Integrasi Pendekatan Multimodal dalam Praktik Anestesiologi dan Terapi Intensif

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Anestesiologi dan terapi intensif telah mengalami perubahan paradigma dari pendekatan terapi tunggal menuju strategi multimodal yang menggabungkan berbagai intervensi untuk mengoptimalkan manajemen perioperatif. Bukti ilmiah menunjukkan bahwa multimodal analgesia pada pembedahan mayor mampu meningkatkan kontrol nyeri, menurunkan konsumsi opioid, serta mempercepat pemulihan pascaoperasi.[1] Temuan ini mengarahkan praktik anestesi modern menuju pendekatan yang lebih komprehensif, terstruktur, dan berorientasi pada luaran klinis yang lebih baik.

Pendekatan multimodal selaras dengan konsep *personalized anesthesia*, yang menekankan penyesuaian pilihan obat, teknik anestesi, dan strategi analgesia berdasarkan profil risiko dan karakteristik individu pasien.[2,3] Dalam kerangka ini, strategi farmakologis, teknik regional, dan pemantauan fisiologis diintegrasikan secara sistematis untuk menjaga stabilitas hemodinamik dan meminimalkan komplikasi. Pada pasien berisiko tinggi, personalisasi strategi multimodal menjadi elemen kunci dalam mencegah perjalanan perioperatif yang tidak stabil.

Perkembangan pemahaman mengenai respons stres perioperatif turut memperkuat urgensi pendekatan multimodal. Peningkatan berbagai sitokin proinflamasi dan biomarker stres telah dikaitkan dengan komplikasi neurologis seperti delirium pascaoperasi.[4] Temuan ini menegaskan bahwa keberhasilan terapi tidak hanya ditentukan oleh stabilitas vital, tetapi juga oleh kemampuan mengendalikan respons biologis yang berlebihan. Integrasi data biomarker dan evaluasi klinis memungkinkan stratifikasi risiko yang lebih akurat, memfasilitasi pendekatan yang lebih individual.

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Dalam aspek farmakologi, penggunaan agonis reseptor alfa-2 seperti dexmedetomidine memberikan kontribusi penting. Agen ini memiliki efek sedasi, analgesia, dan stabilisasi kardiovaskular, serta memengaruhi transduksi nyeri melalui penurunan pelepasan neurotransmiter eksitatorik.[5] Kombinasi dexmedetomidine dalam multimodal analgesia berpotensi menurunkan kebutuhan opioid dan anestetik volatil, sehingga mengurangi efek samping dan memperbaiki kualitas pemulihan.[3] Strategi ini menjadi relevan terutama pada pasien dengan risiko tinggi terhadap komplikasi hemodinamik atau nyeri neuropatik.

Teknik anestesi regional berbasis ultrasonografi juga menempati posisi sentral dalam

multimodal perioperatif. *Ultrasound-guided nerve blocks* meningkatkan presisi tindakan, menurunkan risiko komplikasi, dan memberikan analgesia superior pada berbagai jenis pembedahan, termasuk prosedur fraktur.[6] Ketika dikombinasikan dengan analgesia multimodal, teknik ini dapat menurunkan konsumsi opioid, mengurangi mual muntah, serta memperbaiki kenyamanan pasien dan hasil jangka panjang. Ketersediaan perangkat ultrasonografi di ruang operasi dan ICU karenanya harus dipandang sebagai kebutuhan esensial bagi fasilitas layanan modern.

Penerapan strategi multimodal tidak dapat dilepaskan dari perencanaan sistematis dan kerja sama multidisiplin. Pendekatan ini menuntut koordinasi antara anestesiolog, ahli bedah, perawat, dan tenaga kesehatan lainnya untuk menyusun protokol yang sesuai dengan jenis pembedahan dan profil nyeri yang diantisipasi.[3] Prinsip *patient-centered care* menjadi landasan untuk memastikan bahwa strategi yang diterapkan benar-benar menjawab kebutuhan dan karakteristik setiap pasien.

Meski demikian, sejumlah keberatan terhadap implementasi multimodal dan personalisasi terapi masih ditemui, mulai dari kekhawatiran meningkatnya kompleksitas protokol, beban dokumentasi, keterbatasan sumber daya termasuk ultrasonografi, hingga kebutuhan pelatihan tambahan. Kekhawatiran ini wajar, terutama di fasilitas dengan keterbatasan infrastruktur. Namun bukti menunjukkan bahwa multimodal analgesia memberikan kontrol nyeri lebih baik, menurunkan konsumsi opioid, dan mempercepat pemulihan fungsional.[1,3,6] Secara keseluruhan, strategi ini justru berpotensi mengurangi beban sistemik dan meningkatkan efisiensi layanan dalam jangka panjang.

Jurnal ilmiah memiliki peran penting dalam mendiseminasi pengetahuan, memfasilitasi perkembangan praktik, dan memperkuat budaya ilmiah yang berkelanjutan. Oleh karena itu, komunitas anestesiologi di Indonesia perlu terus melaporkan pengalaman dan inovasi terkait penerapan multimodal, personalisasi terapi, serta pengembangan teknik anestesi regional. Dengan komitmen terhadap integritas ilmiah dan pelayanan yang berpusat pada pasien, integrasi pendekatan multimodal akan menjadi fondasi penting dalam meningkatkan keselamatan dan kualitas layanan anestesiologi dan terapi intensif.

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ORIGINAL ARTICLE

Comparison of IL-6 Levels After Ibuprofen–Paracetamol–Dexamethasone in Percutaneous Nephrolithotomy Patients: an Analytic Observational Study

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Abstract

Introduction: Percutaneous Nephrolithotomy (PCNL) is the therapeutic procedure of choice for kidney stones. IL-6 secretion is stimulated during a secondary inflammatory response due to tissue injury or infection. Proper administration of analgesics can reduce morbidity rates, reduce treatment days, and reduce financing.

Patients and Methods: An analytical observational study with a cross-sectional design at Purwokerto tertiary hospital in the period from December 2024 to January 2025 in patients undergoing PCNL procedures and receiving ibuprofen, paracetamol, and dexamethasone therapy, which met the inclusion and exclusion criteria. The observational group (15 patients each) was: Group A 1000 mg paracetamol and 400 mg ibuprofen and 5 mg dexamethasone; Group B 1000 mg paracetamol and 400 mg ibuprofen. IL-6 levels were measured before and 2 hours after the PCNL procedure. IL-6 levels were measured by ELISA (enzyme-linked immunosorbent assay). Comparative analysis of pre- or post-PCNL IL-6 levels by type of analgesic using unpaired t-test, while the comparison of changes in IL-6 levels was analyzed with the Mann-Whitney test. To determine whether the data distribution was normal, we used the Shapiro-Wilk test. The analysis used SPSS version 25.

Results: Pre- and post-PCNL IL-6 levels were significantly lower in Group A compared to Group B ($p < 0.05$). However, changes in IL-6 levels were not statistically significant ($p = 0.787$). Effect size analysis indicated only a small and clinically negligible difference.

Conclusion: There was no significant difference in IL-6 levels post-PCNL between the two observation groups.

Keywords: Dexamethasone, Ibuprofen, IL6, Paracetamol, PCNL

Perbandingan Kadar IL-6 Setelah Pemberian Ibuprofen–Paracetamol–Deksametason pada Pasien Percutaneous Nephrolithotomy: Studi Observasional Analitik

Abstrak

Pendahuluan: *Percutaneous Nephrolithotomy* (PCNL) adalah prosedur terapi pilihan untuk batu ginjal. Sekresi IL-6 distimulasi selama respon inflamasi sekunder akibat cedera jaringan atau infeksi. Pemberian analgetik yang tepat dapat menurunkan angka morbiditas, menurunkan hari perawatan dan menurunkan pembiayaan.

Pasien dan Metode: Penelitian observasional analitik dengan desain cross sectional di rumah sakit tersier Purwokerto pada periode Desember 2024 hingga Januari 2025 pada pasien yang menjalani prosedur PCNL dan mendapat terapi ibuprofen, paracetamol dan dexametason, yang memenuhi kriteria inklusi dan eksklusi. Kelompok observasional (masing-masing 15 pasien) adalah: Kelompok A 1000 mg parasetamol dan 400 mg ibuprofen dan 5 mg deksametason; Kelompok B 1000 mg parasetamol dan 400 mg ibuprofen. Kadar IL6 diukur sebelum dan 2 jam setelah prosedur PCNL. Kadar IL6 diukur dengan ELISA (*Enzyme-linked immunosorbent assay*). Analisis perbandingan kadar IL-6 pre ataupun post PCNL menurut jenis analgesik menggunakan uji t tidak berpasangan, sedangkan perbandingan perubahan kadar IL-6 dianalisis dengan uji *Mann Whitney*. Analisis normalitas sebaran data dilakukan menggunakan uji *Shapiro Wilk*. Analisis menggunakan SPSS versi 25.

Hasil: Kadar IL-6 pre dan post-PCNL lebih rendah secara signifikan pada kelompok A dibandingkan kelompok B ($p < 0,05$). Namun, perubahan kadar IL-6 antara kedua kelompok tidak berbeda signifikan ($p = 0,787$). Analisis effect size menunjukkan efek kecil dengan interval kepercayaan yang lebar, sehingga perbedaan antar kelompok dianggap terbatas dan tidak bermakna secara klinis.

Kesimpulan: Tidak ada perbedaan yang signifikan dalam kadar IL-6 pasca PCNL antara dua kelompok observasi.

Kata kunci: Dexametasone, Ibuprofen, IL6, Paracetamol, PCNL

Introduction

Nephrolithiasis is a common condition marked by the formation of stones within the renal collecting system. Its prevalence is steadily rising worldwide, with the WHO estimating that 12% of the global population will experience nephrolithiasis at least once in their lifetime.[1] For cases involving large kidney stones or those resistant to conservative treatment, percutaneous nephrolithotomy (PCNL) has become the primary therapeutic approach. Although considered a minimally invasive procedure, PCNL can still provoke inflammatory responses due to tissue trauma during the procedure.[2]

Postoperative inflammatory responses can be monitored via biomarkers such as interleukin-6 (IL-6), a proinflammatory cytokine secreted by various cell types in response to tissue injury. Elevated IL-6 levels have been associated with pain severity and the likelihood of postoperative complications. Therefore, multimodal analgesia is crucial. A combination of drugs such as ibuprofen (NSAID), paracetamol (antipyretic), and dexamethasone (corticosteroid) — each with distinct anti-inflammatory mechanisms — can offer optimal suppression of the inflammatory response.[3,4]

However, data on the effectiveness of this drug combination in reducing IL-6 levels in PCNL patients remain limited in Indonesia.[5] This study aims to address this gap by evaluating whether adding dexamethasone to an ibuprofen-paracetamol regimen offers additional benefits in reducing systemic inflammation, as represented by post-procedural IL-6 levels.

Patients and Methods

This was an analytical cross-sectional observational study conducted at Purwokerto tertiary hospital, between December 2024 and January 2025. Informed consent and ethical clearance were obtained from the research ethics committee (Ref number: 010/KEPK/PE/I/2025). Subjects were adult patients aged 18–65 years undergoing PCNL who met the inclusion criteria and provided informed consent. Patients were excluded if they had received anti-inflammatory medication within 48 hours before the procedure or had autoimmune or active infectious diseases.

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To minimize selection bias, strict inclusion and exclusion criteria were applied, and purposive consecutive sampling was used. Baseline characteristics such as age, gender, BMI, leukocyte count, ASA score, and procedure duration were compared between groups to ensure homogeneity. Potential confounders were controlled statistically. Variables with $p < 0.25$ in univariate analysis were included in a multivariate linear regression model to adjust for their effects on IL-6 levels, allowing assessment of the independent association between analgesic regimen and IL-6 outcomes.

Sample size was calculated for two independent means, assuming a 2.0 pg/mL difference in IL-6 levels between groups, a standard deviation of 2.5, 80% power, and 5% significance. This yielded a requirement of 15 subjects per group, resulting in a total of 30 patients.

Participants were allocated into two groups. Group A received 400 mg ibuprofen, 1000 mg paracetamol, and 5 mg dexamethasone intravenously 30 minutes before the procedure.

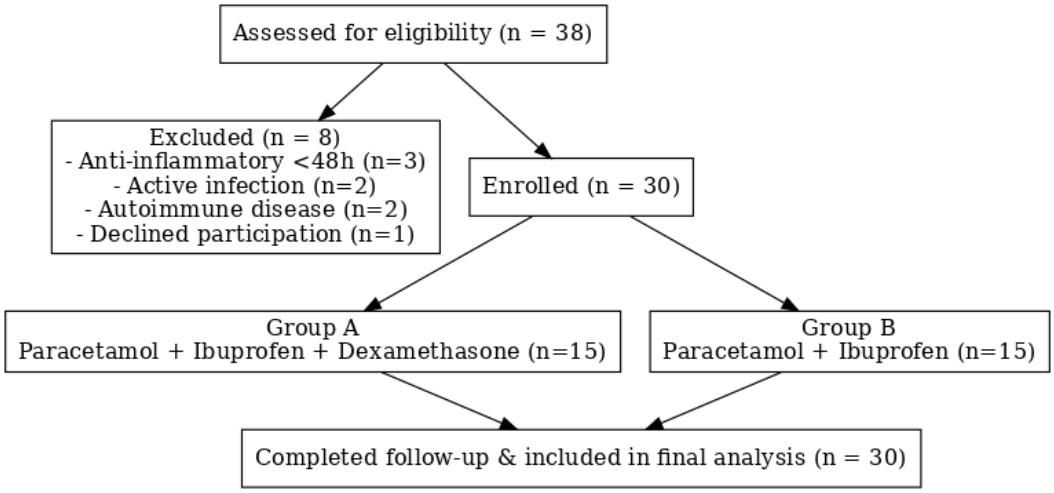

Figure 1. Flow chart of patient recruitment and exclusion process.*

**Thirty patients were enrolled and equally divided between the two groups. The mean age in Group A was 45.6 ± 8.2 years, and in Group B, 44.9 ± 7.5 years. No significant differences were observed in gender distribution or procedure duration between groups.*

Group B received 400 mg ibuprofen and 1000 mg paracetamol. Each group consisted of 15 patients. Blood samples were collected twice—from each patient before and two hours after PCNL—to measure IL-6 levels using enzyme-linked immunosorbent assay (ELISA).

Data were analyzed using SPSS version 25. Normality was assessed with the Shapiro–Wilk test. For normally distributed data, the independent t-test was applied; for non-normally distributed data, the Mann–Whitney test was used. A p-value < 0.05 was considered statistically significant.

Results

A total of 38 patients scheduled for PCNL during the study period were screened for eligibility. Eight were excluded: three had received anti-inflammatory drugs within 48 hours prior to the procedure, two had active infection, two had autoimmune disease, and one declined participation. The remaining 30 patients were enrolled, allocated equally into two groups (n = 15 each), and all completed the study.

Table 1. Patient Characteristics Between Groups

Characteristics	Analgesic types		*p*
	Group A (n = 15)	Group B (n = 15)	
Age, median (min-max) years	52 (38-60)	53 (35-58)	0.884*
Gender, n (%)			
- Male	7 (46.7)	9 (60.0)	0.464^
- Female	8 (53.3)	6 (40.0)	
Education, n (%)			
- SD	5 (38.1)	6 (40.0)	0.833#
- SMP	2 (13.3)	3 (20.0)	
- SMA	6 (40,0)	3 (20,0)	
- D3	1 (6.7)	1 (6.7)	
- S1	1 (6.7)	2 (13.3)	

BMI, n (%)			
- Normal	10 (66.7)	9 (60.0)	0.705^
- Overweight	5 (33.3)	6 (40.0)	
Leukocyte levels, n (%)			
- Above normal	13 (86.7)	10 (66.7)	0.390#
- Normal	2 (13.3)	5 (33.3)	
Surgery duration, median (min-max) minutes	60 (50-80)	60 (50-80)	0.911*
Bleeding volume, median (min-max) cc	200 (150-400)	200 (150-500)	0.743*
ASA score, median (min-max)	2 (1-3)	2 (1-2)	0.608*

*A: paracetamol, ibuprofen & dexamethasone, B: paracetamol & ibuprofen, ^: fisher exact, *: t independen, †: Mann whitney*

Table 1 shows that there were no significant differences in patient characteristics based on the type of analgesic used, as the proportions of each characteristic between Group A and B were not significantly different ($p > 0.05$). It can thus be concluded that patient characteristics were homogeneous and did not confound the effect of analgesic type on IL-6 levels. The median age in Group A was 52 years, similar to that of Group B ($p = 0.884$, Mann-Whitney test). In terms of sex, Group A had a higher proportion of female patients (53.3%), whereas Group B had more male patients (60.0%), though this difference was not statistically significant ($p = 0.464$, Chi-square test). The proportion of patients with elementary school education was similar between Group A and B (38.1% and 40.0%, respectively). Junior high school education was more prevalent in Group B (20.0%) than in Group A (13.3%), while high school education was more common in Group A (40.0%) than in Group B (20.0%). Both groups had equal proportions of diploma (D3) holders, and Group B had a slightly higher proportion of bachelor's degree (S1) holders. Fisher's exact test yielded a p-value of 0.833, indicating comparable educational backgrounds. Regarding BMI, the majority in both Group A and B were of normal weight (66.7% and 60.0%, respectively; $p = 0.705$). Most patients in both groups also had elevated leukocyte levels (86.7% and 66.7%; $p = 0.390$). The mean duration of surgery was identical in both groups at 60 minutes (range 50–80 minutes; $p = 0.911$). The median volume of bleeding was also identical at 200 cc, with a range of 150–400 cc in Group A and 150–500 cc in Group B ($p = 0.743$). The median ASA score was 2 in both groups (range 1–3 in Group A and 1–2 in Group B; $p = 0.608$). No significant differences were observed in operative time, blood loss, or ASA scores ($p > 0.05$ for each, Mann-Whitney test).

Table 2. Comparison of Pre- and Post-PCNL IL-6 Levels Between Analgesic Groups

Measurement time	IL-6 levels (pg/ml)		p-value
	Group A (n = 15)	Group B (n = 15)	
Pre PCNL	0.75 (0.13 – 7.68) (95% CI: 0.3–1.2)	4.00 (0.31 – 96.4) (95% CI: 2.1–5.9)	0.001
Post PCNL	1.25 (0.13 – 171.97) (95% CI: 0.4–2.1)	6.97 (0.64 – 171.66) (95% CI: 3.5–10.4)	0.020

Data are presented as median (min-max); *p<0.05 : significant difference

Table 2 shows that the pre-PCNL IL-6 level in Group A was 0.75 pg/mL (range 0.13–7.68), while in Group B it was 4.00 pg/mL (range 0.31–96.4). The IL-6 data distribution in both

analgesic groups was non-normal and heteroscedastic. Therefore, logarithmic transformation was applied, and the data were re-tested for normality and homogeneity, which were confirmed. An independent t-test on the transformed data yielded a p-value of 0.001 (<0.05), indicating a significant difference in pre-PCNL IL-6 levels between the two groups, with Group A showing lower baseline IL-6 levels.

Post-PCNL IL-6 levels in Group A were 1.25 pg/mL (range 0.13–171.97) compared to 6.97 pg/mL (range 0.64–171.66) in Group B. The data remained non-normally distributed and non-homogeneous until logarithmic transformation was performed, which corrected these issues. An independent t-test showed a significant difference (p = 0.020), with Group A again displaying lower IL-6 levels.

Table 3. Comparison of IL-6 Changes Pre- and Post-PCNL Between Analgesic Groups

Groups*	IL-6 levels (pg/ml)	p-value
	Mean ± SD	
Group A	12.97 ± 43.80 (95% CI: –11.5 to 37.4)	0.787
Group B	26.84 ± 61.44 (95% CI: –6.2 to 59.9)	

Table 3 indicates that changes in IL-6 levels from pre- to post-PCNL between Groups A and B were not significantly different (p = 0.787, Mann-Whitney test).

The median IL-6 level before PCNL was significantly lower in Group A compared to Group B (0.75 pg/mL, 95% CI 0.3–1.2 vs 4.00 pg/mL, 95% CI 2.1–5.9; p = 0.001). Similarly, post-PCNL IL-6 levels were lower in Group A (1.25 pg/mL, 95% CI 0.4–2.1) than in Group B (6.97 pg/mL, 95% CI 3.5–10.4; p = 0.020). However, the change in IL-6 levels between groups was not statistically significant (Group A: 12.97 ± 43.80, 95% CI –11.5 to 37.4 vs Group B: 26.84 ± 61.44, 95% CI –6.2 to 59.9; p = 0.787)

Discussion

In this study, demographic and baseline clinical characteristics, including age, sex distribution, BMI, leukocyte count, ASA score, and surgical duration, were comparable between groups. This homogeneity indicates that the observed outcomes were less likely to be influenced by demographic differences, thereby strengthening the validity of the comparison between treatment groups.

The main finding of this study was that the addition of dexamethasone to an ibuprofen-paracetamol regimen did not significantly alter IL-6 level changes compared to ibuprofen-paracetamol alone. Although both pre- and post-PCNL IL-6 levels were lower in the dexamethasone group, the magnitude of change was not statistically significant. This suggests that the anti-inflammatory benefit of dexamethasone may be limited in the acute postoperative phase when combined with non-opioid analgesics.[6,7]

This study has several limitations. The relatively small sample size may have reduced statistical power to detect subtle differences. IL-6 levels were only measured once postoperatively (2 hours), which might not capture the peak cytokine response. The single-center design may also limit generalizability. In addition, although baseline comparability was achieved, unmeasured variables such as nutritional status or pre-existing inflammation could still act as residual confounders.

The findings suggest that ibuprofen and paracetamol may already provide sufficient

modulation of IL-6 in PCNL patients, and the routine addition of dexamethasone may not provide clinically significant benefit in this context. However, dexamethasone may still have potential value in other settings, such as when longer-term anti-inflammatory effects are required.[8,9,10] These results highlight the need for further trials with larger samples and multiple time-point cytokine measurements to determine the true clinical relevance of adding corticosteroids to multimodal analgesia.

Another important consideration is the potential influence of confounding variables. Although baseline characteristics such as age, sex, BMI, leukocyte count, ASA score, and surgical duration were statistically comparable between groups, unmeasured factors such as pre-existing systemic inflammation, nutritional status, or genetic variability in cytokine expression may still have influenced IL-6 levels. Despite the application of multivariate analysis to adjust for possible confounders, residual confounding cannot be fully excluded.

Moreover, bias related to the relatively small sample size, single-center design, and reliance on a single postoperative IL-6 measurement may have introduced residual bias. These limitations could reduce the generalizability of our findings and suggest the need for larger, multicenter studies with repeated biomarker measurements to confirm these results.

Conclusion

This study concludes that there is no statistically significant difference in IL-6 level changes between PCNL patients receiving a combination of ibuprofen, paracetamol, and dexamethasone and those receiving only ibuprofen and paracetamol. While dexamethasone has known anti-inflammatory potential, its additional effect on IL-6 levels in this setting was not demonstrated. Further longitudinal studies with larger samples are needed to validate these findings.

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Conflicts of Interest

The authors reports no conflict of interest.

Data Availability Statement

The datasets generated and/or analysed for this study are available from the corresponding author upon reasonable request.

Author's Contributions

The author confirms sole responsibility for all aspects of this manuscript, including the conception and design of the work; acquisition, analysis, and interpretation of data; drafting and critical revision of the article; and final approval of the version to be published. The author also agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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ORIGINAL ARTICLE

Dexmedetomidine as Adjuvant in Scalp Nerve Block for Craniotomy: A Double-Blind Randomized Clinical Trial

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Abstract

Introduction: Scalp nerve block (SNB) is an effective adjunct for attenuating hemodynamic responses and reducing postoperative pain in craniotomy. Dexmedetomidine (DEX), with its analgesic and anti-inflammatory properties, may enhance the quality of SNB. This study evaluated the effects of adding DEX to SNB on hemodynamic stability, postoperative pain, inflammatory response, and analgesic duration in craniotomy patients.

Methods: A double-blind, parallel-group randomized clinical trial was conducted on 36 adult patients undergoing elective craniotomy (July–September 2025) at a tertiary hospital Denpasar. Participants received SNB using 0.375% ropivacaine (20 mL) with or without DEX 1 µg/kg under standardized general anesthesia. Outcomes included mean arterial pressure (MAP), Visual Analog Scale (VAS) scores at 12 and 24 hours, neutrophil-to-lymphocyte ratio (ΔNLR), and time to first rescue analgesic (TTFAR). Statistical analyses used mixed ANOVA and Mann–Whitney U tests. Ethical approval number was 2159/UN14.2.2.VII.14/LT/2025.

Results: MAP was significantly lower in the DEX group at 10 minutes (Δ = 4.89 mmHg; 95% CI 1.62–8.16), 20 minutes (Δ = 4.83; 95% CI 1.57–8.10), 30 minutes (Δ = 3.67; 95% CI 0.40–6.94), and upon PACU arrival (Δ = 3.72; 95% CI 0.45–6.99) (all $p < 0.05$). Median VAS scores were significantly lower with DEX at 12 hours (1.50 vs 3.00; $p < 0.001$) and 24 hours (1.00 vs 2.00; $p < 0.001$). ΔNLR was reduced in the DEX group (−0.56 vs 3.08; $p = 0.004$). TTFAR was markedly prolonged (554 vs 257 minutes; $p < 0.001$). No adverse events were reported.

Conclusion: Dexmedetomidine added to scalp nerve block enhances hemodynamic stability, reduces postoperative pain for up to 24 hours, suppresses early systemic inflammation, and prolongs analgesic duration in craniotomy without observed complications. DEX–SNB represents a beneficial component of multimodal analgesia in neuroanesthesia and may support enhanced recovery pathways.

Keywords: Craniotomy, Dexmedetomidine, Hemodynamic stability, Inflammation, Postoperative pain, Scalp block

Efektivitas Penggunaan Dexmedetomidine pada Kraniotomi: Uji Klinis Acak Tersamar Ganda

Abstrak

Pendahuluan: Scalp nerve block (SNB) efektif dalam menurunkan respons hemodinamik dan nyeri pascaoperasi pada kraniotomi. Dexmedetomidine (DEX), yang memiliki efek analgetik dan antiinflamasi, berpotensi meningkatkan kualitas SNB. Penelitian ini mengevaluasi efek penambahan DEX pada SNB terhadap kestabilan hemodinamik, intensitas nyeri pascaoperasi, respons inflamasi, dan durasi analgesia pada pasien kraniotomi.

Metode: Uji klinis acak tersamar ganda dengan desain paralel dilakukan pada 36 pasien dewasa yang menjalani kraniotomi elektif (Juli–September 2025) di Rumah Sakit Tersier Denpasar. Peserta menerima SNB menggunakan ropivacaine 0,375% (20 mL) dengan atau tanpa DEX 1 µg/kg di bawah anestesi umum standar. Luaran meliputi mean arterial pressure (MAP), skor Visual Analog Scale (VAS) pada 12 dan 24 jam, perubahan neutrophil-to-lymphocyte ratio (ΔNLR), dan time to first rescue analgesic (TTFAR). Analisis menggunakan mixed ANOVA dan Mann–Whitney U. Nomor persetujuan etik: 2159/UN14.2.2.VII.14/LT/2025.

Hasil: MAP secara bermakna lebih rendah pada kelompok DEX pada menit ke-10 (Δ = 4,89 mmHg; 95% CI 1,62–8,16), menit ke-20 (Δ = 4,83; 95% CI 1,57–8,10), menit ke-30 (Δ = 3,67; 95% CI 0,40–6,94), dan pascaoperasi (Δ = 3,72; 95% CI 0,45–6,99) (seluruhnya $p < 0,05$). Skor VAS lebih rendah pada kelompok DEX pada 12 jam (1,50 vs 3,00; $p < 0,001$) dan 24 jam (1,00 vs 2,00; $p < 0,001$). ΔNLR lebih kecil pada kelompok DEX (−0,56 vs 3,08; $p = 0,004$). TTFAR lebih panjang secara bermakna (554 vs 257 menit; $p < 0,001$). Tidak ditemukan efek samping.

Kesimpulan: Penambahan dexmedetomidine pada scalp nerve block meningkatkan kestabilan hemodinamik,

menurunkan intensitas nyeri hingga 24 jam, menekan respons inflamasi awal, serta memperpanjang durasi analgesia pada pasien kraniotomi tanpa efek samping yang teramati. DEX–SNB layak dipertimbangkan sebagai bagian dari analgesia multimodal dan berpotensi mendukung protokol pemulihan cepat di bedah saraf.

Kata kunci: Kraniotomi, Dexmedetomidine, Kestabilan hemodinamik, Inflamasi, Scalp blok, Nyeri pascaoperasi

Introduction

Postoperative pain following craniotomy remains a significant challenge in neuroanesthesiology. Inadequately controlled pain can trigger sympathetic activation, elevate blood pressure and heart rate, increase intracranial pressure (ICP), and impair cerebral perfusion, potentially worsening cerebral edema and delaying neurological recovery. Noxious stimuli such as scalp incision, skull pinning, drilling, and dural manipulation are well-known triggers of acute hemodynamic surges during craniotomy. Epidemiological data demonstrate that approximately 10–20% of craniotomy patients experience severe postoperative pain, while over 30% report moderate pain, illustrating the clinical importance of optimizing perioperative analgesia.[1]

Opioids remain a conventional component of analgesia in neurosurgery; however, their use is limited by adverse effects including over-sedation, respiratory depression, nausea, and vomiting, which may impair postoperative neurological evaluation. Therefore, multimodal and opioid-sparing approaches such as the scalp nerve block (SNB) have gained increasing traction. SNB using local anesthetics like ropivacaine has been shown to blunt hemodynamic responses to noxious stimuli and reduce postoperative pain and intraoperative opioid requirements in craniotomy patients.[1–3] Dexmedetomidine (DEX), a selective α_2-adrenergic agonist, has emerged as a promising adjuvant in regional anesthesia due to its analgesic, sedative, sympatholytic, and anti-inflammatory properties. Evidence demonstrates that DEX prolongs sensory blockade, enhances the quality of peripheral nerve blocks, and reduces anesthetic and opioid requirements when combined with local anesthetics.[4,5] Beyond analgesia, DEX attenuates perioperative inflammation by reducing pro-inflammatory cytokines such as IL-6 and TNF-α and is associated with lower postoperative neutrophil-to-lymphocyte ratio (NLR), a biomarker of systemic inflammation.[6,7]

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Although the individual benefits of SNB and dexmedetomidine are well documented, there remains a gap in the literature evaluating their combined effects in craniotomy, particularly studies incorporating hemodynamic outcomes and inflammatory biomarkers simultaneously. Existing trials primarily focus on pain or intraoperative hemodynamic responses without assessing systemic inflammation.[5,8,9] Moreover, no study has been conducted in Indonesia, where patient characteristics, anesthetic practice, and surgical workflows may influence treatment response. This gap highlights the need for a comprehensive evaluation of the dexmedetomidine-assisted scalp nerve block in the local population.

Therefore, this study aims to assess the effectiveness of dexmedetomidine as an adjuvant to scalp nerve block in improving intraoperative hemodynamic stability, reducing postoperative pain intensity, and modulating inflammatory response, as measured by the

change in neutrophil-to-lymphocyte ratio (ΔNLR), in patients undergoing craniotomy at a tertiary care center in Indonesia.

We hypothesize that adding dexmedetomidine to scalp nerve block improves intraoperative hemodynamic stability, reduces postoperative pain, suppresses systemic inflammatory response, and prolongs analgesic duration compared with scalp nerve block using ropivacaine alone.

Patients and Methods

This study was designed as a prospective, double-blind, parallel-group randomized controlled trial to evaluate the effect of adding dexmedetomidine (DEX) to scalp nerve block (SNB) on intraoperative hemodynamic stability, postoperative pain, inflammatory response, and analgesic duration in patients undergoing elective craniotomy. The study was conducted at a tertiary hospital in Denpasar, between July and September 2025. Ethical approval was obtained from the Institutional Ethics Committee (Approval No: 2159/UN14.2.2.VII.14/LT/2025), and all procedures adhered to the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all participants.

The sample size was calculated using a two-mean comparison formula for a superiority design with a significance level of 5% and power of 80%. The calculation was based on a clinically relevant mean difference in mean arterial pressure (MAP) of 17.2 mmHg with a standard deviation of 13.62 mmHg, derived from previously published data on hemodynamic responses to scalp block during craniotomy.[1] This yielded a minimum requirement of 16 subjects per group, and after accounting for an anticipated 10% drop-out rate, a total of 36 subjects were targeted for enrollment.

Participants were recruited consecutively from adult patients scheduled for elective supratentorial craniotomy. Eligible patients were aged 18 to 65 years, classified as ASA physical status I–III, and had a Glasgow Coma Scale (GCS) score of 15. Exclusion criteria included significant cardiac, pulmonary, hepatic, or renal disease; coagulation disorders; moderate-to-severe traumatic brain injury; local infection at the injection site; chronic opioid use; pregnancy; or known allergy to study drugs. Patients were withdrawn from the study if postoperative ventilatory support was required, if intraoperative blood loss exceeded 2 liters, if arrhythmia or hemodynamic shock occurred, if allergic reactions developed, or in the event of perioperative mortality.

Randomization was carried out using a computer-generated sequence produced by an independent statistician via randomizer.org, employing block randomization with a fixed block size of four to ensure balanced allocation in a 1:1 ratio. Allocation codes were placed in sequentially numbered, sealed, opaque envelopes, which were opened only by a research assistant not involved in anesthesia management or postoperative outcome assessment. The study was double-blinded: patients, postoperative evaluators, and the anesthesiologists assessing outcomes remained unaware of group assignments. The anesthesiologist performing the scalp block was not involved in outcome assessment or data analysis. Study solutions were prepared in identical syringes labeled only as “Study Drug A” or “Study Drug B” to ensure allocation concealment.

All patients received standardized general anesthesia consisting of fentanyl 3 µg/kg, propofol 2 mg/kg, and rocuronium 1 mg/kg for induction, followed by maintenance with sevoflurane at 0.8–1.0 MAC in an oxygen–air mixture. After intubation, the scalp nerve block was performed.

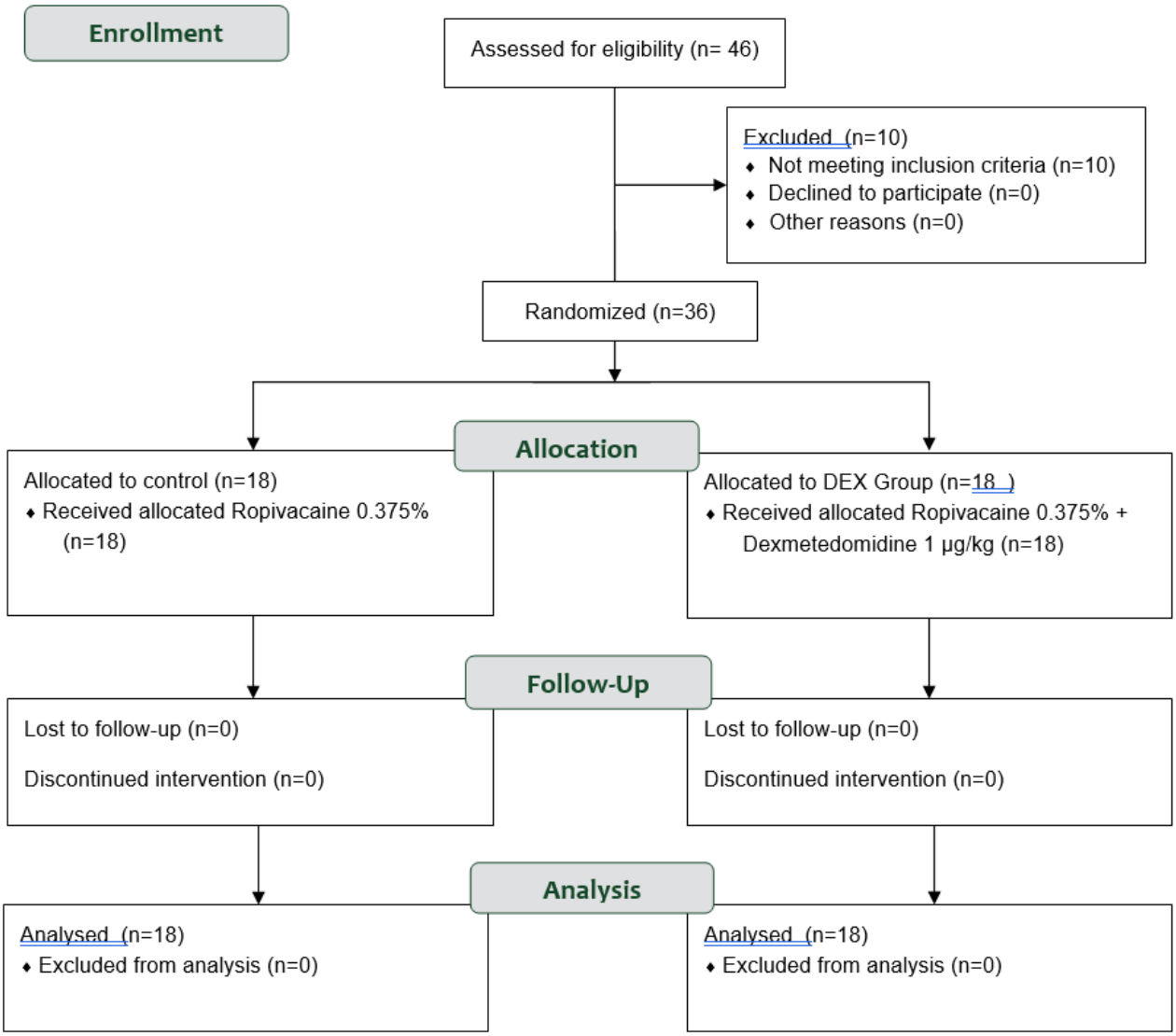

Figure 1. CONSORT diagram

The control group received 20 mL of 0.375% ropivacaine, whereas the DEX group received 0.375% ropivacaine combined with dexmedetomidine at a dose of 1 µg/kg body weight. Dexmedetomidine (100 µg/mL) was diluted in normal saline so that the final injected volume remained 20 mL. The block was administered at the supratrochlear, supraorbital, zygomaticotemporal, auriculotemporal, greater auricular, greater occipital, and lesser occipital nerves, with 3 mL deposited at each anatomical landmark. Mechanical ventilation was performed in volume-controlled mode with end-tidal CO_2 maintained between 35 and 40 mmHg. At the conclusion of surgery, all patients were extubated and transferred to the post-anesthesia care unit (PACU), where they remained under monitoring until achieving an Aldrete score of 10.

The primary outcomes of this study were intraoperative hemodynamic stability, postoperative pain intensity, and systemic inflammatory response. Hemodynamic stability was assessed by MAP measured at baseline (0 minutes), 10, 20, and 30 minutes after incision, and upon PACU arrival. Postoperative pain was evaluated using the Visual Analog Scale (VAS) at 12 and 24 hours after surgery. Inflammatory response was evaluated using the neutrophil-to-lymphocyte ratio (NLR) obtained from venous blood samples collected preoperatively and 12 hours postoperatively. The change in NLR

(ΔNLR) was used as the main inflammatory parameter based on evidence indicating that systemic inflammatory markers peak within 6–24 hours following surgical stress.(6,7) The secondary outcome was the time to first rescue analgesic (TTFAR), defined as the interval between the end of surgery and the first patient-controlled analgesia (PCA) fentanyl demand.

Safety monitoring was conducted intraoperatively and during the first 24 postoperative hours. Adverse events were documented according to predefined clinical criteria: bradycardia was defined as heart rate <50 beats per minute; hypotension as MAP <65 mmHg or ≥20% decrease from baseline; oversedation as a Richmond Agitation–Sedation Scale (RASS) score below –2; and allergic reaction as any occurrence of urticaria, bronchospasm, or hypotension temporally associated with drug administration.

Statistical analysis was performed using IBM SPSS Statistics version 29. Normality of data distribution was assessed with the Shapiro–Wilk test. Normally distributed variables were presented as mean ± standard deviation and compared using the independent t-test, whereas non-normally distributed variables were reported as median and interquartile range and analyzed using the Mann–Whitney U test. Repeated MAP measurements were analyzed using a mixed ANOVA model with Greenhouse–Geisser correction when appropriate. All primary outcomes were presented with 95% confidence intervals. Effect sizes were calculated using Cohen's d for VAS, ΔNLR, and TTFAR, while partial eta squared was used for repeated MAP measures. The primary analysis followed a per-protocol approach, and statistical significance was defined as $p \leq 0.05$.

Results

A total of 46 patients were screened for eligibility during the study period, of whom 36 met the inclusion criteria and were randomized equally into the control group (n = 18) and the dexmedetomidine (DEX) group (n = 18). Ten patients were excluded based on predefined withdrawal criteria. All randomized participants completed the study, and no post-randomization exclusions occurred. Baseline demographic and operative characteristics were comparable between the two groups. The mean age was 39.39 ± 16.28 years in the control group and 44.00 ± 12.86 years in the DEX group ($p = 0.352$). Sex distribution was identical, with 8 males (44.4%) and 10 females (55.6%) in each group. The median duration of surgery was similar between groups (182.5 minutes [IQR 20] vs 190 minutes [IQR 50], $p = 0.748$). All patients were classified as ASA physical status III.

Table 1. Subject Characteristics

Characteristics	Treatment Group		*p*-value
	P1 (n=18)	P2 (n=18)	
Age (years)	39,39 ± 16,28	44 ± 12,86	0,352[T]
Sex			
Male	8 (44,4%)	8 (44,4%)	1,00[C]
Female	10 (55,6%)	10 (55,6%)	
Duration of Surgery (minutes)	182,5 (20)	190 (50)	0,748[M]
ASA Physical Status			
III	100%	100%	-

Mean arterial pressure (MAP) was measured at baseline (0 minutes), 10, 20, and 30 minutes intraoperatively, and upon arrival in the post-anesthesia care unit (PACU). Mixed ANOVA analysis demonstrated a significant overall difference between groups, with consistently lower MAP values in the DEX group. Post-hoc Bonferroni analysis revealed statistically significant reductions in MAP at 10 minutes (Δ = 4.89 mmHg; 95% CI 1.62–8.16; p = 0.004), 20 minutes (Δ = 4.83 mmHg; 95% CI 1.57–8.10; p = 0.004), 30 minutes (Δ = 3.67 mmHg; 95% CI 0.40–6.94; p = 0.028), and in the PACU period (Δ = 3.72 mmHg; 95% CI 0.45–6.99; p = 0.026). Baseline MAP did not differ significantly between groups (p = 0.615). These findings indicate that dexmedetomidine as an adjuvant to scalp nerve block provided superior intraoperative hemodynamic stability.

Table 2. Homogeneity of Variance Test for Parametric Data

Variable	*Levene's Test*		Conclusion
	F Levene	Nilai *p*	
Age	1,619	0,212	Homogeneous
MAP at 0 minutes	9,546	0,004	Heterogeneous
MAP at 10 minutes	1,568	0,219	Homogeneous
MAP at 20 minutes	0,923	0,343	Homogeneous
MAP at 30 minutes	0,573	0,454	Homogeneous
Postoperative MAP	0,166	0,686	Homogeneous
TTFAR	0,164	0,686	Homogeneous

Table 3. Comparative Analysis of Mean Arterial Pressure (MAP) at 0, 10, 20, and 30 Minutes, and Postoperatively in Both Treatment Groups

Characteristics	Treatment Group			*p-value
	P1 (n=18) (EMM ± SE)	P2 (n=18) (EMM ± SE)	Mean Difference 95% CI	
MAP at 0 minutes	78,06 ± 1,17	77,22 ± 1,17	0,83 (−2,44; 4,10)	**0,615**
MAP at 10 minutes	87,83 ± 1,17	82,94 ± 1,17	4,89 (1,62; 8,16)	**0,004**
MAP at 20 minutes	86,06 ± 1,17	81,22 ± 1,17	4,83 (1,57; 8,10)	**0,004**
MAP at 30 minutes	84,44 ± 1,17	80,78 ± 1,17	3,67 (0,40; 6,94)	**0,028**
Postoperative MAP	83,22 ± 1,17	79,50 ± 1,17	3,72 (0,45; 6,99)	**0,026**

Table 4. Comparative Analysis of Visual Analogue Scale at 12 and 24 Hours Postoperatively in Both Treatment Groups

Characteristics	Treatment Group		*p-value
	P1 (n=18)	P2 (n=18)	
VAS at 12 hours postoperatively	3,00 (0)	1,50 (1)	**<0,001[M]**
VAS at 24 hours postoperatively	2,00 (1)	1,00 (1)	**<0,001[M]**

Postoperative pain was assessed using the Visual Analog Scale (VAS) at 12 and 24 hours after surgery. The DEX group demonstrated significantly lower pain scores at both time points. At 12 hours, the median VAS was 1.50 (IQR 1) in the DEX group compared with 3.00 (IQR 0) in the control group ($p < 0.001$). At 24 hours, the DEX group also showed lower scores (1.00 [IQR 1] vs 2.00 [IQR 1], $p < 0.001$). These results confirm a sustained analgesic benefit of dexmedetomidine-assisted scalp nerve block during the first postoperative day.The systemic inflammatory response, measured via the change in neutrophil-to-lymphocyte ratio (ΔNLR) from preoperative to 12-hour postoperative values, was significantly lower in the DEX group. The median ΔNLR was −0.56 (IQR 5.33) in the DEX group compared with 3.08 (IQR 7.60) in the control group ($p = 0.004$), indicating attenuation of the postoperative inflammatory response.

Table 5. Comparative Analysis of Preoperative and Postoperative Neutrophil-to-Lymphocyte Ratio (NLR) in Both Treatment Groups

Characteristics	Treatment Group		*p-value
	P1 (n=18)	P2 (n=18)	
NLR Difference	3,08 (7,60)	-0,56 (5,33)	**0,004[M]**

Analgesic duration, assessed through the time to first rescue analgesic (TTFAR), was markedly prolonged in the DEX group. The median TTFAR was 554 minutes (IQR 45) in the DEX group versus 257 minutes (IQR 53) in the control group ($p < 0.001$). This suggests that dexmedetomidine not only enhanced analgesic quality but also provided a clinically meaningful extension of analgesia duration.

No adverse events—including bradycardia, hypotension, oversedation, or allergic reaction—were observed in either group during the intraoperative period or the first 24 postoperative hours. No participants required withdrawal due to safety concerns.

Table 6. Comparative Analysis of Time to First Analgesia Rescue (TTFAR) Postoperatively in Both Treatment Groups

Characteristics	Treatment Group		*p-value
	P1 (n=18)	P2 (n=18)	
***Time to First Analgesia Rescue* (minutes)**	257 (53)	554 (45)	**<0,001[T]**

Discussion

This randomized controlled trial demonstrated that the addition of dexmedetomidine (DEX) to scalp nerve block (SNB) significantly improved intraoperative hemodynamic stability, reduced postoperative pain intensity, attenuated systemic inflammatory response, and prolonged analgesic duration in patients undergoing elective craniotomy. These findings support the role of DEX as a valuable adjuvant in multimodal neuroanesthesia, complementing existing evidence on the benefits of SNB and α_2-agonist–mediated modulation of nociceptive and inflammatory pathways.

The improved hemodynamic stability observed in the DEX group is consistent with prior studies reporting that DEX attenuates the sympathetic response to noxious cranial stimulation such as scalp incision and skull pinning.[8,9] The magnitude of MAP reduction in this study (3–5 mmHg across key time points) lies within clinically meaningful thresholds for preventing intracranial pressure surges while avoiding hypotension that could compromise cerebral perfusion. From a clinical perspective, even modest stabilization of MAP can facilitate a more controlled surgical field and reduce the risk of bleeding during craniotomy. The hemodynamic benefit observed here likely reflects the synergistic effects of ropivacaine-induced peripheral neural blockade and DEX-induced presynaptic inhibition of norepinephrine release, as described in previous neuroanatomical and pharmacologic studies.[5,10]

Postoperative analgesic outcomes further support the superiority of the DEX–SNB combination. VAS scores were significantly lower at both 12 and 24 hours, accompanied by a substantial prolongation of time to first rescue analgesic. These findings align with meta-analytic data indicating that dexmedetomidine enhances the duration and depth of peripheral nerve block,[4,10] and extend earlier observations by providing a sustained 24-hour analgesic benefit in craniotomy patients—a population in whom early opioid sparing is particularly valuable due to the need for frequent neurological examinations. The large effect sizes observed for pain reduction and TTFAR in this study underscore the clinical significance of these findings.

In addition to hemodynamic and analgesic effects, this study demonstrated a notable reduction in postoperative inflammatory response, as reflected by a significantly lower ΔNLR in the DEX group. This observation is supported by previous reports that DEX suppresses pro-inflammatory cytokines (IL-6, TNF-α) and enhances anti-inflammatory mediators such as IL-10.[6,7] The use of NLR as a biomarker is justified by its sensitivity, simplicity, and established role in detecting systemic inflammation following surgical stress. The selection of the 12-hour time point aligns with evidence that NLR peaks within 6 to 24 hours after major surgery.[6] The suppression of inflammation may contribute to improved recovery profiles and reduced postoperative complications, as indicated by recent trials evaluating DEX in perioperative immunomodulation.[11,12]

The present findings are also relevant within the framework of enhanced recovery after neurosurgery (ERAS-Neuro). By stabilizing hemodynamics, reducing opioid exposure, and modulating inflammation, DEX–SNB can support faster neurological recovery, improve patient comfort, and reduce the risk of secondary brain injury. This aligns with emerging ERAS-Neuro recommendations emphasizing opioid-sparing analgesia, autonomic modulation, and attenuation of inflammatory stress responses during intracranial surgery. While ERAS principles are still evolving in neuroanesthesia, the results of this study provide a compelling rationale for incorporating DEX–SNB into multimodal perioperative pathways.

Comparison with existing literature highlights several unique contributions of this study. Prior investigations have typically evaluated either the hemodynamic impact of DEX-enhanced scalp block,[5,8,9] its analgesic prolongation in peripheral nerve blocks,[4,10] or its systemic anti-inflammatory effects in non-neurosurgical populations.[6,11,12] To our knowledge, no previous study has simultaneously examined all three domains—hemodynamic stability, pain control, and inflammatory modulation—in the context of craniotomy. Furthermore, this is the first study conducted in Indonesia assessing DEX as an SNB adjuvant in neurosurgery, addressing a regional research gap identified in the introduction.

Despite these strengths, several limitations should be acknowledged. The single-center design and relatively small sample size may limit the external validity of the results, particularly for patients with different demographic characteristics or comorbidity profiles. All participants were ASA physical status III, which may restrict generalizability to lower-risk populations. Inflammatory markers were measured only up to 12 postoperative hours, without longer postoperative follow-up or additional biomarkers such as CRP, IL-6, or procalcitonin. No long-term clinical outcomes—including postoperative delirium, neurological recovery, or length of stay—were evaluated. Additionally, although pain and hemodynamic responses were assessed up to 24 hours, the potential benefits of DEX–SNB beyond this period remain unknown. Future multicenter studies with larger sample sizes,

extended follow-up intervals, and comprehensive recovery metrics are warranted to build upon these findings.

In summary, this study reinforces the growing evidence supporting dexmedetomidine as an effective adjuvant to scalp nerve block in craniotomy. The observed improvements in hemodynamic stability, postoperative analgesia, analgesic duration, and attenuation of systemic inflammation highlight its potential to enhance perioperative care within a multimodal neuroanesthesia framework. These findings further support the integration of DEX–SNB into enhanced recovery strategies for neurosurgical procedures, while emphasizing the need for further studies to optimize dosing, timing, and applicability across diverse neurosurgical populations.

Conclusion

This randomized controlled trial demonstrates that the addition of dexmedetomidine to scalp nerve block provides significant perioperative benefits in patients undergoing elective craniotomy. Dexmedetomidine improved intraoperative hemodynamic stability, as reflected by consistently lower mean arterial pressure at multiple surgical time points, without causing hypotension or other adverse effects. Postoperative pain intensity was significantly reduced at 12 and 24 hours, accompanied by a substantial prolongation of time to first rescue analgesic, indicating superior and extended analgesic efficacy. Furthermore, dexmedetomidine attenuated the systemic inflammatory response, evidenced by a markedly lower postoperative ΔNLR compared with scalp block alone.

Dexmedetomidine as an adjuvant to scalp nerve block improves hemodynamic stability, reduces postoperative pain, prolongs analgesia, and attenuates systemic inflammation in craniotomy patients. These benefits support its incorporation into multimodal neuroanesthesia and enhanced recovery pathways. Further multicenter studies are needed to explore long-term outcomes and dosing optimization.

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Conflicts of Interest

The authors report no conflict of interest.

Data Availability Statement

All datasets generated and/or analysed for this study are available from the corresponding author upon reasonable request.

Author's Contributions

All authors contributed significantly to the conception and design of the study, data collection, analysis, and interpretation of the results. All authors participated in writing and critically revising the manuscript for important intellectual content, approved the final version to be published, and are accountable for all aspects of the research.

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Dexmedetomidine pada Blok Thoraco-Lumbar Interfascial Plane Modifikasi: Tinjauan Naratif

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Abstrak

Nyeri pascaoperasi merupakan tantangan klinis utama pada pasien yang menjalani bedah tulang belakang lumbal. Pendekatan analgesia multimodal semakin berkembang, dan blok interfasial torakolumbal (Thoracolumbar Interfascial Plane/TLIP) menjadi salah satu teknik yang efektif dalam mengurangi nyeri dengan risiko minimal terhadap fungsi motorik. Modifikasi teknik TLIP, terutama dengan penambahan adjuvan seperti dexmedetomidine, menawarkan potensi peningkatan durasi dan kualitas analgesia. Tinjauan naratif ini bertujuan merangkum bukti terkini mengenai efektivitas, mekanisme, dan keamanan penggunaan dexmedetomidine sebagai adjuvan pada TLIP modifikasi untuk bedah lumbal. Pencarian literatur dilakukan melalui basis data PubMed, Scopus, dan Google Scholar dengan menggunakan kata kunci "modified TLIP block", "dexmedetomidine", "lumbar spine surgery", dan "postoperative analgesia" untuk artikel berbahasa Inggris atau Indonesia yang diterbitkan antara tahun 2013 hingga 2024. Hasil sintesis menunjukkan bahwa penambahan dexmedetomidine (0,5–1 µg/kg) pada anestesi lokal dapat memperpanjang durasi analgesia hingga 6–8 jam, menurunkan skor nyeri pascaoperasi, serta mengurangi konsumsi opioid tanpa menimbulkan efek samping berat, seperti bradikardia atau hipotensi yang signifikan. Efek analgesik ini terkait dengan aktivasi reseptor α_2-adrenergik di perifer dan spinal yang menghambat transmisi nyeri. Tinjauan ini membahas secara komprehensif dasar fisiologi dan farmakologi kombinasi TLIP–dexmedetomidine, perbandingan dengan blok interfasial lain, bukti klinis terkini, serta arah penelitian yang diperlukan untuk penerapan optimal dalam praktik anestesiologi modern.

Kata kunci: Analgesia pascaoperasi, Bedah tulang belakang, Blok TLIP, Blok torakolumbal interfasial, Dexmedetomidine

Dexmedetomidine in Modified Thoraco-Lumbar Interfascial Plane Block: A Narrative Review

Abstract

Postoperative pain remains a major clinical challenge for patients undergoing lumbar spine surgery. Approaches to multimodal analgesia continue to evolve, and the thoracolumbar interfascial plane (TLIP) block has emerged as an effective technique for reducing pain with minimal risk of motor impairment. Modifications of the TLIP technique, particularly the addition of adjuvants such as dexmedetomidine, offer the potential to enhance both the duration and quality of analgesia. This narrative review aims to summarize current evidence on the efficacy, mechanisms, and safety of dexmedetomidine as an adjuvant in modified TLIP blocks for lumbar spine surgery. Literature searches were conducted through PubMed, Scopus, and Google Scholar using the keywords "modified TLIP block," "dexmedetomidine," "lumbar spine surgery," and "postoperative analgesia" for English- and Indonesian-language articles published between 2013 and 2024. Synthesis of the available evidence indicates that adding dexmedetomidine (0.5–1 µg/kg) to local anesthetics can prolong the duration of analgesia by 6–8 hours, reduce postoperative pain scores, and decrease opioid consumption without causing significant adverse effects such as bradycardia or hypotension. The analgesic effect is attributed to activation of peripheral and spinal α_2-adrenergic receptors that inhibit pain transmission. This review provides a comprehensive discussion of the physiological and pharmacological basis of the TLIP–dexmedetomidine combination, comparisons with other interfascial plane blocks, recent clinical findings, and future research directions necessary for optimal implementation in modern anesthesiology practice.

Keywords: dexmedetomidine; modified TLIP block; postoperative analgesia; lumbar spine surgery; thoracolumbar interfascial plane block

Pendahuluan

Nyeri pascaoperasi masih menjadi masalah klinis yang menantang pada pasien yang menjalani pembedahan tulang belakang. Kompleksitas anatomi, luasnya area insisi, dan keterlibatan jaringan muskuloskeletal menyebabkan stimulus nosiseptif yang kuat. Nyeri yang tidak terkontrol dapat meningkatkan respons simpatis, menghambat mobilisasi dini, serta memperburuk pemulihan fungsional pasien.[1,2] Fenomena ini juga berkontribusi terhadap risiko berkembangnya nyeri kronik pascaoperasi, yang sering kali menurunkan kualitas hidup pasien.[3,4]

Pendekatan analgesia multimodal menawarkan kombinasi berbagai mekanisme kerja farmakologis dan nonfarmakologis untuk menekan nyeri dari berbagai jalur. Blok interfasial seperti TLIP menjadi salah satu teknik yang banyak diminati karena menargetkan saraf dorsal rami dan memberikan analgesia terarah tanpa gangguan motorik.[5] Penggunaan ultrasonografi mempermudah identifikasi bidang interfasial dan meningkatkan akurasi deposisi anestesi lokal; pendekatan TLIP modifikasi telah dideskripsikan dan digunakan secara luas.[6]

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Dalam konteks peningkatan durasi analgesia, berbagai adjuvan telah diteliti, termasuk deksametason, klonidin, dan dexmedetomidine. Di antara ketiganya, dexmedetomidine menonjol karena memiliki efek sinergis terhadap anestesi lokal, mekanisme kerja sentral dan perifer yang jelas, serta profil efek samping yang relatif aman.[7,10] Namun, variasi teknik, dosis, dan protokol klinis yang digunakan dalam penelitian menghasilkan perbedaan temuan yang perlu ditinjau secara kritis agar dapat diterapkan secara rasional dalam praktik klinis. Tinjauan ini menyintesis aspek anatomi dan fisiologi TLIP, farmakologi dexmedetomidine, bukti klinis relevan, serta arah penelitian ke depan.

Anatomi dan Dasar Fisiologi Blok TLIP

Blok interfasial torakolumbal (*thoracolumbar interfascial plane*/TLIP) merupakan teknik yang menargetkan saraf dorsal rami, yaitu cabang posterior dari nervus spinalis yang menyuplai otot multifidus, longissimus, serta jaringan fasial di daerah punggung bawah. Dengan melakukan injeksi anestesi lokal pada bidang antara otot multifidus dan longissimus, impuls nyeri dari jaringan paraspinal dapat dihambat tanpa mengganggu saraf motorik ventral. Teknik ini dikembangkan untuk memberikan analgesia pascaoperasi lumbal tanpa menimbulkan blok motorik atau efek hemodinamik seperti pada blok epidural.[6]

Modifikasi TLIP dilakukan untuk memperluas sebaran anestesi lokal dan mempermudah visualisasi dengan ultrasonografi. Pendekatan modifikasi memungkinkan penyebaran anestesi lebih merata di sepanjang dorsal rami sehingga memberikan efek analgesia yang lebih konsisten. Bukti klinis awal menunjukkan efektivitas TLIP modifikasi pada pembedahan lumbal, termasuk prosedur fusi multilevel.[5,6]

Secara fisiologis, keberhasilan TLIP bergantung pada kemampuan anestesi lokal menembus jaringan fasial dan mencapai dorsal rami dengan konsentrasi yang memadai. Efek blok terutama dihasilkan oleh hambatan transmisi impuls pada serabut saraf A-delta dan C yang membawa sinyal nosiseptif.[2]

Secara teoretis, TLIP memberikan keuntungan selektivitas terhadap target nyeri. Namun, efektivitasnya dapat menurun bila terdapat variasi anatomis individu. Pendekatan berbasis

anatomi secara real time dengan ultrasonografi penting untuk mengurangi variabilitas tersebut. Selain itu, perlu dievaluasi apakah difusi anestesi ke area paraspinal cukup untuk mencakup seluruh segmen insisi, terutama pada operasi lumbal multilevel.

Farmakologi dan Mekanisme Kerja Dexmedetomidine

Dexmedetomidine adalah agonis selektif reseptor α_2-adrenergik dengan afinitas tinggi. Aktivasi reseptor ini menekan pelepasan norepinefrin pada terminal presinaptik, menghambat transmisi nosiseptif, dan menimbulkan hiperpolarisasi neuron postsinaptik di medula spinalis; mekanisme ini menjelaskan efek analgesia sentral dan sedasi.[7,9] Pada perifer, interaksi dengan reseptor α_2 pada ujung saraf aferen menurunkan pelepasan neurotransmiter eksitatorik, sedangkan efek vasokonstriksi lokal memperlambat absorpsi sistemik anestesi lokal sehingga memperpanjang durasi blok.[7,9,10]

Data eksperimental menunjukkan bahwa kombinasi dexmedetomidine dan ropivakain pada saraf perifer dapat meningkatkan kualitas blok tanpa meningkatkan toksisitas bila diberikan dengan teknik yang tepat.[11] Secara klinis, meta-analisis lintas-blok menunjukkan bahwa penambahan dexmedetomidine memperpanjang waktu bebas nyeri dan menurunkan kebutuhan analgesik tambahan.[9,10]

Kombinasi efek sentral dan perifer menjadikan dexmedetomidine sebagai adjuvan yang unik. Namun, perbedaan sensitivitas individu terhadap efek simpatolitik dapat menimbulkan risiko bradikardia atau hipotensi ringan. Titrasi dosis dan pemantauan hemodinamik tetap krusial, sementara konsensus mengenai dosis perineural yang optimal masih memerlukan penelitian dosis–respons lebih lanjut.

Hasil Klinis Dexmedetomidine pada TLIP Modifikasi

Efektivitas blok interfasial torakolumbal (TLIP) modifikasi telah dievaluasi dalam berbagai penelitian klinis. Sebuah penelitian melaporkan bahwa TLIP modifikasi dengan panduan ultrasonografi pada operasi tulang belakang multilevel secara signifikan menurunkan skor nyeri *Visual Analogue Scale* (VAS) dibandingkan kelompok kontrol, baik pada 2, 6, maupun 12 jam pascaoperasi ($p < 0,05$). Durasi analgesia yang diperoleh mencapai rata-rata 14,5 ± 3,2 jam, sedangkan kelompok kontrol hanya 8,3 ± 2,9 jam. Selain itu, kebutuhan analgesik tambahan berkurang sekitar 35% tanpa peningkatan efek samping hemodinamik.[7]

Teknik TLIP modifikasi dideskripsikan sebagai blok yang menempatkan jarum di antara otot multifidus dan longissimus. Studi tersebut menegaskan bahwa penggunaan ultrasonografi memungkinkan visualisasi fasia dengan jelas dan distribusi anestesi lokal yang merata sehingga menghasilkan analgesia pascaoperasi yang optimal.[6] Kedua penelitian ini menyoroti keunggulan TLIP modifikasi dibandingkan teknik interfasial lainnya dalam hal kemudahan identifikasi anatomi serta rendahnya risiko komplikasi.

Terkait penambahan dexmedetomidine, sebuah meta-analisis menunjukkan bahwa penggunaan dexmedetomidine perineural meningkatkan durasi analgesia hingga 4–5 jam dibandingkan anestesi lokal saja pada berbagai blok perifer.[9] Penelitian lain melaporkan bahwa kombinasi dexmedetomidine–ropivakain memperpanjang durasi analgesia rata-rata 160 menit dan menurunkan konsumsi opioid hingga 40% tanpa peningkatan efek samping serius.[10] Bukti eksperimental juga mendukung mekanisme tersebut, menunjukkan bahwa kombinasi ropivakain–dexmedetomidine secara signifikan meningkatkan durasi blok saraf perifer pada model hewan.[11]

Secara keseluruhan, bukti yang tersedia mendukung bahwa penambahan dexmedetomidine memberikan manfaat klinis nyata terhadap durasi dan kualitas analgesia. Namun, belum ada penelitian RCT yang secara langsung menilai kombinasi TLIP–dexmedetomidine pada pasien yang menjalani pembedahan tulang belakang. Mayoritas data

berasal dari blok perifer atau studi nonkomparatif. Oleh karena itu, meskipun dasar farmakologinya kuat dan temuan awal menjanjikan, generalisasi hasil harus dilakukan dengan hati-hati. Penelitian prospektif dengan kontrol aktif diperlukan untuk mengonfirmasi manfaat tersebut secara spesifik dalam konteks TLIP modifikasi.

Perbandingan dengan Teknik dan Adjuvan Lain

Beberapa penelitian membandingkan TLIP dengan teknik interfasial lain, seperti *erector spinae plane block* (ESPB). Dilaporkan bahwa TLIP dan ESPB sama-sama memberikan kontrol nyeri pascaoperasi yang efektif pada pasien yang menjalani pembedahan tulang belakang. Namun, kelompok TLIP menunjukkan skor VAS yang lebih rendah pada 6 dan 12 jam pertama, serta kebutuhan morfin yang lebih sedikit (rata-rata 6,4 ± 2,3 mg dibandingkan 9,1 ± 3,1 mg; p = 0,01).[12] Efek analgesia kedua teknik bertahan hingga 24 jam, tetapi TLIP lebih unggul dalam mempertahankan fungsi motorik dan stabilitas hemodinamik.

Selain itu, sebuah laporan kasus menggambarkan keberhasilan TLIP modifikasi sebagai teknik alternatif yang aman pada pasien dengan sirosis hati dan trombositopenia.[13] Temuan ini memperkuat nilai TLIP modifikasi sebagai prosedur yang relatif minim risiko perdarahan dibandingkan teknik neuraksial seperti epidural.

Dari sisi penggunaan adjuvan, sebuah telaah sistematis menegaskan bahwa agonis α_2-adrenergik, seperti dexmedetomidine, memiliki efek yang paling konsisten dalam memperpanjang durasi analgesia dibandingkan deksametason dan midazolam.[8] Meta-analisis lain juga menunjukkan hasil serupa, di mana penambahan dexmedetomidine menurunkan kebutuhan analgesik tambahan tanpa meningkatkan kejadian efek samping, seperti mual, muntah, atau hipotensi berat.[9,10]

Perbandingan antarteknik menunjukkan bahwa TLIP modifikasi memiliki keunggulan dalam hal spesifisitas area analgesia, kestabilan hemodinamik, dan kemudahan pelaksanaan. Penggunaan dexmedetomidine sebagai adjuvan tampaknya memperkuat manfaat tersebut, terutama dalam menurunkan konsumsi opioid. Namun, pemilihan teknik dan adjuvan sebaiknya tetap disesuaikan dengan kondisi pasien serta karakteristik pembedahan. Evaluasi efektivitas biaya juga penting untuk menentukan apakah peningkatan durasi analgesia sebanding dengan sumber daya dan risiko yang diperlukan.

Kelebihan, Keterbatasan, dan Arah Penelitian ke Depan

Kombinasi blok interfasial torakolumbal (TLIP) modifikasi dengan dexmedetomidine memiliki sejumlah keunggulan klinis yang menjadikannya alternatif menarik dalam manajemen nyeri pascaoperasi tulang belakang. Teknik TLIP yang dimodifikasi, sebagaimana telah dijelaskan sebelumnya, menghasilkan sebaran anestesi lokal yang lebih terarah di bidang antara otot multifidus dan longissimus, dengan visualisasi ultrasonografi yang baik.[6] Studi lanjutan menunjukkan bahwa TLIP modifikasi menurunkan skor nyeri secara signifikan dan memperpanjang durasi analgesia pasca spinal fusion tanpa efek samping bermakna.[7] Jika dibandingkan dengan *erector spinae plane* (ESP) block, TLIP memberikan analgesia yang sebanding dengan kebutuhan opioid yang lebih rendah serta pemeliharaan fungsi motorik yang lebih baik.[12] Selain itu, sebuah laporan kasus turut mendukung penerapan TLIP pada pasien berisiko tinggi, seperti penderita sirosis dengan trombositopenia, sehingga menegaskan keamanan teknik ini pada populasi yang memiliki kontraindikasi terhadap blok neuraksial.[13]

Penambahan dexmedetomidine sebagai adjuvan memperkuat profil analgesia TLIP melalui mekanisme sinergis dengan anestesi lokal. Beberapa meta-analisis menunjukkan bahwa dexmedetomidine memperpanjang durasi analgesia secara bermakna dan menurunkan

kebutuhan opioid tanpa meningkatkan kejadian hipotensi atau bradikardia berat.[9,10] Telaah sistematis yang menilai berbagai adjuvan pada blok perifer juga menegaskan bahwa agonis α_2-adrenergik, termasuk dexmedetomidine, memberikan konsistensi terbaik dalam hal efikasi dan keamanan jika dibandingkan dengan adjuvan lain, seperti deksametason atau midazolam.[8] Dengan demikian, kombinasi TLIP modifikasi dengan dexmedetomidine menawarkan keseimbangan optimal antara efektivitas analgesia, kestabilan hemodinamik, dan kemudahan pelaksanaan di bawah panduan ultrasonografi.

Namun demikian, terdapat beberapa keterbatasan yang perlu diselesaikan. Pertama, sebagian besar bukti berasal dari studi berskala kecil dengan desain yang heterogen dan populasi pasien terbatas, sehingga generalisasi hasil masih terbatas.[6,7,12] Kedua, belum terdapat konsensus mengenai dosis optimal dexmedetomidine untuk injeksi perineural dalam konteks TLIP; sebagian besar penelitian menggunakan dosis 0,5–1 µg/kg berdasarkan ekstrapolasi dari blok ekstremitas.[9,10] Ketiga, durasi *follow-up* pada sebagian besar penelitian masih terbatas hingga 24 jam pascaoperasi, sehingga efek jangka panjang terhadap pemulihan fungsional maupun risiko neuropati belum sepenuhnya diketahui.

Kombinasi TLIP modifikasi–dexmedetomidine memiliki potensi besar untuk menjadi bagian integral strategi analgesia multimodal, terutama pada pembedahan tulang belakang yang memerlukan evaluasi neurologis dini. Penelitian di masa mendatang sebaiknya difokuskan pada uji acak berskala besar dengan protokol dosis yang terstandar, evaluasi farmakokinetik dan farmakodinamik yang spesifik untuk jaringan interfasial, serta pengukuran luaran jangka panjang seperti kualitas tidur, waktu mobilisasi, dan kepuasan pasien. Kajian komparatif langsung antara dexmedetomidine dan adjuvan lain, seperti deksametason, juga diperlukan untuk menentukan pilihan adjuvan terbaik. Pendekatan multidisiplin yang melibatkan bidang anestesiologi, farmakologi, dan rehabilitasi akan memperkuat dasar ilmiah penerapan teknik ini di masa depan.

Kesimpulan

Blok TLIP modifikasi merupakan teknik analgesia regional yang efektif dan aman dalam mengontrol nyeri pascaoperasi tulang belakang lumbal. Pendekatan ini memberikan analgesia yang terfokus pada area insisi tanpa mengganggu fungsi motorik, sekaligus mempertahankan kestabilan hemodinamik pasien. Penambahan dexmedetomidine sebagai adjuvan pada anestesi lokal terbukti memperpanjang durasi analgesia, menurunkan kebutuhan opioid, serta meningkatkan kenyamanan dan kepuasan pasien secara keseluruhan.

Kombinasi TLIP modifikasi dengan dexmedetomidine menunjukkan potensi besar sebagai bagian dari strategi analgesia multimodal dalam praktik anestesiologi modern. Keunggulannya terletak pada keseimbangan antara efektivitas, keamanan, dan kemudahan penerapan dengan panduan ultrasonografi. Meskipun demikian, variasi dosis, teknik injeksi, serta keterbatasan desain penelitian yang ada menuntut dilakukannya uji klinis berskala besar dan studi komparatif yang lebih sistematis.

Dengan pemahaman yang lebih mendalam mengenai anatomi interfasial, mekanisme kerja adjuvan, dan karakteristik respons pasien, kombinasi TLIP–dexmedetomidine berpotensi menjadi salah satu pendekatan analgesia regional yang unggul dalam meningkatkan kualitas pemulihan dan pengalaman perioperatif pasien yang menjalani pembedahan tulang belakang.

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Penelitian ini tidak menerima hibah atau dukungan pendanaan khusus dari lembaga pendanaan di sektor publik, komersial, maupun nirlaba.

Konflik Kepentingan

Para penulis menyatakan bahwa tidak memiliki konflik kepentingan.

Pernyataan Ketersediaan Data

Tidak ada data baru yang dihasilkan atau dianalisis dalam penelitian ini.

Kontribusi Penulis

Seluruh penulis berkontribusi secara signifikan dalam penyusunan dan perancangan penelitian, pengumpulan data, analisis, serta interpretasi hasil. Semua penulis berpartisipasi dalam penulisan dan revisi naskah secara kritis untuk isi intelektual yang penting, menyetujui versi akhir yang akan diterbitkan, serta bertanggung jawab atas seluruh aspek penelitian ini.

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NARRATIVE REVIEW

Efektivitas dan Keamanan Deksmedetomidine Nebulisasi Dibandingkan Rute Intravena sebagai Premedikasi Anestesi: Tinjauan Naratif

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Abstrak

Laringoskopi dan intubasi trakea merupakan prosedur rutin anestesi yang sering memicu respons hemodinamik berupa peningkatan tekanan darah dan denyut jantung, yang dapat berisiko pada pasien dengan komorbiditas kardiovaskular atau serebrovaskular. Deksmedetomidine, agonis reseptor α2 adrenergik selektif, terbukti efektif dalam menekan respon tersebut melalui efek simpatolitik dan sedatif. Namun, pemberian intravena sering menyebabkan efek samping berupa hipotensi dan bradikardia. Tinjauan naratif ini bertujuan membandingkan efektivitas dan profil keamanan deksmedetomidine nebulisasi dengan rute intravena sebagai agen premedikasi untuk mengontrol respon hemodinamik selama laringoskopi dan intubasi. Berdasarkan hasil sintesis, deksmedetomidine nebulisasi mampu menurunkan lonjakan tekanan darah dan denyut jantung secara efektif dengan insidensi hipotensi dan bradikardi yang lebih rendah dibandingkan pemberian intravena, serta mengurangi kebutuhan obat induksi anestesi tanpa menimbulkan komplikasi serius. Dengan demikian, deksmedetomidine nebulisasi berpotensi menjadi alternatif premedikasi yang efektif dan lebih aman untuk stabilisasi hemodinamik selama anestesi, meskipun masih diperlukan uji klinis multisenter berskala besar untuk memperkuat bukti dan menentukan dosis optimal.

Kata kunci: Bradikardi, Deksmedetomidine, Hipotensi, Laringoskopi, Nebulisasi, Premedikasi, Respon hemodinamik

Efficacy and Safety of Nebulized versus Intravenous Dexmedetomidine as Anesthetic Premedication: Narrative Review

Abstract

Laryngoscopy and tracheal intubation are routine anesthetic procedures that frequently elicit hemodynamic responses, such as elevations in blood pressure and heart rate, posing significant risks for patients with cardiovascular or cerebrovascular comorbidities. Dexmedetomidine, a selective α2 adrenergic receptor agonist, has been shown to effectively attenuate these responses through its sedative and sympatholytic properties. However, intravenous administration is frequently associated with adverse events, such as hypotension and bradycardia. This narrative review aims to compare the efficacy and safety profile of nebulized versus intravenous dexmedetomidine as premedication agents for controlling hemodynamic responses during laryngoscopy and intubation. Current evidence indicates that nebulized dexmedetomidine effectively attenuates increases in blood pressure and heart rate, with a lower incidence of hypotension and bradycardia compared to the intravenous route, and reduces anesthetic induction drug requirements without major complications. Therefore, nebulized dexmedetomidine is a promising alternative for maintaining hemodynamic stability during anesthesia, although large-scale multicenter clinical trials are still needed to strengthen the evidence base and determine optimal dosing.

Keywords: Dexmedetomidine, Nebulization, Premedication, Hemodynamic Response, Laringoskopi, Hypotension, Bradycardia

Pendahuluan

Laringoskopi dan intubasi trakeal merupakan prosedur yang dapat memicu aktivasi mendadak sistem saraf simpatis, ditandai dengan peningkatan tekanan darah, denyut jantung, dan kadar katekolamin plasma, yang dapat membahayakan pasien dengan gangguan kardiovaskular atau serebrovaskular karena risiko iskemia miokard dan peningkatan tekanan intrakranial.[1,2] Aktivitas simpatoadrenal selama laringoskopi terjadi akibat stimulasi nosiseptif dari cabang aferen saraf vagus dan glosofaringeus yang memicu pelepasan norepinefrin secara sistemik,

menghasilkan lonjakan hemodinamik yang signifikan namun sementara.

Berbagai agen farmakologis telah digunakan untuk menekan respons ini, termasuk opioid, lidokain, beta-bloker, antagonis kalsium, dan agonis $\alpha 2$ adrenergik.[3-5] Di antara agen tersebut, deksmedetomidine menonjol karena memberikan efek sedasi, analgesia, dan simpatolisis tanpa menyebabkan depresi napas yang signifikan.[6,7] Efek simpatolitik deksmedetomidine menghambat pelepasan norepinefrin di locus coeruleus dan medula spinalis, menghasilkan penurunan denyut jantung dan tekanan darah yang terkontrol.[8,9]

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Secara konvensional, deksmedetomidine diberikan secara intravena, tetapi rute ini sering dikaitkan dengan efek samping berupa hipotensi dan bradikardi yang bersifat dosis tergantung.[2,10] Dalam beberapa tahun terakhir, rute nebulisasi semakin diakui sebagai alternatif yang menarik karena memberikan efek lokal pada mukosa saluran napas atas dan absorpsi sistemik yang lebih lambat, sehingga menurunkan risiko fluktuasi hemodinamik mendadak.[3,7,11] Nebulisasi juga memiliki keunggulan kenyamanan, terutama pada pasien pediatrik atau dewasa yang sulit mendapatkan akses intravena.[12-14]

Berbagai studi telah menilai efektivitas deksmedetomidine nebulisasi dalam menekan respon hemodinamik terhadap laringoskopi dan intubasi. Beberapa penelitian acak terkontrol menunjukkan bahwa nebulisasi menghasilkan penurunan tekanan darah dan denyut nadi yang sebanding, atau bahkan lebih stabil, dibandingkan rute intravena.[2,14,15] Selain itu, efek sedasi yang dihasilkan dianggap memadai dengan insidensi hipotensi dan bradikardi yang lebih renda.[7,10,16] Meta-analisis terbaru juga memperkuat temuan ini, menunjukkan bahwa deksmedetomidine nebulisasi dapat menjadi alternatif noninvasif yang efektif dan aman untuk mengontrol respons hemodinamik periintubasi.[17]

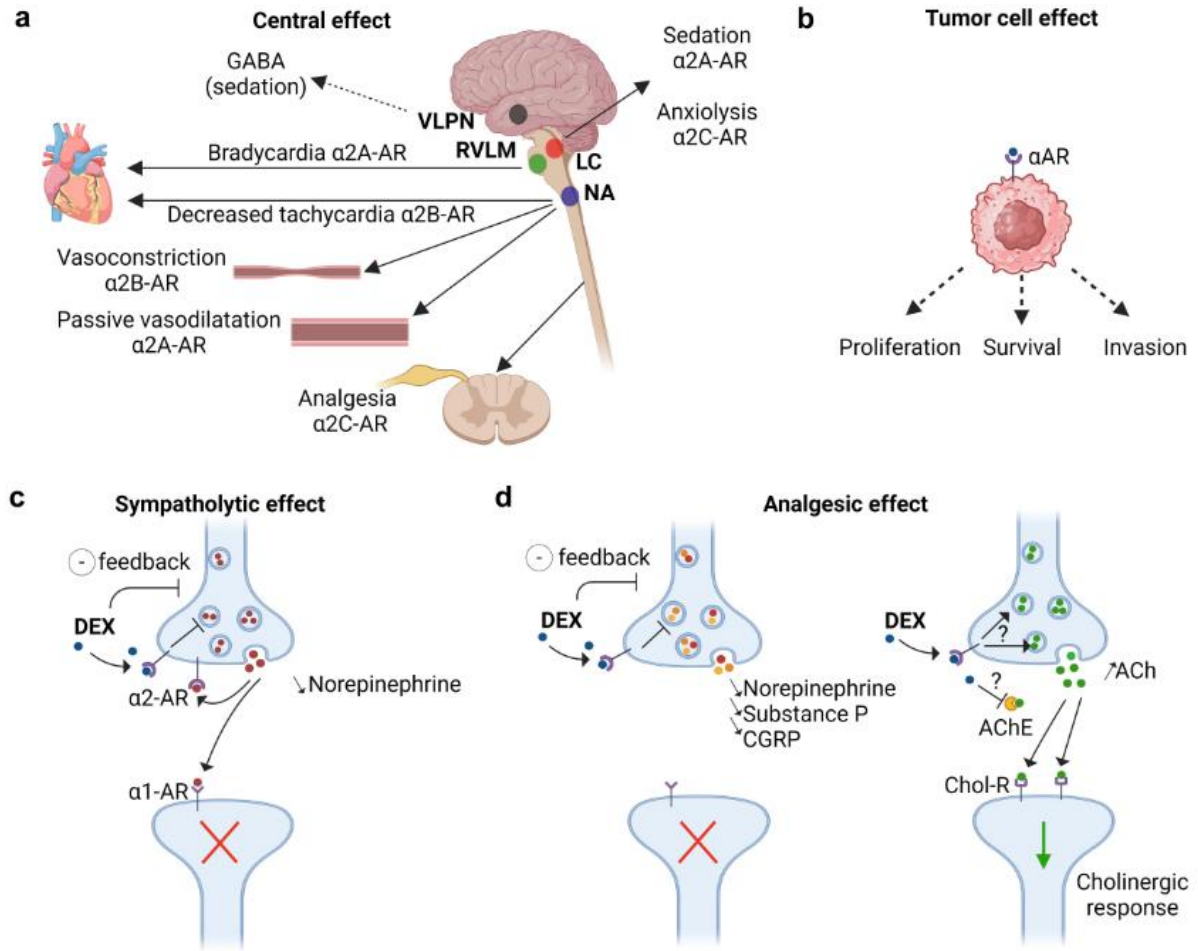
Namun demikian, sebagian besar penelitian yang ada masih terbatas secara geografis—didominasi oleh studi di Asia Selatan—dan memiliki jumlah sampel relatif kecil, sehingga masih diperlukan penelitian lebih lanjut.[17,19] Dengan meningkatnya minat terhadap rute noninvasif dan keterbatasan data komparatif yang ada, diperlukan telaah naratif yang meninjau bukti terkini secara kritis mengenai efektivitas dan keamanan deksmedetomidine nebulisasi dibandingkan dengan rute intravena dalam mengendalikan respon hemodinamik selama induksi anestesi.

Mekanisme Farmakologis dan Rute Absorpsi

Deksmedetomidine merupakan agonis selektif reseptor $\alpha 2$ adrenergik yang bekerja di sistem saraf pusat maupun perifer. Efek utamanya berupa sedasi, analgesia, dan simpatolisis, yang dihasilkan melalui penurunan aktivitas neuron noradrenergik di locus coeruleus dan menghambat pelepasan neurotransmiter eksitatorik di medula spinalis.[10] Aktivasi reseptor $\alpha 2$ presinaptik menghambat pelepasan norepinefrin, sehingga terjadi penurunan tonus simpatis yang berakibat pada penurunan denyut jantung dan tekanan darah, tanpa menyebabkan depresi napas yang bermakna. Selain itu, deksmedetomidine juga menunjukkan efek protektif pada jaringan melalui penurunan stres oksidatif dan inflamasi, yang melibatkan aktivasi jalur *Keap1–Nrf2–ARE*.[19]

Pada tingkat perifer, stimulasi reseptor $\alpha 2$ postsinaptik pada otot polos vaskular dapat menyebabkan vasokonstriksi ringan, namun efek dominannya adalah vasodilatasi sekunder akibat penurunan aktivitas simpatik sentral. Mekanisme ganda ini menjelaskan profil hemodinamik deksmedetomidine yang khas — penurunan tekanan darah moderat disertai bradikardi ringan.

Rute pemberian obat ini memengaruhi farmakokinetika dan intensitas efek klinisnya. Pemberian intravena menghasilkan puncak konsentrasi plasma yang cepat, tetapi juga fluktuasi tekanan darah yang lebih besar. Sebaliknya, rute inhalasi atau nebulisasi memungkinkan absorpsi melalui mukosa saluran napas, memberikan peningkatan konsentrasi sistemik yang lebih bertahap dan stabil.[11] Bioavailabilitas deksmedetomidine melalui rute nebulisasi dilaporkan mencapai 65–82%, dengan waktu puncak sekitar 15–30 menit setelah inhalasi — mirip dengan rute intranasal namun dengan risiko iritasi mukosa yang lebih rendah.



Gambar 1. Efek simpatolitik dan analgesik dari dexmedetomidine dimediasi melalui reseptor α2-adrenoseptor.[10]

Selain efek sedatif dan simpatolitik, sejumlah penelitian praklinis juga menunjukkan potensi aksi pleiotropik deksmedetomidine, termasuk efek antiinflamasi dan sitoprotektif. Dalam model hewan sepsis, deksmedetomidine dilaporkan memperbaiki mikrosirkulasi dan menurunkan mediator inflamasi tanpa menimbulkan depresi kardiovaskular yang signifikan.[11] Hal ini memperkuat rasional klinis bahwa pemberian deksmedetomidine melalui rute noninvasif seperti nebulisasi dapat

mempertahankan efek sistemik yang diinginkan dengan risiko efek samping yang lebih kecil.

Secara fisiologis, rute nebulisasi menawarkan keseimbangan antara efikasi dan keamanan: absorpsi yang cepat namun tidak mendadak, efek sedatif dan analgetik yang cukup untuk premedikasi, serta potensi menurunkan kebutuhan agen anestesi intravena. Mekanisme kerja kombinatif ini menjadi dasar ilmiah bagi banyak penelitian klinis yang membandingkan efektivitas nebulisasi dengan rute intravena pada konteks kontrol respon hemodinamik selama laringoskopi dan intubasi.

Efektivitas Klinis terhadap Respon Hemodinamik

Bukti klinis terkini menunjukkan bahwa deksmedetomidine nebulisasi mampu menekan respon hemodinamik yang diinduksi oleh laringoskopi dan intubasi dengan efektivitas yang setidaknya sebanding dengan rute intravena, serta memberikan stabilitas tekanan darah dan denyut jantung yang lebih konsisten. Beberapa penelitian acak terkontrol mendukung keunggulan rute nebulisasi ini dari sisi kestabilan hemodinamik dan kenyamanan pasien.

Sebuah studi melaporkan bahwa pemberian deksmedetomidine secara nebulisasi menghasilkan penekanan respon tekanan darah arteri rata-rata (*Mean Arterial* Pressure/MAP) dan denyut jantung (*Heart Rate*/HR) yang sebanding dengan rute intravena, tanpa perbedaan signifikan terhadap durasi sedasi atau kejadian efek samping kardiovaskular.[2] Temuan serupa juga ditemukan dalam populasi pasien pembedahan laparoskopi, di mana kelompok nebulisasi menunjukkan fluktuasi tekanan darah yang lebih kecil serta kebutuhan opioid intraoperatif yang lebih rendah.[3]

Studi oleh Kumar et al.[7] menunjukkan bahwa kenaikan HR dan MAP pada menit pertama setelah intubasi secara signifikan lebih kecil pada kelompok nebulisasi dibandingkan intravena, mengindikasikan onset kerja simpatolitik yang memadai dengan efek puncak yang tidak terlalu tajam. Hasil ini diperkuat oleh Singh et al. dan Gandhi et al., yang menemukan bahwa nebulisasi mempertahankan stabilitas hemodinamik selama periode intubasi hingga lima menit setelahnya, dengan efikasi yang setara terhadap penurunan HR dan MAP.[12,15]

Studi terbaru oleh Reshma et al.[20] juga menegaskan efektivitas nebulisasi dalam mengontrol respon hemodinamik pada berbagai jenis operasi umum. Kelompok nebulisasi menunjukkan peningkatan tekanan darah sistolik dan denyut jantung yang lebih kecil dibandingkan kelompok intravena. Konsistensi hasil lintas populasi ini mengindikasikan bahwa rute nebulisasi mampu memberikan efek simpatolitik yang stabil tanpa kehilangan efikasi klinis.

Berbagai uji acak terkontrol menunjukkan bahwa deksmedetomidine nebulisasi efektif dalam menekan peningkatan tekanan darah dan denyut jantung akibat stimulasi laringoskopi dan intubasi, serta dapat menurunkan kebutuhan agen anestesi tambahan. Rute nebulisasi memberikan profil efek yang lebih bertahap dan stabil dibandingkan rute intravena, menjadikannya alternatif premedikasi yang menjanjikan untuk menjaga stabilitas hemodinamik periintubasi.[2,3,7,12,15,20]

Keamanan dan Efek Samping

Selain efektivitasnya dalam menekan respon hemodinamik, aspek keamanan penggunaan deksmedetomidine, khususnya melalui rute nebulisasi, menjadi faktor penting dalam menentukan kelayakan klinisnya. Secara farmakodinamik, deksmedetomidine dapat menimbulkan efek samping berupa hipotensi dan bradikardia yang terkait dengan penurunan aktivitas simpatis dan peningkatan tonus parasimpatis yang dipengaruhi oleh rute pemberian dan kecepatan absorpsi obat.

Shrivastava et al.[4] melaporkan bahwa pemberian deksmedetomidine nebulisasi menimbulkan insidensi hipotensi dan bradikardia yang lebih rendah dibandingkan rute intravena, tanpa perbedaan signifikan terhadap kestabilan tekanan darah. Hal ini menunjukkan bahwa absorpsi bertahap melalui mukosa saluran napas atas mampu menghindari peningkatan kadar plasma mendadak dibandingkan intravena bolus.

Ittoop et al.[6] dalam penelitiannya menemukan bahwa nebulisasi deksmedetomidine tidak hanya menurunkan risiko hipotensi perioperatif, tetapi juga menurunkan kejadian nyeri tenggorokan pascaoperasi, menunjukkan tolerabilitas mukosa yang baik. Temuan tersebut memperkuat keunggulan rute nebulisasi sebagai pilihan noninvasif dengan keamanan mukosa yang tinggi.

Meta-analisis oleh Gupta et al.[8] menunjukkan bahwa nebulisasi secara signifikan menurunkan risiko bradikardia dan hipotensi dibandingkan rute intravena, tanpa peningkatan insiden efek samping respirasi, mual, ataupun muntah. Selain itu, Lin et al.[18] dalam tinjauan sistematisnya terhadap populasi pediatrik menunjukkan bahwa efek samping deksmedetomidine inhalasi bersifat ringan dan reversibel, seperti kantuk dan mulut kering, tanpa depresi pernapasan.

Mekanisme absorpsi mukosa yang lebih lambat pada rute nebulisasi memberikan keuntungan bagi pasien dengan komorbiditas kardiovaskular, di mana fluktuasi tekanan darah atau denyut jantung harus dihindari. Dengan demikian, pemberian nebulisasi dapat menjadi alternatif premedikasi yang lebih aman, terutama pada pasien yang rentan terhadap efek simpatolitik ekstrem.

Secara keseluruhan, bukti ilmiah menunjukkan bahwa deksmedetomidine nebulisasi memiliki profil keamanan yang lebih baik dibandingkan rute intravena, dengan insidensi efek samping kardiovaskular dan respirasi yang lebih rendah serta tolerabilitas mukosa yang baik. Hasil ini memperkuat potensi klinis rute nebulisasi sebagai opsi premedikasi yang aman dan efektif untuk menjaga stabilitas hemodinamik perioperatif.[4,6,8,18]

Aplikasi Noninvasif dan Populasi Khusus

Rute nebulisasi deksmedetomidine tidak hanya memberikan keuntungan dalam hal kemudahan pemberian dan stabilitas hemodinamik, tetapi juga memperluas aplikasinya pada populasi khusus seperti pasien pediatrik, individu dengan kesulitan akses intravena, serta pada prosedur yang memerlukan kesadaran ringan dan kerja sama pasien. Dalam konteks ini, rute noninvasif menjadi solusi praktis yang mempertahankan efikasi klinis tanpa meningkatkan risiko efek samping.

Abdelraheem et al.[5] membandingkan deksmedetomidine intranasal dengan midazolam pada anak-anak yang menjalani MRI dan menemukan bahwa deksmedetomidine memberikan sedasi yang lebih baik dan tingkat kecemasan yang lebih rendah tanpa menimbulkan efek samping kardiovaskular signifikan. Selain itu, Bonagua et al.[9] meneliti nebulisasi deksmedetomidine sebelum pemasangan akses intravena pada anak terdapat penurunan skor kecemasan serta peningkatan kerja sama pasien, tanpa efek pernapasan yang bermakna. Kedua penelitian ini menegaskan potensi deksmedetomidine noninvasif sebagai agen premedikasi pediatrik yang aman dan nyaman.

Gu et al.[3] mengevaluasi kombinasi nebulisasi deksmedetomidine–lidokain pada pasien dewasa yang menjalani bronkoskopi fleksibel dan menemukan tingkat sedasi serta toleransi prosedur yang lebih baik tanpa desaturasi oksigen atau depresi napas. Penelitian serupa oleh Shafa et al.[17] pada anak yang menjalani bronkoskopi menunjukkan hasil yang konsisten, di mana nebulisasi deksmedetomidine memberikan stabilitas

hemodinamik lebih baik dibandingkan lidokain tunggal, sekaligus mempertahankan refleks jalan napas.

Secara praktis, rute nebulisasi meminimalkan ketidaknyamanan akibat pemasangan infus, mengurangi waktu persiapan anestesi, dan meningkatkan kepatuhan pasien. Mekanisme absorpsi mukosa yang efisien memungkinkan efek sistemik yang cukup untuk premedikasi tanpa memerlukan alat invasif tambahan. Pada populasi anak maupun dewasa muda yang rentan terhadap stres atau fobia jarum, hal ini menjadi keuntungan klinis penting dalam menjaga stabilitas fisiologis prainduksi.

Aplikasi deksmedetomidine nebulisasi juga potensial digunakan pada populasi geriatri atau pasien dengan risiko tinggi komplikasi kardiovaskular, di mana kontrol hemodinamik dan kenyamanan menjadi prioritas. Dengan profil efikasi dan keamanan yang mendukung, rute noninvasif ini dapat menjadi pilihan strategis dalam protokol premedikasi modern di berbagai populasi klinis.[5,9,13,17]

Keterbatasan Penelitian dan Arah Riset Selanjutnya

Meskipun berbagai penelitian mendukung efektivitas dan keamanan deksmedetomidine nebulisasi dibandingkan rute intravena, terdapat sejumlah keterbatasan metodologis dan kontekstual yang perlu diperhatikan sebelum generalisasi hasil dapat dilakukan secara luas

Keterbatasan desain dan ukuran sampel

Sebagian besar studi desain uji acak terkontrol memiliki ukuran sampel kecil, dengan jumlah sampel berkisar antara 40 hingga 80 peserta per kelompok.[2–4,7,12,15] Ini menurunkan kekuatan statistik untuk mendeteksi perbedaan kecil dalam parameter hemodinamik, serta meningkatkan risiko bias tipe II. Selain itu, beberapa penelitian tidak melaporkan detail dosis optimal atau waktu pemberian yang distandardisasi, sehingga menyulitkan perbandingan lintas studi.

Bias geografis dan heterogenitas populasi

Sebagian besar literatur berasal dari Asia Selatan, terutama India dan Nepal.[2,3,7,12,15,20] Kondisi ini menimbulkan potensi bias regional, karena perbedaan karakteristik populasi, praktik anestesi, dan ketersediaan fasilitas dapat memengaruhi hasil klinis. Keterbatasan ini menuntut perlunya studi multisenter dengan cakupan geografis yang lebih luas untuk memastikan generalisasi temuan.

Variabilitas dosis dan metode pemberian

Belum terdapat konsensus mengenai dosis ideal dan teknik nebulisasi yang paling efektif. Beberapa studi menggunakan dosis tetap (misalnya 1 µg/kg), sementara lainnya menyesuaikan dosis berdasarkan berat badan atau jenis pembedahan. Variasi dalam waktu pemberian (10–20 menit sebelum induksi) dan durasi inhalasi juga menjadi sumber heterogenitas yang dapat memengaruhi hasil. Standarisasi protokol diperlukan agar bukti yang dihasilkan lebih konsisten.

Keterbatasan pelaporan efek jangka panjang

Sebagian besar penelitian berfokus pada efek akut periintubasi (hingga 10 menit setelah laringoskopi), sementara data tentang efek pascaoperatif, pemulihan kognitif, dan parameter hemodinamik jangka panjang masih sangat terbatas. Penelitian lanjutan perlu mengeksplorasi efek residu deksmedetomidine nebulisasi terhadap kualitas pemulihan anestesi dan waktu *discharge* pasien.

Arah penelitian selanjutnya

Diperlukan uji klinis acak berskala besar dengan desain multisenter yang menilai tidak hanya respon hemodinamik, tetapi juga outcome klinis lain seperti konsumsi anestesi total, kepuasan pasien, dan biaya efektifitas. Selain itu, studi farmakokinetik komparatif antara rute nebulisasi dan intravena akan sangat berharga untuk menentukan dosis optimal yang menyeimbangkan efikasi dan keamanan. Integrasi penelitian translasi mengenai efek

molekuler (misalnya jalur *Keap1–Nrf2–ARE* dan modulasi inflamasi sistemik) juga dapat memperkaya pemahaman mekanistik deksmedetomidine sebagai agen premedikasi noninvasif.

Secara keseluruhan, meskipun hasil yang ada menjanjikan, keterbatasan ukuran sampel kecil, bias regional, dan memiliki variabilitas dosis dan teknik pemberian yang belum distandardisasi masih menjadi hambatan utama dalam penerapan luas deksmedetomidine nebulisasi. Penelitian di masa depan perlu diarahkan untuk memperkuat validitas eksternal dan menghasilkan pedoman dosis baku yang dapat diimplementasikan secara global.

Kesimpulan

Deksmedetomidine nebulisasi merupakan alternatif premedikasi yang efektif dan aman untuk mengendalikan respon hemodinamik selama laringoskopi dan intubasi. Bukti klinis menunjukkan bahwa rute nebulisasi memberikan efek penurunan tekanan darah dan denyut jantung yang sebanding dengan rute intravena, dengan insidensi hipotensi dan bradikardia yang lebih rendah. Keunggulan absorpsi mukosa yang bertahap menjadikan efek simpatolitik lebih stabil tanpa fluktuasi ekstrem. Rute nebulisasi juga menawarkan kenyamanan dan kemudahan penggunaan, terutama pada pasien pediatrik atau individu dengan kesulitan akses intravena. Meskipun demikian, keterbatasan ukuran sampel dan dominasi studi dari satu wilayah geografis menuntut penelitian multisenter berskala besar untuk memperkuat bukti dan menentukan dosis optimal. Secara keseluruhan, deksmedetomidine nebulisasi dapat dipertimbangkan sebagai premedikasi noninvasif yang menjanjikan dengan keseimbangan baik antara efektivitas, keamanan, dan kenyamanan klinis.

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Penelitian ini tidak menerima hibah atau dukungan pendanaan khusus dari lembaga pendanaan di sektor publik, komersial, maupun nirlaba.

Konflik Kepentingan

Para penulis menyatakan bahwa tidak memiliki konflik kepentingan.

Pernyataan Ketersediaan Data

Tidak ada data baru yang dihasilkan atau dianalisis dalam penelitian ini.

Kontribusi Penulis

Seluruh penulis berkontribusi secara signifikan dalam penyusunan dan perancangan penelitian, pengumpulan data, analisis, serta interpretasi hasil. Semua penulis berpartisipasi dalam penulisan dan revisi naskah secara kritis untuk isi intelektual yang penting, menyetujui versi akhir yang akan diterbitkan, serta bertanggung jawab atas seluruh aspek penelitian ini.

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NARRATIVE REVIEW

Efektivitas dan Risiko Pemberian Antibiotik Profilaksis Ceftriaxone pada Pasien Cedera Otak Akut: Tinjauan Naratif

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Abstrak

Cedera otak akut merupakan salah satu penyebab utama mortalitas dan morbiditas pada pasien trauma dan sering disertai komplikasi infeksi nosokomial seperti *ventilator-associated pneumonia* (VAP) dan meningitis. Penggunaan antibiotik profilaksis, termasuk ceftriaxone, banyak diterapkan untuk mencegah komplikasi tersebut karena spektrum kerjanya yang luas dan kemampuannya menembus sistem saraf pusat. Namun, efektivitas dan dampak terhadap resistensi antimikroba masih menjadi perdebatan, terutama dalam konteks praktik intensif dan bedah saraf. Tinjauan naratif ini bertujuan untuk menilai efektivitas, keamanan, dan implikasi klinis pemberian ceftriaxone sebagai antibiotik profilaksis pada pasien cedera otak akut. Berdasarkan hasil uji klinis acak dan kajian sistematis, ceftriaxone menunjukkan penurunan kejadian VAP dini sebesar 14% dibandingkan 32% pada kelompok kontrol, tetapi tidak menunjukkan manfaat signifikan terhadap pencegahan meningitis atau infeksi luka operasi. Beberapa studi juga melaporkan peningkatan risiko resistensi bakteri akibat pemberian berkepanjangan. Hasil sintesis ini menegaskan pentingnya pendekatan selektif dalam pemberian antibiotik profilaksis dengan mempertimbangkan risiko infeksi dan prinsip *antimicrobial stewardship*. Pesan utama dari tinjauan ini adalah perlunya kebijakan penggunaan antibiotik yang lebih rasional dan penelitian prospektif untuk menentukan populasi pasien yang paling diuntungkan serta durasi optimal pemberian profilaksis.

Kata kunci: Antibiotik profilaksis, Cedera otak akut;; Ceftriaxone; Pneumonia terkait ventilator, Resistensi antimikroba.

Effectiveness and Risks of Prophylactic Ceftriaxone Administration in Patients with Acute Brain Injury: A Narrative Review

Abstract

Acute brain injury is a leading cause of mortality and morbidity among trauma patients and is frequently complicated by nosocomial infections such as ventilator-associated pneumonia (VAP) and meningitis. Prophylactic antibiotics, including ceftriaxone, are commonly administered to prevent such infections due to their broad-spectrum activity and excellent central nervous system penetration. However, the efficacy and impact on antimicrobial resistance remain debated, particularly in intensive care and neurosurgical settings. This narrative review aims to evaluate the effectiveness, safety, and clinical implications of ceftriaxone prophylaxis in acute brain injury patients. Evidence from randomized controlled trials and systematic reviews indicates that ceftriaxone reduced early VAP incidence by 14% compared to 32% in controls but showed no significant benefit in preventing meningitis or surgical site infections. Several studies also reported increased bacterial resistance associated with prolonged antibiotic use. The synthesis highlights the importance of a selective approach to prophylactic antibiotic administration based on infection risk and antimicrobial stewardship principles. The key message of this review is the need for rational antibiotic policies and further prospective research to identify high-risk patient populations and determine the optimal duration of prophylaxis.

Keywords: Acute brain injury; Prophylactic antibiotics; Ceftriaxone; Antimicrobial resistance; Ventilator-associated pneumonia

Pendahuluan

Cedera otak akut merupakan salah satu penyebab utama mortalitas dan morbiditas pada pasien trauma. Angka kematian dilaporkan mencapai 30–40%, sementara morbiditas neurologis dapat melebihi 60% dari seluruh kasus cedera otak traumatik di dunia, dengan estimasi sekitar 69 juta kasus setiap tahun.[1] Sebagian besar pasien dengan cedera otak berat memerlukan tindakan pembedahan segera dan

perawatan intensif pascaoperasi. Kondisi ini meningkatkan risiko terjadinya komplikasi infeksi seperti *ventilator-associated pneumonia* (VAP), meningitis, dan *surgical site infection* (SSI), terutama pada pasien dengan tingkat kesadaran rendah atau kebutuhan ventilator mekanik jangka panjang.

Dalam praktik klinis, pemberian antibiotik profilaksis bertujuan untuk menurunkan kejadian infeksi pascaoperasi dan memperbaiki luaran pasien. Salah satu antibiotik yang banyak digunakan adalah ceftriaxone, antibiotik sefalosporin generasi ketiga dengan spektrum luas terhadap bakteri gram negatif dan positif serta penetrasi yang baik ke cairan serebrospinal. Beberapa studi menunjukkan bahwa pemberian ceftriaxone dosis tunggal praoperatif dapat mengurangi kejadian VAP dini,[3] sementara penelitian lain menyebutkan tidak ada perbedaan signifikan antara penggunaan antibiotik profilaksis dan plasebo.[4–6]

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Meningkatnya resistensi antimikroba (*antimicrobial resistance* / AMR) kini menjadi ancaman global. WHO, CDC, dan NICE telah menegaskan perlunya kebijakan rasionalisasi antibiotik untuk mencegah *multidrug-resistant organisms* (MDRO) yang berkontribusi terhadap kegagalan terapi dan peningkatan biaya perawatan.[7] Meskipun demikian, dalam praktik di berbagai rumah sakit, antibiotik profilaksis masih sering diberikan melebihi durasi yang direkomendasikan.

Hingga saat ini, belum terdapat konsensus yang kuat mengenai efektivitas dan keamanan penggunaan antibiotik profilaksis, khususnya ceftriaxone, pada pasien dengan cedera otak akut. Tinjauan naratif ini bertujuan untuk mengevaluasi bukti ilmiah terkini terkait efektivitas dan risiko penggunaan ceftriaxone sebagai antibiotik profilaksis, sekaligus menelaah implikasi klinis serta arah kebijakan penggunaan antibiotik yang rasional dalam tata laksana pasien cedera otak akut.

Rasional dan Dasar Penggunaan Antibiotik Profilaksis pada Cedera Otak Akut

Patofisiologi dan Risiko Infeksi pada Pasien Cedera Otak Akut. Pasien dengan cedera otak akut, terutama yang mengalami *traumatic brain injury* (TBI) berat, memiliki risiko tinggi terhadap komplikasi infeksi akibat berbagai faktor fisiologis dan iatrogenik. Penurunan kesadaran menyebabkan hilangnya refleks protektif jalan napas, sehingga diperlukan intubasi dan ventilasi mekanik jangka panjang. Kondisi ini berkontribusi terhadap terbentuknya biofilm pada saluran endotrakeal, yang menjadi faktor utama penyebab *ventilator-associated pneumonia* (VAP).[2]
Selain itu, pembedahan kraniotomi, fraktur terbuka, dan adanya kebocoran cairan serebrospinal (CSF) meningkatkan risiko infeksi sistem saraf pusat (SSP), termasuk meningitis pascaoperasi. Ketidakseimbangan respons imun pada pasien neurotrauma — seperti imunosupresi sistemik akibat aktivasi aksis hipotalamus–pituitari–adrenal — juga memperburuk kerentanan terhadap infeksi nosokomial.

Farmakologi dan Karakteristik Ceftriaxone sebagai Agen Profilaksis. Ceftriaxone merupakan antibiotik sefalosporin generasi ketiga dengan spektrum luas terhadap bakteri gram negatif dan positif, serta kemampuan penetrasi yang baik ke jaringan otak dan cairan serebrospinal. Waktu paruh yang panjang

(sekitar 8 jam) memungkinkan pemberian dosis tunggal praoperatif untuk mencapai kadar terapeutik yang memadai selama prosedur operasi dan periode awal pascaoperasi.[3]
Berbeda dari cefazolin yang lebih aktif terhadap bakteri gram positif kulit, ceftriaxone memiliki aktivitas yang lebih luas terhadap bakteri gram negatif aerob seperti Klebsiella pneumoniae dan Enterobacter spp., yang merupakan patogen umum penyebab VAP pada pasien ventilasi mekanik. Keunggulan farmakokinetik dan spektrum kerja ini mendasari penggunaannya dalam studi PROPHY-VAP,[3] di mana ceftriaxone terbukti mampu menurunkan insiden pneumonia dini pada pasien yang mengalami koma akibat cedera otak.

Pertimbangan Klinis dan Kebijakan Penggunaan Profilaksis. Pemberian antibiotik profilaksis secara ideal dilakukan dalam 60 menit sebelum insisi pembedahan dan tidak dilanjutkan lebih dari 24 jam setelah operasi.[7] Namun, dalam praktik klinis, banyak rumah sakit masih memperpanjang durasi pemberian antibiotik hingga beberapa hari pascaoperasi, dengan asumsi dapat mengurangi kejadian infeksi sekunder. Bukti terbaru menunjukkan bahwa strategi ini tidak memberikan manfaat tambahan dan justru meningkatkan risiko resistensi antimikroba.[5–7]

Bukti Klinis Efektivitas Ceftriaxone dalam Mencegah Infeksi

Bukti dari Uji Klinis Acak. Sebuah uji klinis acak berskala besar yang dilakukan pada tahun 2024 melibatkan 345 pasien dengan cedera otak akut yang menjalani ventilasi mekanik dan menunjukkan bahwa pemberian dosis tunggal ceftriaxone 2 gram intravena dalam 12 jam pertama setelah intubasi menurunkan kejadian *ventilator-associated pneumonia* (VAP) dini sebesar 14% dibandingkan 32% pada kelompok kontrol, dengan HR 0,60 (95% CI: 0,38–0,95; p=0,030).[3] Sebaliknya, penelitian lain pada tahun 2004 yang meneliti pasien dengan *pneumocephalus traumatic* menemukan bahwa pemberian ceftriaxone 1 gram dua kali sehari selama lima hari tidak memberikan perbedaan bermakna terhadap kejadian meningitis dibandingkan dengan plasebo.[6]

Bukti dari Kajian Sistematis dan Meta-Analisis. Sebuah tinjauan sistematis tahun 2022 melaporkan bahwa antibiotik profilaksis tidak memberikan manfaat signifikan pada penetrating *traumatic brain injury* (pTBI) dengan angka infeksi sistem saraf pusat sebesar 17% pada kelompok antibiotik dan 19% pada kelompok kontrol.[4] Kajian meta-analitik tahun 2020 menunjukkan bahwa pemberian antibiotik pascaoperasi berkepanjangan tidak menurunkan kejadian infeksi luka operasi tetapi justru meningkatkan resistensi antimikroba.[7] Hasil serupa juga dilaporkan oleh penelitian kohort retrospektif tahun 2017 yang melibatkan 808 pasien bedah saraf bersih, di mana tidak terdapat penurunan kejadian infeksi pascaoperasi dan ditemukan peningkatan isolasi bakteri *multidrug-resistant* (MDR).[5]

Sintesis Naratif dan Kesenjangan Penelitian. Secara umum, bukti efektivitas ceftriaxone masih menunjukkan hasil yang kontradiktif. Uji klinis acak berskala besar tahun 2024 menunjukkan penurunan insiden VAP dini sebesar 14% dibandingkan 32% pada kelompok kontrol.[3] Sebaliknya, penelitian pada tahun 2004 menemukan tidak ada perbedaan bermakna dalam kejadian meningitis antara kelompok ceftriaxone dan plasebo.[6] Kajian retrospektif tahun 2017 terhadap 808 pasien bedah saraf bersih juga menunjukkan tidak adanya penurunan kejadian infeksi dan peningkatan isolasi bakteri MDR.[5] Kesenjangan utama yang ditemukan meliputi variasi desain penelitian, heterogenitas populasi, dan minimnya data resistensi bakteri yang terlapor.

Risiko, Keterbatasan, dan Resistensi Antimikroba

Peningkatan kejadian *multidrug-resistant organisms* (MDRO) merupakan kekhawatiran utama pada penggunaan antibiotik profilaksis yang tidak rasional. Sekitar satu dari enam resep antibiotik di rumah sakit digunakan untuk profilaksis bedah, dan hingga 90% pasien di beberapa negara masih menerima antibiotik lebih dari satu hari pascaoperasi.[7]

Durasi pemberian yang berlebihan telah dikaitkan dengan peningkatan kejadian resistensi, gangguan mikrobiota, dan efek nefrotoksik ringan. Analisis meta tahun 2020 menunjukkan bahwa perpanjangan pemberian antibiotik setelah operasi tidak meningkatkan efektivitas pencegahan infeksi luka operasi, namun meningkatkan insidensi resistensi antimikroba.[7] Penelitian retrospektif tahun 2017 terhadap 808 pasien bedah saraf bersih juga menemukan peningkatan isolasi bakteri MDR tanpa adanya penurunan kejadian infeksi.[5] Sebagian besar penelitian tidak menilai resistensi sebagai luaran utama, sehingga data resistensi mikroba masih terbatas.

Pendekatan *antimicrobial stewardship* menekankan pentingnya evaluasi penggunaan antibiotik berdasarkan risiko pasien dan durasi optimal pemberian. Hal ini mencakup penghentian antibiotik segera setelah operasi kecuali terdapat indikasi kuat seperti luka kontaminasi berat atau kebocoran CSF. Implementasi program stewardship di ICU dan unit bedah saraf dapat mengurangi paparan antibiotik yang tidak perlu serta menekan laju resistensi mikroba.

Implikasi Klinis dan Arah Penelitian Masa Depan

Meskipun terdapat bukti bahwa ceftriaxone dapat menurunkan kejadian VAP pada kelompok tertentu, hasil yang tidak konsisten antarstudi menunjukkan perlunya pendekatan selektif. Subkelompok pasien yang berpotensi mendapat manfaat lebih besar antara lain pasien dengan GCS rendah (≤8), ventilasi mekanik jangka panjang, atau luka terbuka dengan kontaminasi.

Penelitian lanjutan perlu difokuskan pada identifikasi pasien berisiko tinggi, evaluasi resistensi mikroba, serta dampak terhadap lama rawat dan mortalitas. Rekomendasi WHO dan CDC menegaskan bahwa antibiotik profilaksis sebaiknya diberikan sesingkat mungkin. Adaptasi kebijakan tersebut di bidang anestesiologi dan terapi intensif di Indonesia diharapkan dapat menekan kejadian MDR dan memperbaiki luaran pasien.

Kesimpulan

Pemberian ceftriaxone sebagai antibiotik profilaksis pada pasien cedera otak akut dapat memberikan manfaat dalam menurunkan kejadian infeksi seperti VAP pada beberapa penelitian. Namun, bukti yang kontradiktif dan meningkatnya resistensi antimikroba menuntut kehati-hatian dalam penerapan rutin.

Diperlukan penelitian prospektif dengan populasi homogen untuk menentukan subkelompok pasien yang paling diuntungkan. Kebijakan *antimicrobial stewardship* tetap menjadi kunci dalam menjaga keseimbangan antara efektivitas klinis dan pencegahan resistensi.

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Penelitian ini tidak menerima hibah atau dukungan pendanaan khusus dari lembaga pendanaan di sektor publik, komersial, maupun nirlaba.

Konflik Kepentingan

Para penulis menyatakan bahwa tidak memiliki konflik kepentingan.

Pernyataan Ketersediaan Data

Tidak ada data baru yang dihasilkan atau dianalisis dalam penelitian ini.

Kontribusi Penulis

Seluruh penulis berkontribusi secara signifikan dalam penyusunan dan perancangan penelitian, pengumpulan data, analisis, serta interpretasi hasil. Semua penulis berpartisipasi dalam penulisan dan revisi naskah secara kritis untuk isi intelektual yang penting, menyetujui versi akhir yang akan diterbitkan, serta bertanggung jawab atas seluruh aspek penelitian ini.

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NARRATIVE REVIEW

Peran Gabapentinoid dalam Strategi Analgesia Preemptif pada Mastektomi Radikal Termodifikasi: Tinjauan Naratif

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Abstrak

Nyeri pascaoperasi tetap menjadi tantangan utama pada pasien kanker payudara yang menjalani prosedur *Modified Radical Mastectomy* (MRM), dengan prevalensi nyeri sedang hingga berat mencapai hampir 70%. Salah satu pendekatan yang menjanjikan adalah penggunaan analgesia preemptif dengan agen gabapentinoid, seperti pregabalin dan gabapentin, yang bekerja menghambat sensitisasi sentral serta menurunkan konsumsi opioid. Tinjauan naratif ini bertujuan mengevaluasi efektivitas kedua agen tersebut dalam mengurangi nyeri pasca-MRM, memperpanjang durasi bebas nyeri, dan menekan kebutuhan analgesik tambahan. Penelusuran literatur dilakukan melalui basis data PubMed, Scopus, ScienceDirect, dan Google Scholar dengan kata kunci "pregabalin", "gabapentin", "preemptive analgesia", "modified radical mastectomy", dan "postoperative pain", mencakup publikasi berbahasa Inggris dan Indonesia periode 2013–2024. Hasil sintesis menunjukkan bahwa pregabalin dan gabapentin secara konsisten menurunkan skor nyeri *Visual Analog Scale* (VAS), memperpanjang waktu hingga permintaan analgesik pertama, dan mengurangi total konsumsi opioid pascaoperasi. Pregabalin dosis 150 mg menunjukkan efektivitas yang setara atau lebih baik dibandingkan gabapentin 900 mg, dengan onset kerja lebih cepat dan profil efek samping yang lebih ringan. Secara keseluruhan, gabapentinoid terbukti efektif dan aman sebagai bagian dari strategi analgesia multimodal pasca MRM, dengan pregabalin menunjukkan keunggulan farmakokinetik dan tolerabilitas yang lebih baik. Penelitian berskala besar dengan populasi homogen masih diperlukan untuk memperkuat rekomendasi klinis berbasis bukti.

Kata kunci: Gabapentin, Gabapentinoid, Mastektomi radikal modifikasi, Nyeri pascaoperasi, Pregabalin

The Role of Gabapentinoids in Preemptive Analgesia for Modified Radical Mastectomy: A Narrative Review

Abstract

Postoperative pain remains a major challenge for breast cancer patients undergoing Modified Radical Mastectomy (MRM), with moderate to severe pain reported in up to 70% of cases. Preemptive analgesia using gabapentinoids such as pregabalin and gabapentin offers a promising strategy to attenuate central sensitization, reduce opioid consumption, and prolong postoperative analgesia. This narrative review aims to evaluate and compare the effectiveness of pregabalin and gabapentin as preemptive analgesic agents in MRM patients, focusing on postoperative pain intensity, time to first rescue analgesia, and total opioid consumption. Literature was searched through PubMed, Scopus, ScienceDirect, and Google Scholar using the keywords "pregabalin," "gabapentin," "preemptive analgesia," "modified radical mastectomy," and "postoperative pain," limited to English and Indonesian publications from 2013 to 2024. The synthesis shows that both pregabalin and gabapentin significantly reduce Visual Analog Scale (VAS) pain scores, extend the pain-free interval before additional analgesia is required, and decrease total opioid use. Pregabalin 150 mg demonstrated comparable or superior efficacy to gabapentin 900 mg, with a faster onset of action and a more favorable safety and pharmacokinetic profile. Overall, gabapentinoids are effective and well-tolerated as part of multimodal analgesia strategies for MRM, with pregabalin showing potential superiority in onset and tolerability. Further large-scale randomized trials with standardized dosing and homogeneous populations are warranted to strengthen clinical recommendations.

Keywords: Gabapentinoid, Pregabalin, Gabapentin, Modified radical mastectomy, Postoperative pain

Pendahuluan

Nyeri pascaoperasi merupakan tantangan klinis yang signifikan pada pasien kanker payudara yang menjalani prosedur Modified Radical Mastectomy (MRM). Prosedur ini, yang melibatkan pengangkatan jaringan payudara secara luas beserta diseksi kelenjar getah bening aksila, sering kali menimbulkan nyeri akut sedang hingga berat dengan prevalensi mencapai hampir 70%.[1] Mekanisme nyeri pasca MRM tidak hanya disebabkan oleh trauma jaringan dan aktivasi nosiseptor perifer, tetapi juga oleh cedera saraf interkostobrakialis yang memicu komponen neuropatik serta proses sensitisasi sentral yang berkontribusi pada risiko berkembangnya Chronic Post-Surgical Pain (CPSP).[2,-4] Kondisi ini dapat menurunkan kenyamanan pasien, memperlambat pemulihan fungsional, serta meningkatkan risiko penggunaan opioid jangka panjang.[5]

Dalam dua dekade terakhir, pendekatan analgesia preemptif berkembang sebagai strategi untuk mencegah aktivasi sistem saraf pusat sebelum stimulus nyeri terjadi. Pendekatan ini menekankan pemberian analgesik sebelum insisi bedah dilakukan, dengan tujuan menekan transmisi nyeri, mengurangi hiperalgesia, serta menurunkan kebutuhan opioid pascaoperasi.[6] Berbagai agen telah dievaluasi untuk tujuan ini, dan perhatian khusus tertuju pada kelompok gabapentinoid—yakni gabapentin dan pregabalin—karena mekanisme kerjanya yang unik pada subunit α2-δ saluran kalsium prasinaptik, yang menurunkan pelepasan neurotransmiter eksitatorik seperti glutamat dan substansi P.[7,8] Mekanisme ini berperan penting dalam menurunkan sensitisasi sentral dan intensitas nyeri akut setelah pembedahan.[9]

Gabapentin telah digunakan secara luas sebagai analgesia preemptif, namun memiliki keterbatasan berupa bioavailabilitas yang menurun pada dosis tinggi dan onset kerja yang lambat.[10] Sebaliknya, pregabalin memiliki farmakokinetik lebih stabil, onset kerja lebih cepat, serta afinitas lebih tinggi terhadap subunit α2-δ.[10] Sejumlah studi menunjukkan bahwa pregabalin dosis 150 mg memberikan efek analgesik yang sebanding atau bahkan lebih baik dibandingkan gabapentin 900 mg, dengan profil efek samping yang lebih ringan.[10,11] Studi lain juga memperkuat temuan tersebut dengan menunjukkan bahwa pregabalin memperpanjang durasi bebas nyeri dan menurunkan kebutuhan opioid dibandingkan gabapentin.[12] Selain itu, meta-analisis oleh Xuan et al. (2022) menegaskan bahwa pregabalin secara signifikan menurunkan skor VAS dan konsumsi opioid pascaoperasi dibandingkan plasebo.[13]

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Kesenjangan pengetahuan tetap ada karena penelitian komparatif langsung antara pregabalin dan gabapentin pada pasien MRM masih terbatas, terutama dalam konteks protokol dosis, waktu pemberian, dan luaran jangka panjang. Oleh karena itu, tinjauan naratif ini bertujuan mengevaluasi secara kritis efektivitas pregabalin dan gabapentin sebagai analgesia preemptif pada pasien yang menjalani Modified Radical Mastectomy, dengan menyoroti aspek farmakologis, luaran klinis, serta relevansinya terhadap strategi analgesia multimodal dalam praktik anestesi modern.

Mekanisme Kerja Pregabalin dan Gabapentin

Mekanisme kerja pregabalin dan gabapentin berpusat pada modulasi aktivitas saraf sensorik

melalui penghambatan saluran kalsium bertipe tegangan (voltage-gated calcium channels / VGCC), terutama subunit α2-δ tipe 1 yang berperan dalam transmisi nyeri. Ekspresi subunit ini meningkat pada kondisi nyeri akibat inflamasi, trauma jaringan, atau pembedahan. Kedua obat merupakan analog struktural gamma-aminobutyric acid (GABA) yang tidak berikatan dengan reseptor GABA secara langsung, melainkan menempel selektif pada subunit α2-δ untuk menghambat masuknya ion kalsium ke neuron prasinaptik. Akibatnya, pelepasan neurotransmiter eksitatorik seperti glutamat, substansi P, dan norepinefrin berkurang, sehingga transmisi dan amplifikasi nyeri turut ditekan.[8,9]

Pregabalin memiliki afinitas lebih tinggi dan lebih selektif terhadap subunit α2-δ dibandingkan gabapentin, menghasilkan onset kerja lebih cepat dengan puncak plasma 1–1,5 jam, sedangkan gabapentin memerlukan 3–4 jam. Pregabalin juga memiliki bioavailabilitas konsisten > 90% yang tidak tergantung dosis, sementara bioavailabilitas gabapentin menurun pada dosis tinggi akibat saturasi transporter absorpsi usus. Keunggulan ini menjadikan pregabalin lebih efektif untuk analgesia preemptif pada fase awal pascaoperasi.[12]

Efek analgesik gabapentinoid berasal dari pengurangan pelepasan neurotransmiter eksitatorik di kornu dorsalis medula spinalis—pusat integrasi sinyal nosiseptif dari perifer. Inhibisi glutamat dan substansi P menurunkan transmisi nyeri dari serabut A-δ dan C ke neuron sekunder, sehingga persepsi nyeri berkurang. Selain itu, efek ini juga memperlemah aktivasi reseptor NMDA secara tidak langsung. Akibatnya, terjadi penurunan ambang rangsang nyeri, perpanjangan waktu hingga kebutuhan analgesik tambahan, serta pengurangan konsumsi opioid sistemik.[8]

Gabapentinoid juga memengaruhi komponen inflamasi dan stres neuroendokrin. Pregabalin dilaporkan menurunkan kadar sitokin proinflamasi seperti IL-6 dan menstabilkan respons simpatis melalui modulasi jalur NF-κB, yang secara klinis berkaitan dengan penurunan nyeri dan pemulihan lebih cepat. Efek ansiolitik keduanya diduga berasal dari penurunan aktivitas noradrenergik di sistem limbik dan korteks prefrontal.[7] Walaupun memiliki struktur mirip GABA, keduanya tidak meningkatkan kadar GABA, tidak berikatan dengan reseptor GABA-A/B, dan tidak memengaruhi metabolisme GABA. Dengan profil farmakokinetik yang lebih baik, pregabalin lebih sesuai untuk kontrol nyeri awal dan kestabilan hemodinamik, sedangkan gabapentin tetap relevan untuk kontrol nyeri jangka menengah.

Efektivitas terhadap Intensitas Nyeri Pascaoperasi (Skala VAS)

Skor *Visual Analog Scale* (VAS) merupakan parameter utama untuk menilai intensitas nyeri akut pascaoperasi. Meta-analisis oleh Jiang et al. (2018) terhadap pasien yang menjalani operasi kanker payudara menunjukkan bahwa gabapentin secara signifikan menurunkan skor nyeri postoperatif dibandingkan kelompok kontrol ($p < 0,001$). Kelompok yang menerima 1200 mg gabapentin 2 jam sebelum operasi menunjukkan penurunan skor VAS segera setelah operasi sebesar –26,00 (95% CI –36,23 hingga –15,77; $p < 0,001$), sedangkan rejimen 400 mg tiga kali sehari mulai malam sebelum operasi hingga hari ke-10 pascaoperasi menghasilkan penurunan skor VAS sebesar –50,00 (95% CI –56,20 hingga –43,80; $p < 0,001$) pada hari pertama pascaoperasi. Hasil ini menegaskan efektivitas gabapentin dalam menurunkan nyeri akut pascaoperasi, khususnya pada populasi operasi kanker payudara termasuk MRM.[10]

Secara komparatif, studi oleh Hetta et al. (2016) menunjukkan bahwa pemberian pregabalin 150 mg dan 300 mg preoperatif secara signifikan menurunkan skor nyeri VAS dibandingkan plasebo ($p < 0,05$). Penurunan nyeri paling bermakna terjadi pada 24 jam

pertama pascaoperasi, dengan *mean difference* (MD) –1,6 (95% CI –2,4 hingga –0,8; p = 0,002) untuk dosis 150 mg dan –1,9 (95% CI –2,6 hingga –1,1; $p < 0,001$) untuk dosis 300 mg. Namun, peningkatan dosis hingga 300 mg disertai efek samping lebih tinggi seperti pusing dan penglihatan kabur, menjadikan 150 mg sebagai dosis optimal dengan keseimbangan terbaik antara efikasi dan tolerabilitas.[11]

Selain itu, meta-analisis oleh Xuan et al. (2022) melaporkan bahwa pregabalin menurunkan skor VAS secara signifikan dibandingkan plasebo pada berbagai interval waktu: 6 jam (MD –13,47; 95% CI –17,83 hingga –9,10; $p <$ 0,001), 12 jam (MD –10,86; 95% CI –15,14 hingga –6,57; $p < 0,001$), dan 24 jam (MD –7,75; 95% CI –10,84 hingga –4,65; $p < 0,001$). Temuan ini menunjukkan kestabilan efek analgesik pregabalin pada fase akut pascaoperasi dengan signifikansi statistik yang kuat, mendukung penggunaannya dalam strategi *multimodal preemptive analgesia* pada pasien MRM.[7]

Durasi Analgesia (Time to First Analgesia Rescue)

Waktu hingga permintaan analgesia tambahan pertama mencerminkan durasi efektivitas analgesik preemptif. Studi Routray et al. (2018) yang membandingkan pregabalin 150 mg dengan gabapentin 900 mg pada pasien operasi tulang belakang menemukan bahwa kelompok pregabalin memiliki durasi analgesia yang lebih panjang secara signifikan dibandingkan gabapentin ($p < 0,01$). Rata-rata waktu hingga permintaan analgesik pertama adalah 180,12 ± 42,5 menit pada kelompok pregabalin dibanding 104,16 ± 38,9 menit pada kelompok gabapentin (MD 76 menit; 95% CI 52,4–99,6; $p < 0,001$).[13]

Efek ini konsisten dengan profil farmakokinetik pregabalin yang memiliki onset lebih cepat dan bioavailabilitas lebih stabil (>90%), sehingga mampu mempertahankan analgesia efektif pada fase awal dan menengah pascaoperasi. Sementara itu, meta-analisis Xuan et al. (2022) juga melaporkan bahwa pregabalin secara signifikan memperpanjang interval bebas nyeri sebelum diperlukan analgesik tambahan dibandingkan plasebo (MD 72,8 menit; 95% CI 41,3–104,2; $p = 0,004$).[7]

Durasi analgesia yang lebih panjang mencerminkan penghambatan sensitisasi sentral yang lebih kuat oleh pregabalin dan pregabalin efektif mempertahankan analgesia stabil pada fase awal-menengah pasca-MRM.

Pengaruh terhadap Konsumsi Opioid Pascaoperasi

Indikator utama keberhasilan analgesia preemptif adalah penurunan kebutuhan opioid pascaoperasi. Dalam meta-analisis oleh Xuan et al. (2022), pregabalin menurunkan total konsumsi opioid kumulatif secara signifikan dibandingkan kontrol pada beberapa titik waktu, yaitu 12 jam (MD –0,48 mg; 95% CI –1,01 hingga –0,04; $p = 0,031$), 24 jam (MD –1,29 mg; 95% CI –1,70 hingga –0,87; $p <$ 0,001), dan 48 jam (MD –1,98 mg; 95% CI –3,27 hingga –0,69; $p = 0,002$). Penurunan ini disertai dengan berkurangnya insidensi mual dan muntah pascaoperasi (*Postoperative Nausea and Vomiting*/PONV) sebesar 24–35%.[7]

Hetta et al. (2016) juga melaporkan bahwa kelompok pregabalin 150 mg menunjukkan penurunan konsumsi morfin dalam 24 jam pertama sebesar 25% dibandingkan plasebo ($p <$ 0,05). Sementara itu, Jiang et al. (2018) menunjukkan bahwa gabapentin 1200 mg preoperatif menurunkan total kebutuhan opioid pascaoperasi secara bermakna sebesar –5,3 mg ekuivalen morfin (95% CI –7,8 hingga –2,8; $p <$ 0,001) serta menurunkan angka PONV sebesar 31%.[11]

Secara komparatif, Routray et al. (2018) mencatat bahwa konsumsi analgesik tambahan, termasuk opioid, lebih rendah pada kelompok

pregabalin (mean 1,8 ± 0,5 dosis) dibanding gabapentin (2,6 ± 0,6 dosis, $p < 0,01$). Hasil ini mendukung bahwa pregabalin 150 mg memiliki efektivitas superior dibandingkan gabapentin dalam mengurangi kebutuhan opioid pascaoperasi dan memberikan kontrol nyeri yang lebih stabil dan berkepanjangan pada pasien yang menjalani MRM.[13]

Gambaran ini menunjukkan pregabalin memiliki efek opioid-sparing lebih kuat, dengan profil efek samping ringan. Integrasi gabapentinoid dapat menekan risiko PONV dan mempercepat pemulihan pasien.

Keterbatasan Metodologi dan Kesenjangan Pengetahuan

Meskipun mayoritas studi menunjukkan efektivitas signifikan pregabalin dan gabapentin sebagai analgesia preemptif, hasil tersebut tetap perlu diinterpretasikan secara hati-hati karena masih terdapat sejumlah keterbatasan metodologis dan potensi bias dalam literatur yang tersedia.

Variasi desain penelitian menjadi salah satu isu utama. Setiap studi menggunakan dosis, waktu pemberian, dan durasi observasi yang berbeda, sehingga kesimpulan mengenai rejimen optimal sulit diseragamkan. Beberapa penelitian menggunakan pemberian tunggal sebelum operasi, sementara yang lain menerapkan rejimen berulang selama beberapa hari; perbedaan ini berpotensi memengaruhi interpretasi efektivitas jangka pendek maupun jangka panjang.

Ukuran sampel pada sebagian besar uji klinis juga relatif kecil, yang dapat menurunkan kekuatan statistik dan meningkatkan risiko kesalahan tipe II (type II error). Selain itu, karakteristik populasi pasien, seperti tingkat nyeri dasar, jenis anestesi, serta penggunaan analgesik multimodal berbeda antara studi satu dengan yang lain, sehingga memungkinkan adanya confounding factors terhadap hasil klinis.

Heterogenitas jenis pembedahan turut menjadi tantangan tersendiri. Sebagian besar penelitian memasukkan berbagai prosedur bedah kanker payudara, bukan MRM secara khusus, sehingga temuan yang diperoleh belum sepenuhnya dapat digeneralisasikan ke pasien MRM. Beberapa publikasi juga tidak menjelaskan secara rinci metode randomisasi, proses blinding, atau penggunaan kontrol plasebo yang setara, sehingga memunculkan potensi bias seleksi dan performa.

Bias publikasi juga mungkin memengaruhi pemahaman terhadap hasil keseluruhan. Studi dengan hasil positif cenderung lebih mudah diterbitkan dibandingkan hasil negatif atau non-signifikan, yang dapat menimbulkan overestimasi terhadap efek analgesik gabapentinoid. Selain itu, sebagian meta-analisis tidak melaporkan uji funnel plot atau Egger untuk menilai simetri data, sehingga sulit menilai secara objektif ada tidaknya bias publikasi

Arah Penelitian Selanjutnya

Berdasarkan sintesis literatur yang ada, masih terdapat sejumlah celah penelitian yang perlu dieksplorasi untuk memperkuat dasar ilmiah penggunaan gabapentinoid sebagai analgesia preemptif pada pasien *Modified Radical Mastectomy* (MRM). Studi masa depan perlu dirancang dengan desain uji klinis acak berskala besar yang homogen, mencakup populasi pasien dengan karakteristik serupa serta protokol dosis dan waktu pemberian yang terstandar. Pendekatan ini akan memungkinkan penentuan rejimen optimal pregabalin dan gabapentin yang memberikan keseimbangan terbaik antara efektivitas dan keamanan.

Selain luaran nyeri akut, penelitian mendatang perlu menilai efek jangka panjang terhadap transisi nyeri akut menjadi nyeri kronik pasca-mastektomi, dengan periode tindak lanjut minimal tiga hingga enam bulan. Evaluasi biomarker inflamasi dan neuroendokrin, seperti IL-6, TNF-α, dan CRP, dapat memberikan

pemahaman yang lebih mendalam mengenai mekanisme anti-inflamasi dan stabilisasi hemodinamik yang dimediasi oleh gabapentinoid.

Dari sisi multidisiplin, integrasi penelitian farmakoekonomi dan *patient-reported outcomes*—termasuk kualitas tidur, tingkat kecemasan, dan kepuasan pasien—akan memperluas perspektif manfaat gabapentinoid tidak hanya dari aspek efikasi analgesik, tetapi juga dari segi efisiensi biaya dan pengalaman pasien secara keseluruhan.

Selain itu, penelitian komparatif lanjutan yang mengombinasikan gabapentinoid dengan modalitas analgesik lain seperti NSAID, dexmedetomidine, atau ketamin melalui pendekatan *network meta-analysis* akan membantu menentukan posisi relatif pregabalin dan gabapentin dalam strategi analgesia multimodal yang lebih komprehensif.

Kesimpulan

Pregabalin dan gabapentin merupakan agen analgesia preemptif non-opioid yang terbukti efektif menurunkan intensitas nyeri, memperpanjang durasi bebas nyeri, serta mengurangi konsumsi opioid pada pasien yang menjalani Modified Radical Mastectomy (MRM). Pregabalin menunjukkan keunggulan dibandingkan gabapentin dalam hal onset kerja yang lebih cepat, bioavailabilitas yang konsisten, serta profil efek samping yang lebih ringan, menjadikannya pilihan rasional dalam strategi multimodal analgesia.

Meskipun bukti yang ada mendukung efektivitas gabapentinoid, variasi dosis, waktu pemberian, dan desain penelitian menimbulkan heterogenitas hasil. Karena itu, dibutuhkan uji klinis acak berskala besar dengan populasi homogen dan tindak lanjut jangka panjang untuk menilai dampak pregabalin dan gabapentin terhadap nyeri kronik pascaoperasi, kualitas hidup, serta pemulihan fungsional pasien.

Secara keseluruhan, integrasi gabapentinoid ke dalam protokol analgesia preemptif sejalan dengan prinsip Enhanced Recovery After Surgery (ERAS) dan berpotensi meningkatkan kenyamanan pasien, mempercepat pemulihan, serta menurunkan ketergantungan terhadap opioid dalam praktik anestesi modern.

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Penelitian ini tidak menerima hibah atau dukungan pendanaan khusus dari lembaga pendanaan di sektor publik, komersial, maupun nirlaba.

Konflik Kepentingan

Para penulis menyatakan bahwa tidak memiliki konflik kepentingan.

Pernyataan Ketersediaan Data

Tidak ada data baru yang dihasilkan atau dianalisis dalam penelitian ini.

Kontribusi Penulis

Seluruh penulis berkontribusi secara signifikan dalam penyusunan dan perancangan penelitian, pengumpulan data, analisis, serta interpretasi hasil. Semua penulis berpartisipasi dalam penulisan dan revisi naskah secara kritis untuk isi intelektual yang penting, menyetujui versi akhir yang akan diterbitkan, serta bertanggung jawab atas seluruh aspek penelitian ini.

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Effectiveness of Dexmedetomidine Compared to Midazolam for Sedation in Mechanically Ventilated Patients: A Narrative Review

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Abstract

Delirium is a common and clinically significant neuropsychiatric complication in mechanically ventilated adult ICU patients, contributing to prolonged hospitalization, increased morbidity, and long-term cognitive impairment. The choice of sedative agent plays a pivotal role in preventing delirium, with dexmedetomidine and midazolam representing the most commonly used drugs with contrasting mechanisms. This narrative review evaluates the clinical efficacy, safety profile, neurocognitive outcomes, and cost-effectiveness of dexmedetomidine compared with midazolam in mechanically ventilated ICU patients. Literature was searched through PubMed, Scopus, ScienceDirect, Cochrane Library, and Google Scholar for studies published between 2020 and 2025 using the keywords dexmedetomidine, midazolam, sedation, mechanical ventilation, delirium, and intensive care units. Seventeen peer-reviewed publications were included and analyzed narratively. Dexmedetomidine consistently reduced the incidence and duration of delirium (RR 0.55–0.65; 95% CI 0.4–0.8), shortened mechanical ventilation by 0.7–1.5 days, and facilitated earlier extubation compared to midazolam. Its α_2-adrenergic agonism at the locus coeruleus produces a sleep-like, cooperative sedation, with mild, dose-dependent bradycardia as the most frequent adverse effect. Despite higher acquisition cost, economic analyses reported average savings of US$ 450–700 (≈ IDR 7–10 million) per patient through reduced ICU stay and delirium-related complications. Overall, dexmedetomidine demonstrates superior efficacy and safety compared with midazolam for ICU sedation, providing both clinical and economic advantages. Integration into light-sedation and delirium-prevention bundles may improve ICU outcomes, particularly in resource-limited settings.

Kata kunci: Delirium, Dexmedetomidine, Intensive care unit, Mechanical ventilation, Midazolam

Efektivitas Dexmedetomidine Dibandingkan dengan Midazolam sebagai Sedasi pada Pasien dengan Ventilasi Mekanik: Tinjauan Naratif

Abstrak

Delirium merupakan komplikasi neuropsikiatrik yang umum terjadi pada pasien dewasa yang menjalani ventilasi mekanik di ICU dan berhubungan dengan peningkatan lama rawat, morbiditas, serta gangguan kognitif jangka panjang. Pemilihan agen sedasi berperan penting dalam mencegah delirium, di mana dexmedetomidine dan midazolam merupakan dua obat yang paling sering digunakan dengan mekanisme kerja yang berbeda. Tinjauan naratif ini bertujuan untuk mengevaluasi efektivitas klinis, keamanan, dampak neurokognitif, serta efektivitas biaya penggunaan dexmedetomidine dibandingkan midazolam pada pasien ICU dengan ventilasi mekanik. Pencarian literatur dilakukan melalui PubMed, Scopus, ScienceDirect, Cochrane Library, dan Google Scholar untuk artikel tahun 2020-2025 menggunakan kata kunci dexmedetomidine, midazolam, sedation, mechanical ventilation, delirium, dan intensive care units. Sebanyak 17 publikasi peer-reviewed memenuhi kriteria dan dianalisis secara naratif. Hasil sintesis menunjukkan bahwa dexmedetomidine secara konsisten menurunkan insidensi dan durasi delirium (RR 0,55–0,65; 95% CI 0,4–0,8), memperpendek durasi ventilasi sebesar 0,7–1,5 hari, serta mempercepat ekstubasi dibandingkan midazolam. Mekanisme α_2-agonis yang bekerja pada locus coeruleus menghasilkan sedasi menyerupai tidur alami dengan risiko bradikardia ringan yang dapat ditangani dengan penyesuaian dosis. Meskipun biaya awal lebih tinggi, analisis ekonomi menunjukkan penghematan rata-rata Rp 7–10 juta per pasien akibat pengurangan lama rawat ICU dan komplikasi delirium. Tinjauan ini menegaskan bahwa dexmedetomidine memiliki keunggulan klinis maupun ekonomis dibandingkan midazolam, mendukung penerapannya dalam strategi sedasi ringan dan pencegahan delirium di ICU, terutama pada fasilitas dengan sumber daya terbatas.

Keywords: Dexmedetomidine, Midazolam, Delirium, Ventilasi mekanik, Unit perawatan intensif

Introduction

Delirium is a multifactorial neuropsychiatric syndrome commonly observed in critically ill patients receiving mechanical ventilation in ICU. It manifests as fluctuating disturbances in attention, cognition, and consciousness, often leading to diagnostic challenges. The incidence of delirium among mechanically ventilated adults can reach up to 80%, representing a major clinical and public health concern. Its occurrence is associated with prolonged ICU and hospital stay, higher mortality, and persistent cognitive deficits that can last months or even years after discharge.[1,2]

Sedation practices considerably influence the development and outcomes of delirium. Among available sedatives, dexmedetomidine and midazolam are two widely used agents with distinct pharmacologic mechanisms and neurocognitive profiles.[3–7] Dexmedetomidine, a highly selective α2-adrenergic agonist, produces light, cooperative sedation resembling natural sleep, allowing for regular neurological assessment and faster awakening. Conversely, midazolam, a GABA-A receptor agonist, induces deeper, less physiologic sedation, which increases the risk of oversedation, delayed extubation, and delirium.[3,4]

In addition to clinical outcomes, sedative selection has important economic implications. Differences in drug acquisition cost, duration of mechanical ventilation, and ICU stay collectively affect healthcare expenditures, particularly in resource-limited environments.[8,9] Therefore, understanding the comparative clinical and economic performance of these sedatives is crucial for optimizing ICU care and improving both outcomes and resource utilization.

This narrative review aims to synthesize current evidence comparing dexmedetomidine and midazolam regarding their efficacy, safety, neurocognitive outcomes, and cost-effectiveness in mechanically ventilated adult ICU patients. Literature was retrieved from PubMed, Scopus, ScienceDirect, Cochrane Library, and Google Scholar for publications between 2020 and 2025, using the keywords dexmedetomidine, midazolam, sedation, mechanical ventilation, delirium, and intensive care units. The review integrates findings from recent randomized trials, observational studies, and meta-analyses to provide an updated understanding of their comparative roles in ICU sedation and delirium prevention.[1–11]

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Pharmacologic Profiles and Delirium Pathogenesis

Dexmedetomidine and midazolam differ substantially in their pharmacodynamic and neurophysiologic properties, which directly influence delirium pathogenesis. Dexmedetomidine is a highly selective α2-adrenergic receptor agonist that acts primarily on the locus coeruleus in the brainstem, suppressing norepinephrine release and producing a light, cooperative sedation that mimics natural non-REM sleep.[3,5] This sedative state allows patients to remain easily arousable and facilitates frequent neurological assessments, which are key strategies in preventing delirium. In contrast, midazolam, a benzodiazepine that potentiates GABA-A receptor activity, produces generalized central nervous system depression, resulting in deeper, less physiologic sedation.[4,6] This pharmacologic difference explains why dexmedetomidine is often associated with a

lower incidence and shorter duration of ICU delirium.[7]

In typical ICU practice, dexmedetomidine is administered at maintenance doses of 0.2–1.4 µg/kg/h after an optional loading dose of 0.5–1 µg/kg over 10 minutes, titrated to achieve a target Richmond Agitation-Sedation Scale (RASS) of –2 to 0.[3,4] Midazolam infusions are typically initiated at 0.02–0.1 mg/kg/h with intermittent boluses as needed, adjusted to organ function and desired sedation depth.[4,6] Excessive or prolonged midazolam exposure has been linked to oversedation, delayed awakening, and accumulation of active metabolites, particularly in patients with hepatic or renal impairment.[4,6] These factors contribute to an increased risk and duration of delirium, delayed extubation, and longer ICU stay.[1,7]

Dexmedetomidine's lighter, sleep-like sedation has been shown to modulate delirium-related neuroinflammation by attenuating the stress-induced catecholamine surge and reducing cortical hyperactivity, thereby supporting cognitive stability.[5,10] In contrast, benzodiazepine-induced deep sedation alters circadian rhythm and suppresses slow-wave sleep architecture, further predisposing to cognitive dysfunction.[4,6] Bradycardia is the most frequently reported adverse event with dexmedetomidine, occurring in approximately 5–13% of cases; however, it is typically mild, dose-dependent, and reversible upon adjustment or cessation of infusion.[3,11]

Collectively, these pharmacologic distinctions clarify the mechanistic rationale behind dexmedetomidine's superiority in minimizing delirium, enabling earlier extubation, and supporting neurological recovery in mechanically ventilated ICU patients. The integration of light-sedation strategies utilizing dexmedetomidine aligns with recent critical care guidelines that recommend minimizing benzodiazepine use to prevent delirium and facilitate early mobilization.[11]

Effectiveness in Reducing Delirium and Duration of Mechanical Ventilation

An expending body of evidence demonstrates that dexmedetomidine provides superior outcomes compared with midazolam in reducing both the incidence and duration of ICU delirium. Several randomized controlled trials and meta-analyses reported that dexmedetomidine significantly decreases delirium risk by approximately 35–45% (RR 0.55–0.65; 95% CI 0.4–0.8) and shortens the duration of mechanical ventilation by 0.7–1.5 days compared with midazolam.[4,6,7] The sedative's α2-adrenergic mechanism promotes lighter, cooperative sedation, allowing consistent neurological assessment and earlier participation in spontaneous awakening and breathing trials—factors known to prevent or shorten delirium episodes.[3,5]

Conversely, midazolam is consistently associated with deeper, less physiologic sedation, which prolongs mechanical ventilation and delays extubation.[4,6] Observational studies indicate that midazolam use correlates with higher rates of prolonged weaning, longer ICU stay, and increased risk of ICU-acquired weakness.[1,4] Furthermore, excessive benzodiazepine exposure is known to alter circadian rhythm and disrupt sleep–wake cycles, exacerbating the cognitive disorientation characteristic of ICU delirium.[6,8]

The clinical advantages of dexmedetomidine extend beyond delirium reduction. Studies in post-cardiac surgery and general ICU populations reveal faster extubation times, reduced need for rescue sedatives, and shorter ICU length of stay when dexmedetomidine is used as the primary sedative agent.[3,6,7] These findings have been reinforced by updated critical care guidelines, which now recommend non-benzodiazepine sedatives—particularly dexmedetomidine or propofol—as first-line

agents for light sedation and delirium prevention.[11]

Nonetheless, some variability exists among studies reporting minimal or non-significant differences between agents. These inconsistencies are often linked to differences in sedation depth targets, patient comorbidities, or the delirium assessment tools used, such as the Confusion Assesment Method for the ICU (CAM-ICU) and Intensive Care Delirium Screening Checklist (ICDSC).[10,12] Despite this heterogeneity, the preponderance of evidence favors dexmedetomidine for achieving optimal sedation quality, faster weaning, and improved cognitive recovery while maintaining hemodynamic safety when appropriately titrated.[3,9,12]

Collectively, the synthesis of contemporary literature demonstrates that dexmedetomidine provides superior clinical efficacy compared with midazolam in ICU sedation. Its integration into light-sedation protocols can improve recovery trajectories, reduce delirium burden, and promote more efficient ICU resource utilization.[6,7,11,13]

Cognitive Recovery and Long-Term Outcomes

Beyond its effects on delirium prevention and ventilation duration, dexmedetomidine has demonstrated additional benefits for cognitive recovery in critically ill and post-surgical populations. Evidence indicates that patients sedated with dexmedetomidine exhibit improved early cognitive function, including orientation, memory, and attention, compared with those who receive midazolam.[3,6] This improvement is largely attributed to dexmedetomidine's ability to maintain natural sleep architecture and permit frequent neurological evaluations, which facilitate early recognition of cognitive fluctuations.[5,9]

In a comprehensive review and meta-analysis of cardiac surgical patients, dexmedetomidine significantly reduced the incidence of postoperative cognitive dysfunction (POCD) and delirium compared with midazolam.[3,6] Similar findings were observed across ICU populations, where dexmedetomidine shortened the duration of sedation and improved recovery scores on standardized tools such as the CAM-ICU and Mini-Mental State Examination.[7,10] These findings reinforce the sedative's neuroprotective properties mediated by α2-adrenergic modulation, which decreases sympathetic excitation, attenuates neuroinflammatory cascades, and mitigates oxidative stress—mechanisms implicated in delirium-related neuronal injury.[5,9]

However, several limitations are noted in the literature. Most available studies are short-term and performed in high-resource settings, with limited representation of low- and middle-income ICUs. Variability in patient comorbidities, sedation protocols, and neurocognitive assessment instruments contributes to heterogeneity and potential bias in reported outcomes.[1,12,14] Longitudinal studies with standardized follow-up beyond six months are still lacking, making it difficult to confirm whether early cognitive improvements persist over time.

Overall, current evidence supports dexmedetomidine as a superior option for sedation to promote early neurocognitive recovery compared with midazolam. By enabling light, cooperative sedation and reducing delirium-associated injury, dexmedetomidine may enhance long-term neurological outcomes and quality of life among ICU survivors.[7,11,13]

Implementation of Delirium Monitoring Protocols

Effective delirium prevention and management in the ICU rely not only on the choice of sedative agent but also on consistent and structured monitoring. The incorporation of validated delirium assessment tools, such as the

CAM-ICU and the ICDSC, has been shown to significantly improve early detection and intervention.[10] Routine monitoring allows clinicians to adjust sedation depth promptly, implement early mobilization, and avoid unnecessary benzodiazepine exposure—measures that collectively reduce the incidence and duration of delirium.[1,11,10]

However, real-world implementation of these monitoring tools remains inconsistent across institutions. A multicenter study demonstrated that even when validated tools are available, adherence rates vary widely depending on staff training, ICU workload, and institutional culture.[10,12] These findings highlight the need for standardized protocols and education programs to ensure reliable delirium assessment by both nurses and physicians. In addition, the empowerment of non-physician staff, such as certified nursing assistants, has proven effective in increasing screening frequency and diagnostic accuracy without compromising workflow.[10]

Recent evidence supports the adoption of care bundles that integrate pharmacologic and non-pharmacologic strategies for delirium prevention. Such bundles typically include light sedation protocols using dexmedetomidine, early mobilization, adequate pain management, sleep promotion, and family engagement.[12,13] Meta-analytic evidence shows that these multidisciplinary interventions reduce delirium prevalence and improve functional recovery at discharge.[12,13,9] When applied consistently, they also contribute to shorter ICU stays and reduced healthcare costs—benefits particularly relevant in resource-limited settings.[8,9]

Despite robust evidence and clear guideline recommendations, several barriers persist in implementing standardized delirium monitoring and prevention strategies. Challenges include limited staff awareness, inconsistent documentation, and variable resource availability.[11,12,14] Addressing these barriers requires institutional commitment, inclusion of delirium screening in quality metrics, and integration of sedation management into routine ICU rounds. Ultimately, sustained adherence to evidence-based protocols combining dexmedetomidine use, structured monitoring, and early mobilization offers the best opportunity to minimize delirium burden and improve long-term patient outcomes.[11,12,15]

Conclusion

Dexmedetomidine consistently demonstrates superiority over midazolam in terms of delirium prevention, sedation quality, and cognitive recovery among mechanically ventilated adult ICU patients. Its unique pharmacologic profile allows for lighter, more cooperative sedation, facilitating neurological monitoring and earlier weaning from ventilation. Furthermore, dexmedetomidine use aligns with current critical care guidelines advocating non-benzodiazepine sedation to reduce delirium incidence and improve overall outcomes. While both clinical and economic data favor dexmedetomidine, implementation of standardized delirium monitoring and multidisciplinary care bundles remains essential to maximize these benefits. Continued research, particularly in diverse and resource-limited settings, is warranted to strengthen long-term evidence and optimize sedation strategies for critically ill patients.

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Conflicts of Interest

The authors report no conflict of interest.

Data Availability Statement

No new data were generated or analysed in this study.

Author's Contributions

All authors contributed significantly to the conception and design of the study, data collection, analysis, and interpretation of the results. All authors participated in writing and critically revising the manuscript for important intellectual content, approved the final version to be published, and are accountable for all aspects of the research.

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CASE REPORT

Low-Flow Anesthesia Management in Pediatric Laparoscopic Choledochal Cyst Excision and Hepaticojejunostomy: A Case Report

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Abstract

Laparoscopic surgery offers significant benefits in pediatric populations but presents anesthetic challenges, especially during prolonged procedures. This case report describes the anesthetic management of an 11-year-old boy who underwent nearly 12 hours of laparoscopic choledochal cyst excision, Roux-en-Y hepaticojejunostomy, and cholecystectomy. Low-flow anesthesia using sevoflurane was administered via a Dräger Perseus A500, enabling precise control of anesthetic delivery, oxygenation, and ventilation. Throughout the procedure, inspired oxygen fraction (FiO_2) was maintained above 30%, and end-tidal CO_2 ($EtCO_2$) remained stable around 35 mmHg. Volatile agent consumption was reduced, with age-adjusted MAC (xMAC) consistently between 0.85 and 0.90. Intraoperative hemodynamics and postoperative recovery were stable, with no immediate complications. This case highlights the safety, efficiency, and cost-effectiveness of low-flow anesthesia in complex pediatric laparoscopic surgery when guided by advanced monitoring systems and supports its broader adoption in resource-limited healthcare settings.

Keywords: Choledochal cyst, Laparoscopic surgery, Low-flow anesthesia; Pediatric anesthesia, Sevoflurane

Manajemen Anestesi Aliran Rendah pada Eksisi Kista Koledokus Laparoskopi Pediatrik dan Hepatikojejunostomi: Laporan Kasus

Abstrak

Bedah laparoskopi memberi banyak manfaat pada populasi pediatrik, namun menghadirkan tantangan anestesi, terutama pada prosedur yang berlangsung lama. Laporan kasus ini menggambarkan manajemen anestesi pada anak laki-laki usia 11 tahun yang menjalani operasi laparoskopi selama hampir 12 jam berupa eksisi kista koledokus, hepaticojejunostomy Roux-en-Y, dan kolesistektomi. Anestesi aliran rendah menggunakan sevoflurane diberikan melalui mesin Dräger Perseus A500, yang memungkinkan kontrol presisi terhadap pemberian anestesi, oksigenasi, dan ventilasi. Sepanjang prosedur, fraksi oksigen terinspirasi (FiO_2) dijaga di atas 30%, dan end-tidal CO_2 ($EtCO_2$) stabil sekitar 35 mmHg. Konsumsi agen volatil berkurang, dengan nilai MAC yang disesuaikan usia (xMAC) konsisten antara 0,85–0,90. Hemodinamik intraoperatif dan pemulihan pascaoperasi stabil tanpa komplikasi. Kasus ini menyoroti keamanan, efisiensi, dan kehematan biaya anestesi aliran rendah pada bedah laparoskopi pediatrik kompleks dengan dukungan pemantauan canggih, serta mendukung penerapannya secara lebih luas di fasilitas dengan sumber daya terbatas.

Kata kunci: Anestesi aliran rendah, Anestesi pediatrik, Kista koledokus, Bedah laparoskopi, Sevoflurane

Introduction

This case is notable for its successful use of low-flow anesthesia during a prolonged pediatric laparoscopic choledochal cyst excision and Roux-en-Y hepaticojejunostomy, an uncommon and technically demanding scenario. Pediatric laparoscopic surgeries are inherently challenging due to altered respiratory mechanics from CO_2 insufflation, limited physiological reserves, and heightened sensitivity to anesthetic agents. These factors increase the risk of hypothermia, hemodynamic instability, and potential neurodevelopmental concerns associated with prolonged exposure to general anesthesia. In this case, careful anesthetic planning was essential to maintain

intraoperative stability and ensure patient safety throughout the complex procedure.[1]

Low-flow anesthesia (LFA), defined as fresh

gas flow below 1 L/min, was employed using sevoflurane as the volatile agent and facilitated by the Dräger Perseus A500 workstation. This approach minimized volatile agent consumption, preserved heat and humidity in the respiratory tract and reduced environmental and occupational exposure to waste anesthetic gases. Sevoflurane's pharmacological profile—particularly its low blood-gas partition coefficient and stability in CO_2 absorbers—makes it well-suited for such techniques. Importantly, the use of low-flow anesthesia also offered significant pharmacoeconomic advantages, making it highly suitable for resource-conscious healthcare systems such as Indonesia's National Health Insurance program (Badan Penyelenggara Jaminan Sosial or BPJS). This case adds to the limited literature documenting the safe and cost-effective application of low-flow techniques in complex pediatric laparoscopic procedures.[2]

Case Presentation

An 11-year-old boy was admitted to a tertiary hospital with a confirmed diagnosis of a choledochal cyst type IVa (Todani classification), accompanied by chronic cholecystitis and gallbladder hydrops. He had a long-standing history of episodic colicky abdominal pain beginning at age one, often associated with high-grade fever, which resolved with symptomatic treatment. There was a history of jaundice without pale stools or tea-colored urine. Two weeks before admission the symptoms worsened, prompting further investigation, including MRCP, which revealed significant intra- and extrahepatic bile-duct dilatation consistent with a choledochal cyst and associated biliary anomalies. At admission there were no complaints of abdominal pain, fever, jaundice, or respiratory symptoms. He was scheduled for elective laparoscopic cyst excision with Roux-en-Y hepaticojejunostomy. He had no significant past medical or surgical history, no known drug or food allergies, and normal developmental milestones for age. There was no family history of similar conditions or relevant genetic disorders. Preoperative examination showed a cooperative patient with stable vital signs and no signs of acute illness. Routine laboratory tests (complete blood count, coagulation profile, renal function, liver enzymes) were within acceptable limits for surgery. Chest radiography was normal, and MRCP confirmed the diagnosis.

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On the day of surgery, standard pediatric anesthetic protocols were followed. Premedication included intravenous midazolam and ketamine. Induction used intravenous propofol and fentanyl; neuromuscular blockade was achieved with atracurium. Endotracheal intubation was performed with a cuffed 6.0 ETT, secured at 17 cm at the lips. Tube position was confirmed by auscultation and capnography. Maintenance anesthesia consisted of oxygen and compressed air as carrier gases with low-flow sevoflurane delivered via the Dräger Perseus A500. Inspired and expired sevoflurane concentrations were maintained at approximately 2.1–2.3% and 2.0–2.2%, respectively, corresponding to xMAC ~0.85–0.90 for age (Figure 1). Ventilation parameters included a tidal volume of 280 mL, respiratory rate of 18 breaths/min , and minute ventilation

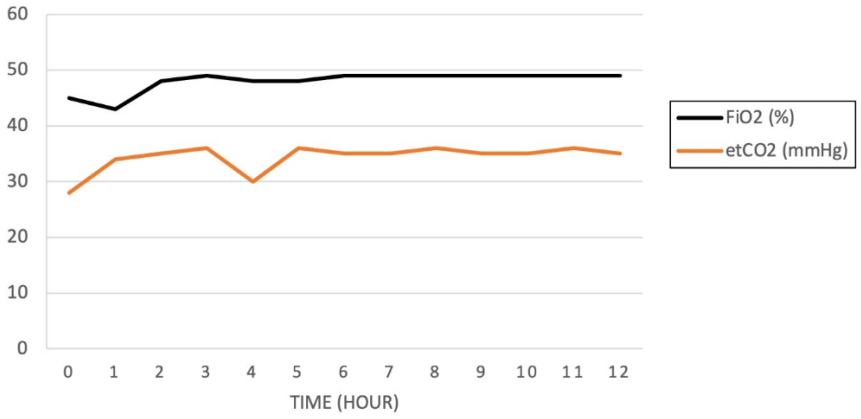

Figure 1. Sevoflurane monitoring demonstrates consistent inSev, etSev, and xMAC values, indicating adequate anesthetic depth during surgery.

of 5.1 L/min. Airway pressures were within normal limits (Paw 19 cmH_2O; PEEP 5 cmH_2O). $EtCO_2$ was stable at ~35 mmHg throughout the procedure. Fraction of inspired oxygen (FiO_2) was maintained at 45–48% with minimal fluctuation, indicating effective oxygenation during LFA (Figure 2). Surgery was performed in the supine position using five laparoscopic ports. Pneumoperitoneum was established with CO_2 insufflation at 12–13 mmHg. Cystic dilatation of the common bile duct was resected; the distal end was closed using a linear stapler. A Roux limb was constructed by dividing the jejunum 25 cm distal to the ligament of Treitz. Hepaticojejunostomy and jejunojejunostomy were completed with absorbable sutures and staplers. Cholecystectomy was performed, and a subhepatic drain (NGT 16 Fr) was placed before closure. Total operative time was approximately 11 hours 55 minutes.

Intraoperative monitoring documented a blood-pressure range of 82–118/43–65 mmHg and heart rate of 81–120 beats/min. Oxygen saturation remained 98–100%. Total intraoperative crystalloid was 1242 mL. Estimated blood loss was 100 mL and urine output 300 mL; no blood products or colloids were required.

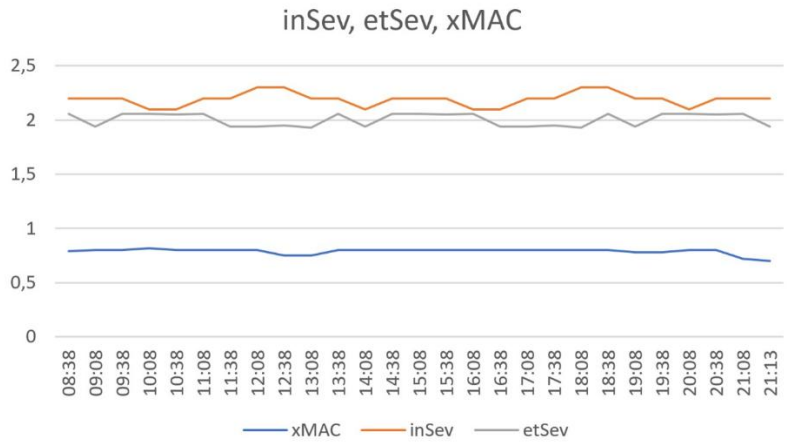

Figure 2. Intraoperative trends of FiO_2 and $etCO_2$, showing stable oxygenation and ventilation throughout the procedure.

At the end of surgery, the patient was transferred to the Pediatric Intensive Care Unit (PICU) for postoperative monitoring and ventilatory support. Analgesia was provided via epidural bupivacaine 0.125% with morphine 0.3 mg in 8 mL every 10–12 hours, plus scheduled paracetamol and ibuprofen. The postoperative course was uneventful; the patient was hemodynamically stable on PICU arrival.

Discussion

The application of LFA in pediatric laparoscopic procedures, such as choledochal cyst excision combined with hepaticojejunostomy and cholecystectomy, presents both opportunities and challenges. Modern anesthesia workstations, like the Dräger Perseus A500, support the effective implementation of LFA through advanced features such as the Low Flow Wizard and Econometer. These tools assist clinicians in optimizing fresh gas flow rates to ensure patient safety, minimize anesthetic agent consumption, and reduce costs. In the presented case, low-flow anesthesia was successfully employed using this workstation. Sevoflurane was chosen as the volatile agent due to its rapid onset and stability, making it particularly suitable for low-flow techniques in pediatric patients. Furthermore, the availability of integrated gas analyzers for monitoring inspired oxygen (FiO_2), end-tidal carbon dioxide ($EtCO_2$), and agent concentrations enhances the safety and practicality of conducting LFA in modern clinical settings. $EtCO_2$ monitoring is crucial in pediatric patients undergoing LFA, as it provides real-time assessment of ventilation and helps detect respiratory abnormalities. Studies have shown that $EtCO_2$ values remain within acceptable ranges during LFA, indicating its safety and efficacy in maintaining adequate ventilation.[2,3]

One of the primary advantages of low-flow anesthesia is the significant reduction in the consumption of anesthetic gases. A comparative study demonstrated that sevoflurane consumption was significantly lower in the low-flow group (4.17 ± 0.70 mL) compared to the standard-flow group (8.96 ± 1.11 mL), highlighting the efficiency of LFA in reducing anesthetic usage.[4] Studies have reported that with high-flow anesthesia (e.g., 5 L/min), approximately 80–90% of anesthetic agents and gases are wasted. In contrast, low-flow anesthesia minimizes this wastage, leading to considerable cost savings and reduced environmental impact.[5] This is particularly relevant in healthcare systems focused on cost-efficiency, such as Indonesia's BPJS program, without compromising patient safety or anesthetic quality.

While low-flow anesthesia offers significant benefits such as reduced anesthetic gas consumption and improved cost-efficiency, it is not without its challenges. One of the primary concerns is the risk of hypoxia due to rebreathing, particularly when fresh gas flows are reduced. Studies have shown that maintaining a minimum inspired oxygen concentration (FiO_2) above 30% is critical to preventing hypoxic episodes during low-flow techniques. For example, research by Baum et al. emphasized that careful monitoring and adjustment of FiO_2 are essential in pediatric low-flow anesthesia to ensure patient safety. [5] In the present case, this principle was applied effectively, with FiO_2 consistently maintained above 30% throughout the nearly 12-hour procedure. This demonstrates that with appropriate monitoring and vigilance, low-flow anesthesia can be safely implemented even in complex pediatric laparoscopic surgeries.

Additionally, effective ventilation is paramount in laparoscopic surgeries due to the use of CO_2 insufflation, which can increase systemic CO_2 absorption and elevate end-tidal CO_2 ($EtCO_2$) levels. This issue is particularly significant in pediatric patients, who have a higher per-body-weight metabolic rate and increased CO_2 absorption. Nevertheless, in the present case,

$EtCO_2$ was successfully maintained around 35 mmHg, demonstrating well-controlled ventilation and gas exchange. These findings underscore that with vigilant intraoperative monitoring, low-flow anesthesia can be safely and effectively applied even in lengthy and complex pediatric laparoscopic surgeries.[6]

Comparatively, standard high-flow anesthesia techniques may offer more straightforward management of gas concentrations and quicker adjustments to changes in patient physiology. However, they come with increased consumption of anesthetic agents and greater environmental impact. Moreover, high-flow techniques may lead to more significant heat and humidity loss from the respiratory tract, which can be detrimental, especially in pediatric patients. [5,7]

This case reinforces the viability of low-flow anesthesia as a safe and efficient technique in prolonged pediatric laparoscopic surgery. Despite the inherent challenges in managing ventilation and oxygenation in children, the combination of modern anesthesia technology and continuous intraoperative monitoring allowed for stable physiological parameters throughout the procedure. The significant reduction in volatile agent use underscores its pharmacoeconomic value, particularly in resource-limited settings. Ultimately, this report supports the broader adoption of low-flow anesthesia in pediatric practice, provided that careful monitoring and appropriate equipment are in place.

Acknowledgement

Nil.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of Interest

The authors report no conflict of interest.

Data Availability Statement

De-identified patient data from this case report will be made available upon reasonable request to the corresponding author following publication, subject to institutional data-sharing policies and ethics approval.

Author's Contributions

All authors contributed significantly to the conception and design of the study, data collection, analysis, and interpretation of the results. All authors participated in writing and critically revising the manuscript for important intellectual content, approved the final version to be published, and are accountable for all aspects of the research.

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CASE REPORT

Graded Epidural Anesthesia with Real-Time Hemodynamic Monitoring for Cesarean Delivery in Severe Mitral Stenosis: A Case Report

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Abstract

This case report highlights the successful management of a high-risk obstetric patient with severe rheumatic mitral stenosis (MS) and acute decompensated heart failure (ADHF) using graded epidural anesthesia guided by real-time hemodynamic monitoring. A 34-year-old woman, in her second pregnancy following a previous abortion, presented at 34 weeks and 5 days of gestation with progressive dyspnea and orthopnea. Echocardiography confirmed severe MS accompanied by pulmonary hypertension and preserved left ventricular systolic function. After multidisciplinary optimization, an elective cesarean delivery was performed under graded epidural anesthesia with incremental dosing of lidocaine and ropivacaine. Beat-to-beat cardiac output monitoring using the MostCare™ PRAM (Pressure Recording Analytical Method) system guided vasopressor titration with phenylephrine, maintaining hemodynamic stability. The patient remained hemodynamically stable throughout the intraoperative and postoperative periods, with no pulmonary edema or arrhythmias, and was discharged on postoperative day four. This case demonstrates that graded epidural anesthesia, when combined with advanced hemodynamic monitoring and collaborative care, represents a safe and effective alternative to general anesthesia in parturients with severe valvular heart disease.

Keywords: Cesarean section, Graded epidural anesthesia, Hemodynamic monitoring, Mitral stenosis, Rheumatic heart disease

Anestesi Epidural Bertahap dengan Pemantauan Hemodinamik *Real-Time* pada Seksio Sesarea dengan Stenosis Mitral Berat: Laporan Kasus

Abstrak

Laporan kasus ini menggambarkan keberhasilan penatalaksanaan pasien obstetri berisiko tinggi dengan stenosis mitral (MS) berat akibat penyakit jantung rematik dan gagal jantung dekompensasi akut (ADHF) menggunakan anestesi epidural bertahap yang dipandu oleh pemantauan hemodinamik *real-time*. Seorang wanita berusia 34 tahun pada kehamilan kedua dengan riwayat abortus datang pada usia kehamilan 34 minggu 5 hari dengan keluhan sesak progresif dan ortopnea. Ekokardiografi menunjukkan MS berat disertai hipertensi pulmonal dengan fungsi sistolik ventrikel kiri yang masih terjaga. Setelah dilakukan optimalisasi multidisiplin, pasien menjalani operasi seksio sesarea elektif dengan anestesi epidural bertahap melalui titrasi dosis lidokain dan ropivakain. Pemantauan curah jantung *beat-to-beat* dengan sistem *MostCare™ PRAM* (*Pressure Recording Analytical Method*) memandu pemberian vasopresor fenilefrin untuk menjaga stabilitas hemodinamik. Pasien tetap stabil selama operasi dan periode pascaoperasi tanpa edema paru atau aritmia, dan dipulangkan pada hari keempat pascaoperasi. Kasus ini menunjukkan bahwa anestesi epidural bertahap, bila dikombinasikan dengan pemantauan hemodinamik canggih dan kerja sama multidisiplin, dapat menjadi alternatif yang aman dan efektif terhadap anestesi umum pada pasien obstetri dengan penyakit katup jantung berat.

Kata kunci: Penyakit jantung rematik, Stenosis mitral, Anestesi epidural bertahap, Pemantauan hemodinamik, Seksio sesarea

Introduction

Rheumatic heart disease (RHD) remains a major contributor to maternal morbidity and mortality in low- and middle-income countries, where limited access to cardiac intervention leads to high-risk pregnancies with complex valvular lesions.[1] Severe MS poses a particularly critical challenge. The normal physiological changes of pregnancy—especially a 40–50% increase in cardiac output

and plasma volume—can unmask or exacerbate underlying MS, predisposing patients to ADHF, pulmonary hypertension, and arrhythmias.[2,3] Up to half of pregnant women with severe MS experience symptomatic heart failure by the third trimester, with mortality rates reported as high as 10–50% in those with New York Heart Association (NYHA) class III–IV or mWHO class IV disease.[1,2]

Anesthetic management in these patients requires a careful balance between maintaining maternal hemodynamic stability and ensuring uteroplacental perfusion. While general anesthesia allows controlled airway management, it carries significant risks in fixed cardiac output states—particularly due to tachycardia, increased pulmonary vascular resistance, and myocardial depression.[4] Conversely, neuraxial anesthesia, especially graded epidural, offers theoretical advantages by minimizing sympathetic surges and avoiding volatile anesthetics; however, it remains controversial in severe MS due to potential precipitous decreases in preload and afterload.[5,6]

Recent case series and case reports have demonstrated that carefully titrated graded epidural anesthesia, combined with real-time hemodynamic monitoring and judicious vasopressor use, can be safely implemented in high-risk obstetric patients with severe valvular disease.[7–10] Hemodynamic monitoring technologies such as MostCare™ PRAM enable continuous assessment of cardiac output and systemic vascular resistance, guiding precise pharmacologic and fluid management.[11] Integration of these technologies, within a multidisciplinary approach involving anesthesiology, cardiology, and obstetrics, aligns with recent international guidelines emphasizing individualized, physiology-based care.[1,3,4]

This case report presents a 34-year-old pregnant woman with severe rheumatic MS and ADHF who successfully underwent cesarean delivery under graded epidural anesthesia guided by beat-to-beat cardiac output monitoring. The case highlights the feasibility and safety of this approach in a mWHO class IV patient and contributes to the growing body of evidence supporting neuroaxial anesthesia with hemodynamic guidance as a viable alternative to general anesthesia in critically ill parturients with valvular heart disease.

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Case Presentation

A 34-year-old woman in her second pregnancy after a previous abortion, at 34 weeks and 5 days of gestation was referred for elective cesarean delivery due to severe rheumatic MS and ADHF. She presented with progressively worsening exertional dyspnea and orthopnea, requiring three pillows at night. There was no chest pain, palpitations, or fever. Her medical history included RHD with severe MS (Wilkins score 7, valve area < 1 cm²), pulmonary hypertension, paroxysmal atrial fibrillation, and mild tricuspid regurgitation. She was categorized as mWHO class IV, NYHA class III, and ASA physical status III. Her comorbidities included mild anemia (Hb 8.7 g/dL) and well-controlled bronchial asthma.

On admission, she appeared tachypneic with a respiratory rate of 24/min, heart rate 92 bpm, and blood pressure 109/66 mmHg. Oxygen saturation was 98% on 3 L/min via nasal cannula. Echocardiography demonstrated

marked left atrial enlargement, a left ventricular ejection fraction of 54.4% consistent with low-normal systolic function, and diastolic dysfunction attributable to severe rheumatic mitral stenosis with a valve area of less than 1.0 cm^2. Estimated pulmonary artery pressures were in the moderate range, reflecting clinically significant pulmonary hypertension. These findings were consistent with fixed cardiac output physiology and highlighted the need for meticulous perioperative hemodynamic control. Chest X-ray showed mild pulmonary congestion. Arterial blood gas analysis revealed mild respiratory alkalosis, while spirometry indicated a moderate restrictive pattern ($FEV_1 \approx$ 70% predicted).

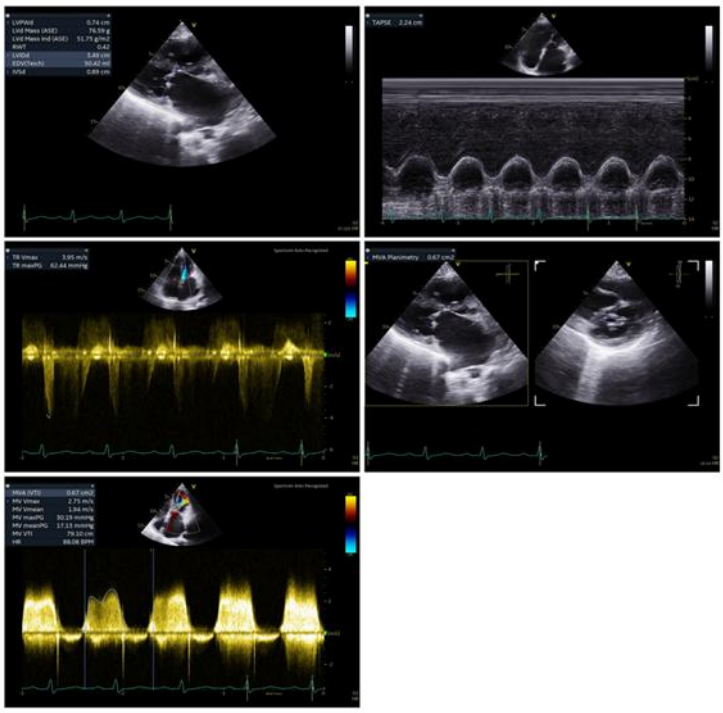

Figure 1. Echocardiography showed LA and LV dilation, reduced EF (54.38%), uncoordinated septal wall motion, severe mitral stenosis (MS), mild tricuspid regurgitation, high probability of pulmonary hypertension, and undetermined diastolic function due to severe MS.

A multidisciplinary team consisting of cardiology, obstetrics, pulmonology, and anesthesiology, planned an elective cesarean section after preoperative optimization. The patient received bisoprolol 2.5 mg daily, furosemide 40 mg IV on the morning of surgery, benzathine penicillin G for rheumatic prophylaxis, and antenatal corticosteroids for fetal lung maturity.

A graded epidural anesthesia technique was selected because it provides a controlled and physiologically gentle approach to sympathetic blockade, which is essential in patients with severe MS and fixed cardiac output physiology. Unlike single-shot spinal anesthesia, which produces a rapid and dense block that can suddenly reduce systemic vascular resistance and venous return, a graded epidural permits slow titration of segmental anesthesia. This allows the anesthesiologist to monitor the hemodynamic response after each dosing increment and adjust therapy accordingly. The stepwise onset of epidural anesthesia is aligned with current European Society of Cardiology (ESC), American College of Cardiology (ACC/AHA), and SOAP guidance, which recommend avoiding abrupt reductions in preload and afterload in high-risk valvular lesions. By selecting a graded technique, the team minimized the risks of acute hypotension, tachyarrhythmias, and pulmonary edema while still achieving adequate anesthesia for cesarean

delivery. Under aseptic conditions, an epidural catheter was placed at the L1–L2 interspace, with the tip directed to T9–T10. MostCare™ PRAM monitoring was used to obtain beat-to-beat measurements of cardiac output, stroke volume, and systemic vascular resistance, enabling titrated management.

In this patient with severe MS and ADHF, clearly defined hemodynamic targets were established prior to initiating neuraxial anesthesia. The primary objectives included maintaining a heart rate between 60 and 70 beats per minute to prolong diastolic filling time and reduce the transmitral gradient, preserving a mean arterial pressure of approximately 70–80 mmHg to ensure adequate coronary perfusion, and avoiding abrupt decreases in preload that might precipitate pulmonary congestion. Particular attention was also given to preventing increases in pulmonary vascular resistance, as this could worsen right ventricular strain and aggravate pulmonary hypertension. These goals served as the physiologic framework for anesthetic decision-making throughout the procedure and guided both fluid administration and vasopressor therapy.

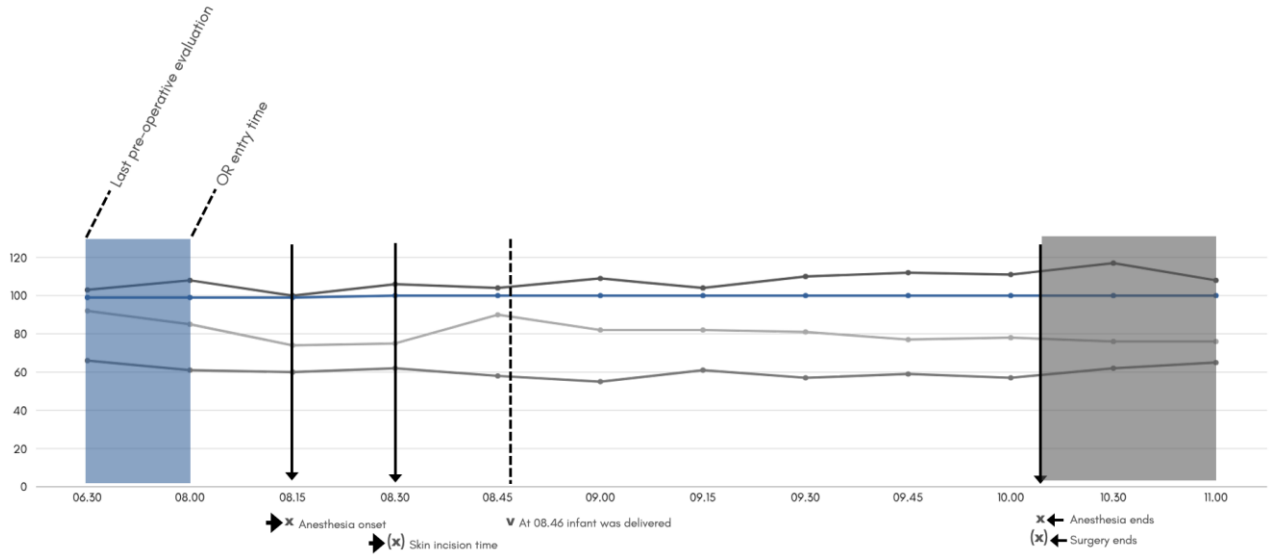

Figure 2. Intraoperative Hemodynamic Monitoring Timeline and Key Events

Incremental dosing was initiated with lidocaine 2% (6 mL) followed by ropivacaine 0.5% (8 mL), attaining a sensory block level of T6–L1. The selection of lidocaine and ropivacaine for the epidural regimen was based on their complementary pharmacologic profiles and safety considerations in patients with compromised cardiac function. Lidocaine 2% was used initially due to its rapid onset and predictable spread, allowing early assessment of block adequacy. Ropivacaine 0.5% was subsequently administered to provide more stable sensory anesthesia with minimal motor blockade and reduced cardiotoxicity compared with bupivacaine. Delivering these agents in small, carefully titrated aliquots allowed the anesthetic level to advance progressively while enabling real-time evaluation of cardiac output, systemic vascular resistance, and stroke volume trends on PRAM monitoring. This incremental dosing strategy helped maintain preload and afterload within the targeted physiologic range and reduced the likelihood of sudden hemodynamic deterioration. A phenylephrine infusion (25 µg/min, titrated) was administered to maintain systolic blood pressure ≥ 90 mmHg. Hemodynamics remained stable (BP 82–108/62–73 mmHg, HR 63–78 bpm, SpO_2 99–100%). A male infant weighing 2270 g was delivered with Apgar scores of 7 and 9 at one and five minutes, respectively. Estimated blood

loss was 500 mL, and urine output was 1 L during the procedure.

Real-time hemodynamic monitoring with the MostCare™ PRAM system provided continuous measurements of cardiac output, stroke volume, systemic vascular resistance, and ventricular contractility indices. These data allowed early detection of subtle downward trends in cardiac output or stroke volume during the incremental epidural dosing. Any reduction exceeding approximately 10% from baseline prompted temporary cessation of further neuraxial dosing and adjustment of the phenylephrine infusion to restore vascular resistance and support forward flow. This dynamic, physiology-guided approach ensured that the anesthetic block progressed in a hemodynamically safe manner and allowed precise titration of vasopressor support based on objective beat-to-beat hemodynamic data rather than intermittent noninvasive measurements alone.

The postoperative analgesic regimen was designed to maintain hemodynamic stability by preventing pain-induced sympathetic surges and tachycardia, both of which can critically worsen transmitral gradients in severe MS. A low-dose epidural regimen using dilute bupivacaine combined with intermittent low-dose morphine provided effective analgesia while avoiding the respiratory depression and hypercapnia that may occur with systemic opioids and potentially exacerbate pulmonary hypertension. This technique ensured stable postoperative heart rate and afterload conditions, supporting safe recovery and minimizing the risk of pulmonary edema during the vulnerable early postpartum period, when abrupt fluid shifts commonly occur.

The patient was monitored in a high-dependency unit for 48 hours. Analgesia was provided via epidural Bupivacaine 0.0625% + Morphine 0.5 mg q12h, supplemented with Paracetamol 1 g IV q8h. Furosemide 20 mg IV was administered post-delivery to prevent volume overload. No pulmonary edema or arrhythmias occurred. She was discharged in stable condition on postoperative day 4 with a plan for percutaneous balloon mitral valvotomy.

Discussion

Pregnancy induces significant cardiovascular adaptations, including increased blood volume and cardiac output, which may precipitate heart failure in women with severe MS.[1,2,4] These patients have fixed cardiac output and limited ability to tolerate tachycardia or decreased afterload. The goal of anesthesia is therefore to maintain controlled heart rate, stable preload, and adequate SVR.

General anesthesia may provoke sympathetic surges, tachycardia, and myocardial depression, increasing maternal and fetal risk.[4,6] Conversely, graded epidural anesthesia, when performed cautiously, provides controlled sympathetic blockade and gradual hemodynamic change.[5–7] Previous studies have reported improved outcomes with the use of incremental epidural techniques in patients with MS during pregnancy.[7,8] The present case contributes to this evidence by incorporating real-time cardiac output monitoring via the MostCare™ PRAM system, allowing physiology-guided titration of vasopressors and fluids.[11]

Phenylephrine, a pure α-agonist, was selected for vasopressor support due to its ability to maintain SVR without increasing heart rate, consistent with SOAP and ESC recommendations.[1,3,4] Controlled fluid administration and postoperative diuresis minimized pulmonary congestion risk, while beta-blockade optimized diastolic filling.[1,3,4,9]

Our findings align with recent literature demonstrating that hemodynamic-guided graded epidural anesthesia can be safely employed in mWHO class IV patients with

valvular disease.[7–10] The main strengths of this case include integration of advanced monitoring and a multidisciplinary perioperative approach. Limitations include single-case nature and short follow-up period.

The present case underscores the importance of adhering to strict hemodynamic goals during anesthetic management of severe mitral stenosis in pregnancy. Maintaining controlled heart rate, stable preload, and adequate afterload is essential to prevent hemodynamic collapse in fixed cardiac output states. The combination of graded epidural anesthesia and PRAM-guided monitoring provided a controlled and adaptable environment in which sympathetic blockade developed gradually and cardiovascular responses were immediately visible. This approach allowed early correction of minor hemodynamic deviations, prevented abrupt decreases in systemic vascular resistance, and minimized the need for large vasopressor boluses. The real-time insight into cardiovascular performance further supported individualized anesthetic management and reduced the risk of peripartum decompensation, reinforcing the feasibility of neuraxial anesthesia even in mWHO class IV patients when applied with careful physiologic guidance.

Graded epidural anesthesia guided by real-time cardiac output monitoring and multidisciplinary planning, can be safely applied in pregnant patients with severe mitral stenosis and acute heart failure. Key management principles include incremental dosing, maintenance of SVR with phenylephrine, and strict fluid control. This physiology-based approach supports the evolving paradigm of precision, hemodynamic-guided anesthesia for high-risk obstetric cardiac disease.

Acknowledgement

Nil.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of Interest

The authors report no conflict of interest.

Data Availability Statement

De-identified patient data from this case report will be made available upon reasonable request to the corresponding author following publication, subject to institutional data-sharing policies and ethics approval.

Author's Contributions

All authors contributed significantly to the conception and design of the study, data collection, analysis, and interpretation of the results. All authors participated in writing and critically revising the manuscript for important intellectual content, approved the final version to be published, and are accountable for all aspects of the research.

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CASE SERIES

Renal Resistive Index in Early Detection of AKI after Neurosurgery: A Case Series

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Abstract

Postoperative acute kidney injury (AKI) is a frequent yet underrecognized complication in neurosurgical patients, often contributing to increased morbidity and mortality. Brain injury can trigger systemic effects, including sympathetic overactivation, inflammatory responses, and hemodynamic instability, all of which predispose patients to renal dysfunction. The Renal Resistive Index (RRI), obtained by Doppler ultrasonography, reflects intrarenal vascular resistance and has emerged as a promising early marker of AKI. This case series describes three patients undergoing decompressive craniectomy for intracranial hemorrhage who had normal preoperative renal function and subsequently developed stage 1 AKI according to Kidney Disease; Improving Global Outcome (KDIGO) guideline within 24 hours postoperatively. In each case, an elevated RRI (>0.7) measured during the early postoperative period preceded the rise in serum creatinine and the reduction in urine output. The consistent pattern across these patients highlights the potential utility of RRI as a noninvasive, bedside predictor of postoperative AKI in neurosurgical populations. The findings support the clinical relevance of integrating RRI into perioperative monitoring, particularly in high-risk patients where early detection of renal dysfunction may guide timely interventions to optimize hemodynamic stability and prevent further injury. Further prospective studies with larger cohorts are warranted to validate these observations and establish standardized thresholds for practice.

Keywords: Acute kidney injury; Intracranial hemorrhage; Neurosurgery; Postoperative care; Renal resistive index

Renal Resistive Index dalam Deteksi Dini AKI Pasca Bedah Saraf: Kasus Serial

Abstrak

Cedera ginjal akut pascaoperasi (*Acute Kidney Injury*/AKI) merupakan komplikasi yang sering terjadi namun kurang dikenali pada pasien bedah saraf. Hal ini berkontribusi pada peningkatan morbiditas serta mortalitas. Cedera otak dapat memicu efek sistemik, termasuk aktivasi simpatis berlebihan, respons inflamasi, dan ketidakstabilan hemodinamik, yang semuanya dapat meningkatkan risiko disfungsi ginjal. *Renal Resistive Index* (RRI), yang diperoleh melalui ultrasonografi Doppler, merefleksikan resistensi vaskular intrarenal dan muncul sebagai penanda awal yang menjanjikan untuk AKI. Seri kasus ini melaporkan tiga pasien yang menjalani kraniektomi dekompresi akibat perdarahan intrakranial dengan fungsi ginjal preoperatif normal. Namun, dalam 24 jam pascaoperasi berkembang menjadi AKI stadium 1 menurut kriteria *Kidney Disease; Improving Global Outcome* (KDIGO). Pada setiap kasus, peningkatan nilai RRI (>0,7) pada periode awal pascaoperasi mendahului kenaikan kadar kreatinin serum serta penurunan produksi urin. Pola konsisten yang ditemukan pada ketiga pasien ini menekankan potensi RRI sebagai prediktor noninvasif di samping tempat tidur untuk AKI pascaoperasi pada populasi bedah saraf. Temuan ini mendukung relevansi klinis integrasi pemantauan RRI dalam manajemen perioperatif, khususnya pada pasien berisiko tinggi di mana deteksi dini disfungsi ginjal dapat mengarahkan intervensi tepat waktu untuk mengoptimalkan stabilitas hemodinamik dan mencegah kerusakan lebih lanjut. Studi prospektif dengan jumlah sampel yang lebih besar masih diperlukan untuk memvalidasi temuan ini dan menetapkan ambang baku yang dapat diterapkan dalam praktik klinis.

Kata kunci: Cedera ginjal akut; Perdarahan intrakranial; Bedah saraf; Perawatan pascaoperasi; *Renal resistive index*

Introduction

Acute kidney injury (AKI) is among the most frequent complications after major surgery, associated with prolonged hospitalization and increased mortality.[1] A systematic review of 19 studies (82,514 patients) reported a pooled incidence of 13.4% after major abdominal surgery. Another meta-analysis estimated an

overall postoperative AKI rate of 16%, with variations across surgical types. Gynecological procedures had the lowest incidence (6%), while digestive and mixed abdominal surgeries reached 15% and 19%, respectively.[1,2] In contrast, cardiac surgery showed wider variability (5–42%). At our hospital, AKI occurs in 7–30% of intensive care patients, contributing to longer stays, higher costs, and mortality.[3] Despite its importance, postoperative AKI following neurosurgery remains underreported, indicating a need for further research.

In neurosurgical patients, diagnosis is often delayed as attention focuses on neurological recovery. Yet, studies show cerebral injury may disrupt renal function through autonomic, inflammatory, and hemodynamic mechanisms.[4] Thus, monitoring kidney function in intracranial hemorrhage surgery is clinically relevant.

The Renal Resistive Index (RRI), assessed by Doppler ultrasonography, is a simple noninvasive indicator of intrarenal vascular resistance. Values above 0.7 suggest early renal impairment.[5] Unlike serum creatinine, which increases only after significant damage, RRI detects early perfusion changes, making it useful for perioperative monitoring.[6]

This case series presents three patients with intracranial hemorrhage undergoing emergency craniectomy who developed postoperative AKI despite normal baseline renal function. Increased RRI consistently preceded biochemical AKI markers, emphasizing its potential as an early predictor of renal dysfunction in neurosurgical cases.

Case Presentation

Case I

A 59-year-old male with no chronic kidney disease presented with sudden severe headache and decreased consciousness (GCS 7, BP 160/95 mmHg, HR 96 bpm). Baseline renal function was normal (creatinine 1.03 mg/dL; clearance 71 mL/min). CT revealed a large intracerebral and epidural hematoma with midline shift, and emergency decompressive craniectomy was performed. With balanced fluids and intermitten vasopressor support. At 12 hours postoperatively, RRI was 0.81 and urine output 0.44 mL/kg/h. At 24 hours, creatinine rose to 1.51 mg/dL (clearance 48.4 mL/min), fulfilling stage 1 AKI. Conservative management with fluid optimization and monitoring was applied.

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Case II

A 60-year-old hypertensive female presented with altered consciousness after a traumatic fall (GCS 7, BP 150/90 mmHg, HR 88 bpm). Baseline renal function was normal (serum creatinine 1 mg/dL; clearance 66.7 mL/min). Head CT revealed a large intracerebral and intraventricular hemorrhage with significant mass effect, prompting emergency craniectomy. Postoperatively, hemodynamics remained stable under standard anesthetic and intensive care management. At 12 hours, Doppler ultrasound showed an RRI of 0.763 with urine output 0.34 mL/kg/h; at 24 hours, serum creatinine increased to 2.22 mg/dL (clearance 3.03 mL/min), fulfilling stage 2 AKI criteria. Neurological status remained stable, and conservative management effectively prevented additional complications.

Case III

A 47-year-old hypertensive male presented with sudden loss of consciousness (GCS 9, BP 160/90 mmHg, HR 102 bpm). Preoperative renal function was normal (serum creatinine 1.05 mg/dL; clearance 104.5 mL/min). CT scan showed spontaneous intracerebral hemorrhage, and urgent decompressive craniectomy was performed. The intraoperative course was stable with adequate fluid and vasopressor support. At 12 hours postoperatively, RRI was 0.77 with urine output 0.31 mL/kg/h; at 24 hours, serum creatinine increased to 1.4 mg/dL, consistent with stage 1 AKI. Conservative renoprotective management restored urine output to 1.5 mL/kg/h without complications.

Table 1. Demographic and Clinical Characteristics of Patients

Charateristics	Case I	Case II	Case III
Gender	Male	Male	Male
Age (years)	59	60	47
Diagnosis	Moderate TBI + tEDH R Temporal + tICH R Temporoparietal + tSAH R FrontoTemporal + IVH R Lateral Ventricle	sICH R FrontoTemporal + sIVH	sICH L External Capsule ec Rupture MCA Bifurcation Aneurysm + sIVH L Lateral Ventricle + sSAH + Acute Non Communicating Hydrocephalus
Type of Surgery	Decompressive Craniectomy	Decompressive Craniectomy	Decompressive Craniectomy + EVD
Co-morbidities	None	Hypertension	Hypertension
Baseline Scr (mg/dL)			
Intraoperative	1.03	1.00	1.05
Postoperative (24 hr)	1.51	2.22	1.40
Baseline BUN (mg/dL)			
Intraoperative	12.8	10.8	11.1
Postoperative (24 hr)	19.2	16.2	16.6
Baseline CCT (mg/dL)			
Intraoperative	71.0	66.6	104.5
Postoperative (24 hr)	48.4	30.3	78.4
Urine Output (mL/kgBB/hr)			
Intraoperative	2.08	0.41	0.93
Postoperative (12 hr)	0.44	0.34	0.31
Postoperative (24 hr)	0.58	0.57	1.50
KDIGO Stage	I	II	1
RRI Postoperative (12 hr)	0.810	0.763	0.770
Outcome	Improved after optimization	Improved after optimization	Improved after optimization

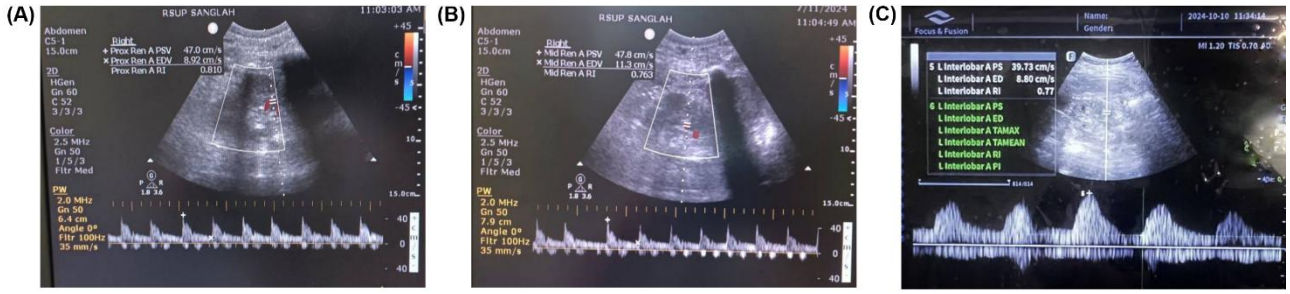

Figure 1. Postoperative Doppler Assessment of RRI

Discussion

RRI measurement is most valuable after achieving hemodynamic stability, typically within 12–24 hours post-surgery, when the transition from intraoperative stress to recovery occurs. A persistently elevated RRI (>0.7) during this phase may indicate subclinical renal hypoperfusion, even when serum creatinine and urine output remain normal. Detection of a high RRI should prompt reassessment of mean arterial pressure, fluid status, and vasoactive drug use.[2]

This case series highlights the utility of RRI as an early indicator of postoperative AKI in neurosurgical patients. Despite stable perioperative hemodynamics and normal baseline renal function, all three cases developed stage 1–2 AKI within 24 hours of craniectomy. Notably, RRI values >0.7 consistently preceded biochemical changes, suggesting that RRI may allow earlier identification of renal impairment than conventional laboratory parameters.

The brain–kidney interaction has gained increasing attention in neurosurgical care, as AKI occurs in 3–20% of patients and contributes to poorer outcomes.[7,8] In those undergoing intracranial hemorrhage surgery, systemic complications often extend beyond the central nervous system, with AKI representing an underrecognized contributor to morbidity and mortality.[9]

Several mechanisms explain the brain–kidney interplay (Figure 2). Neurohumoral activation following brain injury triggers sympathetic overactivity and stimulation of the renin–angiotensin–aldosterone system (RAAS), leading to vasoconstriction, sodium retention, and renal hypoperfusion.[4,10] Systemic inflammation driven by cytokines such as interleukin-6 and TNF-α further impairs endothelial and microvascular function.[10,11] Oxidative stress and mitochondrial dysfunction add to tubular injury and reduce renal adaptive capacity, making the kidneys more vulnerable to perioperative insults.[12]

Moreover, neurosurgical procedures themselves pose hemodynamic challenges. Tight blood-pressure control, osmotic diuretics, vasopressors, and anesthetic agents can compromise renal perfusion. Combined with systemic inflammatory responses and surgical stress, these factors create a “perfect storm” predisposing patients to postoperative AKI.[4]

In this case series, all patients displayed a consistent pattern: early RRI elevation followed by AKI within 24 hours, underscoring RRI’s potential to bridge neurological and renal monitoring. RRI reflects renal vascular resistance and perfusion in real time.[1] Brain injury induces sympathetic activation, inflammation, and circulatory disturbances that can impair renal perfusion before creatinine elevation or oliguria occur.[7,8] As a bedside Doppler parameter, RRI enables early detection of these changes. Prior studies in intensive care and surgical populations have similarly linked elevated RRI to AKI, particularly in cardiac and abdominal procedures, suggesting comparable mechanisms in neurosurgical

settings where renal monitoring is often secondary.[1,5]

Nonetheless, RRI interpretation requires caution. It is influenced by systemic factors such as arterial compliance, intra-abdominal pressure, and vasoactive drug use.[5] The limited number of cases precludes statistical inference, and operator expertise may affect reproducibility, highlighting the need for standardized measurement protocols. In this series, certified anesthesiologists performed RRI assessment 12 hours postoperatively using portable Doppler ultrasonography to detect early renal perfusion changes. AKI was defined by using both creatinine and urine output, ensuring diagnostic accuracy and alignment with international recommendations.

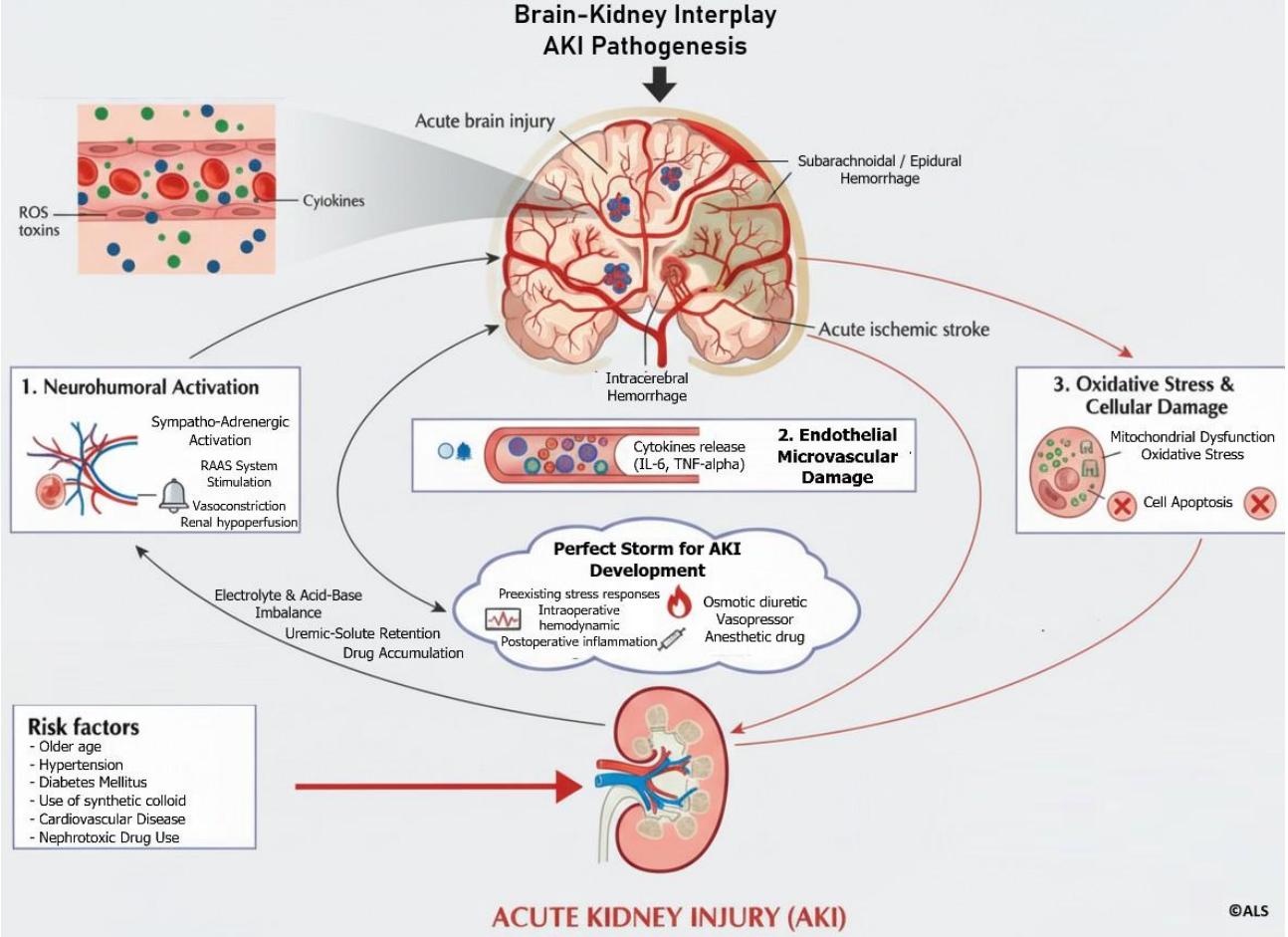

Figure 2. Schematic of Brain–Kidney Interplay in Postoperative AKI [4,10–12]

All patients received careful fluid management, hemodynamic optimization, and avoidance of nephrotoxins.[2] Although AKI was not prevented, early identification enabled intensified monitoring and supportive interventions that may have mitigated progression. Neurosurgical patients should thus be monitored not only for intracranial stability but also for early renal vulnerability.[4,8] Larger, prospective studies are needed to determine whether RRI-guided management improves renal outcomes in this population.

This report remains limited by its small sample size, lack of a control group, and absence of long-term renal follow-up. Consequently, the prognostic value of early postoperative RRI elevation requires confirmation through larger, controlled studies employing standardized ultrasonography protocols and defined RRI thresholds for intervention.

Acknowledgement

Nil.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of Interest

The authors report no conflict of interest.

Data Availability Statement

De-identified patient data from this case report will be made available upon reasonable request to the corresponding author following publication, subject to institutional data-sharing policies and ethics approval.

Author's Contributions

All authors contributed significantly to the conception and design of the study, data collection, analysis, and interpretation of the results. All authors participated in writing and critically revising the manuscript for important intellectual content, approved the final version to be published, and are accountable for all aspects of the research.

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NARRATIVE REVIEW

Anesthetic Approach to Placenta Previa with Associated Bladder Rupture: A Case Report

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Abstract

This case report outlines the anesthetic management of total placenta previa with high-risk features of placenta accreta spectrum (PAS) complicated by bladder rupture, representing a rare but clinically significant form of invasive placentation. A 29-year-old G2P1001 at 35+3 weeks' gestation presented with recurrent antepartum bleeding and ultrasonographic features consistent with PAS, including grade III lacunae, bridging vessels, severe myometrial thinning, and a Placenta Accreta Index (PAI) score of 6. Spinal anesthesia was initiated for delivery, followed by a controlled conversion to general anesthesia to facilitate hysterectomy, two-layer bladder repair, ureteral reconstruction, and Double-J stent placement. Hemodynamic stability was maintained using tranexamic acid, colloid co-loading, invasive arterial monitoring, and norepinephrine titration. An estimated blood loss of 2,300 mL was managed with targeted transfusion, resulting in favorable maternal recovery and neonatal outcomes (Apgar 7 and 9). This case underscores the importance of early PAS recognition, structured anesthetic planning, and coordinated multidisciplinary care, supporting the benefit of a staged neuraxial-to-general anesthesia strategy in complex PAS with urologic involvement.

Keywords: Anesthetic management, Bladder rupture, Caesarean hysterectomy, Placenta Accreta spectrum, Placenta previa

Pendekatan Anestesi pada Kasus Plasenta Previa dengan Komplikasi Ruptur Buli: Laporan Kasus

Abstrak

Laporan kasus ini menjabarkan penatalaksanaan anestesi pada plasenta previa total dengan fitur risiko tinggi *placenta accreta spectrum* (PAS) yang disertai ruptur buli, sehingga menimbulkan tantangan maternal dan pembedahan yang signifikan. Seorang perempuan G2P1001 berusia 29 tahun dengan usia kehamilan 35+3 minggu datang dengan perdarahan antepartum berulang serta temuan ultrasonografi yang mengarah pada PAS, termasuk lakuna grade III, pembuluh darah *bridging*, penipisan miometrium yang berat, dan skor *Placenta Accreta Index* (PAI) sebesar 6. Anestesi spinal diberikan untuk proses persalinan, diikuti konversi terencana ke anestesi umum untuk memfasilitasi tindakan histerektomi, perbaikan buli dua lapis, rekonstruksi ureter, serta pemasangan stent Double-J. Stabilitas hemodinamik dipertahankan melalui pemberian asam traneksamat, *co-loading* koloid, pemantauan arteri invasif, dan titrasi norepinefrin. Perkiraan kehilangan darah sebesar 2.300 mL ditangani dengan transfusi terarah, dan luaran maternal maupun neonatal (Apgar 7 dan 9) menunjukkan hasil yang baik. Kasus ini menegaskan pentingnya deteksi dini PAS, perencanaan anestesi yang terstruktur, dan koordinasi multidisipliner, serta menyoroti manfaat pendekatan anestesi kombinasi neuraksial–umum pada kasus PAS kompleks dengan keterlibatan urologis.

Kata Kunci: Histerektomi sesarea, Manajemen anestesi, Plasenta previa, Ruptur buli, Spektrum plasenta akreta

Introduction

Placenta previa is characterized by abnormal implantation of placental tissue in the lower uterine segment and is classified as total placenta previa when the placenta completely covers the internal cervical os.[1] This condition carries considerable maternal and neonatal morbidity, particularly when occurring concurrently with PAS, which substantially increases surgical risk and complexity. The strongest risk factor for placenta previa is a prior cesarean delivery, and with rising global cesarean rates, its incidence has increased to approximately 1 in 200 pregnancies.[2]

When abnormal placentation invades adjacent organs such as the bladder, operative complexity and mortality risk rise significantly, with maternal mortality up to 9.5% and neonatal mortality up to 24%.[3] Given its life-threatening potential, placenta previa requires meticulous hemorrhage risk assessment and comprehensive anesthetic planning, including preoperative evaluation and intraoperative hemodynamic management.[1]

This case is notable due to the presence of total placenta previa with high-risk sonographic indicators of PAS, complicated by intraoperative bladder rupture that necessitated extensive urologic reconstruction. The combination of complex obstetric pathology, massive hemorrhage risk, and the need for a staged anesthetic strategy—from neuraxial anesthesia for delivery to planned conversion to general anesthesia—provides important insight into multidisciplinary perioperative management in high-acuity PAS cases.

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Case Presentation

A 29-year-old woman (G2P1001) at 35+3 weeks' gestation was admitted with total placenta previa and high suspicion of PAS (PAS 3, S2, Type 4), supported by grade III lacunae, bridging vessels, severe myometrial thinning (<1 mm), and a PAI score of 6.0. She had a history of recurrent vaginal bleeding since 27 weeks of gestation, including a significant episode shortly before admission. An ultrasound at 30 weeks had shown findings consistent with PAS, and elective readmission had been advised. She denied systemic symptoms, urinary or gastrointestinal complaints, and reported no allergies or significant medical history. Her surgical history included an uncomplicated cesarean section under regional anesthesia in 2022. She did not consume tobacco or alcohol.

On admission, she was hemodynamically stable with a pulse of 113 beats/min, blood pressure of 100/70 mmHg, respiratory rate of 18 breaths/min, and SpO_2 of 97% on room air. Physical examination showed a fundal height of approximately 28 cm and ongoing spotting, with normal fetal heart tones at 148 beats/min. Airway evaluation was unremarkable (Mallampati II). Laboratory tests revealed microcytic hypochromic anemia (Hb 8.8 g/dL, MCV 81.1 fL, MCH 24.9 pg, MCHC 30.7 g/dL), normal coagulation profile, preserved renal and liver function, and albumin 3.2 g/dL. Transabdominal ultrasound confirmed a live cephalic fetus and an anterior placenta completely covering the cervical os, with grade III lacunae, bridging vessels, and myometrial thickness <1 mm, consistent with high suspicion for PAS. The patient was classified as ASA physical status III.

In anticipation of massive hemorrhage, multidisciplinary preparation included two large-bore intravenous lines, arterial catheterization, blood product readiness, vasoactive agents, and equipment for controlled transition to general anesthesia. Spinal anesthesia with 10 mg of 0.5% hyperbaric bupivacaine was administered at L3–L4, with confirmed sensory block. She received oxygen via nasal cannula and prophylactic medications including tranexamic acid, paracetamol, ondansetron, and vitamin K. After delivery of the neonate, the anesthetic was converted to general anesthesia using intravenous lidocaine, fentanyl, propofol, and atracurium. Endotracheal intubation was successful, and anesthesia was maintained with sevoflurane

and intermittent atracurium. Norepinephrine was titrated to maintain a mean arterial pressure above 65 mmHg.

Estimated blood loss was 2,300 mL, managed with crystalloid, colloid, and 682 mL packed red cells. In addition to hysterectomy, intraoperative findings included bladder and ureteral injury requiring two-layer bladder repair, end-to-end ureteral anastomosis, left ureteral reimplantation, and placement of a double-J stent.

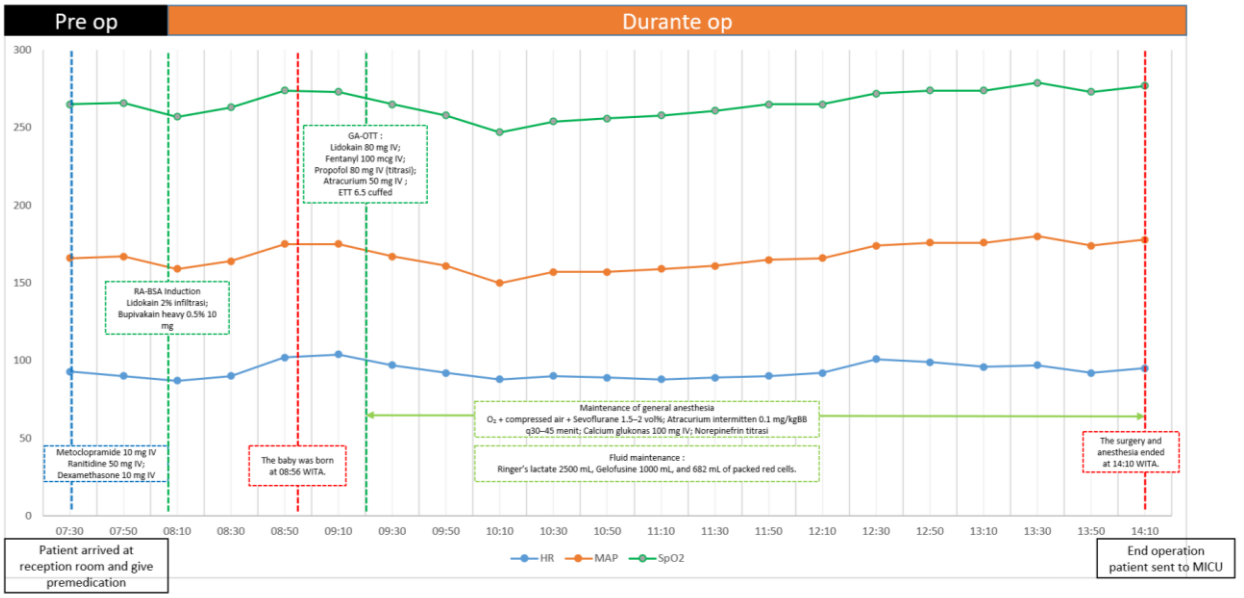

Figure 1. Haemodynamic profile preoperation and during operation

Postoperatively, the patient was managed in the maternal intensive care unit with multimodal analgesia consisting of a low-dose morphine–ketamine infusion and paracetamol. Her clinical condition improved progressively: she tolerated oral intake, achieved stable urine output, and ambulated independently by day 4, when the abdominal drain was removed. No adverse or unexpected complications occurred. She was discharged with a plan for follow-up 7–10 days later.

Discussion

Effective perioperative management is vital in placenta previa complicated by PAS, particularly when bladder invasion is suspected.[1] Advanced imaging such as MRI may better delineate placental invasion into the myometrium and adjacent organs.[4]

Anesthetic technique selection must be individualized, balancing hemorrhage risk, fetal exposure, airway management, and anticipated surgical complexity. Neuraxial anesthesia offers maternal awareness, minimal impact on uterine tone, reduced fetal exposure to systemic agents, and superior postoperative analgesia, though unplanned conversion to general anesthesia (GA) may be required. GA provides early airway control but is associated with increased risks of hemorrhage, difficult intubation, and fetal anesthetic exposure. A combined strategy—initiating with neuraxial anesthesia and transitioning to planned GA—may optimize both maternal and neonatal outcomes but involves the challenge of intraoperative intubation.[5,6] In high-risk abnormal placentation, anesthetic technique may influence hemodynamic stability.[4]

In this case, spinal anesthesia minimized fetal exposure, while planned conversion to general anesthesia optimized surgical access and hemodynamic control.[7] A controlled conversion to GA after delivery (propofol induction, atracurium neuromuscular blockade,

sevoflurane maintenance) enabled safe hysterectomy and urologic reconstruction.[8] This approach balanced neonatal benefits associated with neuraxial anesthesia with the airway control and hemodynamic precision of GA.[9] Although unplanned conversions carry risk of hemodynamic instability, GA alone in abnormal placentation also increases hypotension and vasopressor requirement.[5]

Adequate vascular access and invasive hemodynamic monitoring are essential to mitigate hemorrhage-related instability and support rapid transfusion.[10] Bladder invasion increases the risk for massive hemorrhage and reconstructive surgery, underscoring the need for blood availability and readiness to activate massive transfusion protocols.[7,9] In this case, pre-incision colloid co-loading and tranexamic acid were implemented. Blood loss was managed with targeted packed red cell transfusion.

Surgical management prioritized hemorrhage control via hysterectomy and restoration of urinary tract integrity through cystorrhaphy, ureteral anastomosis, and stent placement. Hemodynamic management during hemorrhage is crucial. Norepinephrine was titrated to maintain MAP >65 mmHg, and tranexamic acid served as part of multimodal hemorrhage control.[9] Continuous invasive monitoring and readiness for transfusion reduce the severity and duration of hypotension, helping prevent organ injury.[13] Intraoperatively, blood pressure was maintained with vasopressor support.

Postoperative intensive care facilitates early recognition and management of residual hemorrhage, anemia, fluid imbalance, or organ dysfunction.[10] Multimodal analgesia—morphine–ketamine infusion and paracetamol—offered adequate pain control while minimizing respiratory depression, reducing risk of pulmonary and infectious complications.[12,13] No postoperative infection or hemodynamic instability occurred.

Despite favorable outcome, opportunities for improvement include optimizing preoperative anemia, enhancing MRI access, strengthening massive transfusion readiness, and improving multidisciplinary preparedness. Preoperative anemia limited physiologic reserve; when feasible, optimizing hematologic status may reduce transfusion needs. Blood product availability and blood bank responsiveness remain important system-level determinants. Earlier access to MRI could refine preoperative mapping of placental invasion and improve urologic planning. Variability in outcomes among similar cases often reflects differences in institutional preparedness and multidisciplinary coordination. While uterine artery embolization or conservative measures may be considered in selected scenarios, bladder invasion with extensive PAS typically requires hysterectomy and urogenital reconstruction.[13,14]

This case illustrates that early recognition of PAS, structured anesthetic planning, and coordinated multidisciplinary care are essential for optimizing outcomes in placenta previa complicated by bladder rupture. A staged neuraxial-to-general anesthesia approach offers significant benefit in complex PAS requiring extensive urologic reconstruction.

Acknowledgement

Nil.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of Interest

The authors report no conflict of interest.

Data Availability Statement

De-identified patient data from this case report will be made available upon reasonable request to the corresponding author following publication, subject to institutional data-sharing policies and ethics approval.

Author's Contributions

All authors contributed significantly to the conception and design of the study, data collection, analysis, and interpretation of the results. All authors participated in writing and critically revising the manuscript for important intellectual content, approved the final version to be published, and are accountable for all aspects of the research.

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