

ARTIGO ORIGINAL / ORIGINAL ARTICLE

Comparison of Opioid-Free and Opioid-Based Anesthesia for Postoperative Analgesia in Laparoscopic Urological Surgery: A Randomized Controlled Trial

Comparação entre Anestesia Sem Opioides e Anestesia com Opioides na Analgesia Pós-Operatória em Cirurgia Urológica Laparoscópica: Ensaio Clínico Randomizado

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Afiliações

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Keywords

Analgesics, Opioid; Dexmedetomidine; Laparoscopy; Pain Management; Postoperative Nausea and Vomiting; Postoperative Pain; Urologic Surgical Procedures.

Palavras-chave

Analgésicos Opioides; Dexmedetomidina; Dor Pós-Operatória; Gestão da Dor; Laparoscopia; Náusea e Vômito Pós-Operatórios; Procedimentos Cirúrgicos Urológicos.

ABSTRACT

Introduction: Opioid-free anesthesia (OFA) aims to reduce opioid-related adverse effects and enhance recovery. This study compared opioid-free versus opioid-based anesthesia for postoperative analgesia in elective laparoscopic urological surgery.

Methods: In this randomized controlled trial, 70 adult patients scheduled for elective laparoscopic urological procedures were assigned to either an opioid-free (OF) or an opioid-based (OB) anesthesia group. The OF group received dexmedetomidine (loading dose 1 µg/kg over 10 minutes, maintenance 0.5 µg/kg/h), while the OB group received fentanyl at equivalent dosing. The primary outcome was the Visual Analog Scale at Rest (VAS-R) 1 hour after surgery. Secondary outcomes included VAS-R and VAS during coughing (VAS-C) at 0, 1, 2, 4, 6, 24 h; rescue analgesia; total 24-h tramadol use; and adverse events.

Results: VAS-R at 1 hour was significantly lower in the OF group (mean difference -0.94 [1.21], $p < 0.005$). Fewer OFA patients required rescue tramadol (28.6% vs 77.1%, $p < 0.001$). Postoperative nausea and vomiting (PONV) occurred less frequently in the OF group (0% vs 14.3%, $p < 0.05$). No serious adverse events occurred.

Conclusion: Dexmedetomidine-based OFA improved early postoperative analgesia, reduced opioid consumption, and lowered PONV rates compared with fentanyl anesthesia. OFA appears to be safe and consistent with enhanced recovery after surgery (ERAS) recommendations.

RESUMO

Introdução: A anestesia sem opioides (ASO) tem como objetivo reduzir os efeitos adversos associados aos opioides e melhorar a recuperação. Este estudo comparou a anestesia sem opioides com a anestesia baseada em opioides na analgesia pós-operatória em cirurgia urológica laparoscópica eletiva.

Métodos: Neste ensaio clínico randomizado, 70 doentes adultos submetidos a procedimentos urológicos laparoscópicos eletivos foram distribuídos para um grupo de anestesia sem opioides (SO) ou um grupo com opioides (CO). O grupo SO recebeu dexmedetomidina (dose de carga de 1 µg/kg durante 10 minutos, seguida de manutenção de 0,5 µg/kg/h), enquanto o grupo CO recebeu fentanil em doses equivalentes. O desfecho primário foi a Escala Visual Analógica em Repouso (VAS-R) 1 hora após a cirurgia. Os desfechos secundários incluíram VAS-R e VAS durante a tosse (VAS-C) aos 0, 1, 2, 4, 6 e 24 horas; necessidade de analgesia de resgate; consumo total de tramadol nas primeiras 24 horas; e eventos adversos.

Resultados: A VAS-R à 1 hora foi significativamente inferior no grupo SO (diferença média -0,94 [1,21]; $p < 0,005$). Um menor número de doentes no grupo SO necessitou de tramadol de resgate (28,6% vs 77,1%, $p < 0,001$). Náuseas e vômitos pós-operatórios (NVPO) ocorreram com menor frequência no grupo SO (0% vs 14,3%, $p < 0,05$). Não se registaram eventos adversos graves.

Conclusão: A ASO baseada em dexmedetomidina melhorou a analgesia pós-operatória precoce, reduziu o consumo de opioides e diminuiu a incidência de NVPO em comparação com a anestesia com fentanil. A ASO parece ser segura e consistente com as recomendações de recuperação otimizada após cirurgia (ERAS).

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INTRODUCTION

Minimally invasive laparoscopic urological surgery offers advantages in terms of reduced pain and faster recovery. However, pneumoperitoneum and Trendelenburg positioning can affect respiratory mechanics and anesthesia requirements.¹ Enhanced recovery after surgery (ERAS) guidelines emphasize minimizing perioperative opioid exposure due to risks of nausea, vomiting, ileus, and delayed recovery.² Opioid-free anesthesia (OFA), commonly employing dexmedetomidine, may improve pain control and reduce opioid-related complications, but evidence in laparoscopic urology is limited. This randomized controlled trial compared dexmedetomidine-based OFA versus fentanyl-based anesthesia on postoperative pain and opioid requirements.

MATERIAL AND METHODS

Study Design

Prospective, randomized, parallel-group, single-center controlled trial conducted at Safdarjung Hospital, New Delhi (June 2023–December 2024).

Ethics and Registration

The Institutional Ethics Committee approved the study (IEC/VMMC/SJH/Thesis/2023-03/CC-58). Written informed consent was obtained. The trial was prospectively registered with the Clinical Trials Registry of India (CTRI/2023/05/052926). Full protocol is available upon request from the corresponding author.

Participants

Inclusion Criteria

- Adults aged 18–65 years
- American Society of Anesthesiologists (ASA) physical status I–II
- Undergoing elective laparoscopic urological surgery

Exclusion Criteria

- Chronic opioid therapy
- Contraindications to transversus abdominis plane (TAP) block
- Cognitive inability to use the Visual Analog Scale (VAS)
- Known dexmedetomidine or fentanyl allergy

Randomization and Allocation Concealment

Sequence Generation

Computer-generated block randomization (block size = 10) with a 1:1 allocation ratio.

Allocation Concealment

Sequentially numbered, opaque, sealed envelopes prepared by an independent statistician.

Implementation

- Sequence generated by an independent statistician.
- Enrollment performed by the investigator.
- Non-investigating anesthesiologist opened the envelope immediately before induction and administered the assigned intervention.

Blinding

- Participants: Blinded
- Surgeons: Blinded
- Postoperative assessors: Blinded
- Anesthesiologist: Not blinded due to nature of interventions.

Drugs were prepared in identical syringes by a separate anesthesiologist not involved in intraoperative care.

Interventions

Opioid-Free Anesthesia (OF) Group

- Dexmedetomidine 1 µg/kg IV over 10 min
- Continuous infusion 0.5 µg/kg/h until port closure

Opioid-Based Anesthesia (OB) Group

- Fentanyl 1 µg/kg IV over 10 min
- Infusion 0.5 µg/kg/h until port closure

Standardized Anesthesia (Both Groups)

- Induction: propofol 2 mg/kg, vecuronium 0.1 mg/kg
- Maintenance: isoflurane 0.7–1 MAC with oxygen/air 50%
- Bilateral ultrasound-guided TAP block: 15 mL of 0.25% bupivacaine each side
- Ventilation: tidal volume 6–8 mL/kg; end-tidal CO₂ 35–45 mmHg
- Reversal: neostigmine 0.05 mg/kg with glycopyrrolate 0.01 mg/kg

Outcomes

Primary Outcome

- VAS at rest (VAS-R) 1 hour postoperatively.

Secondary Outcomes

- VAS-R and VAS during coughing (VAS-C) at 0, 1, 2, 4, 6, 24 hours
- Time to first rescue analgesic
- Total tramadol consumption in 24 hours
- Adverse events: postoperative nausea and vomiting (PONV), sedation, desaturation, bradycardia, hypotension

All outcomes were pre-specified.

Sample Size

Sample size calculation was based on VAS differences reported by Toleska *et al*³ (mean difference 1.86, standard deviation 2.2). Assuming $\alpha = 0.05$, power = 80%, and 10% attrition, a total of 70 patients (35 per group) was required.

Statistical Analysis

- Normality: Kolmogorov–Smirnov test
- Continuous variables: Student t-test or Mann–Whitney U as appropriate
- Categorical variables: Chi-square or Fisher's exact test
- Effect sizes: mean differences with 95% confidence intervals (CI) and risk ratios with CI
- *p*-value <0.05 considered significant

No missing data occurred; therefore, a complete-case analysis was performed.

RESULTS

Participant Flow Diagram (Fig. 1).

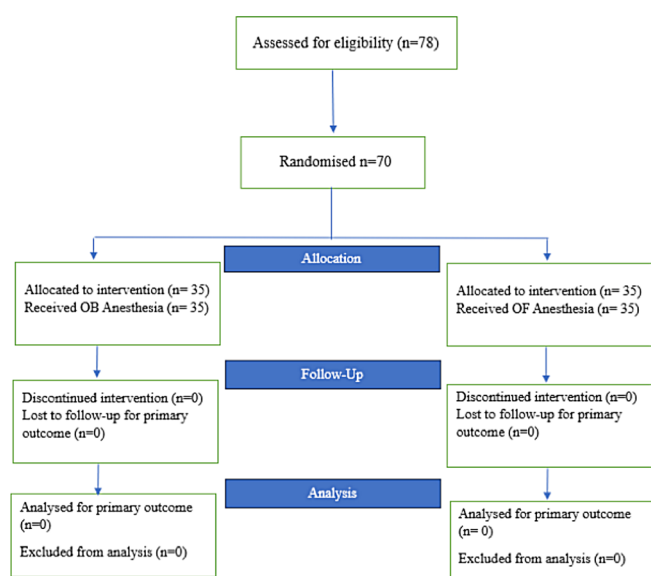


Figure 1. Participant Flow Diagram.

Participant Flow (Fig. 1)

A total of 78 patients were assessed for eligibility. Eight patients were excluded (4 declined to participate, 2 were receiving chronic opioid therapy, and 2 had cognitive limitations preventing VAS assessment).

Seventy patients were randomized in a 1:1 ratio.

- Opioid-free (OF) group: **35 allocated** and included in the final analysis
- Opioid-based (OB) group: **35 allocated** and included in the final analysis

No patients were lost to follow-up or excluded after randomization.

All randomized patients (n = 70) were analyzed.

Baseline Characteristics

Groups were comparable for demographic and clinical variables.

Table 1. Baseline Characteristics.

Variable	OF Group (n = 35)	OB Group (n = 35)	p-value
Age (years), Mean ± SD	38.4 ± 13.5	39.1 ± 12.9	0.82
Sex, n (%)			0.621
Male	23 (65.7%)	21 (60.0%)	
Female	12 (34.3%)	14 (40.0%)	
Weight (kg), Mean ± SD	62.5 ± 4.8	61.9 ± 5.0	0.67
ASA Grade, n (%)			0.122
I	27 (77.1%)	21 (60.0%)	
II	8 (22.9%)	14 (40.0%)	

Primary Outcome

- VAS-R at 1 hour was significantly lower in the OF group:
 - Mean difference: 0.20 ± 0.41
 - $p < 0.005$ (Table 2, Fig. 2)

Table 2. VAS-R and VAS-C scores.

Time (h)	VAS-R (Mean ± SD)		VAS-C (Mean ± SD)	
	OF	OB	OF	OB
0*	0.03 ± 0.17	1.17 ± 1.04	0.20 ± 0.41	2.03 ± 1.46
1*	0.94 ± 1.21	1.66 ± 1.24	1.31 ± 1.51	2.37 ± 1.86
2	0.80 ± 1.02	0.80 ± 0.63	1.20 ± 1.47	1.20 ± 0.80
4	0.77 ± 1.06	1.11 ± 1.28	1.46 ± 1.62	1.66 ± 1.55
6	1.11 ± 0.99	2.03 ± 1.92	1.69 ± 1.35	3.06 ± 2.70
24*	1.00 ± 0.94	1.60 ± 1.35	1.66 ± 1.30	2.60 ± 1.87

OF: opioid-free anesthesia; OB: opioid-based anesthesia.

Secondary Outcomes

• Pain Scores

OF significantly reduced early VAS-R and VAS-C (0 and 1 h). At 24 hours, VAS-C remained lower ($p = 0.031$).

• Rescue Analgesia

- OF: 10/35 (28.6%)
- OB: 27/35 (77.1%)
- $p < 0.001$

• Total Tramadol Consumption

Significantly lower in OF at 6 h ($p < 0.001$) and 24h ($p = 0.013$), Table 3, Fig. 3.

Table 3. Analgesic Requirements and Adverse Events.

Parameter	OF Group (n = 35)	OB Group (n = 35)	Statistical Test	p-value
Rescue Analgesia Required, n (%)	10 (28.6%)	27 (77.1%)	$\chi^2 = 16.57$	<0.001
Rescue Analgesia Not Required, n (%)	25 (71.4%)	8 (22.9%)		
Analgesic Use by Time Interval, n (%)				
0 h (Tramadol use)	0 (0.0%)	5 (14.3%)	$\chi^2 = 3.45$	0.054
6 h (Tramadol/PCM)	1 (2.9%) / 11 (31.4%)	13 (37.1%) / 4 (11.4%)	$\chi^2 = 10.80$	<0.001
24 h (Tramadol/PCM)	1 (2.9%) / 9 (25.7%)	9 (25.7%) / 18 (51.4%)	$\chi^2 = 5.72$	0.013
Adverse Events (0 h)				
Nausea, n (%)	0 (0.0%)	4 (11.4%)	Fisher's Exact	0.002
Vomiting, n (%)	0 (0.0%)	5 (14.3%)	Fisher's Exact	0.002
No Adverse Event, n (%)	35 (100%)	26 (74.3%)		

OF: opioid-free anesthesia; OB: opioid-based anesthesia; PCM: paracetamol; VAS-R: Visual Analog Scale at rest; VAS-C: Visual Analog Scale during coughing..

Harms (CONSORT Harms Reporting)

- PONV: 0% vs 14.3% ($p = 0.002$)
- No desaturation or serious adverse events
- Sedation was mild and similar across groups
- No patient withdrawals for adverse events

DISCUSSION

In this randomized controlled trial, dexmedetomidine-based OFA was associated with significantly improved early post-operative pain control, reduced tramadol consumption, and

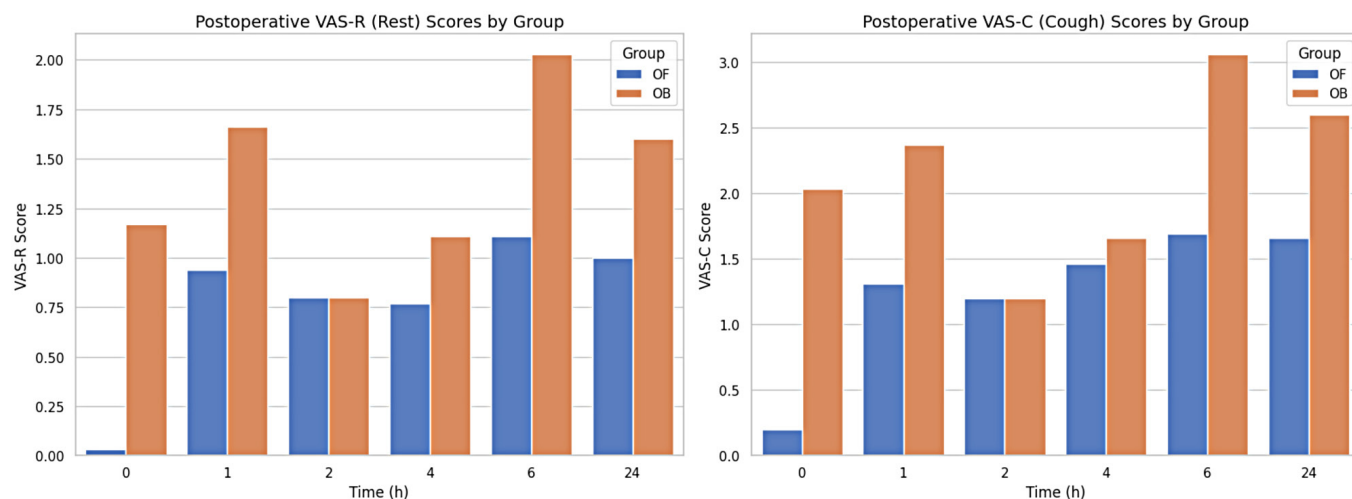


Figure 2. Postoperative Pain Scores (VAS-R and VAS-C).

Mean postoperative visual analog scale for rest & cough (VAS-R, VAS-C) scores at various time points in the OF and OB groups. The graph presents the mean VAS-R & VAS-C scores (with standard error bars) recorded at 0, 1, 2, 4, 6, and 24 h after surgery. OF: Opioid-free group; OB: Opioid-based group.

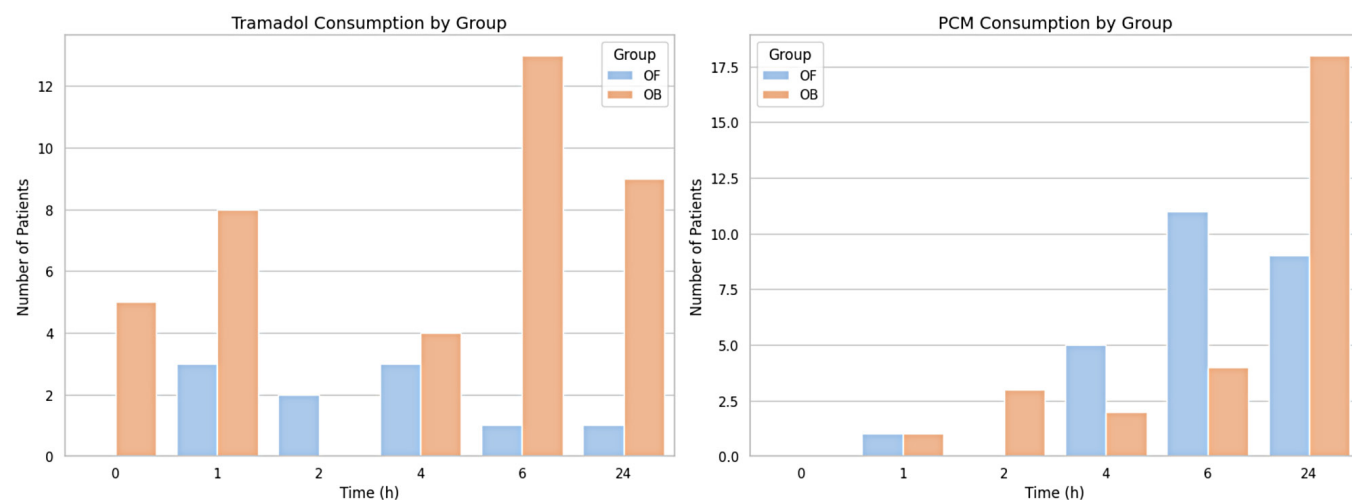


Figure 3. Postoperative Analgesic Requirement.

Postoperative tramadol & PCM requirements in the OF and OB groups at various time points. The bar graph shows the number and percentage of patients requiring tramadol & PCM at 0, 1, 2, 4, 6, and 24 h postoperatively in each group. Groups OF (blue bars) and OB (orange bars) indicate different treatment regimens. OF: Opioid-free group; OB: Opioid-based group.

a lower incidence of PONV in patients undergoing laparoscopic urological surgery. These findings are consistent with previous studies by Koo *et al.*⁴ Olausson *et al.*⁵ and Chen *et al.*⁶ which demonstrated the benefits of opioid-sparing anesthetic techniques. Furthermore, the observed reduction in opioid requirements is in accordance with ERAS recommendations, which advocate minimizing perioperative opioid use to improve recovery outcomes.

This study has several strengths. It employed a randomized, assessor-blinded design, which reduces the risk of bias. In addition, anesthesia and analgesia protocols were standardized across both groups, enhancing internal validity. Complete follow-up was achieved, with no missing outcome data, thereby strengthening the reliability of the findings.

However, some limitations should be acknowledged. The study was conducted at a single centre, which may limit the generalizability of the results. The sample size was moderate and may not have been sufficient to detect less frequent

adverse events. Additionally, long-term outcomes, such as chronic postoperative pain, were not evaluated. Finally, blinding of the anesthesiologist was not feasible due to the nature of the interventions, which may have introduced performance bias.

The findings of this study are applicable to adult patients with ASA physical status I–II undergoing elective laparoscopic urological surgery, particularly in centres equipped with ultrasound-guided regional anesthesia and standard intraoperative monitoring.

CONCLUSION

Dexmedetomidine-based opioid-free anesthesia significantly improves postoperative pain outcomes and reduces opioid requirements while minimizing PONV. OFA represents a safe, effective, and ERAS-consistent anesthetic strategy for laparoscopic urology.

PROTOCOL AVAILABILITY

Full protocol available from the corresponding author upon reasonable request.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

SP: Writing - original draft, Writing - review & editing, Conceptualization, Data curation: Formal analysis, Methodology, Project administration, Funding acquisition, Visualization, Investigation, Resources.

SA: Writing - original draft, Writing - review & editing, Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Visualization, Resources.

TY: Writing - review & editing, Formal analysis, Project administration, Visualization, Resources.

All authors approved the final version to be published.

SP: Redação – rascunho original, Redação – revisão e edição, Conceitualização, Organização dos dados, Análise formal, Metodologia, Gestão do projeto, Obtenção de financiamento, Visualização, Investigação, Recursos.

SA: Redação - rascunho original, Redação - revisão e edição, Conceitualização, Curadoria de dados, Análise formal, Metodologia, Administração do projeto, Visualização, Recursos.

TY: Redação - revisão e edição, Análise formal, Administração do projeto, Visualização, Recursos.

Todos os autores aprovaram a versão final a ser publicada.

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2024 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

Ethical Disclosures

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2024).

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

Submissão: 8 de janeiro, 2026 | Received: 8th of January, 2026

Aceitação: 29 de março, 2026 | Accepted: 29th of March, 2026

Publicado: 1 de abril, 2026 | Published: 1st of April, 2026

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