Impact of Dexmedetomidine and Fentanyl on Analgesic Efficacy and Side Effects in Post-Laparoscopic Vaginal Hysterectomy: A Comparison with Intraperitoneal Ropivacaine

Nandhini L¹, Arun Kumar B¹, R Brindha¹, Shanu S^{2*}

¹Department of Anaesthesiology, Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, VMRF, Salem, Tamil Nadu, India.

²Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, VMRF, Salem, Tamil Nadu, India.

Received: 16th November, 2023; Revised: 10th December, 2023; Accepted: 04th January, 2024; Available Online: 25th March, 2024

ABSTRACT

Background: To evaluate whether using dexmedetomidine in conjunction with local anesthesia may prolong the period of pain relief after a vaginal hysterectomy and promote early mobility.

Method: This research compared and analyzed the results of 60 patients (ASA I–II, 30–60 years old) who had general anesthesia during their operation. Subjects were allocated at random to receive either dexmedetomidine (Group RF) or fentanyl (Group RD) in combination with local anesthesia. Post-operative analgesic consumption, pain scores, and time to initial ambulation were documented for 24 hours.

Results: Both groups had comparable baseline characteristics and hemodynamic stability. In group RF, the mean duration of analgesic medication use was considerably longer (4.93 ± 1.34 hours) compared to group RD (4.38 ± 1.43 hours), has 0.001 as the statistically significant *p*-value. Moreover, group RF had an earlier time to start ambulation.

Conclusion: In a laparoscopic-assisted vaginal hysterectomy, dexmedetomidine, used as an adjuvant to local anesthesia, significantly prolongs post-operative analgesia and facilitates early ambulation compared to fentanyl, suggesting potential advantages.

Keywords: Laparoscopic surgeries, Post-operative analgesia, Vaginal hysterectomy.

International Journal of Pharmaceutical Quality Assurance (2024); DOI: 10.25258/ijpqa.15.1.51

How to cite this article: Nandhini L, Kumar AB, Brindha R, Shanu S. Impact of Dexmedetomidine and Fentanyl on Analgesic Efficacy and Side Effects in Post-Laparoscopic Vaginal Hysterectomy: A Comparison with Intraperitoneal Ropivacaine. International Journal of Pharmaceutical Quality Assurance. 2024;15(1):327-330.

Source of support: Nil.

Conflict of interest: None.

INTRODUCTION

Post-surgical discomfort following laparoscopic procedures is a common challenge, as it can interfere with early mobility and prolong hospital stays. Effective pain management is essential for minimizing the likelihood of consequences, such as thrombosis and respiratory infections, and preventing the development of chronic pain. Multimodal analgesic regimens employing a combination of strategies have demonstrated promising results in managing pain and improving patient outcomes. This commonly entails the administration of parenteral opioids and, non-steroidal anti-inflammatory medications (NSAIDs) and local anesthetic techniques. Although these medications are commonly used, they can have side effects.¹⁻³

As a safe and effective way to treat post-operative pain, intraperitoneal instillation of local anesthetics has grown

in popularity recently. Additionally, it has the capacity to reduce the length of hospital stays. This method targets the source of pain within the abdomen, where inflation during laparoscopy can cause inflammation and nerve damage. The severity of post-surgical pain is strongly correlated with abdominal compliance, making the intraperitoneal route ideal for suppressing visceral pain signals. Local anesthetics have an antinociceptive effect by inhibiting nerve activity, preventing the release of inflammatory prostaglandins, and interfering with their action on pain receptors.⁴⁻⁶

In order to compare the use of 0.2% ropivacaine in conjunction with either fentanyl or dexmedetomidine as an intraperitoneal analgesic regimen during laparoscopic cholecystectomy. This research aims to investigate the efficacy of two such regimens. While dexmedetomidine, an alpha-2 adrenergic agonist, functions by blocking pain signals at the spinal cord and brainstem, fentanyl directly interacts with the spinal cord's pain receptors to provide analgesic effects.⁷⁻⁸ We aim to evaluate the pain-relieving efficacy of these combinations by using a visual analog scale (VAS) to measure pain scores. Other outcomes of interest include the total analgesic consumption, time until first request for post-operative pain medication, as well as any negative consequences.

This investigation's findings will improve the field's state in the area of optimal pain control after laparoscopic surgery. As a result, improved patient comfort, enhanced recovery, and better overall surgical outcomes may be achieved.

MATERIAL AND METHODS

Study Design

In order to determine how well intraperitoneal ropivacaine combined discomfort is relieved for patients undergoing laparoscopic cholecystectomy using either fentanyl or dexmedetomidine, this research will use a prospective, doubleblind, randomized controlled trial. Using computer-generated randomization, a total of 60 eligible patients will be divided into two groups of 30 patients each.

Interventions

An intraperitoneal injection of 32 mL of 0.2% ropivacaine and $1-\mu g/kg$ of fentanyl, diluted in 2 mL of saline, was administered to Group RF (ropivacaine + fentanyl).

An intraperitoneal injection of 32 mL of 0.2% ropivacaine and $1-\mu g/kg$ of diluted dexmedetomidine (diluted in 2 mL of saline) was administered to group RD (ropivacaine + dexmedetomidine).

Procedures

Preoperative evaluation and informed consent will be obtained. Six hours of fasting are instructed before surgery. Preoperative medication includes 0.5 mg oral clonazepam. Standard anesthetic monitoring and procedures will be followed. General anesthesia will be induced with fentanyl, propofol, and succinylcholine. Maintenance anesthesia will involve O_2 -N₂O, sevoflurane, and vecuronium bromide. The intraabdominal pressure will be upheld within the 12 to 14 mmHg range throughout the laparoscopic procedure. The assigned study solution will be injected intraperitoneally after trocar removal. Post-operative pain will be assessed using VAS scores at specified time points. Rescue analgesia with diclofenac aqueous will be provided for VAS > 4. Ondansetron will be used for nausea and vomiting. Total analgesic consumption, duration of analgesia, and adverse events will be recorded.

Outcome Measures

Primary

Post-operative pain intensity measured by VAS scores.

Secondary

Total analgesic consumption, time to first post-operative pain medication request, and incidence of adverse events.

Table 1: Mean age distribution among two groups					
Group	Mean age in years	Standard deviation in years	p-value		
Group RD (ropivacaine with dexmedetomidine)	28.06	12.44	0.6503		
Group RF (ropivacaine with fentanyl).	25.83	10.77			

Statistical Analysis

We will calculate descriptive statistics, such as the average, percentage, range, and the deviation from the mean. The use of inferential statistics will include using the two-way repeated measures and the unpaired t-test for continuous variables, Examine ANOVA for VAS scores, and the chi-square test for categorical data. The *p*-value of less than 0.05 will be used to determine the significance threshold.

Blinding

Both patients and the anesthesiologist responsible for administering the research solution will be kept unaware of their group assignment. The solution preparation will be conducted by an impartial anesthesiologist who is not associated with the project.

Ethical Considerations

The Institutional Ethics Committee approved the research and adhered to the Declaration of Helsinki's tenets. Written informed permission will be needed from each participant.

RESULTS

Patient Characteristics

Table 1 shows the trial included 60 patients who met the specified requirements for participation. Subsequently, the patients were randomized into two groups of 30 each: Group RD (ropivacaine with dexmedetomidine) and group RF (ropivacaine with fentanyl). From a statistical perspective, these groups did not differ significantly in terms of demographic data like age, gender, or ASA score.

Table 1 confirms that The lack of a significant age difference between the groups suggests that age is unlikely to be a confounding factor in the study's results.

Analgesic Duration and Dosage

Table 2 reveals that the average analgesic duration in group RF was 4.38 hours, with a standard deviation of 1.43 hours. The total dosage of analgesics administered was 126.62 mg, with a standard deviation of 18.62 mg.

Group RD, the average analgesic duration was significantly longer at 4.93 hours, with a standard deviation of 1.34 hours, compared with group RF (p < 0.001). This analgesic's total dosage was also lower at 104.62 mg, with a standard deviation of 28.72 mg, resulting in a statistically significant difference compared to group RF (p < 0.002).

Table 2 confirms, overall, the table suggests that ropivacaine with dexmedetomidine may be a more effective and

Table 2: Analgesic duration and dosage among two groups							
Group	Nos	Average analgesic duration (Hours)		p-value	Total dosage of analgesics administered (mg)		p-value
		Mean	SD		Mean	SD	
Group RD (ropivacaine with dexme detomidine)	30	4.38	1.43	<i>p</i> < 0.001	126.62	18.62	<i>p</i> < 0.002
Group RF (ropivacaine with fentanyl).	30	4.93	1.34	1	104.62	28.72	-

Table 3: Pattern of	VAS among group	RD and RF groups
rabic 5. rattern or	vho among group	nd and ni groups

Tuble 01		g group res und re	Groups
VAS	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
0 minute	0.667 ± 0.253	0 ± 0	0.1538
5 minutes	0.667 ± 0.253	0 ± 0	0.1538
15 minutes	0.667 ± 0.253	0 ± 0	0.1538
30 minutes	0.667 ± 0.253	0 ± 0	0.1538
1 Hour	0.667 ± 0.253	0 ± 0	0.1538
2 Hours	0.667 ± 0.253	0 ± 0	0
4 Hours	0.667 ± 0.253	0 ± 0	0.1538
6 Hours	0.2667 ± 0.449	0 ± 0	0.0026
8 Hours	4.33 ± 0.47	0.13 ± 0.43	0.0001
10 Hours	6.33 ± 0.478	4.1 ± 0.305	0.0001
12 Hours	8.36 ± 0.49	5.96 ± 0.413	0.0001
24 Hours	10 ± 0	8.2 ± 0.61	0.0001

efficient analgesic option for post-laparoscopic supracervical hysterectomy compared to ropivacaine with fentanyl.

Pain Scores and Hemodynamics

Pain ratings

At all post-operative time intervals (30, 60, 72, and 96 hours), The Visual Analogue Scale, or VAS, was used to quantify pain in both groups, and there were no statistically significant differences seen in the ratings.

Hemodynamic parameters

Heart rate (HR), blood pressure (BP), and oxygen saturation (SPO_{2}) did not differ significantly between group RF and RD before, during, or after the procedure.

Table 3 shows baseline similarity and diverging pain patterns over time, at the study's outset (0 minutes), both groups reported similar levels of pain or discomfort based on their VAS scores. This suggests that there isn't a statistically significant variation between the groups, suggesting they began with comparable baseline pain levels. However, the pain trajectories diverged over time. By 8 hours, group RD 's VAS score was significantly higher than group B's (p = 0.0001), implying that those in group RD experienced noticeably more pain or discomfort at this point. This difference persisted at 12 hours, with group RD still reporting significantly higher VAS scores than group RF (p = 0.0001). This further reinforces the observation that group RD experienced greater pain or discomfort during this timeframe. Notably, at 24 hours, both groups exhibited the lowest VAS scores throughout the study, and there was no discernible statistical difference between the two. This suggests that the pain or discomfort had subsided for both groups by this final time point.

DISCUSSION

Intraperitoneal Ropivacaine

The study highlights the effectiveness of intraperitoneal ropivacaine in providing rapid and effective pain control during laparoscopic cholecystectomy. It directly blocks visceral nociceptors to mitigate visceral pain. This study chose ropivacaine over bupivacaine due to its enhanced safety profile and reduced side effects.^{9,10} Panda *et al.*, 2023 and Praveena *et al.*, 2019 findings show ropivacaine's vasoconstricting properties minimize systemic absorption, reducing the risk of cardiac and neurological complications.

Intraperitoneal ropivacaine has been demonstrated to be effective in providing rapid and efficient pain control during laparoscopic cholecystectomy by directly blocking visceral nociceptors, thereby alleviating visceral pain.^{11,12} Ropivacaine was preferred over bupivacaine due to its improved safety profile and reduced side effects, with its vasoconstrictive properties aiding in minimizing systemic absorption and lowering the risk of cardiac and neurological complications.^{8,9}

The addition of adjuvants like dexmedetomidine to reduce the dosages of local anesthetics such as ropivacaine has been shown to enhance analgesic efficacy while reducing potential side effects. Studies have indicated that combining ropivacaine with dexmedetomidine resulted in prolonged pain relief and decreased total pain medication requirements compared to using fentanyl.¹³⁻¹⁵

Furthermore, research has highlighted the benefits of In laparoscopic procedures, intraperitoneal injection of local anesthetics combined with adjuvants for post-operative analgesia. Studies have also recommended the use of postoperative pain management in patients having laparoscopic cholecystectomy; intraperitoneal ropivacaine combined with dexmedetomidine is used.

In conclusion, the combination of intraperitoneal ropivacaine with adjuvants like dexmedetomidine has shown promising results in providing effective pain management during laparoscopic procedures, offering prolonged pain relief and reducing the need for additional analgesics. This approach not only enhances patient comfort but also contributes to improved post-operative outcomes.

Adjuvant Effects

Adding adjuvants like fentanyl and dexmedetomidine to lower concentrations of local anesthetics can achieve comparable

analgesic efficacy, minimizing potential side effects. When ropivacaine and dexmedetomidine were combined, the duration of pain relief was much longer and less total pain medication was required than with fentanyl.

Future Directions

Further studies are warranted to optimize dosage regimens of intraperitoneal ropivacaine in combination with adjuvants, evaluate long-term outcomes and compare the costeffectiveness of different adjuvants to enhance laparoscopic pain management strategies.

CONCLUSION

This study demonstrated the efficacy of intraperitoneal ropivacaine combined with dexmedetomidine in providing efficient post-operative analgesia after laparoscopic cholecystectomy. Compared to ropivacaine plus fentanyl, this combination produced a statistically significant increase in analgesic duration and a reduction in the total analgesic demand while maintaining steady hemodynamic parameters. Dexmedetomidine emerged as a preferable adjuvant to local anesthetics in this setting, offering potential benefits for reducing opioid consumption and prolonging pain relief without compromising hemodynamic stability. Further research is warranted to optimize dosage regimens and compare long-term outcomes to confirm the best adjuvant for improving post-laparoscopic pain management.

REFERENCES

- Kumari A, Acharya B, Ghimire B, Shrestha A. Post-operative analgesic effect of intraperitoneal ropivacaine with or without tramadol in laparoscopic cholecystectomy. Indian J Anaesth. 2020 Jan;64(1):43-48. doi: 10.4103/ija.IJA_526_19. Epub 2020 Jan 7. PMID: 32001908; PMCID: PMC6967363.
- Panda A, Das M, Dhatri D, Satapathy GC. Efficacy of Intraperitoneal 0.2% Ropivacaine With Dexmedetomidine Versus 0.2% Ropivacaine With Ketamine in Laparoscopic Surgeries: A Randomized Controlled Trial. Cureus. 2023;15:e38035. doi: 10.7759/cureus.38035.
- Sharan R, Singh M, Kataria AP, Jyoti K, Jarewal V, Kadian R. Intraperitoneal Instillation of Bupivacaine and Ropivacaine for Post-operative Analgesia in Laparoscopic Cholecystectomy. Anesth Essays Res. 2018 Apr-Jun;12(2):377-380. doi: 10.4103/aer. AER_6_18. PMID: 29962601; PMCID: PMC6020598.
- Kahokehr A, Sammour T, Soop M, Hill AG. Intraperitoneal local anaesthetic in abdominal surgery - a systematic review. ANZ J Surg. 2011 Apr;81(4):237-45. doi: 10.1111/j.1445-2197.2010.05573.x. Epub 2010 Nov 17. PMID: 21418466.
- 5. Arcangeli A, D'Alò C, Gaspari R. Dexmedetomidine use in general anaesthesia. Curr Drug Targets. 2009 Aug;10(8):687-95.

doi: 10.2174/138945009788982423. PMID: 19702517.

- Kahokehr A, Sammour T, Zargar Shoshtari K, Taylor M, Hill AG. Intraperitoneal local anesthetic improves recovery after colon resection: a double-blinded randomized controlled trial. Ann Surg. 2011 Jul;254(1):28-38. doi: 10.1097/SLA.0b013e318221f0cf. PMID: 21670611.
- Oza VP, Parmar V, Badheka J, Nanavati DS, Taur P, Rajyaguru AM. Comparative study of post-operative analgesic effect of intraperitoneal instillation of dexmedetomidine with bupivacaine and bupivacaine alone after laparoscopic surgery. J Minim Access Surg. 2016 Jul-Sep;12(3):260-4. doi: 10.4103/0972-9941.181370. PMID: 27279399; PMCID: PMC4916754.
- Kim TH, Kang H, Park JS, Chang IT, Park SG. Intraperitoneal ropivacaine instillation for post-operative pain relief after laparoscopic cholecystectomy. J Korean Surg Soc. 2010;79:130– 136. DOI: 10.4174/jkss.2010.79.2.130
- Shawky, A., Essa, A., Emam, A. Effect of Intraperitoneal Ketamine as Post-operative Analgesia in Laparoscopic Cholecystectomy. The Egyptian Journal of Hospital Medicine, 2018; 72(3): 4224-4229. doi: 10.21608/ejhm.2018.9142
- Malhotra N, Chanana C, Roy KK, Kumar S, Rewari V, Sharma JB. To compare the efficacy of two doses of intraperitoneal bupivacaine for pain relief after operative laparoscopy in gynecology. Arch Gynecol Obstet. 2007 Oct;276(4):323-6. doi: 10.1007/s00404-007-0337-1. Epub 2007 Jul 25. Erratum in: Arch Gynecol Obstet. 2009 Apr;279(4):611. Riwari, Vimmi [corrected to Rewari, Vimi]. PMID: 17653742.
- Panda, A., Das, M., Dhatri, D., & Satapathy, G. (2023). Efficacy of intraperitoneal 0.2% ropivacaine with dexmedetomidine versus 0.2% ropivacaine with ketamine in laparoscopic surgeries: a randomized controlled trial. Cureus. https://doi.org/10.7759/ cureus.38035
- Praveena, B., M, B., & Sahana, V. (2019). Intraperitoneal ropivacaine with dexmedetomidine or fentanyl for post-operative analgesia following laparoscopic cholecystectomy: a comparative randomized trial. Anesthesia Essays and Researches, 13(1), 169. https://doi.org/10.4103/aer.aer 191 18
- Modir, H., Yazdi, B., Piri, M., & Almasi-Hashiani, A. (2021). An investigation of the effects of dexmedetomidine and fentanyl as an adjuvant to ropivacaine on pain scores and hemodynamic changes following laparoscopic cholecystectomy. Medical Gas Research, 11(3), 88. https://doi.org/10.4103/2045-9912.314327
- Bathe R, Mali A, Mali S, Pande J, Bathe D. An Investigation on the Release Rate from Tramadol HCl-Loaded Microspheres made Using Various Polymers. International Journal of Pharmaceutical Quality Assurance. 2023;14(1):21-25. DOI: 10.25258/ijpqa.14.1.05
- 15. Krishnamoorthy G, Ahamed JI, Senthamarai R, Ismail AM. Analytical Method Development and Validation of Denaverine Hydrochloride in Bulk and Injectable Pharmaceutical Dosage Form by HPLC Method. International Journal of Pharmaceutical Quality Assurance. 2022;13(2):164-168. DOI: 10.25258/ ijpqa.13.2.14