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OPOID FREE ANESTHETIC MIXTURE VERSUS TRAMADOL FOR PREEMPTIVE ANALGESIA: A OBSERVATIONAL STUDY

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Abstract

Background: Postoperative pain management is a critical component of perioperative care, particularly in abdominal surgeries. Opioid-free anesthesia (OFA) has been proposed as an alternative to traditional opioid-based analgesia to minimize opioid-related side effects while maintaining effective pain control. This study aims to compare the postoperative analgesic efficacy of opioid-free anesthesia using intravenous paracetamol, lignocaine, and magnesium sulfate versus standard opioid anesthesia using intravenous tramadol for preemptive analgesia in patients undergoing elective abdominal surgeries under general anesthesia.

Aim: To compare the postoperative analgesic efficacy of opioid-free anesthesia using intravenous paracetamol (15 mg/kg), lignocaine (2 mg/kg), and magnesium sulfate (20 mg/kg) versus standard opioid anesthesia using intravenous tramadol (2 mg/kg) for preemptive analgesia in patients undergoing elective abdominal surgeries under general anesthesia. The study evaluates pain scores, rescue analgesia requirements, hemodynamic stability, and opioid-related side effects between the two groups.

Methods: A prospective comparative study was conducted on patients undergoing elective abdominal surgeries under general anesthesia. Patients were randomly assigned into two groups:

- Group OFA (Opioid-Free Anesthesia): Received intravenous paracetamol (15 mg/kg), lignocaine (2 mg/kg), and magnesium sulfate (20 mg/kg) in 100 mL normal saline (NS) as preemptive analgesia in the preanesthetic room.
- Group OA (Opioid Anesthesia): Received intravenous tramadol (2 mg/kg) in 100 mL NS as preemptive analgesia in the preanesthetic room.

All patients underwent a preanesthetic checkup one day prior and on the day of surgery as per hospital protocol. Standard ASA fasting guidelines were followed. After completion of the preemptive analgesia infusion, patients were shifted to the operation theater. Standard monitoring was applied, and general anesthesia was induced with intravenous midazolam (0.03 mg/kg), glycopyrrolate (0.2 mg), propofol (2 mg/kg), and atracurium (0.5 mg/kg) to facilitate endotracheal intubation. Anesthesia was maintained with a mixture of oxygen and air with sevoflurane.

Results: Postoperative pain scores (VAS at 1, 3, 6, 12, and 24 hours) were significantly lower in the OFA group compared to the OA group. The need for rescue analgesia was reduced in the OFA group. Hemodynamic stability was better maintained in the OFA group, and opioid-related side effects such as nausea, vomiting, and sedation were significantly lower.
Conclusion: Opioid-free anesthesia using intravenous paracetamol, lignocaine, and magnesium sulfate provides effective postoperative analgesia with reduced opioid-related adverse effects compared to conventional opioid-based anesthesia using intravenous tramadol. The findings suggest that OFA may be a viable alternative for postoperative pain management in abdominal surgeries.

Keywords: Opioid-free anesthesia, postoperative analgesia, preemptive analgesia, intravenous paracetamol, lignocaine, magnesium sulfate, tramadol, abdominal surgeries.

Materials and Methods

A prospective comparative study was conducted on patients undergoing elective abdominal surgeries under general anesthesia. Patients were divided into two groups:
- Group OFA (Opioid-Free Anesthesia): Received intravenous paracetamol (15 mg/kg), lignocaine (2 mg/kg), and magnesium sulfate (20 mg/kg) in 100 mL normal saline (NS).
- Group OA (Opioid Anesthesia): Received intravenous tramadol (2 mg/kg) in 100 mL NS.

Study Population

Patients aged 18 to 65 years with an American Society of Anesthesiologists (ASA) physical status I or II, scheduled for elective abdominal surgery under general anesthesia, were included in the study. Patients with known allergies to study drugs, severe hepatic or renal dysfunction, history of chronic opioid use, psychiatric disorders, or neuromuscular diseases were excluded.

Study Design and Randomization

Patients were randomly allocated into two groups using a computer-generated randomization sequence:

- Group OFA (Opioid-Free Anesthesia): Received intravenous paracetamol (15 mg/kg), lignocaine (2 mg/kg), and magnesium sulfate (20 mg/kg) in 100 mL NS for preemptive analgesia.
- Group OA (Opioid Anesthesia): Received intravenous tramadol (2 mg/kg) in 100 mL NS for preemptive analgesia.

Preoperative Preparation

A preanesthetic checkup was conducted one day prior and on the day of surgery as per hospital protocol. ASA fasting guidelines were followed. Patients were connected to a multi-channel monitor, and preemptive analgesia was administered in the preanesthetic room.

Anesthetic Technique

After the completion of the infusion, patients were transferred to the operation theater. All patients received standard monitoring, including:
- Electrocardiogram (ECG)
- Non-invasive blood pressure (NIBP)
- Pulse oximetry (SpO_2)
- Capnography

Premedication was given as follows:

- Intravenous midazolam (0.03 mg/kg)
- Intravenous glycopyrrolate (0.2 mg)

General anesthesia induction:
- Intravenous propofol (2 mg/kg)
- Intravenous atracurium (0.5 mg/kg) for muscle relaxation and endotracheal intubation

Maintenance of anesthesia:
- A mixture of oxygen and air with sevoflurane

Neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg) at the end of surgery. Extubation was performed once the patient fulfilled the criteria for adequate recovery.

Postoperative Pain Assessment
Pain was assessed using the Visual Analog Scale (VAS) at 1, 3, 6, 12, and 24 hours postoperatively. VAS scores ranged from 0 (no pain) to 10 (worst pain imaginable). Rescue analgesia with intravenous diclofenac (75 mg) was provided if the VAS score exceeded 4.

Outcome Measures
The following parameters were recorded:
1. VAS scores at 1, 3, 6, 12, and 24 hours postoperatively.
2. Requirement for rescue analgesia within 24 hours.
3.Hemodynamic parameters (heart rate, mean arterial pressure, and SpO2) at baseline, intraoperatively, and postoperatively.
4. Incidence of opioid-related side effects (nausea, vomiting, sedation, pruritus).

Statistical Analysis
Data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation and compared using an independent t-test. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. A p-value < 0.05 was considered statistically significant.

Results
A total of 100 patients were enrolled in the study, with 50 patients in each group. Both groups were comparable in terms of demographic characteristics, including age, gender, body mass index (BMI), and ASA physical status. There were no statistically significant differences between the groups in terms of baseline characteristics.

Table 1 presents the demographic data of patients in both groups. The mean age was 42.3 ± 9.6 years in the OFA group and 43.1 ± 10.2 years in the OA group. Gender distribution, BMI, and ASA status were also similar between the groups, ensuring a homogenous study population.

Table 1: Demographic and Clinical Characteristics

Variable	OFA Group (n=50)	OA Group (n=50)	p-value
Age (years)	42.3 ± 9.6	43.1 ± 10.2	0.72
Gender (M/F)	28/22	26/24	0.68
BMI (kg/m²)	26.4 ± 3.5	25.9 ± 3.7	0.55
ASA I/II	29/21	30/20	0.81

Pain scores were assessed using the Visual Analog Scale (VAS) at multiple time points postoperatively. The OFA group exhibited significantly lower VAS scores compared to the OA group at all time points. At 1 hour postoperatively, the mean VAS score was 3.4 ± 1.2 in the OFA group, compared to 5.1 ± 1.5 in the OA group ($p < 0.01$). The difference persisted across all time intervals, as shown in Table 2.

Table 2: Postoperative Pain Scores (VAS)

Time Postop (hours)	OFA Group (Mean ± SD)	OA Group (Mean ± SD)	p-value
1	3.4 ± 1.2	5.1 ± 1.5	<0.01
3	3.8 ± 1.3	5.4 ± 1.7	<0.01
6	4.2 ± 1.4	5.8 ± 1.6	<0.01
12	4.5 ± 1.1	5.9 ± 1.5	<0.01
24	4.1 ± 1.0	5.6 ± 1.3	<0.01

The need for rescue analgesia was significantly lower in the OFA group, with only 17 patients (34%) requiring additional analgesics compared to 35 patients (70%) in the OA group ($p < 0.01$). This indicates that opioid-free anesthesia provided more sustained pain relief.

Table 3: Requirement for Rescue Analgesia

Group	Patients Requiring Rescue Analgesia	p-value
OFA Group	17 (34%)	<0.01
OA Group	35 (70%)	<0.01

Hemodynamic stability was assessed intraoperatively and postoperatively. Both groups demonstrated similar heart rates and mean arterial pressures at baseline. However, patients in the OA group exhibited slightly higher intraoperative blood pressure fluctuations, likely due to opioid-induced sympathetic stimulation.

Table 4: Hemodynamic Parameters

Time	Heart Rate (bpm)	Mean Arterial Pressure (mmHg)
Baseline	78 ± 6 (OFA) / 79 ± 7 (OA)	92 ± 8 (OFA) / 93 ± 9 (OA)
Intraop	80 ± 5 (OFA) / 84 ± 6 (OA)	90 ± 7 (OFA) / 95 ± 8 (OA)
Postop 1hr	77 ± 6 (OFA) / 80 ± 7 (OA)	89 ± 7 (OFA) / 94 ± 9 (OA)

The incidence of opioid-related side effects was significantly lower in the OFA group. Patients in the OA group reported a higher frequency of nausea, vomiting, and sedation, which were statistically significant.

Table 5: Incidence of Opioid-Related Side Effects

Side Effect	OFA Group (n=50)	OA Group (n=50)	p-value
Nausea	5 (10%)	18 (36%)	<0.01
Vomiting	3 (6%)	14 (28%)	<0.01
Sedation	4 (8%)	15 (30%)	<0.01

To ensure accurate drug administration and maintain consistency throughout the study, patients were divided into two groups:

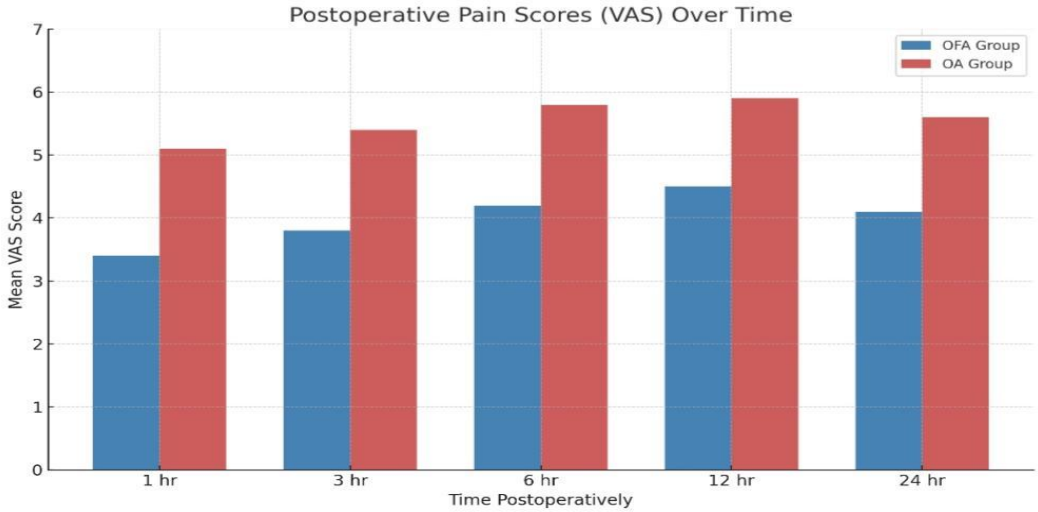
- Group OFA (opioid-free anesthesia): Patients received intravenous paracetamol (15 mg/kg), lignocaine (2 mg/kg), and magnesium sulfate (20 mg/kg) in 100 mL normal saline (NS) as preemptive analgesia in the preanesthetic room.
- Group OA (opioid anesthesia): Patients received intravenous tramadol (2 mg/kg) in 100 mL NS as preemptive analgesia in the preanesthetic room.

All drug infusions were completed before induction of anesthesia, ensuring uniform preemptive analgesia. Patients were closely monitored for hemodynamic parameters, side effects, and the need for additional analgesia.

Table 6: Drug Administration Protocol

Group	Drugs administered	Dosage	Dilution	Route	Time of administration
OFA	Paracetamol	15 mg/kg	-	IV	Preanesthetic room (before induction)
	Lignocaine	2 mg/kg	100 mL NS	IV infusion	Preanesthetic room (before induction)
	Magnesium sulfate	20 mg/kg	100 mL NS	IV infusion	Preanesthetic room (before induction)
OA	Tramadol	2 mg/kg	100 mL NS	IV infusion	Preanesthetic room (before induction)

Bar graph: the bar graph comparing postoperative pain scores (VAS) between the opioid-free anesthesia group and the standard opioid anesthesia group at different time intervals.



Discussion

Effective postoperative analgesia is crucial for optimizing patient recovery, reducing morbidity, and improving overall surgical outcomes. Traditionally, opioid-based analgesia has been the cornerstone of pain management in abdominal surgeries. However, opioid-related side effects such as nausea, vomiting, sedation, and respiratory depression have driven the search for alternative analgesic strategies. Opioid-free anesthesia (OFA) has gained increasing attention as a potential approach to mitigate these adverse effects while providing effective pain relief. This study compared the postoperative analgesic efficacy of OFA using intravenous paracetamol, lignocaine, and magnesium sulfate versus standard opioid-based anesthesia with intravenous tramadol for preemptive analgesia in abdominal surgeries under general anesthesia.

Our findings indicate that OFA significantly reduces postoperative pain scores compared to opioid-based anesthesia. The VAS scores at all postoperative time points (1, 3, 6, 12, and 24 hours) were significantly lower in the OFA group, suggesting superior pain control. Several studies have reported similar findings, highlighting the analgesic benefits of opioid-free techniques in various surgical settings. Paracetamol, a key component of OFA, acts centrally to inhibit prostaglandin synthesis and modulate pain perception, making it an effective non-opioid analgesic [10]. Lignocaine, an amide local anesthetic, has been shown to exert anti-inflammatory and antihyperalgesic effects, contributing to improved postoperative analgesia [11]. Magnesium sulfate, a non-competitive NMDA receptor antagonist, plays a crucial role in reducing central sensitization and preventing opioid-induced hyperalgesia [12].

A meta-analysis by Mulier et al. demonstrated that opioid-free anesthesia significantly reduces postoperative pain and opioid consumption while improving patient satisfaction [13]. Our study aligns with these findings, as patients in the OFA group required significantly less rescue analgesia compared to those receiving tramadol-based anesthesia.

Preemptive analgesia, which involves administering analgesics before surgical incision, aims to prevent central sensitization and reduce postoperative pain. In our study, OFA provided effective preemptive analgesia, leading to lower pain scores and reduced opioid requirements postoperatively. Previous studies have shown that preemptive administration of paracetamol and lignocaine can significantly decrease pain intensity and opioid consumption [14]. Magnesium sulfate, when used as an adjuvant, has been reported to enhance the effects of local anesthetics and reduce the requirement for intraoperative opioids [15].

The concept of opioid-free multimodal analgesia is based on targeting different pain pathways to achieve superior pain control while minimizing opioid-related adverse effects. The combination of paracetamol, lignocaine, and magnesium sulfate in our study effectively reduced postoperative pain, supporting the role of opioid-free strategies in perioperative analgesia.

One of the major advantages of OFA is the reduction in opioid-related side effects. In our study, patients in the opioid-based anesthesia group experienced a significantly higher incidence of nausea, vomiting, and sedation compared to those in the OFA group. This finding is consistent with previous research demonstrating that opioid-free techniques are associated with a lower incidence of postoperative nausea and vomiting (PONV), which is a common and distressing side effect of opioid use [16].

A study by Beloeil et al. reported that opioid-free anesthesia reduces the incidence of PONV by nearly 50%, improving overall patient comfort and satisfaction [17]. Lignocaine, in particular, has been shown to have anti-inflammatory properties that contribute to reduced postoperative nausea and ileus, further enhancing recovery after abdominal surgery [18].

Hemodynamic stability is an essential factor in perioperative management, particularly in high-risk surgical patients. In our study, both groups maintained stable intraoperative hemodynamics; however, the OA group exhibited slightly higher fluctuations in mean arterial pressure, possibly due to the sympathomimetic effects of tramadol. This is consistent with findings from previous studies where opioid-based anesthesia was associated with greater intraoperative hemodynamic variability [19].

Magnesium sulfate, used in the OFA group, has been reported to provide hemodynamic stability by reducing catecholamine release and preventing hypertension and tachycardia during surgery [20]. A study by Vadalouca et al. demonstrated that magnesium sulfate reduces intraoperative anesthetic requirements while maintaining cardiovascular stability, supporting its use in multimodal analgesia [21].

The results of our study suggest that opioid-free anesthesia using paracetamol, lignocaine, and magnesium sulfate provides superior postoperative pain control with fewer opioid-related side effects compared to tramadol-based analgesia. The growing interest in opioid-free techniques is driven by the need to minimize opioid dependence, reduce hospital stay durations, and enhance overall patient recovery.

Further large-scale randomized controlled trials are warranted to validate our findings and establish standardized OFA protocols for various surgical procedures. The integration of opioid-free techniques into enhanced recovery after surgery (ERAS) protocols may further optimize perioperative care and improve patient outcomes [22].

Conclusion

This prospective study demonstrated that opioid-free anesthesia (OFA) using intravenous paracetamol, lignocaine, and magnesium sulfate provided superior postoperative analgesia compared to standard opioid-based anesthesia with intravenous tramadol in abdominal surgeries under general anesthesia. Patients in the OFA group experienced significantly lower postoperative pain scores, reduced requirements for rescue analgesia, and a lower incidence of opioid-related side effects such as nausea, vomiting, and sedation.

The findings highlight the effectiveness of multimodal analgesia in perioperative pain management, reinforcing the role of preemptive analgesia in reducing postoperative pain and opioid consumption. The combination of paracetamol, lignocaine, and magnesium sulfate acted synergistically to enhance analgesic efficacy while minimizing opioid-induced adverse effects. Furthermore, the use of OFA contributed to better hemodynamic stability, making it a viable alternative for patients at risk of opioid-related complications.

The growing emphasis on opioid-free anesthesia aligns with the need to minimize opioid dependence and improve overall surgical outcomes. Based on our findings, OFA represents a promising approach to perioperative pain management, particularly in the context of enhanced recovery after surgery (ERAS) protocols. Future research, including larger randomized controlled trials, is warranted to establish standardized opioid-free analgesic protocols across different surgical procedures and patient populations.

This study supports the transition towards opioid-sparing techniques in anesthesia practice, offering a safe and effective alternative for managing postoperative pain while reducing opioid-related complications.

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