ORIGINAL ARTICLE

Opioid Sparing Effect of Opioid Free Anesthesia in Laparoscopic Gynecological Surgeries with ERAS Protocol

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Abstract

Background: ***Laparoscopic gynecological surgery has surpassed open surgery as the preferred form of gynecological care due to its minimally invasive nature. Although the laparoscopic approach often results in less postoperative discomfort than the open approach, Twenty percent to forty percent of patients report moderate to severe discomfort following laparoscopic procedures. Laparoscopic gynecological procedures can benefit from opioid-free anesthesia and the ERAS protocol, which can optimize patient recovery by shortening hospital stays without increasing mortality or morbidity rates.***

Aim and objectives: ***To evaluate the opioid sparing effect of opioid free anesthesia regarding pain control reflected on hemodynamics in laparoscopic gynecological surgeries, so we compare between opioid free anesthesia vs opioid based anesthesia.***

Subjects and methods: ***This prospective randomized single-blind controlled study was carried out on 90 patients divided into two groups. Opioid anesthesia group (OA): the patients will receive fentanyl (2mcg/kg). Opioid free anesthesia group (OFA): which will receive IV Paracetamol (15mg/kg), dexamethasone (8mg) and loading dose of dexmedetomidine (1mcg/kg) followed by maintenance dose of dexmedetomidine (0.1-0.3 mcg/kg/hr), ketamine (0.3 mcg/kg/hr) and lidocaine (1.5 mg/kg/hr) until end of surgery.Both groups underwent elective laparoscopic gynecological surgeries admitted to Al-Azhar University Hospitals, Cairo, Egypt in the duration from Jun 2023 till January 2025.***

Results: ***Opioid anesthesia (OA) patients needed more rescue fentanyl, and the overall amount of fentanyl was much higher than in the opioid free anesthesia (OFA) patients. Neither group showed a statistically significant difference in agitation score. Opioid anesthesia (OA) patients had a substantially greater risk of postoperative nausea, vomiting, and pruritus compared to opioid free anesthesia (OFA) patients.***

Conclusion: ***In gynecological laparoscopic surgery following the ERAS protocol, opioid-free anesthesia using the ERAS protocol is a safe and effective way to manage pain.***

Keywords: Titanium Elastic Nailing System ; Intramedullary Fixation; Middle third clavicular Fractures

1. Introduction

To get the most out of opioid-free anesthesia, gynecological laparoscopy might be the way to go. During the perioperative period, patients undergoing gynecologic surgery are administered intravenous opioids due to the moderate degree of discomfort that is expected.[1]

Research has demonstrated that postoperative pain impacts neuroendocrine function, which in turn causes changes in the body's internal environment through activation of the sympathetic nervous system and a series of stress reactions, as well as changes in the patient's mental and psychological condition following surgery.[2]

Opioids are the most often utilized intravenous analgesics, although they have the potential to induce adverse effects such as nausea, vomiting, disorientation, respiratory depression, pruritus, and constipation. Academics around are apprehensive about the detrimental effects of opiate misuse and consumption.[3]

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Along with the introduction of the concept of Enhanced Recovery After Surgery (ERAS), there is a pressing need for better pain management that lessens the possibility of adverse reactions while yet providing appropriate analgesia.

Accelerated recovery after surgery is possible with the use of ERAS techniques because they maintain organ function before surgery and reduce the substantial stress reaction afterwards. The foundation of ERAS treatments is preoperative counseling, nutritional optimization, consistent analgesic and anaesthetic regimens, and early mobility.[4]

In gynecological laparoscopic surgery, OFA with the ERAS protocol provided several benefits over the use of opioid based anesthesia. Opioid-free anaesthesia was investigated in the randomized controlled study, conducted by Massoth et al.[5]

The aim of this study was to evaluate the opioid sparing effect of opioid free anesthesia with regard to pain control reflected on hemodynamics in laparoscopic gynecological surgeries.

2. Patients and methods

This prospective randomized single-blind controlled study was carried out on 90 female patients underwent elective laparoscopic gynecological surgeries admitted to Al-Azhar University Hospitals, Cairo, Egypt in the duration from Jun 2023 till January 2025. The study was approved by the Ethics Committee of Faculty of Medicine, Al-Azhar University, Egypt. An informed written consent was obtained from each patient.

Sample size calculation:

Sample size was calculated using G*Power software (latest ver. 3.1.9.7; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). Considering a confidence level of 95%, a power of 90%, and an α error of 5%, the representative sample should be at least 80 patients. Estimating a 10% dropout during follow-up (f), then the total number of cases would be 30 cases in each group. Expected dropout rate (f) = 10% q = 1 ÷ (1-f), q= 1÷0.9=1.1, n=80x1.1=88≈90 cases.

Inclusion criteria:

Age from 21 to 45 years old, American Society of Anesthesiologists (ASA)[6] I and II, female patients underwent elective laparoscopic gynecological surgeries.

Exclusion criteria:

Patients' refusal, allergy to study drugs, preoperative chronic dependence upon opioid or non-steroidal anti-inflammatory drugs (NSAIDS), major organ dysfunction, kidney and liver insults, coagulopathies, BMI ≥ 35kg/m2, patients who use rate control drugs, uncontrolled hypertension, and patients who need to be converted to open surgery with more tissue trauma.

Randomization and Blindness:

An opaque sealed envelope was employed to store each patient's code, and computer-generated randomization numbers were utilized for random allocation. In a parallel fashion, patients were randomly divided into two groups with an allocation ratio of 1:1: Participants in Group-OA (n=45) were given opioid anesthesia, while those in Group-OFA (n=45) were given opioid free anesthesia.

Method:

This prospective randomized single-blind controlled study was carried out on 90 patients divided into two groups.

Opioid anesthesia group (OA): the patients will receive fentanyl (2mcg/kg).

Opioid free anesthesia group (OFA): which will receive IV Paracetamol (15mg/kg), dexamethasone (8mg) and loading dose of dexmedetomidine (1mcg/kg) followed by maintenance dose of dexmedetomidine (0.1-0.3 mcg/kg/hr), ketamine (0.3 mcg/kg/hr) and lidocaine (1.5 mg/kg/hr) until end of surgery.

Preoperative:

Our team meticulously documented each patient's medical and surgical background, conducted thorough physical examinations, and ran standard laboratory testing, including complete blood counts, renal function tests, liver function tests, and coagulation profiles. Prior to receiving clear fluids 2 hours before surgery, patients were required to fast from solid foods for 6-8 hours.

After surgery, all patients were taught how to use the Visual Analogue Scale (VAS) to measure their discomfort. Scale from 0 (no pain) to 10 (the worst pain possible), with 1–3 representing mild pain, 4–6 representing considerable pain, 7–9 representing severe pain, and 10 representing extreme pain.[7]

For the purpose of diagnosing patients with anticipated difficult intubation, the Mallampati score was utilized in every instance for airway evaluation. As part of the examination, the patient will be asked to look into a mirror and expand their jaw so they may protrude their tongue. The degree to which specific anatomical features are visible determines the final score.[8]

Intraoperative:

Pulse oximetry (SpO2), electrocardiography (ECG), non-invasive blood pressure monitoring, temperature probe and capnography was utilized for the standard monitoring of patients. IV access was inserted after EMLA cream. General anaesthesia was induced following 3 min of preoxygenation with propofol 2mg/kg.

In order to facilitate tracheal intubation, 0.6-0.8 mg/kg of rocuronium bromide was administered intravenously. Afterwards,

sevoflurane (1MAC) and a combination of air and oxygen (50%:50%) were administered mechanically to all patients at a flow rate of 3 L/min.

The goal was to keep the end-tidal CO2 (EtCO2) between 35 and 40 mmHg; therefore, the tidal volume was regulated to 6-8 ml/kg, and the respiratory frequency to a certain level. Every half an hour, GA was maintained with 0.1-0.2 mg/kg rocuronium bromide and 1MAC sevoflurane. The opioid free anesthesia patients (OFA) were given the following medications: intravenous paracetamol (15 mg/kg), dexamethasone (8 mg), and a loading dose of dexmedetomidine (1 mcg/kg) 10 minutes before the anesthesia was induced. Then, dexmedetomidine (0.1-0.3 µg/kg/hr), ketamine (0.3 mg/kg/hr), and lidocaine (1.5 mg/kg/hr) were continuously infused into the veins until the operation was completed. For intraoperative pain relief, patients in group OA were given fentanyl at a dosage of 2 µg/kg.

Intraoperative pain relief. If the changes in systolic blood pressure and heart rate rose by 20% or more compared to the baseline values, fentanyl was given intravenously at a dose of 0.5 mcg/kg as an opioid rescue.

During recovery, the degree of agitation was measured using the Riker sedation-agitation scale.

Postoperative:

It was standard practice to administer the modified Aldrete score every ten minutes to patients being discharged to the post anesthetic care unit (PACU) in order to track their recovery quality. All patients received postoperative controlled intravenous analgesia (PCIA). Any patients with VAS equal to or more than 4, received a rescue analgesia of 30 mg intravenous pethidine every 20 min, until VAS became equal or less than 3.

Results

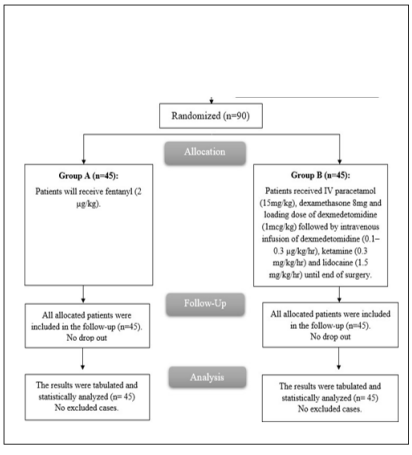

Figure 1. enrolled patients' CONSORT flowchart.

Table 1. The demographic information and length of surgery for the groups under study.

		GROUP (OA) N=45	GROUP (OFA) N=45	P-VALUE
AGE (YEARS)	Mean ±SD Range	36.18±6.09 24-46	33.78±7.69 22-45	0.104
WEIGHT (KG)	Mean ±SD Range	82.91±11.03 63-99	81.13±12.61 61-100	0.479
HEIGHT (CM)	Mean ±SD Range	167.11±6.45 156-178	166.67±5.07 159-176	0.717
BMI (KG/M^2)	Mean ±SD Range	29.63±3.09 23.1-34.3	29.1±3.55 22.2-34.7	0.451
ASA PHYSICAL STATUS	I II	32(71.11%) 13(28.89%)	37(82.22%) 8(17.78%)	0.213
DURATION OF SURGERY (MIN)	Mean ±SD Range	88.67±18.9 50-120	91.33±19.41 60-120	0.511

There was no significant difference between the two groups in terms of age, height, weight, BMI, ASA physical status, or length of operation, (table 1; figures 2&3).

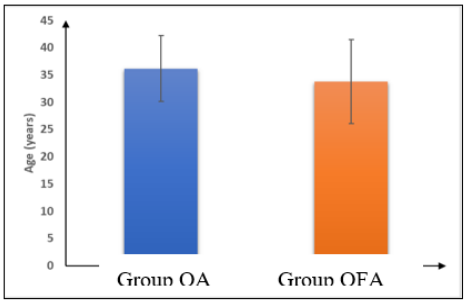

Figure 2. Age of the groups under study

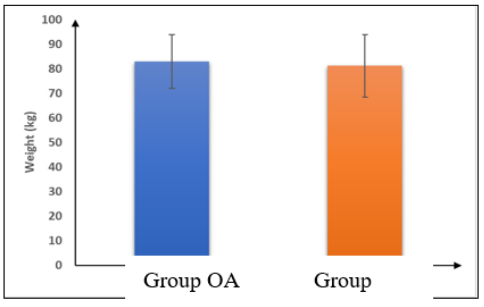

Figure 3. Weight of the groups under study.

Table 2. Heart rate of the studied groups (beats/min)

	GROUP-OA (N=45)	GROUP-OFA (N=45)	P-VALUE
T0	86.62±7.34	84.64±7.52	0.210
T1	83.93±7.36	81.71±7.58	0.162
T2	81.24±7.74	79.04±7.34	0.170
T3	79.93±10.08	78.04±10.66	0.390
20MIN	79.82±7.65	77.09±7.41	0.089
30MIN	78.18±8.11	75.71±8.96	0.174
40MIN	77.73±10.02	74.16±9.04	0.079
50MIN	76.49±8.58	73.58±9.05	0.121
END OF SURGERY	79.4±7.27	76.71±8.96	0.122

Heart rate was insignificantly different between both groups (table 2 figure 4).

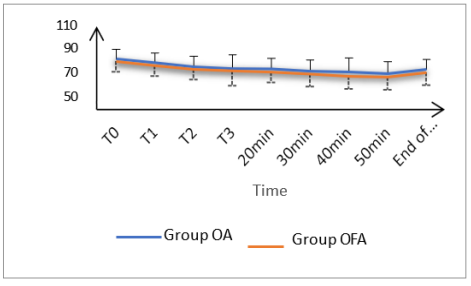

Figure 4. Heart rate of the groups under study.

Table 3. The analyzed groups' mean arterial pressure (mmHg).

	GROUP OA N=45	GROUP OFA N=45	P-VALUE
T0	90.49±8.14	88.4±6.83	0.191
T1	86.16±8.24	83.78±6.95	0.143
T2	85.44±10.52	81.98±7.4	0.074
T3	83.82±11.27	80.27±8.19	0.091
20 MIN	81.47±8.87	78.96±7.62	0.153
30 MIN	80.87±8.83	79±8.2	0.302
40 MIN	79.96±7.75	77.58±7.07	0.132
50 MIN	79.64±8.33	76.58±6.82	0.059
END OF SURGERY	82.64±8.14	80.33±6.73	0.146

The difference in mean arterial pressure between the two groups was negligible, (table 3; figure 5)

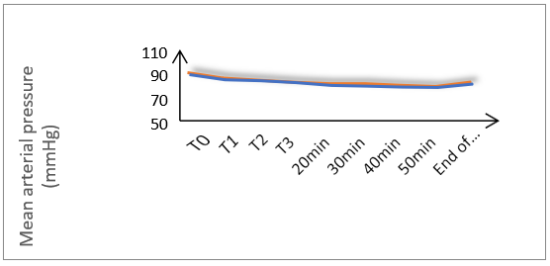

Figure 5. Mean arterial pressure of the studied groups.

Table 4. Intraopearive Number of patients rescue fentanyl required, average total fentanyl consumption(micrograms) per patient and agitated score of the studied groups.

		GROUP OA (N=45)	GROUP OFA (N=45)	P-VALUE
NUMBER OF PATIENTS RESCUE FENTANYL REQUIRED (MCG)		11(24.44%)	3(6.67%)	0.039*
AVERAGE TOTAL FENTANYL CONSUMPTION (MCG) PER PATIENT	Range	170	20	0.012
AGITATED SCORE		4(3-5)	3(2-4)	0.168

*: significant as P-value≤ 0.05.

Number of patients rescue fentanyl required, total fentanyl consumption was significantly higher in group-OA than OFA (P-value=0.039 and 0.004 respectively). Agitated score was insignificantly different between both groups, (table 4; figure 6).

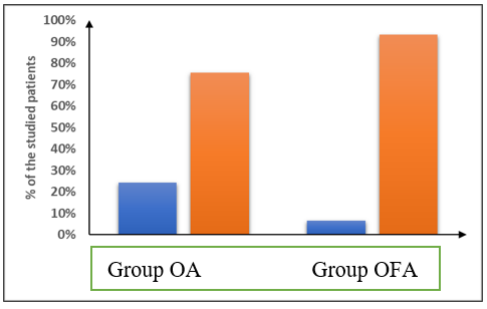

Figure 6. Number of patients rescue fentanyl required of the studied groups.

Table 5. Time of first postopertive rescue analgesia (hours) and average total postoperative rescue pethidine consumption (mg) per patient of the studied groups.

		GROUP OA (N=45)	GROUP-OFA (N=45)	P-VALUE
TIME OF FIRST RESCUE ANALGESIA (H)	Mean±SD	7.02±0.84	5.13±0.84	<0.001*
	Range	6-8	4-6	
AVERAGE TOTAL PETHIDINE CONSUMPTION (MG) PER PATIENT		10	15	0.038*

Group OA experienced a substantially delayed time of initial rescue analgesia compared to group OFA (P-value<0.001). Group OFA consumed substantially more total postoperative rescue pethidine than group OA (P-value = 0.038), (table 5).

Table 6. Complications of the studied groups

	GROUP OA (N=45)	GROUP OFA (N=45)	P VALUE
BRADYCARDIA	2 (4.44%)	4 (8.89%)	0.67
HYPOTENSION	3 (6.67%)	6 (13.33%)	0.485
PONV	14 (31.11%)	5 (11.11%)	0.020*
PRURITIS	5 (11.11%)	0 (0%)	0.02*
RESPIRATORY DEPRESSION	6 (13.33%)	0 (0%)	0.026*

Data presented as frequency (%).

3. Discussion

The most popular medications for treating acute pain in the initial postoperative phase are opioids, which are also frequently given for analgesia and further sedation during general anesthesia. Opioids offer steady intraoperative hemodynamics and efficient analgesia, both of which are beneficial throughout the perioperative phase. Nonetheless, it is dangerous to utilize opioids during the perioperative phase.[9]

Among the numerous possible side effects of opioids are respiratory depression, opioid-induced hyperalgesia (OIH), and postoperative nausea and vomiting (PONV). Patients and healthcare systems are put under more strain as a result of these consequences, which lead to longer recovery times, more time spent in the post-anesthetic care unit (PACU), later hospital discharge, and even unanticipated hospitalization.[10]

Throughout our investigation, we found no significant differences in heart rate, mean arterial pressure (MAP), SPO2, and end-tidal CO2 between the two groups at various time intervals and at the end of the operation.

Consistent with our results, Vishnuraj et al.,[11] studied 88 patients who had a laparoscopic cholecystectomy and were the subjects of a randomised controlled trial. The subjects were split into two groups: one that received opioids and another that did not. Both the opioid and non-opioid groups showed no statistically significant differences in heart rate or mean

arterial pressure (MAP)

Supporting our findings, Chen et al.[12] performed gynecological laparoscopic surgery on seventy-seven adult female patients as part of a non-inferiority randomized controlled trial. They were split into two groups: one that received opioid anesthesia (OA) using sufentanil and remifentanil, and another that received esketamine and dexmedetomidine. Both the OFA and OA groups showed statistically insignificant differences in heart rate and MAP.

In the same line with our findings, Tochie et al.,[13] 36 women who had elective gynecological surgeries participated in a pilot trial that was randomized. Both the OFA group and the CGA group, which stands for customary general anesthesia, were given equal weights. There was no discernible change in mean arterial pressure (MAP) or heart rate between the OFA and CGA groups, and the former demonstrated superior intraoperative hemodynamic stability.

Also, Aboelela et al.,[14] studied 68 patients who had gynecological surgeries in the abdomen, who were the subjects of a prospective randomized controlled trial. Two groups were formed: one that used opioids for anesthesia and another that did not. The researchers discovered no statistically significant difference in heart rate or MAP between the groups that received opioid-based anesthesia and those that did not.

Group OA showed considerably larger numbers of patients requiring rescue fentanyl and total fentanyl consumption compared to group OFA. However, the group OFA had higher total postoperative rescue pethidine use. Neither group showed a statistically significant difference in agitation score. First rescue analgesia onset was also noticeably later in the OA group compared to the OFA group.

Supporting our findings, Vishnuraj et al.,[11] discovered that the opioid group consumed more opioids overall than the opioid-free group. Opioid groups had shorter times to first rescue analgesia than opioid-free groups. Their usage of 0.5 mcg/kg/h of dexmedetomidine and our use of 0.1-0.3 mcg/kg/h may explain the discrepancy.

Also, Abdelmoniem et al.,[15] findings showed that compared to the opioid-free anesthesia group, the opioid-based anesthesia group had a much higher number of patients requiring opioids and overall opioid use.

Also, Aboelela et al.,[14] demonstrated that the opioid-based group's total opioid consumption and the number of patients requiring rescue opioids were significantly higher than those of the opioid-free group. On the other hand, the opioid-based group had a considerably higher agitated score and a considerably faster time to first rescue analgesia than the opioid-free group. Our use of dexmedetomidine in addition to ketamine and lidocaine, as well as the fact that their usage of only these two anesthetics, could explain these discrepancies.

We found that compared to group OA, group OFA had a considerable delay in awakening time. Because the two groups used different methods to alleviate pain, the opioid-free group required much more time to wake up than the opioid-based group. Opioids shorten the time it takes to recover from anesthesia because they give excellent analgesia with a more predictable offset.

Medications used in opioid-free regimens, such as non-opioid analgesics, can have different sedative effects and might cause recovery to take longer.[16]

Supporting our findings, Chen et al.,[12] discovered that the time it took for the OFA group to wake up was noticeably longer than the OA group.

Also, Salem et al.,[17] showed that the time from PACU arrival to discharge was insignificantly different between the groups.

In addition, Hakim et al.,[18] reported that PACU discharge time was statistically insignificant

different between the OF group and the OA group.

However, Aboelela et al.,[14] found that the opioid-based group required far more time to recover than the opioid-free group.

4. Conclusion

With less opioid consumption and a lower incidence of postoperative nausea and vomiting (PONV), pruritus, and respiratory depression, the opioid-free anesthesia technique (OFA) is an effective and safe way to manage pain during gynecological laparoscopic surgery according to the ERAS protocol. However, the technique may lengthen the time it takes to awaken.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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