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Opioid Free Anesthesia (OFA) for Laparoscopic Cholecystectomy in Low Resource Settings

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Abstract **Case Report**

Laparoscopic Cholecystectomy is a common minimally invasive surgical procedure done under general anesthesia using an opioid-based regimen. Although laparoscopic cholecystectomy is a minimally invasive surgical procedure, some patients may have significant discomfort in the postoperative period in the first 24 to 72 hours. Inadequate pain control, PONV, and delayed recovery are common postoperative issues. This case report shows that OFA is a safe, opioid-sparing, and feasible option that provide stable perioperative hemodynamics, good analgesia, and an uneventful recovery profile to patients undergoing laparoscopic cholecystectomy.

Keywords: Opioid Free Anesthesia, Multimodal analgesia, Laparoscopic surgery.

INTRODUCTION

Laparoscopic Cholecystectomy is a standard surgical procedure for cholelithiasis and gallstone disease. Pneumoperitoneum is created using Carbon dioxide, and a camera and dissecting instruments are introduced in the abdominal cavity. Initiation and maintenance of pneumoperitoneum cause hemodynamic stress, which is attenuated by adequate anesthesia depth and often multimodal analgesia. Although laparoscopic cholecystectomy is a standard minimally invasive surgical procedure, some patients may have significant morbidity in the first 24 to 72 hours during the postoperative period. Opioids are commonly used for intraoperative analgesia and sedation during general anesthesia and are among the most widely used agents for treating acute pain in the immediate postoperative period. Opioids are known to provide adequate analgesia and stable intraoperative hemodynamics, which are the most critical concerns during the perioperative period. Although opioids are an essential constituent of balanced anesthesia, their use has been questioned due to severe and significant adverse effects [1]. Moreover, the availability of potent opioids in low-resource settings is also a remarkable challenge. To tackle this situation several suitable alternatives were explored. Preemptive and multimodal analgesia is an established care model that minimizes perioperative opioid consumption, thereby minimizing adverse effects and promoting positive outcomes after surgery [2]. These techniques combine the pharmacologic effects of multiple analgesics to achieve a synergistic effect of their different modes of action and curtail individual drug doses, thereby minimizing their side effects. Opioid-free anesthesia (OFA) [3], is a well-defined technique that may achieve similar goals. OFA is an anesthetic technique where opioids are not used in the perioperative period; thereby, the number of opioid-related adverse effects will be reduced. The present case report stresses the feasibility, efficacy, and safety of the OFA regimen during laparoscopic surgeries conducted under general Anesthesia.

Conduct of Cases Using OFA

Ten American Association of Anesthesiologists (ASA) I and II patients scheduled for elective laparoscopic cholecystectomy are included. A single surgeon did all cases. The youngest patient was 30-year-old, and the oldest was 60 years. Patients with ASA >II, allergic to tramadol, lidocaine, magnesium, ketamine, and paracetamol; patients who chronically use benzodiazepines or opioids; patients who were pregnant or breastfeeding; patients with chronic pain; patients with cardiac, renal, and hepatic failure; patients with diabetes and psychiatric illness were not included. Written informed consent was taken from all the patients during the pre-anesthetic check-up. They were kept overnight (8 hrs.) nil orally as per standard fasting

guidelines. After taking the patients inside the operation theater, ASA standard monitors were attached, including a pulse oximeter, five lead ECG, Non-invasive blood pressure and Capnography, and a fraction of inspired oxygen (FiO_2). Injection of midazolam 1 mg and injection of Ketamine 25 mg with the injection of Glycopyrrolate 0.2 mg were given to each patient, followed by Shiv- mix-3 (injection Paracetamol 1 gram + injection tramadol 25 mg + injection MgSO4 1 gm + preservative free injection Lignocaine 1.5 mg/kg body weight) was infused over 15 to 20 minutes in all patients before induction of General anesthesia through 18 Gauze intravenous cannula. Patients were induced using an induction dose of Propofol (2 mg/kg body weight) and injection of Rocuronium 0.6 mg/kg body weight after ventilating with 100% oxygen through a non-rebreathing face mask at 10 liter/minute. Dexamethasone 4 mg and an injection of diclofenac sodium 75 mg were given intravenously before the skin incision. The surgical team infiltrated the port site with 0.25% bupivacaine before the incision. Anesthesia was maintained with propofol infusion @ 100 microgram/kg/minute, continued until pneumoperitoneum was maintained. Patients were put on mechanical ventilation using an oxygen and nitrous oxide mixture in a 1:2 ratio. Injection fentanyl and injection esmolol were kept ready to combat intraoperative hypertension and tachycardia. No patient needed an extra top-up dose of relaxant. Intraoperative hemodynamic stability was maintained in all patients during surgery except one patient who required a 20 mg bolus dose of Esmolol and 50 micrograms of fentanyl, and 30 mg Propofol to combat the rise in blood pressure and tachycardia.

All the patients were extubated in the operation theatre after surgery. The residual neuromuscular blockade was antagonized with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/ kg, and when the patient had regular spontaneous breathing, tracheal Extubation was performed. Then patients were transported to the Post-Anesthesia Care Unit (PACU), and their heart rate and oxygen saturation from pulse oximeter were monitored. Postoperative pain was measured on a numerical rating scale (NRS). NRS values fall between 0 and 10, where 0 denotes no pain and 10 expresses the worst pain imaginable. In our patients, it remained 2-3 in nine patients, and in one patient, it was four at rest, on voluntary deep breathing immediately, and one h after Extubation. No patient required any extra analgesics apart from paracetamol 1 g plus tramadol 50 mg given eight hourly in the postoperative period. There was no episode of respiratory depression, nausea, vomiting, shoulder tip pain, or pruritus in any patient. All patients were fully awake and following commands immediately after reversal. Patients were discharged the next day from the hospital.

Table 1: Patient characteristics

Details of patients	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age	38	30	60	54	40	42	54	47	45	35
Gender	F	F	M	M	F	M	F	F	M	F
BMI	22	21	23	22	24	23	28	22	24	24.5
ASA	I	I	II	II	II	I	II	I	II	I
HTN	No	No	Yes	No	Yes	No	Yes	No	Yes	No
DM	No	No	Yes	Yes	N	No	No	No	No	No
Duration of anesthesia* (Minute)	31	29	39	34	33	30	32	24	32	34
Duration of surgery** (Minute)	20	20	30	25	25	22	26	15	27	27

* From the start of induction till extubation.

**From first skin incision to complete skin closure.

Table 2: Recovery profile

Recovery characteristics						
Patients	**Pain score on deep breathing (just after Extubation)**	**PONV**	**Respiratory Depression**	**Consciousness at Extubation**	**Shoulder tip pain**	**Pruritus**
1	2	Nil	Nil	Fully awake	Nil	Nil
2	3	Nil	Nil	Fully awake	Nil	Nil
3	4	Nil	Nil	Fully awake	Nil	Nil
4	2	Nil	Nil	Fully awake	Nil	Nil
5	3	Nil	Nil	Fully awake	Nil	Nil
6	2	Nil	Nil	Fully awake	Nil	Nil
7	2	Nil	Nil	Fully awake	Nil	Nil
8	1	Nil	Nil	Fully awake	Nil	Nil
9	3	Nil	Nil	Fully awake	Nil	Nil
10	3	Nil	Nil	Fully awake	Nil	Nil

DISCUSSION

Pain is an important factor in the perioperative period in surgical patients and may lead to unstable hemodynamics, unwanted prolonged postoperative recovery, increased usage of analgesics in the postoperative period, prolonged hospital stays, and surgeon and patient dissatisfaction. *Harless M et al.*, reported 75% of surgical patients had inadequate pain treatment in the postoperative period [4]. Opioids are the traditional choice for intraoperative pain management in most operative procedures. Extensive use of opioids is found to be associated with various side effects, such as itching, urinary retention, respiratory depression, postoperative nausea and vomiting, and constipation [5]. Moreover, in recent years, the use of opioids has been linked to influencing cancer recurrence [6]. To combat these problems, the model of multimodal balanced anesthesia by using a combination of non-opioid drugs has been introduced in order to curtail the usage of opioids in the perioperative period, thereby avoiding opioid-related adverse effects. Multimodal opioid-free anesthesia (OFA) has been used to reduce the incidence of these side effects. Several non-opioid medications are used, including but not limited to Clonidine [7] and Dexmedetomidine (alfa-1 agonists) [8], low dose Ketamine (NMDA antagonist) [9], Dexamethasone [10]. Tramadol [11], Magnesium sulfate, [12, 13] Low dose preservative free Lignocaine [14, 15], etc. These medications are used as supplemental or sole analgesics perioperatively. Shiv-Mix is one such example described elsewhere [16]. Ketamine is an N-methyl D-aspartate (NMDA) receptor antagonist. It acts by blocking the release of potassium from the cell and thus prevents the transmission of painful impulses. Preemptive administration of ketamine has been shown to have an opioid-sparing effect in perioperative period [17]. Lidocaine is a local anesthetic with analgesic, anti-hyperalgesic, and anti-inflammatory effects. Infusion of Lidocaine in surgical patients reduced the need for opioids, decreased postoperative nausea and vomiting, faster return of intestinal motility, and a shortening of hospital stay [18]. Magnesium sulfate also acts as an antagonist at NMDA receptors by blocking the entry of calcium and sodium into the cell, thereby preventing pain transmission. Using magnesium in the intra-operative period reduces pain, nausea, and vomiting in the postoperative period [19]. Dexamethasone is a corticosteroid with an established antiemetic effect. Its anti-inflammatory and edema-reducing property interferes with the pain pathway. This drug has an opioid-sparing effect and reduced pain score at rest and during movement, and its use is associated with a lesser incidence of PONV [20].

Several studies show the efficacy and feasibility of OFA in literature [21, 22]. It has been shown that when all these drugs are given together, they alter the pathophysiologic process involved in nociception. In that way, more effective intra-operative analgesia with fewer side effects is obtained [23]. *Hontoir et al.*, also observed improved postoperative recovery using an opioid-free approach in breast surgery patients [24]. These findings align with the goals of ERAS (enhanced recovery after surgery) protocol as providing optimal perioperative analgesia facilitates early recovery with a minimal adverse effect of an opioid-based regimen [25]. In our cases, we found stable perioperative hemodynamics, adequate postoperative analgesia, and no incidence of PONV and other feared side effects, leading to smooth recovery, a comfortable patient, and a satisfied surgeon.

CONCLUSION

This case report shows that OFA using Shiv-Mix infusion preoperatively is a safe, opioid-sparing, and feasible option that provide good perioperative analgesia, stable hemodynamics, and an uneventful recovery profile.

DECLARATION OF PATIENT CONSENT

The authors certify that informed consent was obtained from all patients regarding the method of anesthesia and the use of their data to be reported in an academic journal. The patients understand that their names and initials will not be published, and due efforts will be undertaken to conceal their identity.

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Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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