

*Research Article***Efficacy and Safety of Intraperitoneal Bupivacaine versus Bupivacaine - Nalbuphine for Postoperative Analgesia After Laparoscopic Cholecystectomy**

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Abstract

Introduction: Laparoscopic cholecystectomy (LC) is a proven, gold standard surgical procedure for management of gallbladder stones. **Aim of the work:** This prospective randomized, double-blinded, placebo-controlled study was performed to compare between postoperative analgesic effects of intraperitoneal instillation of bupivacaine 100 mg (20 ml, bupivacaine 0.5%) with that of bupivacaine 100 mg (20 ml, bupivacaine 0.5%) combined with nalbuphine 10 mg in patient undergoing laparoscopic cholecystectomy. **Patients and Methods:** This prospective, randomized, double-blinded, placebo-controlled study was conducted in El-Minia University Hospital during the period from March 2017 to November 2017, after approval of the university ethical committee and obtaining informed consent from all patients. **Results:** A total of ninety participants were enrolled in this study, they were randomized into three groups (n=30) with no patient dropout. Recommendations Based on the current study, we recommend: This technique must be adopted for control of postoperative pain after laparoscopic surgeries. Multicentric studies are required to confirm these findings including patients categorized under ASA III or IV. Future researches to test wide range of different nalbuphine doses. In addition, trying other adjuvants.

Keywords: Intraperitoneal, laparoscopic cholecystectomy, bupivacaine, nalbuphine ANOVA: Analysis of variance, ASA: American Society of Anesthesiologists, CBD: Common bile duct.

Introduction

Laparoscopic cholecystectomy (LC) is a proven, gold standard surgical procedure for management of gallbladder stones. Early and easily recovery, less operative morbidities, less postoperative pain, earlier return of bowel function, improved cosmesis, an earlier return to full activity, less hospitalization day and decreased overall cost are the superiorities of laparoscopic cholecystectomies comparing with open surgical procedures.⁽¹⁾ The pain in the conventional cholecystectomy is mainly a parietal pain while in laparoscopic cholecystectomy, pain is mainly visceral pain. In 17% to 41% of the patients, pain is the main cause for staying overnight in the hospital in the day of surgery and the primary reason why the patients have a longer convalescence. Postoperative abdominal pain usually occurs during the first 24 hours, while shoulder pain most commonly appears the second day after laparoscopic cholecystectomy.⁽²⁾

Incidence rate of PONV after (LC) is higher than that after other types of surgery. A rate of

46% to 75% has been reported for patients who did not receive antiemetic treatment after LC⁽³⁾.

Because postoperative pain after laparoscopic surgery is complex, specialists suggest that effective analgesic treatment should be a multimodal support. Several methods have been used for pain relief after laparoscopic surgeries such as administration of intraperitoneal local anesthetics alone or in combination with opioid analgesics⁽⁴⁾

Aim of the work

This prospective randomized, double-blinded, placebo-controlled study was performed to compare between postoperative analgesic effects of intraperitoneal instillation of bupivacaine 100 mg (20 ml, bupivacaine 0.5%) with that of bupivacaine 100 mg (20 ml, bupivacaine 0.5%) combined with nalbuphine 10 mg in patient undergoing laparoscopic cholecystectomy.

Patients and Methods

This prospective, randomized, double-blinded, placebo-controlled study was conducted in El-Minia University Hospital during the period

from March 2017 to November 2017, after approval of the university ethical committee and obtaining informed consent from all patients. A total of 90 adult patients aged between 18-60 years old, of either sexes, belonging to American Society of Anesthesiologists grade I or II, and scheduled to undergo elective laparoscopic cholecystectomy surgery under general anesthesia were included in the study.

Exclusion criteria:

Patients with history of allergy to the studied drugs or acute cholecystitis. Patients with Morbid obesity (body mass index >35 kg/m²). Patients with severe cardiac, pulmonary, renal, hepatic, or neurological diseases. Patients with Previous abdominal surgery. Patients in whom surgery had to be converted to open cholecystectomy or with complications which could increase postoperative pain such as biliary spillage due to puncture of the gall bladder or extensive dissection due to adhesions. Patients with drug abuse or on analgesics for any reason.

Study groups:

The patients were randomly allocated into three groups using computer generated table numbers each contain (30) patient.

Control group (C): received intraperitoneal 50 ml normal saline (Normal saline, Otsoka, Egypt). Bupivacaine group (B): received intraperitoneal bupivacaine 100 mg (20 ml, bupivacaine 0.5%), diluted with normal saline to total volume of 50 ml. Bupivacaine-Nalbuphine group (BN): received intraperitoneal bupivacaine 100 mg (20 ml, bupivacaine 0.5%) with 10 mg nalbuphine (Nalufin® AMOUN PHARMACEUTICAL CO. El-Obour city, Cairo, Egypt), diluted with normal saline to total volume of 50 ml. The study solutions were drawn into precoded sterile syringes by an anesthetist not involved in the study and given to the surgeon after completion of surgery for intraperitoneal instillation in a double-blinded manner. The protocol was opened after the study had been completed.

Preoperative assessment and preparation:

Preoperative assessment was done for the patients by taking careful medical history, and performing general and physical examination including blood pressure, heart rate, respiratory rate, chest, heart and abdomen. Then, routine

and relevant investigations were carried out such as complete blood picture, renal and liver function tests, random blood sugar, and electrocardiogram were performed and analyzed in detail prior to procedure. Proper explanation of the visual analogue scale (VAS) was done, VAS consists of a straight vertical 10 cm line; the bottom point (0 cm) represents no pain and the top (10 cm) represents the worst imaginable pain. Patients were fasted for 6 hours for solid foods and 2 hrs. for water and clear liquids.

Technique of study:

On arrival to the operating theatre, standard monitoring was applied including noninvasive blood pressure (NIBP), Electrocardiography (ECG) and pulse oximetry (Datex. Ohmeda monitor, model: IMEC12- Filand). Then an intravenous 18 G cannula was inserted after sterilization of the skin and preloading with Ringer's lactate solution 10-15 ml/kg was given. Conventional balanced anesthesia was administered for all patients after preoxygenation with oxygen with well fitted face mask for 3 min. and pre-medication with midazolam 0.05 mg/kg. Induction of anesthesia was achieved with atropine 0.01 mg/Kg, fentanyl 1µg/kg and 2 mg /kg propofol 1 % until loss of verbal response, followed by atracurium 0.5 mg/kg to facilitate tracheal intubation with an appropriate size cuffed endotracheal tube.

Anesthesia was maintained with inhalational isoflurane (MAC 1-1.5 in O₂) and atracurium bolus 0.1 mg/kg. Ventilation was controlled with tidal volume of 6-8 ml/kg and respiratory rate of 12-14 breaths/min. The ventilation parameters were adjusted to keep end-tidal CO₂ at 30-35 mmHg with PEEP of 3-5 cmH₂O and O₂ flow of 5 L /min. Intravenous fluid therapy was given according to the calculated formula (4/2/1rule) per fasting hours for maintenance of fluid requirements, 4 ml/kg/h for third space loss and replacement of surgical bleeding if present. Nasogastric tube was inserted for all patients after intubation and was removed at the end of the surgery. Induction of pneumoperitoneum was created by insufflation of carbon dioxide CO₂ to maintain intra-abdominal pressure between 12 and 15 mm Hg throughout the surgical procedure and placement of laparoscopic ports was done.

After removal of the gall bladder, hemostasis, washing of the peritoneal cavity and suctioning

of the fluid used for irrigation were performed. Then, the study solutions were instilled by the surgeon

intraperitoneally using metallic suction cannula keeping its knob at irrigation point and syringe nozzle attached to the inlet, while keeping suction outlet closed and secured ensuring no spillage or loss of study medications. The instillation was done under direct vision into the right hepatodiaphragmatic space and on the gall bladder bed. 12), with the patient in trendelenberg's position. All the operations were performed by a team of surgeons that has at least 3 years' experience in laparoscopic surgery.

Results

A total of ninety participants were enrolled in this study, they were randomized into three groups (n=30) with no patient dropout. Changes in (VAPS) are summarized in Table (1) where Comparison among the three study groups detects a statistically significant difference in at 0,1,2,4,6, 8,10,12,16 & 24 hrs immediately.after full recovery where the score was significantly lower in group (BN) when compared to each of other groups except at 12 hrs. It was significantly higher than group (B). In comparing group (B) with group (c) a significant decrease in VAPS at all times recorded except at 8 hrs. there is significant increase.

Table (1): Changes in the visual analogue pain score (VAPS): Data are presented as median and Inter-Quartile Range.

Time	Group C (n=30)	Group B (n=30)	Group BN (n=30)	P value		
Immediately (after recovery) Median IQR	6 (5-6)	1 (0-1)	0 (0-0)	<0.001*		
				C vs B	C vs BN	B vs BN
				<0.001*	<0.001*	<0.001*
1 h Median IQR	# 2 (2-3)	# 1 (1-1)	0 (0-0)	<0.001*		
				C vs B	C vs BN	B vs BN
				<0.001*	<0.001*	<0.001*
2 h Median IQR	# 4 (4-4)	# 1 (1-2)	# 1 (1-1)	<0.001*		
				C vs B	C vs BN	B vs BN
				<0.001*	<0.001*	0.028*
4 h Median IQR	# 4 (3-5)	# 2 (1-2)	# 1 (1-1)	<0.001*		
				C vs B	C vs BN	B vs BN
				<0.001*	<0.001*	<0.001*
6 h Median IQR	# 3 (3-4)	# 2 (2-2)	# 1 (1-1)	<0.001*		
				C vs B	C vs BN	B vs BN
				<0.001*	<0.001*	<0.001*
8 h Median IQR	# 3 (3-4)	# 4 (4-5)	# 1 (1-2)	<0.001*		
				C vs B	C vs BN	B vs BN
				0.042*	<0.001*	<0.001*
10 h Median IQR	# 4 (3-4)	# 3 (2-4)	# 2 (2-2)	<0.001*		
				C vs B	C vs BN	B vs BN
				0.022*	<0.001*	<0.001*
12 h Median IQR	# 3 (3-4)	# 1 (1-2)	# 2 (1-4)	<0.001*		
				C vs B	C vs BN	B vs BN
				<0.001*	0.003*	0.044*
16 h Median IQR	# 3 (3-4)	1 (1-1)	0 (0-2)	<0.001*		
				C vs B	C vs BN	B vs BN
				<0.001*	<0.001*	<0.001*
24 h Median IQR	# 4 (3-4)	1 (1-1)	0 (0-0)	<0.001*		
				C vs B	C vs BN	B vs BN
				<0.001*	<0.001*	<0.001*

- *: Significant difference at p value < 0.05

- #: Significant difference within each group at p value < 0.05

Discussion

Laparoscopic cholecystectomy is gold standard surgery for symptomatic gall stone disease which is the commonest disease needs surgical management. LC offers various advantages over open cholecystectomy like short duration of hospital stay, better recovery, lesser morbidities and less postoperative pain. However postoperative pain after laparoscopic cholecystectomy remains an issue, it can prolong hospital stay and leads to increase morbidity, it is affected by several factors including patient demographics, nature of underlying disease, surgical factors such as rupture of blood vessels caused by rapid distension of the peritoneum, traumatic traction on the nerves, trauma to the abdominal wall during port insertion, volume of residual gas, type of gas used for pneumoperitoneum, and the pressure created by the pneumoperitoneum⁽⁵⁾.

Post laparoscopic cholecystectomy pain is multifactorial and methods for short-term analgesia cannot improve postoperative functions or shorten hospitalization⁽⁷⁾. So, multimodal efforts like parenteral non-steroidal anti-inflammatory drugs and opioids have been done to reduce overall pain, but in spite of their efficacy, all parenteral medications are associated with adverse effects. Where routine use of systemic NSAIDs may produce adverse side effects, such as gastric bleeding, renal impairment, or increased bleeding, caused by inhibition of platelet activity.

Also parenteral opioids for post-operative analgesia have recently been critically challenge because of the development of tolerance or opioid-related side effects such as nausea, vomiting, sedation, depression of brainstem control of respiratory drive, hypotension and urinary retention. So that another techniques were described to reduce post-laparoscopy pain including preincisional infiltration and intraperitoneal instillation of levobupivacaine 0.25%, intraperitoneal ropivacaine and a gas drain, intraperitoneal levobupivacaine with

epinephrine, intraperitoneal application of bupivacaine plus morphine, preincisional injection of bupivacaine, preemptive intraperitoneal injection of ropivacaine and intraperitoneal lidocaine combined with intravenous or intraperitoneal tenoxicam⁽⁶⁾

Recommendations

Based on the current study, we recommend: This technique must be adopted for control of postoperative pain after laparoscopic surgeries. Multicentric studies are required to confirm these findings including patients categorized under ASA III or IV.

Future researches to test wide range of different nalbuphine doses. In addition, trying other adjuvants.

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