Original research article

Intraperitoneal Bupivacaine alone or with Dexmedetomidine for Post-Operative Analgesia and Haemodynamic Changes following Laparoscopic Cholecystectomy: A Comparative Evaluation

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Abstract

Background and Objective: Laparoscopic surgery has now become the most accepted surgical and safe technique for a number of surgery including cholecystectomy , appendcectomy , etc .Advantages over open procedures include lesser haemorrhoage , better cosmetic results , lesser post operative pain and better results . To compare the analgesic effect of intraperitoneal application of bupivacaine and bupivacaine with dexmedetomidine in laparoscopic cholecystectomy . To assess the quality of analgesia by visual analgesia scale score (VAS).

Material and Method: This study was an interventional, prospective, double blind, parallel group, randomised clinical study conducted on patients undergoing laparoscopic cholecystectomy surgeries. Institutional Ethical Committee Approval was obtained and written informed consent was obtained from all the patients before the screening in the study. Total of 162 patients were selected in which 81 were randomly allocated in each group using table of randomisation. Study Duration Period 2 Sep 2020 To 2 March 2021.

Conclusion: Hence our study showed that intraperitoneal instillation of dexmedetomidine 1 µgm/kg in combination with bupivacaine 0.25% in elective laparoscopic cholecystectomy significantly reduces the post-operative pain and significantly reduces the analgesic requirement in post-operative period as compared to bupivacaine 0.25% alone.

Keywords: dexmedetomidine, bupivacaine, cholecystectomy.

Introduction

Laparoscopic surgery has now become the most accepted surgical and safe technique for a number of surgery including cholecystectomy , appendcectomy , etc[1] .Advantages over open procedures include lesser haemorrhoage , better cosmetic results , lesser post operative pain and better results$_2$. The pain in laparoscopic surgeries is mainly confined to the first 24 hours and gradually subsides[3] . The type of pain in laparotomy is different from laparoscopy . In the former the pain is parietal in nature while in the latter the pain is visceral in nature . Causes of pain in laparoscopy includes stretching of intra abdominal cavity , peritoneal inflammation and diaphragmatic irritation[5] causes by residual carbon dioxide in the peritoneal cavity[6] . Pain after laparoscopy can result in increased hospital stay , increased morbidity and increased costs . Various methods have been proposed to relieve post operative pain after laparoscopic cholecystectomy . Peritoneal inflammation caused by carbon dioxide pneumoperitoneum provides rationale for use of non steroidal anti inflammatory drugs[8] . NSAIDs use after laparoscopy yield controversial results . Moreover the safety of NSAIDs may be questionable because of pathophysiological changes of renal blood flow induced by pnuemoperitoneum . Application of local anaesthetics in incision area after laparoscopic cholecystectomy resulted

in lower post operative pain as compared to open cholecystectomy . Local anaesthesia infiltration at trocar site of laparoscopic cholecystectomy resulted in lower post operative pain as was shown by another study. Other methods to reduce post operative pain , involved instillation of local anaesthetic (80 ml of bupivacaine 0.125% with epinephrine 1:2,00,000) under right diaphragm to reduce shoulder pain after minor gynaecological laparoscopic surgeries. Significant morphine sparing analgesia could be achieved for 4 hours after total abdominal hysterectomy when combination of intraperitoneal and incisional bupivacaine with epinephrine was used. Intraperitoneal administration of levobupivacaine with epinephrine is associated with modest analgesia following laparoscopic cholecystectomy with reduced morphine consumption . This technique however seemed ineffective in relieving pain after laparoscopic cholecystectomy. The differences may be due to differences in study protocol (volume and concentration of local anaesthetic instilled : 20 ml of bupivacaine 0.25% and 100 ml of bupivacaine with epinephrine in concentration of 1:1,50,000 and/or use of two different laparoscopic procedures .

Intraperitoneal administration of bupivavaine 0.25% 30 ml with morphine 2 mg reduced analgesic requirements during the first 6 post operative hours as compared with control group undergoing laparoscopic cholecystectomy as shown by study. Intraperitoneal administration of local agents alone[7] or in combination with opoids α_2 agonists such as clonidine and dexmedetomidine reduces post operative pain following laparoscopic cholecystectomy . Local anaesthetics had been used with epinephrine , opoids such as morphine , tramadol , fentanyl and α_2 agonists such as clonidine in earlier studies and has shown to prolong analgesia . Dexmedetomidine is a highly selective α_2 agonist like clonidine with more effect on α_2 receptors , provides sedation , anxiolysis , analgesia and sympatholysis Use of dexmedetomidine in regional anaesthesia is due to its high selectivity for α receptors . The purpose of our study is to compare the analgesic effect of intraperitoneal application of bupivacaine and bupivacaine in combination with dexmedetomidine and associated haemodynamic changes in laparoscopic cholecystectomy surgeries at the end of procedure .

Objectives

To assess the quality of analgesia by visual analgesia scale score (VAS)
To assess the time to the first request to resume analgesia
The total dose of analgesic in first 24 hours
To assess the haemodynamic effects – heart rate , blood pressure and respiratory rate at various time intervals
Adverse effects if any (hypotension , bradycardia , respiratory depression ,dry mouth , nausea, vomiting , sedation)

Material and Method

This study was an interventional, prospective, double blind, parallel group, randomised clinical study conducted on patients undergoing laparoscopic cholecystectomy surgeries. Institutional Ethical Committee Approval was obtained and written informed consent was obtained from all the patients before the screening in the study. This study was conducted at Drabhanga Medical College and hospital , Darbhanga. Study duration period Sep2, 2020 To March2,2021. Patients who were eligible under inclusion and exclusion criteria were included in the study. Interventions were done in the operation theatre under indoor hospital settings. Total of 162 patients were selected in which 81 were randomly allocated in each group using table of randomisation.

Inclusion

- Age group of 18-60 years
- Patient of either sex
- ASA grade I and II
- Body weight between 50-60 kg
- Patient undergoing laparoscopic cholecystectomy

Exclusion

- Patient refused to participate in the study
- ASA grade III and IV
- History of allergy to local anaesthetics and study drugs
- Patients with acute cholecystitis
- Any history of cardiopulmonary, renal, neurological and psychiatric disorders

The study procedure was explained to the patient and informed consent was taken. Preparation included fasting of 6 hours before the surgery, premedication was given a night before and in the morning of surgery with oral tablet alprazolam 0.25mg and tab ranitidine 200 mg. All patients were transported to the operating room without premedication. On arrival to operating room, an 18-gauge intravenous (IV) catheter was inserted and 6 ml/kg/h crystalloid was infused. Intraoperative monitoring of electrocardiography, non-invasive blood pressure, oxygen saturation (SpO_2) was started and baseline values were recorded. Pre-oxygenation with 100% oxygen was done for 3 min. General anaesthesia was induced with IV fentanyl 1.5 ug/kg, propofol 2.0-2.5 mg/kg followed by succinylcholine 2 mg/kg to facilitate orotracheal intubation. The trachea intubated with a cuffed orotracheal tube of appropriate size, lubricated with lidocaine jelly 2% & maintained with 60% NO in oxygen with 0.5-1% isoflurane.

Vecuronium bromide will be used to achieve muscle relaxation, minute ventilation adjusted to maintain normocapnia (end tidal carbon-dioxide [$EtCO_2$] between 34 and 38 mm Hg) and monitoring done . All the study patients will be instructed about the use of the VAS score before induction of anaesthesia (VAS score 0 - no pain, VAS score 10 -worst possible pain). Patients who will be reported VAS 3 or >3 will be given infusion paracetamol 15mg/kg as rescue analgesia. Patients will also be observed for post-operative nausea and vomiting. Patients who will be suffered nausea or vomiting were given ondansetron 4 mg IV.

Demographic data was analysed using unpaired Student's t-test (for comparison of parameters among groups). Comparison was carried out using Chi-square (x2) test and Wilcoxon test with a p value reported at 95% confidence level. Level of significance used was P = 0.05 assuming equal variance for both the study groups. The intensity of post-operative pain recorded for all the patients using VAS score at 0.5, 1, 2,4,6,12,24 hours after surgery and over all VAS score i.s. mean of all VAS scores were analyzed.

Results

Table 1 : Distribution of participants according to gender

Gender	Group			Chi-Squared Test	
	B	BD	Total	X^2	P Value
Male	15 (18.5%)	28 (34.6%)	43 (26.5%)	5.350	0.021
Female	66 (81.5%)	53 (65.4%)	119 (73.5%)		

Gender	Group			Chi-Squared Test	
	B	BD	Total	X^2	P Value
Total	81 (100.0%)	81 (100.0%)	162 (100.0%)		

The distribution of study subjects according to sex is given in Table 1. The females were less in both the groups compared to males. The results of chi-square test show that there is significant association between sex and groups (p value=0.021).

COMPARISON ON THE BASIS OF AGE

Table 2: Comparison of age in years between the groups

		Group B	Group BD	t value	p value
Age	Mean	38.20	36.67	1.063	0.289
	SD	11.28	12.06		

The mean age of patients in group B (38.20) was higher than that of group BD (36.37). The results of independent sample test reveal that the relationship between between mean age of groups B and BD (p value >0.05) is not statistically significant Table 2. and there is no significant association between mean age and groups (p value =0.289).

Table 3: Distribution ofparticipants according to diagnosis

Diagnosis	Group			Chi-Squared Test	
	B	BD	Total	X^2	P Value
Cholelithiasis	81 (100.0%)	81 (100.0%)	162 (100.0%)	-	-
Total	81 (100.0%)	81 (100.0%)	162 (100.0%)		

In both groups B and BD all the patients were diagnosed with Cholelithiasis. Chi-squared test was used to explore the association between 'Group' and 'Diagnosis'.

100.0% of the participants in the group Group: B had Diagnosis: Cholelithiasis. 100.0% of the participants in the group Group: BD had Diagnosis: Cholelithiasis. The distribution of study subjects according to surgery is given in Table 6. All the study participants underwent Laparoscopic cholecystectomy.

Table 4: Distribution of participants according to procedure

Procedure	Group			Chi-Squared Test	
	B	BD	Total	X^2	P Value
Laparoscopic Cholecystectomy	81 (100.0%)	81 (100.0%)	162 (100.0%)	-	-
Total	81 (100.0%)	81 (100.0%)	162 (100.0%)		

Comparison of total dose of analgesic in 24 hours

Table 5: Comparison of total dose of analgesic in 24 hours between the two groups

Total dose of analgesic in 24 hours		Group B	Group BD	p value
	Mean	1552.96	741.67	0.001
	SD	105.46	41.89	

The mean dose for analgesic requirement in group B (1552.96 mg of paracetamol) was higher as compared to group BD (741.67 mg of paracetamol). The results of Independent sample t test reveal that the difference between mean dose for analgesic requirement of groups is stastistically significant (p value <0.05) .

Table 6: Association Between Group and Nausea (n = 162)

Nausea	Group		
	B	BD	Total
Present	3 (3.7%)	1 (1.2%)	4 (2.5%)
Absent	78 (96.3%)	80 (98.8%)	158 (97.5%)
Total	81 (100.0%)	81 (100.0%)	162 (100.0%)

3.7% of the participants in the group Group B had nausea while only 1.2% of the participants in the group Group BD had nausea

Table 7: Association Between Group and Vomiting (n = 162)

Vomiting	Group		
	B	BD	Total
Present	2 (2.5%)	1 (1.2%)	3 (1.9%)
Absent	79 (97.5%)	80 (98.8%)	159 (98.1%)
Total	81 (100.0%)	81 (100.0%)	162 (100.0%)

\2.5% of the participants in the group Group B had vomiting while only 1.2% of the participants in the group Group BD had Vomiting.

Table 8: Association Between Group and Sedation (n = 162)

Sedation	Group		
	B	BD	Total
Present	13 (16.0%)	47 (58.0%)	60 (37.0%)
Absent	68 (84.0%)	34 (42.0%)	102 (63.0%)
Total	81 (100.0%)	81 (100.0%)	162 (100.0%)

16.0% of the participants in the group Group B had Sedation as compared to 58.0% of the participants in the group Group BD who had Sedation.

Discussion

Laparoscopic surgery, also called minimally invasive surgery is a modern surgical technique used for various surgeries like cholecystectomy, appendicectomy, hernia repair. Pain after laparoscopic surgery is due to skin incision site, creation of pneumoperitoneum, tissue trauma created by surgical procedure[9]. Postoperative pain after laparoscopic surgery are mainly due to stretching of intra abdominal cavity (visceral pain), phrenic nerve irritation by residual carbon dioxide in the peritoneal cavity (shoulder pain) and surgical incision (parietal pain)[6]. In this modern era of surgery, intra peritoneal instillation of local anaesthetic agents has become an important method to control post operative pain, nausea, vomiting and reduced hospital stay[10,11]. In laparoscopic surgeries because of gas insufflation and raised intra peritoneal pressure, there is peritoneal inflammation and neuronal rupture with a linear relationship between abdominal compliance and resultant severity of postoperative pain[12].

Hence, we chose intra peritoneal route because it blocks the visceral afferent signals and modifies visceral nociception. The local anaesthetic agents provide anti nociception by affecting nerve membrane associated proteins and by inhibiting the release and action of prostaglandins which stimulates the nociceptors and cause inflammation[13]. As pain after laparoscopic surgery is multifactorial and multimodal analgesia is necessary to counter this pain. Dexmedetomidine is a potent and more selective alpha-2 agonist and reduces pain scores after laparoscopic cholecystectomy with multimodal analgesia. The anti nociceptive effects of dexmedetomidine occurs at dorsal root neuron level, where it blocks the release of substance P in the nociceptive pathway and through action on inhibitory G protein, which increases the conductance through potassium channels[14]. In the present study, out of 162 study participants, 81 were randomized into 2 groups each i.e. group B - bupivacaine and group BD bupivacaine in combination of dexmedetomidine), in which 43 were male patients and 119 were female patients. The mean age of the study participants in group B was 38.20 and group BD was 36.63. This shows that all the study participants were falls under the mid age group. Out of 162 patients, 128 patients were coming under ASA grade I (normal healthy patients) and 34 patients were falls under ASA grade II (patients with mild systemic disease) in both the study groups. Among 162 patients,all 162 were diagnosed with cholelithiasis and all the patients have undergone for Laparoscopic cholecystectomy. The MP grades 1 were more in both groups when compared to MP grade 2. Vital parameters like heart rate, blood pressure are important indicators of patient's comfort and the findings were correlated well with the VAS scores. Statistical analysis revealed that the mean heart rate of patients who receive bupivacaine alone was higher when compared with the patients who received bupivacaine in combination of dexmedetomidine. The mean systolic blood pressure of patients who receive bupivacaine alone was higher when compared with the patients who received bupivacaine in combination of dexmedetomidine and diastolic blood pressure revealed reverse trend i.e. in patients who receive bupivacaine alone was lower when compared with the patients who received bupivacaine in combination of dexmedetomidine. Similarly, the mean respiratory rate of patients who receive bupivacaine alone was lower when compared with the patients who received bupivacaine in combination of dexmedetomidine. Bhattacharjee et al.[15] concluded that dexmedetomidine improves intra and post-operative hemodynamic stability during laparoscopic surgeries without prolongation of recovery and similar results were obtained by Bakhamees et al. [16]. Our study hemodynamic findings also support the previous reported study. All our study findings fulfilled the study objectives and proved the antinociceptive effect of intraperitoneal application of bupivacaine in combination of dexmedetomidine in laparoscopic surgery showed better results than the bupivacaine alone with quality VAS score, better hemodynamic values, less doses of analgesic requirement on post operative period and minimal adverse events. Limitation of the present study is the post-operative pain, which is a subjective experience and can be difficult to quantify objectively and compare when comparing various treatment options.As there are very few studies in the past on addition of dexmedetomidine to intraperitoneal bupivacaine, further studies with different doses of dexmedetomidine, timing, and concentrations of local anaesthetics and routes of administration are needed to provide maximal benefit in terms of postoperative pain relief with minimal adverse effects after laparoscopic surgeries.

Conclusion

Hence our study showed that intraperitoneal instillation of dexmedetomidine 1 µgm/kg in combination with bupivacaine 0.25% in elective laparoscopic cholecystectomy significantly reduces the post-operative pain and significantly reduces the analgesic requirement in post-operative period as compared to bupivacaine 0.25% alone.

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