To Evaluate the Analgesic Efficacy of Port Site Infiltration of Dexmedetomidine for Postoperative Pain Relief after Laproscopic Procedure in Comparison with Bupivacaine

Nandkishor Agrawal[1], Shreshtha Singh[2]

ABSTRACT

Introduction: Laproscopic procedures have advantages such as less haemorrage, better cosmetic results, lesser post operative time causing lesser hospital stay and less expenditure. The aim of this study was to compare the analgesic efficacy of port-site infiltration of bupivacaine with Dexmedetomidine and placebo in reducing postoperative pain after laparoscopic procedures.

Material and Methods: The study was carried out in the department of Anaesthesia AVBRH, a unit of Jawaharlal Nehru Medical College Sawangi Wardha, from December 2016 – December 2017. At the end of surgery, the study Group I (GI) received 50 mL saline; Group II (GII), received 50 mL bupivacaine 0.25% (125 mg) and Group III (GIII),0.25% (125 mg)+1µg/kg Dex (Dexmedetomidine) equally at all the ports sites. Assessment of postoperative pain was based on a 0 to 10 visual analogue scale (VAS, 0: no pain, 10: the worst imaginable pain) at 0, 4, 8, 12 hours postoperatively.

Results: Demographic data, in type of surgery, and duration showed no significant difference between the groups (P>0.05). There was no significant differences regarding hemodynamic variables (NIBP, pulse rate) measured during the intraoperative and postoperative period and in sedation scores among all of the groups (P>0.05). There was a significant reduction in pain as measured by VAS in GIII at baseline, 2 hours, 4hours, and 24 hours postoperatively in comparison to the other two groups (P<0.05). The time of the first rescue analgesic requirement was significantly prolonged in GIII (9.5067.5) in comparison to other two groups (P50.002), with no significant differences observed between GI (0.6060.6) and GII (0.8060.7).

Conclusion: Portsite administration of 1 mcg/ kg Dexmedetomidine combined with bupivacaine provides better quality and duration of analgesia and has an analgesic-sparing effect compared with bupivacaine alone without significant adverse effects in patients undergoing Laparoscopy cholecystectomy surgery.

Keywords: Dexmedetomidine, VAS Score, Analgesia, Portsite

INTRODUCTION

Laparoscopic cholecystectomy as opposed to open cholecystectomy is currently the most accepted surgical technique for cholelithiasis. Laparoscopic procedures have advantages such as less hemorrhage, better cosmetic results, lesser hospital stay and less expenditure. Severity of post operative pain and opioid consumption is less with better pulmonary function in laproscopic procedures compared to open cholecystectomy.[1]

After laparoscopic surgery, visceral pain is experienced due to stretching of intraperitoneal cavity, peritoneal inflammation and phrenic nerve irritation caused by residual carbon dioxide in the peritoneal cavity, whereas open procedures are mainly somatic in nature.[2]

Many methods have been used to decrease the post operative pain including NSAIDs, opioids, intraperitoneal local anesthetics with variable success.[3] Portsite administration of local anesthetic (IPLA), either during or after surgery, is used by many surgeons as a method of reducing postoperative pain. The main advantage of portsite administration of local anesthetic (LA) is that it is simple and does not involve additional central neuroaxial block.[4] Local anaesthetics are effective in mitigating postoperative pain and are safe with less side effects. Bupivacaine a long acting aminoamie local anaesthetic containing equal proportions of S and R enantiomers.

Another approach to reducing postoperative pain involves α_2-adrenergic agonists. α_2-adrenergic agonists have been introduced to clinical anesthesia for their sympatholytic, sedative, anesthetic- sparing, and hemodynamic-stabilizing properties.[5,6] Their central actions are mediated through α_2 adrenoceptors, which are situated at locus coeruleus and dorsal horn of spinal cord.[7]

Dexmedetomidine (Dex) is a highly selective α_2-adrenoceptor agonist recently introduced to anesthesia that produces dose dependent sedation, anxiolysis, and analgesia (involving spinal and supraspinal sites) without respiratory depression.[8] Dexmedetomidine features a high selectivity for the α_2- versus α_1- AR, and in binding studies it is eight times more specific to α_2-ARs than clonidine (the α_2-/ α_1- AR selectivity ratio of Dex is 1,620:1, compared with 220:1 for clonidine).[9] Furthermore, Dex has no agonistic activity toward α_1-ARs in the concentration needed to stimulate α_2-ARs. From a pharmacokinetic perspective, Dex (Dexmedetomidine) has a half life of nearly 2 hours and duration of action of

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nearly 4 hours which is shorter than clonidine.[10] The adverse effects of Dex (Dexmedetomidine) include hypotension, hypertension, nausea, bradycardia, atrial fibrillation, and hypoxia.[11] Given the above characteristics of α_2-adrenoceptor agonism in managing pain, it is reasonable to consider its intraoperitoneal application use in combination with LA for laparoscopic surgery.

The aim of this study was to compare the analgesic efficacy of port-site infiltration of bupivacaine with Dexmedetomidine and placebo in reducing postoperative pain after laparoscopic procedures

MATERIALAND METHODS

The study was carried out in the department of Anaesthesia AVBRH, a unit of Jawaharlal Nehru Medical College Sawangi Wardha, from December 2016 – December 2017. Written informed consent from all patients and approval from ethical committee of our institution were obtained. The preoperative anaesthetic evaluation were done using history, general and systemic examination and routine investigation like HB, CBC, ESR, LFT, KFT, BUN and HbS ag

Inclusion criteria

1. Patients of ASA status I-II of both sexes, undergoing laparoscopic cholecystectomies
2. Aged between 18 and 65 years
3. All the patients who are willing to give informed consent

Exclusion criteria

1. Patients not willing,
2. Patient who were allergic to study drugs,
3. Patients with acute cholecystitis,
4. Patients with severe cardiac, pulmonary, and neurological diseases,
5. Those patient in whom procedure had to be converted to open cholecystectomy,
6. Those patient in whom abdominal drain has to be put.
7. Patient with history of psychological disturbance or chronic pain before laparoscopy

Patients were randomly divided, by computer generated data into three groups, each consisting of 15 patients. On arrival to the operating room, an intravenous line was inserted and premedication with 0.25 mg/kg intravenous ranitidine was given to all patients. Monitoring was done by noninvasive blood pressure (NIBP), O_2 saturation, temperature and electrocardiography. Anesthesia was induced for all participating patients with 1.5–2 lg/kg fentanyl, 2–3 mg/kg propofol, and 1.5 mg/kg lidocaine. Endotracheal intubation was facilitated by 0.15 mg/kg atracurium. Anesthesia and muscle relaxation were maintained by 1–1.5 MAC isoflurane in 50% oxygen/air mixture and 0.03 mg/kg atracurium, respectively. Intravenous crystalloid solution was administered according to the patients' requirement. No other analgesics were given. A nasogastric tube was inserted to monitor end-tidal carbon dioxide ($ETCO_2$) after intubation. Intra abdominal pressure was limited to 12 mm Hg for cholecystectomy. The mean duration of operation was 50 minutes in all the groups. Ventilation was adjusted to maintain an ETCO2 of approximately 35–40 mm Hg. A pneumoperitoneum was created by insufflation of CO2. Surgery was conducted in the supine position.At the end of surgery, the study Group I (GI) received 50 mL saline; Group II (GII), received 50mL bupivacaine 0.25% (125 mg) and Group III (GIII), received 50mL bupivacaine 0.25% (125 mg)+1µg/kg Dex equally at all the ports sites. Postoperative pain intensity was assessed by Visual Analogue Scale (VAS, 0: no pain, 10: the worst imaginable pain). Pain intensity was assessed at 0, 4, 8, 12 hours postoperatively, with 0 hour being defined as the time of arrival in the postoperative ward. Patients with VAS score of 3 or above received 2m/kg of intravenous tramadol. In addition 75mg of diclofenac was given intramuscularly if the patient had VAS score of 3 or more within 6 hours of receiving tramadol. Tramadol was repeated if the patient had a VAS score of 3 or more 6 hours after the initial dose of tramadol.

STATISTICAL ANALYSIS

Statistical analysis was done with the help of SPSS. Chi square test was done to calculate the p value.

RESULTS

There was no significant difference between the groups in terms of demographic data, type and duration of surgery as well as regarding hemodynamic variables(NIBP, pulse rate) and sedation scores measured during intraoperative and postoperative period($P>0.05$; Table 1).

There was a significant reduction in pain as measured by VAS score in GIII at baseline ($P = 0.049$) and at 2 ($P = 0.001$), 4 ($P = 0.022$), and 24 ($P = 0.002$) hours postoperatively in comparison to the other two groups ($P<0.05$; Figure 1 and

Demographic data	Group I	Group II	Group III
Age (yrs)			
Mean ±SD	51.76±8.12	52.34±7.98	49.87±8.21
Range	35-65	36-66	36-60
P-value		0.867	
Weight			
Mean ±SD	73.76±8.97	73.10±9.23	75.12±8.67
Range	54-90	55-89	59-89
P-value		0.912	
Male:Female	7/8	9/6	8/7
Surgery Time (hour)			
Mean ±SD	5.05±0.67	5.0±0.76	5.12±0.55
Range	3.5-6.5	3.5-6	3.5-6.5
P-value		0.961	

Table-1: Demographic data and duration of surgery

Time (hr)	Group I	Group II	Group III	P value
0	3.5±1.1	3.5±1.1	2.5±1.1	<0.05
2	4±1.2	3.7±1.2	2±1.4	<0.05
4	3±1.3	2.5±1.3	2±1.3	<0.05
6	2.8±1.1	2.6±1.2	2.2±1.2	<0.05
8	2.6±1.3	2.4±1.4	2.3±1.4	<0.05
12	2.7±1.1	2.6±1.3	2.4±1.2	<0.05
24	2.5±1.3	2.5±1.1	2±1.1	<0.05

Table-2: VAS (Visual Analogue Score)

Postoperative analgesia	Group I	Group II	Group III	P value
Time for first rescue analgesia	1.2±0.9	1.75±1.0	9.5 ± 1.4(hr)	<0.05

Table-3: Comparison between 3 groups regarding post operative analgesia

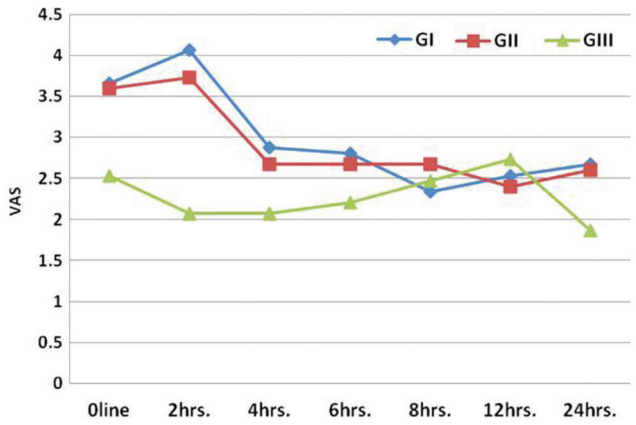

Figure-1: VAS postoperatively

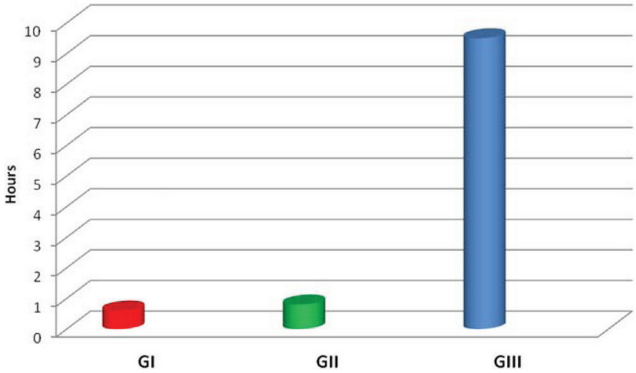

Figure-2: Time of first analgesic request

Table 2).

The time of the first rescue analgesic requirement was significantly prolonged in GIII (9.5067.5) in comparison to other two groups (P50.002), with no significant differences observed between GI (0.6060.6) and GII (0.8060.7) (Figure 2 andTable 3).

DISCUSSION

Our study demonstrated that portsite administration of Dex with bupivacaine significantly reduces postoperative pain and reduces the use of postoperative rescue analgesic consumption, as well as prolong the time to first rescue analgesic request within first 24 hours postoperatively when compared with portsite administration of bupivacaine alone and placebo.

Nearly 80% of patients after laparoscopic surgery need opioid analgesia in the postoperative period.[12,13] Visceral pain signaling is complex. It occurs through the enteric nervous system with a vast network of distinct, and functionally diverse, neuronal subtypes and is partly independent of central nervous system.[14] The main advantage of these local anesthetic agents is that they do not exhibit the adverse effects of opioids, such as postoperative sedation, nausea, gastrointestinal paralysis, and respiratory depression, and they act directly on the tissue to which they are applied.[15]

It had already been shown in various studies that IPLA is beneficial in patients undergoing open hysterectomy[16,17], laparoscopic gynecological procedures[18,19], and laparoscopic cholecystectomy[20], where instilled LAs block visceral afferent signaling, and potentially modify visceral nociception by blocking sodium channels[21], and this may explain the minimal difference in outcome between groups I and II.

Memis D et al found in their study that the combination of bupivacaine plus clonidine administered intraperitoneally in total abdominal hysterectomy operations provides more effective analgesia than bupivacaine alone during the early postoperative period.[22]

Clonidine has several limitations as the vascular responses to clonidine might represent the sum of its effects on both α_1- and α_2-ARs. From a practical standpoint, more problems with clonidine exist in its pharmacokinetic properties, primarily a long duration of effect (6–10 hours), a long elimination half-time (t1/ 256–23 hours), and a prolonged dose-dependent duration of side effects, contributing to prolonged sedation.[9]

Dex has been used to premedicate and sedate patients undergoing day-case procedures without adverse effects.[23] In a study by Esmaoglu et al.[24] it was shown that addition of Dex to lidocaine for intravenous regional anesthesia has better analgesic effect, increased time to the first postoperative analgesic requirement, and reduced total analgesic requirement. Our results are in agreement with those of Ahmed et al.[25] who demonstrated that intraperitoneal administration of Dex with bupivacaine in laparoscopic gynecologic surgeries was associated with a reduction in postoperative analgesic requirements and increased time to first request for postoperative morphine. There is dual action of α_2-adrenergic agonists. It inhibits the release of substance P at the level of the dorsal root neuron[26] and prevents norepinephrine release at nerve endings.[27] It also causes local vasoconstriction, which resulst in higher concentrations of Las near the nerves and enhances analgesia.[28] In this study there was a large difference in the total amount of the rescue analgesic used but there was no significant difference in the sedation score between the groups. The higher dose of rescue analgesics used in groups I and II were not high enough to cause significant sedation in the first 24 hours.

CONCLUSION

Portsite administration of 1 mcg/ kg Dexmedetomidine combined with bupivacaine provides better quality and duration of analgesia and provides an analgesic-sparing effect compared with bupivacaine alone without significant adverse effects in patients undergoing laparoscopy cholecystectomy surgery.

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