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Original Research Article

Randomized control trial of intra-peritoneal instillation of bupivacaine versus placebo for post-operative analgesia after laparoscopic hysterectomy

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ABSTRACT

Background: Laparoscopy is an established method to perform major surgeries, with many advantages over open surgeries. Hysterectomy is a common procedure performed with increased use of laparoscopy, having postoperative pain management is a major issue. Effective pain management promotes early ambulation, lowering the risk of DVT and PE.

Methods: The present study aimed to assess effect of bupivacaine intraperitoneally during laparoscopic hysterectomy to reduce postoperative pain. 48 women undergoing laparoscopic hysterectomy under ASA I and II general anesthesia were included, divided into 2 groups, group A receiving 0.25% bupivacaine intraperitoneally; group B receiving saline. A blind observer observed both groups for 6 hours post-surgery or until the VAS was 4, whichever came first, need for rescue analgesia, side-effects, and total dose of analgesia required in 24 hours. Diclofenac sodium and paracetamol was used as rescue analgesia for both groups.

Results: There was no significant difference reported in demographic parameters between two study groups. The VAS scores at 6, 12 and 24 hours after laparoscopy was significantly lower in group A than group B. There was significant increase in the time required for 1st analgesia, while amount of analgesia required was significantly low in group A as compared to group B. There were significantly more number of patients in group B who needed opioids than group A.

Conclusions: Peritoneal bupivacaine instillation after laparoscopic hysterectomy was found to be useful to reduce the pain as compared to use of saline (placebo), significant reduction in need for analgesics in the postoperative period.

Keywords: Laparoscopy, hysterectomy, pain management, bupivacaine

INTRODUCTION

Laparoscopy is an established method to perform major surgeries, advantages over open surgeries include: less haemorrhage, better cosmetic results, less postoperative pain and shorter recovery time, leading to shorter hospital stay and less expenditure. Hysterectomy is one of the most common gynaecologic procedures and 90% of cases due to benign diseases. It can be performed abdominally, vaginally or laparoscopically depending on the patient's

clinical characteristics and surgeon's expertise and preference. Laparoscopic hysterectomies have been increased recently due to several advantages of minimally invasive surgery.¹

Postoperative pain management remains major challenge after laparoscopic procedures. Effective pain control encourages early ambulation which significantly reduces the risk of deep vein thrombosis and pulmonary embolism.²

Pain after laparoscopic surgeries has two components, 1) visceral component due to surgical handling, tissue injury and the stretching of nerve endings. Pneumoperitoneum stretches the peritoneum and diaphragmatic muscle fibers, which irritates phrenic nerve endings. Carbon dioxide is another factor for diaphragmatic irritation 2) somatic component of post laparoscopy is pain due to holes made in abdominal wall for trocars entry.³

Intraperitoneal instillation of local anaesthetics has been shown to minimise post-operative pain after laparoscopic surgeries. A high quality of postoperative pain management improves recovery and reduces the risk of postoperative acute and chronic adverse effect.⁴

Intraperitoneal instillation of bupivacaine with or without dexmedetomidine, ropivacaine are used for postoperative analgesia after laparoscopic procedures.⁵

These are very effective and do not have any added risk for complications. Simultaneous instillation of local anaesthetic into the peritoneal cavity along with local infiltration alleviates the post-operative discomfort due to both the visceral and somatic component of the pain.⁶

With the help of this study we plan to assess the effect of use of bupivacaine locally and intraperitoneally during laparoscopic hysterectomy to reduce postoperative pain.

METHODS

The present randomized double blind control study was conducted in the Department of Obstetrics and Gynaecology, Bharati Vidyapeeth (DTU) Medical College and Hospital, Pune and Dinanath Mangeshkar Hospital, Pune. The sample size was calculated to be 48 women (24 women in each group). Therefore, the study included 48 women for a duration of 9 months from 1st April 2021 to 31st December 2021. All women who presented for Laparoscopic hysterectomy age between 39 to 65 years with indications for hysterectomy- Any benign condition were included, patient unfit for the laparoscopic surgery, genital malignancy and/or any allergy to used drug were excluded from the study.

Methodology

48 women who presented for laparoscopic hysterectomy under General Anaesthesia ASA I and II were recruited for the study. The patients who fulfil the inclusion criteria were recruited and written informed consent was obtained. The patients were randomized using simple randomization method by chits in two groups:

Group A: Intraperitoneal instillation bupivacaine.

Group B: Intraperitoneal instillation normal saline.

The patients who were selected for the group 'A' received intraperitoneal instillation of 0.25% bupivacaine dose of

20 ml (in supra-hepatic region). The patients selected for group 'B' received normal saline instead of bupivacaine. Both groups were induced as per standard protocol for general anaesthesia. Both groups received any other analgesia/diclofenac suppository during the surgery and in the post-operative period was noted.

Both groups were monitored by a blind observer for visual analogue pain score (VAS) at every hour post-surgery for 6 hours or till the VAS is 4, whichever was earlier, need of rescue analgesia at VAS score of 4, any side-effects, total dose of analgesia required in 24 hours. Rescue analgesia for both groups was inj. diclofenac sodium 75 mg aqueous solution intramuscular/inj. paracetamol 1 gm. IV. Further post-operative analgesia was inj. diclofenac 75 mg intramuscularly 12 hourly/inj. paracetamol 1 gm. intravenously 8 hourly.

Statistical analysis

The collected data was coded and entered in Microsoft excel sheet. The data was analysed using SPSS version 25.0 software. The qualitative data was presented as ratios and proportions, and compared between groups using chi-square test. The quantitative data was presented as mean \pm standard deviation (SD), Students 't' test was used to compare difference between two means. The p value of <0.05 was considered significant.

RESULTS

The present study was aimed to compare the efficacy of intraperitoneal instillation of bupivacaine versus placebo for post-operative analgesia after laparoscopic hysterectomy. Total 50 patients undergoing hysterectomy were included in the study, which were divided into 2 groups with 25 patients in each group viz. group A received intraperitoneal instillation of 0.25% bupivacaine dose of 20 ml and group 'B' received normal saline.

Between the two study groups there was no any significant difference in the means for demographic parameters including age and BMI was reported, also there was no significant difference in the distribution of patients as per previous surgery/LSCS. The results are shown in Table 1.

Table 1: Comparison of basic demographic features and operative variable between 2 study groups.

	Group A (n=25)	Group B (n=25)	P value
Age (years)			
Range	40-49	40-49	0.4945
Mean \pm SD	44.2 \pm 2.43	43.72 \pm 2.5	
BMI			
Range	22.5-33.7	22.8-37.2	0.4308
Mean \pm SD	27.81 \pm 3.11	28.16 \pm 3.12	
Previous surgery/LSCS			
Number (%)	4 (16)	4 (16)	0.6997

The indications for hysterectomy among both the study groups were noted and presented in Table 2. Adenomyosis was reported to be the most common indication, followed by presence of multiple fibroids, large uterine fibroid etc.

Table 2: Indications for hysterectomy among the study groups.

	Group A (n=25)		Group B (n=25)	
	N	%	N	%
AUB with endometrial hyperplasia	2	8	0	0
AUB with adenomyosis	10	40	14	56
AUB with endometrial hyperplasia	0	0	2	8
AUB with multiple fibroid	7	28	4	16
Large uterine fibroid	1	4	1	4
Large broad ligament fibroid	1	4	0	0
Large left lateral wall fibroid	1	4	0	0
large multiple uterine fibroid	1	4	0	0
large posterior wall fibroid	0	0	1	4
large right lateral wall fibroid	0	0	1	4
multiple uterine fibroid	1	4	1	4
Severe endometriosis with large fibroid	1	4	1	4

The VAS scores at 6, 12 and 24 hours after laparoscopy was assessed and compared between the study groups. At every time interval the VAS score was significantly low in group A than group B. The results of VAS scores is showed in Table 3.

Table 3: Comparison of pain score (VAS) between study groups at different time interval.

	Group A (n=25)	Group B (n=25)	P value
After 6 hours			
Range	5-7	7-9	<0.0001*
Mean±SD	5.64±0.69	8.08±0.63	
After 12 hours			
Range	3-4	5-7	<0.0001*
Mean±SD	3.4±0.49	5.92±0.48	
After 24 hours			
Range	2-3	4-5	<0.0001*
Mean±SD	2.16±0.37	4.32±0.47	

Postoperative analgesia was assessed by observing the time required for 1st analgesic dose, amount of analgesia needed, and need for opioids. There was a significant increase in the time required for 1st analgesia in group A as compared to group B, while amount of analgesia

required was significantly low in group A as compared to group B. There were significantly more number of patients in group B who needed opioids than group A. The results are depicted in Table 4.

Table 4: Comparison of postoperative analgesia between the study groups.

	Group A (n=25)	Group B (n=25)	P value
Time for 1st analgesia (in hours)			
Range	4-9	1-3	<0.0001*
Mean±SD	5.54±1.04	2.32±0.73	
Amount of analgesia needed (1 mg/100 ml bottles)			
Range	1-2	3-4	<0.0001*
Mean±SD	1.60±0.49	3.40±0.49	
Need for opioids			
Number (%)	3 (12)	14 (56)	0.0028*

DISCUSSION

Hysterectomy is one of the most common gynaecologic procedure performed. Despite the fact that traditional gynaecologic surgery was done through an open abdominal incision, advances in minimally invasive gynecologic surgery have resulted in a significant increase in the use of the laparoscopic approach.^{25,30}

This is largely due to the fact that laparoscopic hysterectomy has been shown to have a number of benefits over the traditional abdominal approach, including reduced pain and a faster return to normal activities.^{25,31}

Postoperative pain management remains a major challenge after laparoscopic procedures. Effective pain control encourages early ambulation, which significantly reduces the risk of deep vein thrombosis and pulmonary embolism; enhances patient's ability to take deep breaths to decrease the risk of pulmonary complications (e.g., atelectasis and pneumonia); and decreases the incidence of tachycardia and unnecessary investigations related to it.³

Intraperitoneal instillation of local anesthetics, with or without adjuncts, has become a popular way to manage postlaparoscopic pain.³²

The present study was aimed to compare the efficacy of intraperitoneal instillation of bupivacaine versus placebo for post-operative analgesia after laparoscopic hysterectomy. Among 2 groups with 25 patients in each group viz. group A received intraperitoneal instillation of 0.25% bupivacaine dose of 20 ml and group 'B' received normal saline.

Between the two study groups there was no any significant difference in the means for demographic parameters including age and BMI was reported, also there was no

significant difference in the distribution of patients as per previous surgery/LSCS. Adenomyosis was reported to be the most common indication for hysterectomy, followed by presence of multiple fibroids, large uterine fibroid etc. In each group 4 females had undergone previous LSCS surgeries.

Arden et al reported abnormal uterine bleeding, pelvic pain, and symptomatic leiomyomas to be the most common indications for hysterectomy.²⁵ Also in their study in bupivacaine group and in placebo group, 70% and 77% of patients had undergone one or more previous abdominal surgeries, similar to present study cesarean delivery was the most common of them.

At 6, 12 and 24 hours after laparoscopy the VAS score was significantly improved among patients in group A compared to group B.

Similar results were reported by Elbeialy et al for use of intraperitoneal bupivacaine with nalbuphine compared to magnesium postoperatively at 6 and 12 hours but it was opposite at 1, 2, 4, and 12 hours.³²

Badawy et al reported significantly lower VAS in Bupivacaine and Magnesium Sulphate group at 6, 12 and 24 hours after laparoscopy than a placebo group, while difference was insignificant after 7 days.³ A significant reduction in pain intensity was noted in bupivacaine and magnesium sulphate group.

The intensity of pain at 0.5, 1, 2, 4, 6, 24 h after surgery by Kaarthika et al, and reversal from anaesthesia did not show any statistical difference between the groups using intraperitoneal instillation of additional dexmedetomidine or clonidine along with bupivacaine.²⁹

According to Arden et al rated postoperative pain at 1, 2, 4, 6, 12, and 24 hours, median VAS scores at all postoperative time points ranged from 2.0 to 4.3 with no statistically significant difference between the groups intraperitoneal instillation of bupivacaine and placebo at any time point.²⁵ Toleska et al reported significantly lower VAS score at all times in the patients those received instillation bupivacaine 0.5% than patients those did not receive any intraperitoneal instillation.²⁸

Pati also reported similar results about VAS at different time interval after laparoscopy was less in group receiving instillation of bupivacaine with dexmedetomidine compared to patients receiving instillation of only bupivacaine which was statistically significant.²⁷ Intraperitoneal instillation of ropivacaine plus dexmedetomidine (RD) was analysed by Chiruvella et al, the overall VAS score at 24 hours was significantly lower in RD group compared to patients who received instillation of only ropivacaine.³³

Since 1951, intraperitoneal local anesthetics (IPLAs) have been used. IPLA has been shown to decrease shoulder tip

pain, overall pain, nau-sea and vomiting, and hospital stay time.^{28,34}

Local anesthetics inhibit the release of prostaglandins that stimulate nociceptors and boost the inflammatory process by blocking visceral afferent signals and modifying visceral nociception. They also provide antinociception by affecting nerve membrane-associated proteins and inhibiting the release of prostaglandins that stimulate nociceptors and boost the inflammatory process.³²

Systemic absorption of local anesthetic from the peritoneal cavity may also play a part in reduced nociception although this would be expected to occur after any local anesthetic technique. Systemic levels of local anesthetic are detectable in the serum circulation as soon as 2 minutes after bolus instillation into the peritoneum.^{28,35}

In the present study there was a significant increase in the time required for 1st analgesia, while amount of analgesia required was significantly low among patients who received bupivacaine vs placebo and there were significantly more number of patients in placebo group who needed opioids than patients received intraperitoneal instillation of bupivacaine.

According to Elbeialy et al regarding total diclofenac consumption per 24 h, it was significantly higher in BM group when compared with BN group.³² Moreover, rescue analgesia time was significantly shorter in BM group when compared with BN group. Badawy et al noted a significant increase in the time required for 1st analgesia in bupivacaine and magnesium sulphate group than without instillation group, also the amount of analgesia needed was significantly less in study group than comparison group, and number of patients need for opioids in were more in group receiving no any intraperitoneal instillation than compared to patients receiving instillation of bupivacaine and magnesium sulphate.³

The range of total opioid medication use did not differ significantly in study group compared to placebo group by Arden et al.²⁵

The amount of rescue opioid fentanyl required was lower in bupivacaine dexmedetomidine (BD) group and bupivacaine clonidine (BC) group compared to only bupivacaine group. BC group required less amount of fentanyl when compared to BD group. The mean time to first request for analgesia in minutes was significantly less in BC group than BD group, but without significant difference in the number of doses and total dose of paracetamol received. None of the patients from group BD and BC needed a second dose of rescue fentanyl in comparison with only bupivacaine group.²⁹

Chiruvella et al reported significant longer time for first dose of rescue analgesia in ropivacaine plus dexmedetomidine (RD) group than in only ropivacaine, indicating better and longer pain relief in the RD group,

with high consumption of analgesic by patients in ropivacaine receiving group than in RD group.³³ Total diclofenac consumption was also low in RD group.

Pati et al reported significant increase in the time required for 1st rescue analgesia in BD group than group B, with significantly less amount of paracetamol needed in group BD than group B.²⁷

CONCLUSION

In conclusion as compared to the placebo (saline) group, intraperitoneal instillation of bupivacaine in laparoscopic hysterectomy significantly reduces postoperative pain and significantly reduces the need for analgesics in the postoperative period.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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