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Original Research Paper

Anaesthesiology

TO COMPARE THE EFFICACY OF INTRAPERITONEAL INSTILLATION OF BUPIVACAINE ALONE VERSUS BUPIVACAINE PLUS DEXMEDETOMIDINE VERSUS BUPIVACAINE PLUS TRAMADOL FOR POST OPERATIVE ANALGESIA FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY.

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ABSTRACT

Background: Nowadays laparoscopic surgeries are commonly performed on a day care basis. Although of less intensity, laparoscopic surgeries do have some amount of pain. **Aims and objectives:** To compare the efficacy of intraperitoneal instillation of Bupivacaine alone versus Bupivacaine plus Dexmedetomidine versus Bupivacaine plus Tramadol for postoperative analgesia following laparoscopic cholecystectomy. **Method:** Total 81 patients of American Society of Anesthesiologist status(ASA) grade I/II of either sex scheduled to undergo elective laparoscopic cholecystectomy under general anesthesia were included in the study. Patients were divided in 3 groups,27 in each group. Group B (n = 27): Intraperitoneal Bupivacaine 40 ml (0.25%) + 5 ml normal saline ,Group BD (n = 27) : Intraperitoneal Bupivacaine 40 ml (0.25%) + Dexmedetomidine 1 μg/kg (diluted in 5 ml NS), Group BT (n = 27) :Intraperitoneal Bupivacaine 40 ml (0.25%) + Tramadol 1 mg/kg (diluted in 5 ml NS) was given. Patients demographic details, hemodynamic status and visual analogue scale (VAS) was assessed. **Result:** The demographic details were comparable in all 3 groups. Post-operative VAS at different time interval were significantly higher in group B, as compared to group BD and BT. Mean time to first requirement of rescue analgesic in the post operative period for group BD, BT and B was 367.40 ± 111.47, 233.55 ± 23.06 and 109.07 ± 28.42 respectively. Mean of the total analgesic requirement in 24 hours was 105.55 ± 42.92, 133.33 ± 48.04 and 186.11 ± 43.48 mg in study groups BD, BT and B respectively. **Conclusion:** Bupivacaine (0.25%) plus 1 mcg/kg Dexmedetomidine and Bupivacaine(0.25%) plus 1 mg/kg Tramadol provides longer duration of postoperative analgesia as compared to Bupivacaine (0.25%) alone.

KEYWORDS : Bupivacaine, Post operative analgesia, Laparoscopic cholecystectomy, Dexmedetomidine

INTRODUCTION:

Nowadays laparoscopic surgeries are commonly performed on a day care basis.[1] Although of less intensity, laparoscopic surgeries do have some amount of pain.[2] This post-operative pain, to some extent, limits early post operative recovery and extends hospital stay. Incisional (somatic), intra abdominal (visceral) & shoulder tip pain result from a number of reasons after laparoscopy. Post operative pain occur due to stretching of parietal peritoneum from insufflation of gases intra-peritoneally, release of inflammatory mediators of pain, irritation caused by blood clots and phrenic nerve irritation caused by CO_2 in the peritoneal cavity.[2]

Several methods have been tried till date for post operative analgesia after laparoscopic surgeries such as systemic NSAIDs, epidural analgesia, analgesic suppositories, intravenous opioids and infiltration of wounds with local anesthesia.[1] Intraperitoneal instillation of local anesthetic agents have been found to be useful as anti nociceptive technique for post operative analgesia after laparoscopic surgeries.[3]

Bupivacaine is routinely used LA for post operative analgesia procedures. Literatures are available on widespread use of Bupivacaine intra-peritoneally to provide post-operative analgesia with safety in different laparoscopic surgeries in different doses, concentrations and volumes of the drug.[4-6] Various agents such as, Clonidine, Dexmedetomidine, Tramadol, Morphine, Dexamethasone, Fentanyl, Meperidine are used along with LA, as an additives to provide better analgesia.[1,7-9] These adjuvant drugs act at a site different from that of local anesthetic agents and potentiates the action of LA.[1]

MATERIALS AND METHODS

This randomized control trial was conducted in the department of Anesthesiology at a namo medical collage over a period of 1 year to compare the efficacy of intra-peritoneal instillation of Bupivacaine alone versus Bupivacaine plus Dexmedetomidine versus Bupivacaine plus Tramadol for post- operative analgesia after laparoscopic cholecystectomy.

After obtaining approval from Institutional Ethical committee, a total 81 patients of American Society of Anesthesiologist status(ASA) I/II of either sex scheduled to undergo elective laparoscopic cholecystectomy under general anesthesia were included in the study by closed envelop randomization method. A written, informed consent was obtained from all the patients. Patients with history of allergy, long term use of analgesic drugs, ASA status III or IV, pregnant and lactating females, not willing for participation were excluded.

Detailed history and pre-anesthetic evaluation was done one day prior to surgery of all the patients to rule out any associated disease. Necessary investigations were done as an when required. Pre-operatively, all the patients were informed about the procedure. Patients were instructed on how to use a 0-10 graded Visual Analogue Scale for pain with anchors ranging from `no pain' to 'worst possible pain, in the post-operative period.

Monitoring of Electrocardiography, non-invasive blood pressure and oxygen saturation (Sp02), $EtCO_2$ was started and baseline parameters like heart rate (HR), systolic blood (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were recorded as pre-operative vitals.

Patients were pre medicated with inj. Glycopyrolate (4 mcg/kg) and inj. Fentanyl (2 mcg/kg). Pre-oxygenation was done with 100% oxygen for 3 minutes. A standard general anesthesia was administered to all the patients with inj. Propofol (2 mg/kg) for induction and inj. Succinylcholine (2 mg/kg) to facilitate tracheal intubation. Anesthesia was maintained with 50% $O_2$and 50% N_2O with 1-1.5% .

The study drug solution was instilled intra-peritoneally at the end of surgery according to the group allocation.

- Group B (n=27): Intraperitoneal Bupivacaine 40 ml (0.25%) + 5 ml normal saline
- Group BD (n=27): Intraperitoneal Bupivacaine 40 ml (0.25%) +Dexmedetomidine 1 μg/kg (diluted in 5 ml NS),
- Group BT (n=27): Intraperitoneal Bupivacaine 40 ml (0.25%) + Tramadol 1 mg/kg (diluted in 5 ml NS)

At the end of surgery, the study drug was instilled intra-peritoneally into the gall bladder fossa, hepato-diaphragmatic space and around the hepatoduodenal ligament before removal of trocars with the table in head low and right tilt position, allowing collection of drug solution into the sub-diaphragmatic space. Study period started from immediate post extubation till 24 hours post-operatively.

VAS was assessed at 0 minute (immediate post extubation), every 15 minutes till 1 hour, hourly till 10 hours, and at 12, 16, 20 and 24 hours. Pain was graded as VAS < 3: no pain, 3-5: mild pain, 6 - 7: moderate pain and > 7: severe pain. Patients heart rate and blood pressure was also measured at 0 ,30 minutes and at 1,4,8,12 hour.

Statistical analysis

In our study, data were presented as Mean ± SD, proportion or n (%). One-way analysis of variance (ANOVA) and t-test were used for comparison between groups and P values < 0.05 were considered significant. Statistical analysis was done using software Open Epi and SPSS.

RESULTS:

A total of 81 patients were included in the study.

Table1: Distribution of patients according to age, sex and weight (Mean ± S.D.)

Variables		Group BD	Group BT	Group B	p value
Age		38.40 ± 11.13	42.55 ± 14.58	39.88 ± 11.68	0.503
Weight		56.77 ± 8.19	63.14 ± 11.44	61.14 ± 10.16	0.064
Sex	Male	4(14.81%)	2(7.41%)	6(22.22%)	0.309
	Female	23(85.19%)	25(25%)	21(77.78)	

Patients studied in the three study groups were between 18-60 years of age and between 45 to 85 kg. The distribution of patients according to age, sex and weight were found to be statistically insignificant amongst the three groups (P > 0.05) and the three groups were comparable.

There was female preponderance in all the three study groups. M: F ratio was 1:5.75 (4:23) in group BD, 1:12.5 (2:25) in group BT and 1:3.5 (6:21) in group B.

Table 2: Duration Of Surgery

Variables	Group BD	Group BT	Group B
Duration of surgery (minutes)	66.29 ± 8.88	64.44 ± 9.16	68.51 ± 7.79
p value	0.228		

Statistically no difference was found in overall duration of surgery in between all three groups.(P > 0.05) Mean duration of surgery in group BD, BT and B was 66.29 ± 8.88, 64.44 ± 9.16 and 68.51 ± 7.79 respectively.

Patients were assessed for post- operative analgesia by using VAS at 0 minute (immediate post extubation), every 15 minutes till 1 hour, hourly till 10 hours, at 12th, 16th, 20th and at 24th hours. Overall mean VAS score was statistically significant (p< 0.05) between the three study groups BD, BT and B at all the time interval except at 4th, 6th, 20th and 24th hour postoperatively.

Mean VAS score was statistically significant (p< 0.05) within the group BD and group BT at all time interval except at immediate post extubation time, 4th, 6th, 20th and 24th hour postoperatively. Mean VAS score was statistically significant(p< 0.05) within the group BD and group B at immediate post extubation time, 15 min, 30 min, 45 min, 1st, 3rd, 5th, 6th and 24th hour postoperatively. Mean VAS score was statistically significant (p< 0.05) within the group BT and group B at all time except at immediate post extubation time, 4th , 8th, 20th and 24th hour postoperatively.[Figure 1]

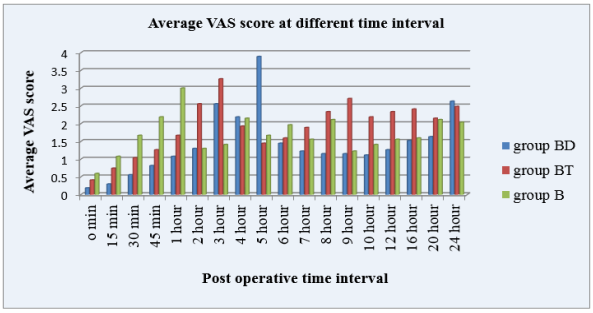

Figure 1: Average VAS score at different time interval

Rescue Analgesia Requirement

Patients were administered intravenous inj. Diclofenac aqueous 75 mg as a rescue analgesic if VAS ≥ 4. The number of patients requiring rescue analgesia at different post-operative time intervals in the three study groups is shown in the figure 2 .

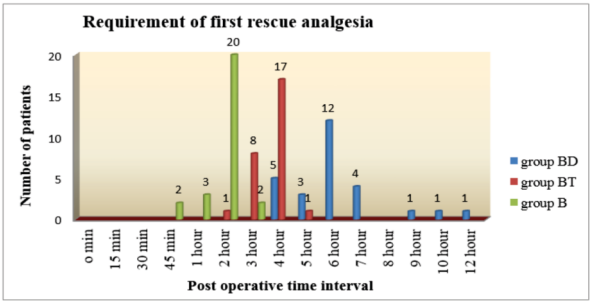

Figure 2: Requirement of first rescue analgesia

Out of 27 patients in group BD, maximum number of patients i.e. **12 (44.44%)** required rescue analgesia at 6th hour. Among group BT, maximum number of patients i.e. **17 (62.96%)** required rescue analgesia at 4th hour. Out of 27 patients in group B, maximum number of patients i.e. **20 (74.07%)** required rescue analgesia at 2nd hour.

Table 3: Comparison of postoperative heart rate (HR) (Mean ± S.D)

Post operative Time interval	Group BD (Mean ± S.D)	Group BT (Mean ± S.D)	Group B (Mean ± S.D)	Over all 'P' value	p values of different group		
					BD vs BT	BD vs B	BT vs B
0 min	95.48 ± 6.49	109.56 ± 7.83	114.51 ± 7.08	0.000	0.000	0.000	0.015
30 min	86.89 ± 7.41	96.29 ± 6.34	97.78 ± 6.17	0.000	0.000	0.000	0.385
1 hour	82.89 ± 5.37	86.59 ± 4.83	92 ± 10.25	0.000	0.010	0.000	0.017
4 hour	87.78 ± 6.41	91.78 ± 7.30	92.15 ± 6.35	0.034	0.037	0.015	0.843
8 hour	86.44 ± 5.80	81.78 ± 7.65	87.33 ± 10.26	0.030	0.015	0.696	0.028
12 hour	86 ± 6.15	82.22 ± 8.19	84.59 ± 8.13	0.184	0.060	0.476	0.290
24 hour	88.07 ± 5.90	84 ± 6.32	83.26 ± 6.71	0.014	0.018	0.007	0.678

Post operatively mean HR was on higher side in group BT and B as compared to group BD which was persistently on lower side. The difference in mean HR between the three study groups BD, BT and B was statistically significant at all the time intervals till 2 hours post- operatively (P<0.05) The difference after 2 hours was not significant (P<0.05) between three study groups at all the time intervals except 8 and 24 hours.

Table 4: Comparison of postoperative mean arterial

pressure (MAP)(Mean ± S.D)

Post operative Time interval	Group BD (Mean ± S.D)	Group BT (Mean ± S.D)	Group B (Mean ± S.D)	Overall 'P' value	p values of different group		
					BD vs BT	BD vs B	BT vs B
0 min	93.33 ± 4.68	102.19 ± 5.65	101.48 ± 4.79	0.000	0.000	0.000	0.620
30 min	89.58 ± 6.92	93.53 ± 7.80	91.98 ± 4.99	0.097	0.054	0.149	0.389
1 hour	85.60 ± 5.75	81.42 ± 4.99	82.81 ± 5.11	0.016	0.006	0.065	0.316
4 hour	90.96 ± 8.97	94.64 ± 6.69	91.53 ± 7.81	0.188	0.093	0.804	0.122
8 hour	90.84 ± 7.65	81.97 ± 4.65	86.52 ± 7.10	0.000	0.000	0.036	0.007
12 hour	86.37 ± 9.07	83.90 ± 7.12	85.03 ± 7.87	0.532	0.270	0.564	0.582
24 hour	87.23 ± 7.45	82.91 ± 4.97	84.59 ± 6.25	0.045	0.017	0.167	0.279

Mean arterial pressure was slightly on lower side in group BD as compared to group BT and B at all the time intervals post-operatively. The difference in MAP was statistically not significant between the three groups BD, BT and B at different time intervals except immediate after extubation, at 1 hr,8 and 24 hours. The difference in MAP amongst group BD vs BT, BD vs B and group BT vs B was not significant post- operatively (P>0.05.)MAP was never beyond acceptable limits at any point of time in all the three study groups post- operatively.

DISCUSSION:

Laparoscopic surgeries being minimally invasive procedures offer many advantages to the patients and hospital services. In comparison to conventional laparotomy, laparoscopic surgeries have reduced hemorrhage, smaller and more cosmetic incision, which reduces pain, reduced risk of acquiring infections thus shorten recovery time, less hospital stay and less expenditure.

A randomized study done by Ranjita Acharya et al [1] used IP Ropivacaine(0.2%, 40 ml) combined with 0.5 mcg/kg Dexmedetomidine that provide superior post operative analgesia without any side effects as compared to Ropivacaine alone. A prospective study done by Anurag and colleagues[7] used 100 mg Tramadol along with Bupivacaine (0.25%, 30 ml) and 50 mg/kg of $MgSO_4$along with Bupivacaine for intraperitoneal instillation after laparascopic cholecystectomy for post operative analgesia. A randomized placebo controlled trial conducted by Nishith Govil et al[9] used intraperitoneal Levobupivacaine with Clonidine (1 mcg/kg) for pain relief after laparoscopic Cholecystectomy. In present study we used Dexmedetomidine (1 mcg/kg) and Tramadol (1 mg/kg) as an additives to Bupivacaine.

In current study, demographic profile in terms of age (p=0.503) and weight (p=0.064) of the patients were comparable in the study population. Gender distribution among the three study groups was not significant statistically (p = 0.309). However, there was female preponderance in all the three study groups. The mean duration of surgery in all the study groups were comparable.(p=0.228)

In the present study, overall mean VAS score was statistically significant (p< 0.05) between the three study groups BD, BT and B at all the time except at 4th, 6th, 20th and 24th hour postoperatively which was comparable to bhardwaj et al [6] and shukla et al. [10]

In the post – operative period, mean time to first requirement of rescue analgesic for group BD, BT and B was 367.40 ± 111.47, 233.55 ± 23.06 and 109.07 ± 28.42 respectively. There was statistically significant difference found in the meantime to first requirement of rescue analgesia between the study groups BD, BT and B and also within the groups BD vs BT, group BD vs B, and group BT vs B (P<0.05). Total duration of analgesia was approximately 6 hours, 4 hours and 2 hours in Group BD, BT and B respectively.

In concern of hemodynamic, post operatively mean HR was on higher side in group BT and B as compared to group BD which was on lower side till 2 hours, difference was significant. (p<0.005). The difference in MAP was statistically not significant between the three groups BD, BT and B at different time intervals

Nishith Govil and Parag Kumar and colleagues et al [9] conducted a randomized, double-blind, placebo-controlled trial tocompare the effect of Intraperitoneal Levobupivacaine with or without Clonidine for Pain Relief after Laparoscopic Cholecystectomy. Patients were divided into three groups. Group I received 20 ml of 0.9% normal saline (placebo group), group II received 20 ml of 0.5% Levobupivacaine and group III received 20 ml of 0.5% Levobupivacaine with 1mcg/kg Clonidine. VAS was highest in Group I and was lowest in Group III at all time intervals, the difference was statastically significant. Time to first supplemental analgesic requirement was maximum in Group III than in Group II and was minimum in Group I and the difference is statistically significant ($P < 0.01$).

Anurag Yadava, Sunil K Rajput, Sarika Katiyar and colleagues et al [7] conducted a prospective, randomized study for comparison of intraperitoneal bupivacaine-tramadol with Bupivacaine-magnesium sulphate for pain relief after laparoscopic cholecystectomy. Patients were randomly divided into two groups. Group TB received 30 ml of 0.25% Bupivacaine along with 100 mg Tramadol,Group MB received 30 ml of 0.25% Bupivacaine along with 50 mg/kg of $MgSO_4$. The mean of VAS pain score at 1, 2, 4, 6 and 24 h after surgery was more in TB group compared to MB group, and the difference was statistically significant ($P < 0.05$). The mean time interval of thefirst rescue analgesiawas also longer in MB group (7.39 hour) compared to TB group (4.94 hour) which was also statistically significant ($P < 0.05$). The results of following study was contradictory to our study.

CONCLUSION:

Intraperitoneal instillation of local anesthetic agent provides better postoperative analgesia in laparoscopic chole cystectomy where visceral pain forms a major component of pain. Bupivacaine(0.25%) plus 1 mcg/kg Dexmedetomidine and 0.25% Bupivacaine plus 1 mg/kg Tramadol provides longer duration of postoperative analgesia compared to 0.25% Bupivacaine alone. Highest result was achieved with 0.25%bupivacaine plus 1 mcg/kg Dexmedetomidine. So, looking to safety profile, longer duration of postoperative analgesia and patient satisfaction, 0.25% Bupivacaine plus 1 mcg/kg Dexmedetomidine can be an attractive combination for intraperitoneal instillation in laparoscopic surgeries.

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