A Prospective Comparative Study to Assess-Post Operative Analgesic Effect of Intraperitoneal Instillation of Bupivacaine with Dexmedetomidine to Bupivacaine with Tramadol in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract

Objective: Tocompare post operativeanalgesic effect of intraperitoneal instillation of bupivacaine with dexmedetomidine, to bupivacaine with tramadol in patients undergoing laparoscopic cholecystectomy.

Method: Sixty patients belonging to age group 20 to 50 years, from both sexes posted for laparoscopic cholecystectomy under general anesthesia were enrolled in our study. They were randomized in two groups, Group A and Group B with 30 patients each. ASA1 & ASA2 physical status were selected. A written and informed consent was taken from all the patients. The group A received 35 ml of 0.25% Bupivacaine with 50 mcgdexmedetomidine and Group B received 35 ml of 0.25% bupivacaine with 50 mg tramadol before removal of trocar. The sites selected for instillation were hepato-diaphragmatic space (10ml), sub hepatic (10ml), on gall bladder bed (10ml) and near and above hepatoduodenal ligament (5ml), at the end of surgery. Intraoperative hemodynamic monitoring was done. Postoperative pain relief was assessed hourly for first 6 hours by VASscore. Time to requirement of first dose of rescue analgesia was noted and this was the endpoint of this study, although the patients were monitored for 24 hours. Sideeffects like postoperative nausea, vomiting and respiratory depression were noted.

Results: We noted that intraperitoneal instillation of bupivacaine with dexmedetomidine prolonged the duration of post operative analgesia compared to bupivacaine & tramadol combination. The requirement of first dose of rescue analgesic is delayed more inbupivacaine dexmedetomidine group as compared to bupivacaine tramadol group. Also the incidence of post operative nausea and vomiting was found to be less in group Ai.e. bupivacaine dexmedetomidine group.

Conclusion: From this study it can be concluded that the use of intraperitoneal instillation of bupivacaine with dexmedetomidine significantly reduces the requirement of post operative analgesics in patients undergoing laparoscopic cholecystectomy with better compliance.

Keywords: *Bupivacaine, Tramadol, Intraperitoneal Instillation, Laparoscopic cholecystectomy.*

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Introduction

Pain in post laparoscopic procedure is common complaint which prolongs the duration of hospital stay and morbidity. Use of local anesthetics for post operative pain relief is a growing practice forlaparoscopic surgeries in recent times. Various studies are available in medical

literature on the different types of anesthetics and adjuvant drugs. Rajan et al studied about the Intrathecal Clonidine and Dexmedetomidine on Characteristics of Bupivacaine Spinal Anesthesia[1]. Jejani et al conducted a study of Intrathecal Buprenorphine for Postoperative Analgesia after Cesarean Section[2]. Singh et al conducted a Comparative Evaluation of Dexmedetomedine versus Clonidine as an Adjuvant in Supraclavicular Brachial Plexus Block[3]. Traditionally, opioids or NSAID'S in various combinations have been used for post operative analgesia after laparoscopic procedures[4,5,6]. Intraperitoneal instillation of local anesthetic agents alone or in combination of opioids[2,3], alpha-2 agonists dexmedetomidine and clonidine have been found to reduce post operative pain following laparoscopic cholecystectomy[7,8]. Pain due to laparoscopic surgeries is because of, stretching and peritoneal inflammation. Shoulder pain is due to irritation of phrenic nerve. Parietal pain is due to incision. Peritoneal origin of pain suggests that analgesia delivered locally to the peritoneal cavity may be of benefit post operatively[9,10].

Methodology

This is a prospective observational study to compare the post operative analgesic effects of intraperitoneal instillation of bupivacaine with dexmedetomidine to bupivacaine with tramadol in patients undergoing laparoscopic cholecystectomy. This study was conducted from Oct 2019 to April 2020 at SMRHC Wanadongri in collaboration with the data collected from AVBRH, JNMCSawangi and some private practitioners. Ethical committee clearance was obtained. Written and informed consent was taken. Group of 60 patients were evaluated in the age group of 20 to 50 years of either gender with ASA1 and ASA2 physical status. Two groups were made;Group A -B upivacaine with Dexmedetomidine and Group B -Bupivacaine with Tramadol.

The patients in whom the procedure was converted to open cholecystectomy, where abdominal drain was put and the patient who did not give consent for the study were excluded from the study.

A detailed preoperative evaluation was done a day prior to surgery pertaining to a detailed general and systemic examination and biochemical tests for each patient and the patients were categorized as ASA1 and ASA 2 physical status accordingly. A written and informed consent was taken from all the patients and VAS scale was explained. The patient was given Tab Alprazolam 0.25 mg on the night prior to surgery and was kept nil by mouth since 10 pm. On the day of surgery after entering the operation theater,standard monitors as ECG, Pulseoxymeter and NIBP were attached, 20G iv access was secured. Prior to induction all the patients were preoxygeneted with 100% oxygen for 3 minutes. After this as premedication, inj glycopyrrolate 0.2 mg IV, injondenseteron 4 mg IV and inj fentanyl 2mg/kg was given. Induction was done with inj Propofol 2 mg/kg. Inj vecuronium 0.01 mg/kg was given to facilitate laryngoscopy and intubation. Adequate depth of anesthesia was maintained with O2:N2O 50:50 with sevoflurane in the range of 1.5 -2% dial concentration. Relaxation was maintained with intermittent doses of 1mg vecuronium ½ hourly. Monitoring of vitals was done. Minute ventilation and respiratory rate were adjusted to maintain the Etco2 in between 35-38. Intra abdominal pressure post Co2 insufflations was maintained in between 12-14 mm of Hg. The patients were randomly placed in two groups of 30 each. Group A - 35 ml of 0.25%bupivacaine with 50 mcg/kg dexmedetomidineand Group - B35 ml of 0.25% bupivacaine with 50 mg Tramadol. Towards the end of the procedure,Co2 was slowly released and the surgeon was asked to instill the drug intraperitoneally; into the hepato-diaphragmatic space (10ml), sub hepatic area (10ml) on gall bladder bed (10ml) and near and above hepatoduodenal ligament (5ml). Patient was reversed with inj glycopyrrolate 0.5mg IV and inj neostigmine 2.5 mg. The patient was shifted to postoperative recovery room and monitored for vitals, pain & any side effects like nausea vomiting, excessive sedation, shivering & pruritus. The intensity of post-operative pain was recorded for all the patients using VAS score at 1, 2, 4, 6 hours after surgery and over all VAS score (mean of all VAS scores) was recorded. (VAS score 0 - no pain, VAS score 10 - worst possible pain) Patients who reported VAS >3 were given Inj paracetamol 1g intravenously as rescue analgesia. Though time of rescue analgesia was considered as the end point of study all patients were followed up for 24 hours.

Statistical Analysis: The statistical analysis was performed by statistician by using Windostat Version 9.2*T-tests* to analyze differences between two groups.

Differences in parameters such as VAS score,time of 1st request of analgesia,any adverse effects over time were analyzed using ANOVA Test.

Observation and Results

The demographic data pertaining to Age, Sex, Weight,duration of surgery and ASA physical status was comparable in both groups and was not significant. ANOVA is applied for age and duration of surgery .P value<0.05 is considered significant t test applied.

Table 1: Demographic Parameters of patients

Parameters	Group A	Group B
Age in years	43.56±9.8	45.44±7.9
Weight in kgs	66.11±7.8	62.7±7.1
Duration of surgery (min.)	63.4±4.5	66.04±4.1

Table 2: Comparison of ASA physical status and gender

Parameters	Group A [n=30]	Group B [n = 30]
Sex (M/F)	11/19	13/17
ASA 1/ASA2	19/11	20/10

Table 3: Comparison of mean VAS Score over 6 hrs

Time [hrs]	Group A (Mean VAS score)	Group B (Mean VAS score)	p Value
1	0.5±0.49	1.5±0.5	0.0009
2	0.93±0.66	1.8±0.45	0.0008
3	1± 0.4	2.3± 0.6	0.0007
4	1.39±0.5	2.5±0.7	0.009
5	1.5±0.5	2.5± 0.5	0.000
6	1.6±0.5	2.7±0.8	0.0089

The above table shows comparison of mean VAS score at specified time intervals that is at 1,2,3,4,5 and 6 hours. p value was <0.05 and is significant.

Table 4: Comparison of VAS score in 6 hours, Time of 1st request of analgesics.

Variable	Group A (Mean±SD)	Group B (Mean±SD)	P value
Overall VAS score in 6 hours	1.16 ± 0.56	2.08 ± 0.63	0.007
Time of first dose of analgesics (min) inj paracetamol 1 gm	315.6±33.3	211.6±23.6	0.009

P value < 0.05 is significant.

Time required for first dose of rescue analgesia was longer in group A (315.6±33.3 min) than in group B (211.6±23.6 min), indicating better and longer pain relief in group A as compared to group B.

Table 5: Showing comparision of heart rate in between two groups at various time intervals during the study.(p value is >0.05)and is not significant.

Heart Rate	Group A (N=30)	Group B (N=30)	P value
PreOp	78.7	80.7	0.6617
Induction	82	78	0.6513
Start OF procedure	81	82	0.5812
IntraOp 15 min	79.7	79	0.712
IntraOp 30 min	82	81	0.618
IntraOp 45 min	81	80	0.762
IntraOp 60 min	78	79	0.823
PostOp	76	73	0.612
PostOp 1 hour	65	70	0.423
PostOp 2 hour	64	74	0.222
PostOp 3 hour	63	72	0.245

Heart Rate	Group A (N=30)	Group B (N=30)	P value
PostOp 4 hour	64	70	0.355
PostOp 5 hour	66	74	0.185
PostOp 6 hour	65	78	0.155

Table 6: showing comparision in systolic blood pressure in between two groups at various time intervals during the study.(p value is >0.05 and is not significant.

Systolic Blood Pressure	Group A (mm Hg)	Group B (mm Hg)	P Value
PreOp	113	114.4	0.5896
Induction	124	124.4	0.9847
Start OF procedure	110	120.4	0.722
IntraOp 15 min	111	118.4	0.7419
IntraOp 30 min	119.4	116.4	0.6493
IntraOp 45 min	113	121.4	0.9103
IntraOp 60 min	115.5	114.4	0.623
PostOp	120	115.4	0.8287
PostOp 1 hour	116	110.4	0.6841
PostOp 2 hour	118	117.4	0.5823
PostOp 3 hour	117.6	119.4	0.7423
PostOp 4 hour	124	122	0.8774
PostOp 5 hour	118	120.4	0.7455
PostOp 6 hour	120	119.6	0.6551

Discussion

Good postoperative analgesia aims to produce long-lasting, continuous effective analgesia with minimum side effects. Laparoscopic cholecystectomy is considered superior to open cholecystectomy with reduced post-operative pain, morbidity and duration of convalescence[6]. The intensity of pain usually peaks during the initial postoperative period.

In this study we compared intraperitoneal instillation of dexmedetomidine and tramadol as an adjuvant to study their analgesic efficacy when added with 0.25% bupivacaine in patients undergoing laparoscopic cholecystectomy.

Dexmedetomidine, an imidazole derivative, a highly selective α2-adrenoreceptor agonist, decreases systemic adrenaline and noradrenaline production and has negative chronotropic and inotropic effect.[13]

Dexmedetomidine when added to local anaesthetic or given intravenous prolongs the duration of sensory block of local anaesthetic during peripheral nerve block.[14]

Dexmedetomidine has antinociceptive effects at dorsal root neurons, decreasing substance P release and stimulating the inhibitory G protein, which increases potassium channel conductivity.[15]

Tramadol also has sensory blockade and similar mechanism of action to that of local anaesthetic in the form of blocking of voltage gated sodium channels[11]. So we used tramadol as the adjuvant in our study.

Shukla et al compared the analgesic effects of dexmedetomidine and tramadol with bupivacaine to bupivacaine alone intraperitoneally after laparoscopiccholecystectomy. Dexmedetomidine group had remarkable less shoulder pain than tramadol group., Time to first request of analgesia (min) was (128 ± 20, & 118 ± 22) in Dexmedetomidine & Tramadol group respectively which is similar to the result of our study[11].

Golubovic et al reported that analgesic effects of intraperitoneal injection of bupivacaine and tramadol in patients with laparoscopic cholecystectomy were effective for treatment and management of pain after surgery[8].

Memis et al studied effects of tramadol and clonidine added to intraperitoneal bupivacaine on post operative pain in Total abdominal hysterectomies and found combination of tramadol or clonidine with intraperitoneal bupivacaine to be more effective than bupivacaine alone.

Ahmed et al compared the analgesic effect of intraperitoneal instillation of Ropivacaine alone to Ropivacaine with dexmedetomidine. In this, the time of requirement of first request of analgesia is longest that is 487± 40.96(min) in ropivacaine dexmededtomidine combination and 242.5 ± 19.85 min with ropivacaine alone.

In a study conducted by Radhe Sharan,Manjit S & Rohit Kadian, 20 ml of 0.5% bupivacaine was compared to 0.5% ropivacaine after intraperitoneal instillation in laproscopic cholecystectomy patients[16].In this group side effects as arrythmia and hypotension were noted in group 0.5% bupivacaine group as compared to 0.5 % ropivacaine group.

As a result we took a lower concentration of bupivacaine that is 0.25% in our study.

Rapolu et al studied the antinociceptive effect of 0.25% bupivacaine with saline to 0.5% bupivacaine with 1 mcg/kg dexmedetomidine after intraperitoneal instillation in patients of laproscopic cholecystectomy and named them as Group B and Group BD respectively. They found that the time to first dose of analgesia was longer in group BD as compared to Group B and also the side effects were not significant[17,18].

In our study we found that dexmedetomidine group has significantly lower VAS score at all points of time((1.80 ± 0.36)P< 0.05. and statistically lower than tramadol which was in agreement with the study done by Shukla et al and Ropulo et al.

In our study minimal side effects in the form of nausea and vomiting were observed and that too were statistically insignificant(p value=0.171).There were no major side effects like respiratory depression.

This study results show that a combination of bupivacaine with dexmedetomidine was superior to the combination of bupivacaine with tramadol in terms of post operativepain, time to the first request of analgesia and adverse effects. General demographics such as age,sex,weight,ASA status and duration of surgery between the two groups had no statistical difference.

The results of our study are consistent with above studies. Time to first rescue analgesia in post operative period was significantly delayed in group A as compared to Group B in our study. There were few post operative complications like nausea and vomiting in both the groups. The incidence was more in the group B than the group A. We have found this to be statistically insignificant (P = 0.171).

Conclusion

We conclude that intraperitoneal instillation of dexmedetomidine 50µg in combination with 35ml of 0.25% bupivacaine in elective laparoscopic cholecystectomy significantly reduces the post operative pain and significantly reduces the analgesic requirement in post-operative period as compared to 35ml of 0.25% bupivacaine combined with tramadol. This is simple to use with minimal side effects and discomfort to the patient and hence can be suggested for routine use.

Limitation: End point of our study was the time for first requirement of rescueanalgesia. VAS score over 24 hours was not taken into consideration. Also the total dose of analgesics was not calculated. We need to take a larger sample size & include a control group of plain bupivacaine without any adjuvant to have a better comparison. Last but not the least cost of dexmedetomidine can not be ignored. We need to compare it with the cost of total analgesics required post operatively.

Ethical Clearance: Taken from institutional ethics committee.

Source of Funding: Self.

Conflict of Interest: Nil.

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