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Original Research Article

Comparison of Efficacy of Bupivacaine Plus Tramadol with Bupivacaine Plus Dexmedetomidine as Preincisional Infiltration in Patients Undergoing Abdominal Surgery Under General Anasthesia: A Prospective Randomised Double Blinding Study

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to assess the efficacy of bupivacaine plus tramadol with bupivacaine plus dexmedetomidine as pre-incisional infiltration in patients undergoing abdominal surgery under general anesthesia.

Methods: The Prospective randomized and double-blind study was conducted at of Indira Gandhi Institute of Medical Sciences, Patna. The study protocol, informed consent form (in Hindi & English) and case report form (CRF) were submitted to the ethical committee of Indira Gandhi Institute of Medical Sciences, Patna for approval. Study was done after taking approval from institute ethical committee. Written informed consent was taken from each participants of the study. The Data was collected between – May 2019 to November 2020. Total 60 samples were included in the study (30 in each group).

Results: It was observed that maximum number of patients were in the group T 35-44 years age group (26.674%) and group D, 55-60 years age group (30%). Mean age ± SD of patients in Group T was 41.63±13.46 years while that of group D was 41.80±14.37 years. On comparing the data statistically observed among the groups in the height distribution. The result of Independent sample t test reveals that there was significant difference between mean VAS Score of groups in 4 hour and 6 hours. There was no significant difference in group T and Group D in mean heart rate of the patients. The mean basal MAP in Group T was 96.38±2.93 mmHg and Group D was 96.34±3.02 mmHg. Mean MBP decreased at 3 & 20 minutes interval in two groups. On statistical analysis the mean oxygen saturation among the two groups were insignificant.

Conclusion: We concluded that skin infilteration of 1µg/kg dexmedetomidine 0.2 ml/kg of 0.25% Bupivacaine in abdominal surgery significantly reduces the post-operative pain and reduces the analgesic requirement in post-operative period as compared to 2mg/kg Tramadol in 0.2ml/kg of 0.25% Bupivacaine.

Keywords: bupivacaine, dexmedetomidine, tramadol, abdominal surgery

Introduction

Laparoscopic cholecystectomy as opposed to open cholecystectomy is currently the most accepted surgical technique for cholelithiasis. [1] Laparoscopic procedures have many advantages over open procedures such as lesser haemorrhage, better cosmetic results, lesser post-operative pain, and shorter recovery time, leading to shorter hospital stay and less expenditure. [2] Pain results from stretching of the intra-abdominal cavity, [3] peritoneal inflammation, and diaphragmatic irritation caused by residual carbon-dioxide in the peritoneal cavity. [4] Many methods have been proposed to relieve post-operative pain following laparoscopic cholecystectomy. [5]

Analgesics or Local Anaesthetics given before the surgical stimulus may prevent the increase in excitability of the CNS & prevent or attenuate post operative pain. [6,7] Tramadol is synthetic racimic compound made up of two isomers that have opioid & nonopioid activities, and used mainly for inhibition of pain. Tramadol is a central analgesic with low affinity for opioid receptors. The rate of production of its M1 metabolite (O-demethyl tramadol) is influenced by debrisoquine-type polymorphism, and this metabolite shows a higher affinity for opioid receptors than the parent drug. Experimental and clinical data suggest that tramadol may also exert its analgesic effect through direct modulation of central monoaminergic pathways. Indeed, after a single oral dose, the role of the μ-receptor agonist component of the antinociceptive effect of tramadol appears to be minor, with most of the analgesic effect being attributable to nonopioid properties of the parent compound. Approximately 2-fold accumulation of the parent compound and the M1 metabolite may be expected during multiple dose treatment. The duration of analgesic effect after a single oral dose of tramadol 100 mg is about 6 hours. Clinical experience has confirmed that tramadol is an effective and relatively safe analgesic that may be of value in several pain conditions not requiring treatment with strong opioids. Additionally, the Local Anaesthetic effect of tramadol had been demonstrated in both clinical & lab study. [8-13]

Dexmedetomidine is new alpha-2 agonist that was approved by FDA in 1999, for use in humans as a short term medication for sedation/ analgesia in the intensive care unit. Dexmedetomidine, a highly selective a2-adrenoreceptor agonist, has been used for premedication and as an adjunct to general anesthesia. Intravenous dexmedetomidine premedication before general anesthesia provides preoperative sedation, analgesia, and hemodynamic stability and reduces requirements for intraoperative inhalational agents and postoperative analgesics. [14,15]

Tramadol and Dexmedetomidine when added as an adjunct to Local Anaesthetics for preincisional infilteration in patients undergoing abdominal surgery effectively reduces analgesics consumption in first 24 hour of postoperative period. The aim of the present study was to assess the efficacy of bupivacaine plus tramadol with bupivacaine plus dexmedetomidine as preincisional infiltration in patients undergoing abdominal surgery under general anasthesia.

Materials and Methods

The Prospective randomized and double blind study was conducted at of Indira Gandhi Institute of Medical Sciences, Patna. The study protocol, informed consent form (in Hindi & English) and case report form (CRF) were submitted to the ethical committee of Indira Gandhi Institute of Medical Sciences, Patna for approval. Study was done after taking approval from institute ethical committee. Written informed consent was taken from each participant of the study. The Data was collected between – May 2019 to November 2020. Total 60 samples were included in the study (30 in each group).

CTRI Registration Number: CTRI/2019/05/ 019201

Inclusion Criteria

- Patients of ASA physical status 1 and 2.
- Age between 18 - 60 years.
- Those who were willing to give written informed consent

Exclusion Criteria

- Patients' refusal to participate
- Patients with Pregnancy, morbid obesity, full stomach and emergency surgery
- Patients with ASA physical status III and above.

In this Prospective double blind study, 60 ASA I or II adult patients scheduled for Abdominal surgery under general anesthesia were randomly allocated to either

Group-T (n=30) to receive 2mg/kg Tramadol in 0.2ml/kg of 0.25% Bupivacaine or

Group-D (N=30) to receive 1mcg/kg dexmedetomidine in 0.2 ml/kg of 0.25% Bupivacaine. After calculated the required amount of drug as per body weight. The total volume of drugs in both group was made up to 15 ml. After obtaining written informed consent, the patients were randomized by computer-generated random table numbers inserted into an envelope and assigned into two groups.

Group - T – Bupivacaine + Tramadol

Group - D – Bupivacaine + Dexmedetomidine

Patients were graded according to ASA classification. A linear visual analogue scale (VAS) on a scale of 0-10 cm (where 0 states no pain and 10 states worst pain) was explained to each patient. An informed and written consent was obtained from the parents or legal guardian after explaining the anesthetic procedure and the risk involved.

Preparation of Operating Room

The anesthesia machine with oxygen delivery system was checked. Appropriate size endotracheal tube, working laryngoscope, suction apparatus, other resuscitation equipments, anesthetic drugs and emergency drug tray were checked and kept ready.

Blinding

These injections were prepared by in independent anaesthesiologist. The patient and attending anaesthesiologist and surgeons was unaware of the group allocation. After preoxygenation for 5 minutes all patients was induced by injection morphin 1 mg/kg intravenous and propofol 1.5-2 mg/kg intravenous slow till loss of communication followed by injection Vecuronium 0.1 mg/kg. Patients was ventilated with an inhalational agent in 100% oxygen for 3 minutes. Tracheal intubation was performed with on appropriate sized cuffed endotracheal tube. Anaesthesia was maintained with controlled ventilation with nitrous oxide 50% and oxygen 50% with an inhalational agent (Isoflurane) and interminent bolus vecuronium 0.025 mg/kg.

After induction by general anaesthesia the group received either locally administered 2 mg/kg Tramadol in 0.2 ml/kg of 0.25% bupivacaine (Group T, n=50) or 1 mcg/kg Dexmedetomidine in 0.2ml/kg of 0.25% bupivacaine. (Group D, n=50) 3 minute before incision by a surgeon. Age, sex, body weight, duration of surgery and perioperative hemodynamic changes of the patient was recorded. Visual Analogue Score (VAS) a pain scoring tools ranging from 0-10 will be used to evaluate the severity of pain. The evaluations will be performed postoperatively hourly for 6 hour in Post Anaesthesia Care Unit (PACU) by anaesthesiology who had unaware of group allociation. Then pain score was evaluated every 6 hourly for 24 hours. Rescue analgesia will be provided by Morphine 0.05 mg/kg if VAS score is more than 5.

- **Timing of rescue analgesia**

Analgesics were avoided until demand by the patient. The time interval for the first analgesic consumption was noted.

Assessment of analgesia

Pain was assessed by Visual analogue score (VAS)

First advocated by Revill and Robinson in 1976, VAS consists of a 10cm line anchored at one end labelled as 'No pain' and at the other end labelled as 'Worst pain imaginable' or 'Pain as Bad as can Be'. The patients simply mark the line to indicate the pain intensity then measures the length of the line to mark a point scale. All the patients were instructed about the VAS and to point out the intensity of pain on the scale.

0 = No pain 10 = Worst pain

Statistical Analysis:

All the data were analyzed using SPSS package (Stata, version 26.0 SPSS INC, Chicago, IL, USA) for windows. The data were presented as descriptive statistics for continuous variables and percentage for categorical variables and was subjected Chi-square test, t test & Anova test. Other values were represented in number, proportions (%) and mean ± SD.

Results

Table 1: Patient details

Age group	Group T		Group D		P. Value
	No.	%	No.	%	
18-24	4	13.33	4	13.33	
25-34	6	20	6	20	
35-44	8	26.67	7	23.33	
45-54	4	13.33	4	13.33	
55-60	8	26.67	9	30	
Total	30	100.00	30	100.00	
Mean ±SD	41.63±13.46		41.80±14.37		0.964
Gender					
Male	10	33.33	16	53.33	
Female	20	66.67	14	46.67	

It was observed that maximum number of patients were in the group T 35-44 years age group (26.674%) and group D, 55-60 years age group (30%). The age of patients ranged from 18-60 years, mean age ± SD of patients in Group T was 41.63±13.46 years while that of group D was 41.80±14.37 years. On comparing both groups, significant difference was not found. (P. Value = 0.964). In Group T, there were 10 (33.33%) male and 20 (66.67%) were female and group D had 16 (53.33%) male and 14 (46.67%) had female subjects.

Table 2: Weight distribution in groups

Weight	Group T	Group D	P. Value

	No.	%	No.	%	
≤50	13	43.33	4	13.33	0.127
51-60	17	56.67	23	76.67	
61-70	0	0	3	10	
Total	30	100.00	30	100.00	
Mean±SD	49.83±4.19		55.30±5.18		

It was observed that maximum number of patients were in the group T 51-60 kg weight (56.67%) and group D, 51-60 kg weight (76.67%). The weight of patients mean±SD in Group T is 49.83±4.19 kg while that of group D is 55.30±5.18 kg. Significant difference was not found on comparing the data of both groups. (P. Value = 0.127).

Table 3: Height distribution in groups

Height	Group T		Group D		P. Value
	No.	%	No.	%	
148-158	11	36.67	11	36.67	0.711
159-169	17	56.67	15	50	
>169	2	6.67	4	13.33	
Total	30	100.00	30	100.00	
Mean±SD	161.20±7.64		162.03±6.47		

t was observed that maximum number of patients were in the group T 159-169 Height 17 (56.67%), Group D, 159-169, 15 (50%) . The height of patients mean±SD in Group T was 161.20±7.64, Group D is 162.03±6.47. On comparing the data statistically observed among the groups. (P. Value = 0.711).

Table 4: VAS Score

	Group T	Group D	't' Value	P. Value
	Mean ±SD	Mean ±SD		
1 hr	1.06±0.691	1.16±0.698	-1.795	0.083
2 hrs	1.83±0.530	1.93±0.520	-1.795	0.083
3hrs	3.00±1.41	2.73±0.980	1.765	0.088
4 hrs	4.96±2.00	3.83±1.59	2.583	0.015
5 hrs	4.33±2.49	3.43±2.25	1.568	0.128
6hrs	2.20±1.54	4.36±2.82	-3.486	0.002
12hrs	6.23±1.27	6.43±0.858	-0.711	0.483
18hrs	5.83±1.89	5.73±1.85	0.219	0.828
24hrs	1..70±1.41	1.81±0.949	-0.459	0.650

The mean VAS Score of study subjects in Group T initially showed increasing trend up to 5 hours and 12 hour to 18 hours and later it decreased in 6 hours and 24 hrs. In Group D, initially the mean VAS score shown increasing trend up to 12th hour and later it decreased in 18th and 24 hours. The result of Independent sample t test reveals that there was significant difference between mean VAS Score of groups in 4 hour and 6 hours.

Table 5: Mean Heart Rate in study Groups at different time interval

In Min	Group T		Group D		't' test	P. Value
	N	Mean±SD	N	Mean±SD		
0	30	78.76±3.56	30	79.6±4.01	38.6	0.12
3	30	77.9±6.26	30	76.6±4.62	36.2	0.14
10	30	77.42±5.28	30	75.3±9.76	36.2	0.6
20	30	76± 4.56	30	74.17±8.06	36.9	0.15
30	30	71.94±1.88	30	72.07±1.76	33.3	0.17

At baseline, the mean heart rate in Group T was 78.76±3.56 beats per minute whereas in Group D, the mean value was 79.6±4.01 beats per minute showing no significant difference among groups. (P. Value = 0.12). At 20 minutes, in group T the heart rate was 76± 4.56 beats per minute and in Group D was 74.17±8.06 beats per minute showing no significant difference among groups. The heart rate gradually returned to around baseline at 30 minutes, mean heart rate was 71.94±1.88 beats per minute in Group T, 72.07±1.76 beats per minute in Group D. There was no significant difference in group T and Group D. The mean value of heart rate remained stable.

Table 6: Mean arterial pressure in study Groups at different time interval

In Min	Group T	Group D	't' test	P. Value

	N	Mean±SD	N	Mean±SD		
0	30	96.38±2.93	30	96.34±3.02	11.49	0.18
3	30	87.8±7.88	30	89.94±4.64	14.35	0.17
10	30	90.28±7.63	30	91.8±5.82	14.43	0.20
20	30	91.9±6.89	30	93.14±5.48	12.21	0.41
30	30	93.46±5.80	30	94.64±4.57	12.06	0.42

The mean basal MAP in Group T was 96.38±2.93 mmHg and Group D was 96.34±3.02 mmHg. Mean MBP decreased at 3 & 20 minutes interval in two groups.

Table 7: Mean Oxygen saturation in study Groups at different time interval

In Min	Group T		Group D		't' test	P. Value
	N	Mean±SD	N	Mean±SD		
0	30	98.8 ± 1.36	30	98.84 ±1.15	0.79	0.19
3	30	99.76±0.64	30	99.74±0.65	0.80	0.17
10	30	100 ±0.49	30	99.96± 0.48	0.80	0.16
20	30	100 ±0.49	30	100 ±0.49	1.5	0.16
30	30	100 ±0.49	30	100 ±0.49	1.5	0.16

The mean basal Oxygen saturation in Group T was 98.8 ±1.36 and Group D was 98.84±1.15. There is statistically insignificant. At 3 minute oxygen saturation in Group T was 99.76±0.64 and Group D was 99.74±0.65. The mean oxygen saturation remained stable between 98 to 100 at all intervals. On statistical analysis the mean oxygen saturation among the two groups were insignificant. (P > 0.05).

Discussion

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 emboli (PE); 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. [16] Postoperative pain may be transient and most of the time lasts for 24 hours and sometimes even up to 3 days. Intensity of pain is more immediately after surgery and less after 24 hours.

The present study observed that maximum number of patients were in the group T of 35-44 years age group (26.674%) and group D, 55-60 years age group (30%). The age of patients ranged from 18-60 years, mean age ± SD of patients in Group T was 41.63±13.46 years while that of group D was 41.80±14.37 years. On comparing both group, significant difference was not found. (P. Value = 0.964). This present study observed that Group T there were 10 (33.33%) male and 20 (66.67%) were female and group D had 16 (53.33%) male and 14 (46.67%) had female subjects. This study observed that maximum number of patients were in the group T 51-60 kg weight (56.67%) and group D, 51-60 kg weight (76.67%). The weight of patients mean±SD in Group T is 49.83±4.19 kg while that of group D is 55.30±5.18 kg . Significant difference was not found on comparing the data of both groups. (P. Value = 0.127). The present study observed that maximum number of patients were in the group T 159-169 Height 17 (56.67%), Group D, 159-169, 15 (50%) . The height of patients mean±SD in Group T was 161.20±7.64, Group D was 162.03±6.47. On comparing the data statistically observed among the groups. (P. Value = 0.711). The present study observed that the mean VAS Score of study subjects in Group T, initially showed increasing trend up to 5 hours and 12 hour to 18 hours and later it decreased in 6 hours and 24 hrs. In Group D, initially the mean VAS score shown increasing trend up to 18th hour and later it decreased in 24 hours. The result of Independent sample t test reveals that there is significant difference between mean VAS Score of groups in 4 hour and 6 hours. (P value <0.05)

Verma GR, & Cantore F, [17,18] suggest that predominant cause of pain is parietal but in contrast many other studies emphasized that in early convalescent period, major portion is occupied by visceral pain because as compared to small incisions and limited trauma to the abdominal wall, the surgical manipulation and tissue destruction in visceral organs is much more. El-Labban GM, Tobias JD. Abdulla S, Salihoglu Z et al [19-22] Multimodal efforts like parenteral opioids, non-steroidal anti-inflammatory drugs or local wound infiltration have been done to reduce overall pain and benefit post-operative conditions of patients undergoing laparoscopic surgeries. Golubovic *et al*. [23] assessed the analgesic effects of intraperitoneal instillation of bupivacaine and/or tramadol in patients undergoing laparoscopic cholecystectomy and concluded that intraperitoneal instillation of bupivacaine or tramadol or combination of both are effective method for management of pain after laparoscopic cholecystectomy and they significantly reduce post-operative analgesic and antiemetic medication.

On the contrary, we found bupivacaine in combination with tramadol (Group BT) has significantly lower VAS score at all points of time ($P < 0.05$) and overall VAS score, and post-operative analgesia was statistically lower than with Group B.

Memis *et al*. [24] studied the effects of tramadol or clonidine added to intraperitoneal bupivacaine, on post-operative pain in total abdominal hysterectomy and found that combination of tramadol or clonidine with intraperitoneal bupivacaine to be more effective than bupivacaine alone. They found no significant difference between tramadol and clonidine groups in terms of efficacy but we found dexmedetomidine to have significantly better efficacy than tramadol in combination with bupivacaine. The prominent effect of dexmedetomidine may be due to its higher efficacy in our study and higher efficacy of clonidine in the study by Memis *et al*. Ahmed *et al*. [32] which has shown that intraperitoneal instillation of mepiridine or dexmedetomidine in combination with bupivacaine 0.25% significantly decreases the post-operative analgesic requirements and decreased incidence of shoulder pain in patients undergoing laparoscopic gynaecological surgeries. Memis *et al*. [24] found no difference between tramadol or clonidine groups and in present study, the time was significantly shorter in tramadol group than dexmedetomidine group ($P = 0.03$). Time to first request of analgesia in post operative period was significantly delayed in Group T as compared to Group D ($P = 0.000$).

Chudrigar et al [25] had done the same study in laproscopic cholecystectomy and they found less VAS Score in the study group patients for 3 hours. This difference is suggestive of prolong duration of analgesia by adding Dexmedetomidine with Bupivacaine. Golubovic et al.[22] assessed the analgesic effects of intraperitoneal instillation of bupivacaine and /or tramadol in patients undergoing laproscopic cholecystectomy and reported that intraperitoneal instillation of Bupivacaine or Tramadol or combination of both are effective method for management of pain after laproscopic cholecystectomy and they significantly reduce post-operative analgesic and antiemetic medication.

The present study observed that at baseline, the mean heart rate in Group T was 78.76±3.56 beats per minute whereas in Group D, the mean value was 79.6±4.01 beats per minute showing no significant difference among groups. (P. Value = 0.12). At 20 minutes, in group T the heart rate was 76± 4.56 beats per minute and in Group D was 74.17±8.06 beats per minute showing no significant difference among groups. The heart rate gradually returned to around baseline at 30 minutes, mean heart rate was 71.94±1.88 beats per minute in Group T, 72.07±1.76 beats per minute in Group D. There was no significant difference in group T and Group D. This study observed that the mean basal MAP in Group T was 96.38±2.93 mmHg and Group D was 96.34±3.02 mmHg. Mean MBP decreased at 3 & 20 minutes interval in two groups. The present study observed that the mean basal Oxygen saturation in Group T was 98.8 ±1.36 and Group D was 98.84±1.15. There is statistically insignificant. At 3 minute oxygen saturation in Group T was 99.76±0.64 and Group D was 99.74±0.65. The mean oxygen saturation remained stable between 98 to 100 at all intervals. On statistical analysis the mean oxygen saturation among the two groups were insignificant.

Conclusion

In this study, males and females were found to be equally. We concluded that skin infilteration of 1μg/kg dexmedetomidine 0.2 ml/kg of 0.25% Bupivacaine in abdominal surgery significantly reduces the post-operative pain and reduces the analgesic requirement in post-operative period as compared to 2mg/kg Tramadol in 0.2ml/kg of 0.25% Bupivacaine. The results can be better when bupivacaine combined with dexmedetomidine.

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