Section: Anaesthesiology

Original Research Article

COMPARATIVE STUDY OF SURGICAL SITE INFILTRATION WITH COMBINATION OF BUPIVACAINE WITH TRAMADOL VERSUS BUPIVACAINE WITH DEXMEDETOMIDINE FOR POSTOPERATIVE ANALGESIA FOLLOWING ABDOMINAL SURGERY

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Abstract

Background: To compare the efficacy and quality of postoperative analgesia achieved with surgical site infiltration of a combination of Bupivacaine with Tramadol versus Bupivacaine with Dexmedetomidine. **Materials and Methods:** A prospective randomised study was undertaken in patients posted for elective abdominal surgeries under spinal anaesthesia. 60 patients under ASA I and II were randomly divided into two groups; Group BT: Surgical site infiltration with 2mg/kg Tramadol diluted in 30ml of 0.25% Bupivacaine and Group BD: Surgical site infiltration with 1µg/kg Dexmedetomidine diluted in 30ml of 0.25% Bupivacaine. **Result:** VAS score was significantly low in the BD group compared to the BT group at 6 hrs, 8 hrs, and 12 hrs with mean VAS score of 2.27 ±0.449 vs 2.67±0.479, 2.7 ± 0.466 vs 3.27 ± 0.691, and 3.3 ± 0.466 vs 3.6 ± 0.498 with a p-value of 0.0015, 0.004 and 0.0192 respectively. The time to reach VAS ≥4 was significantly longer in the BD group compared to the BT group. The time to give 1st rescue analgesia was 10.6 ± 1.631 hours in the BT group and 13.067 ± 1.574 hours in the BD group. **Conclusion:** Thus, dexmedetomidine and tramadol seem to be an attractive adjuvant to bupivacaine for surgical site infiltration in patients undergoing abdominal surgeries; however, the combination of bupivacaine with dexmedetomidine provides superior pain relief compared to bupivacaine with tramadol.

INTRODUCTION

Effective postoperative pain control is an essential & humanitarian need of every surgical procedure. Inadequate pain control may result in increased morbidity, delayed recovery & increased hospital stay. Abdominal surgeries are one of the most commonly performed surgeries in hospitals which are associated with moderate to severe postoperative pain which is often multifactorial and can attribute to incision pain, pain from deeper visceral structures, and dynamic pain on movement such as during respiration, coughing or mobilizing that may be severe. Management of postoperative pain relieves suffering and leads to earlier mobilization, shortened hospital stay, reduced hospital costs, and increased patient satisfaction. When compared to various modes of providing postoperative analgesia, the wound infiltration technique is the older technique with better analgesia and the least side effect profile acts by inhibition of pain impulses originating from peripheral nerves innervating the surgical site with local anesthetic alone or added with adjuvants which can improve the quality and duration of analgesia. Wound infiltration with bupivacaine has been shown to reduce the levels of interleukin.[1] Local anaesthetic administered subcutaneously exhibit bacteriostatic and bactericidal action, but the important limitation of bupivacaine is its short duration of action. If used alone its effect usually remains for about 5-6 hours. To overcome this limitation bupivacaine is usually mixed with an adjuvant such as epinephrine, α2 adrenoceptor agonists, ketorolac, magnesium, sodium bicarbonate, and hyaluronidase which can improve the quality and

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duration of analgesia. This study aims to compare the analgesic efficacy of tramadol and dexmedetomidine as adjuvants for wound infiltration with bupivacaine for postoperative analgesia in patients undergoing abdominal surgeries under spinal anesthesia. Tramadol is a synthetic analog of codeine that acts through the mechanism of action of both opioids (weak opioid receptor agonist) and nonopioids (noradrenaline, which prevents the reuptake of serotonin). When added as an adjuvant to the local anesthetic agent, it can modify the effects of local anesthetic by directly or indirectly affecting sodium channels, thus contributing to a better analgesic effect. Dexmedetomidine is a potent α2 adrenoreceptor agonist that can potentiate and prolong the duration of local anesthetic wound infiltration for pain relief.

This study was conducted given only a few studies were available for the combination of bupivacaine with adjuvants namely Tramadol or Dexmedetomidine in surgical site infiltration.

MATERIALS AND METHODS

This Prospective randomized study was conducted at PES Medical College Hospital from January 2018 until June 2019. After taking written informed consent, 60 Adult patients of the age group18-60 of both gender with ASA physical status Grade I and II who were posted for elective abdominal surgeries like Mesh Hernioplasty for Inguinal Hernia, Umbilical Hernia and Incisional Hernia, Elective LSCS, Total Abdominal Hysterectomy, Umbilical sinus tract excision and Open Appendectomy under spinal anaesthesia were enrolled in the study. Patients who were allergic to local anaesthetics, dexmedetomidine and tramadol; patients using analgesic medications continuously for chronic pain; patients having renal or hepatic diseases; patients having coagulation abnormalities; on anticoagulant therapy; Age > 60 years and < 18 years; ASA physical status grade III & IV; patient refusal were excluded from the study. Sample size estimations was done based on the results of a previous study [2], and assuming an α level of 0.05 and ß error of 0.8; 27 patients were needed per group to detect a one-point difference on the 0 to 10 visual analogue pain scale score. To account for the possible loss of follow-up, it was decided to include 30 patients per group. 60 patients of both genders were randomly allocated into two groups; Group BT: Surgical site infiltration with 2mg/kg Tramadol diluted in 30ml of 0.25% Bupivacaine and Group BD: Surgical site infiltration with 1µg/kg Dexmedetomidine diluted in 30ml of 0.25% Bupivacaine. Randomisation was done using sequentially numbered, opaque sealed envelopes depending upon drugs used for surgical site infiltration at the end of surgery.

After a thorough pre-anaesthetic evaluation, all patients were given the anxiolytic drug Alprazolam 0.5 mg orally on the previous day at bedtime. In the preoperative room, the anaesthetic procedure was explained to the patient, and written informed consent was taken as per institutional protocol. Patients were taken to the operation theatre. After obtaining intravenous access with18G cannula, the infusion of 500ml Ringer lactate was started. The patient was connected to monitor and baseline heart rate, SBP, DBP, MAP, and SpO2 were recorded including E.C.G . Under complete aseptic precautions, a lumbar puncture was performed at L3-L4 intervertebral space through a midline approach using 25G Quincke spinal needle. The correct spinal placement was identified by the free flow of cerebrospinal fluid, and 3 ml (15mg) of hyperbaric bupivacaine 0.5% was given for the subarachnoid block. Surgery was performed after achieving a complete sensory block at T8 dermatome, as assessed by a pinprick. Standard monitoring was done throughout the operative procedure. E.C.G. and pulse oximetry(SpO2) were monitored continuously while non-invasive blood pressure (NIBP) was monitored every 3 min for the first 15 min, after that every 5min till the completion of surgery. At the end of the surgical procedure, but before the closure of the surgical wound, the surgeon was asked to infiltrate all layers of the surgical incision under direct visualization in a controlled and meticulous manner using a 22-gauge, 1.5-inch needle which was inserted approximately 0.5 to 1 cm into the tissue plane (i.e., peritoneal, Musculofascial, and subdermal planes) and study drugs were Infiltrated with moving needle technique to optimize the distribution of the local anaesthetic solution. Infiltration was 1 to 1.5 ml for every 1 to 2 cm of surgical incision per layer. The total volume of study drugs was 30 ml, with 10 ml injected into the peritoneal plane, 10 ml injected into the musculofascial plane, and 10 ml injected into the subdermal plane. The total amount of Bupivacaine used in the study, including spinal anaesthesia and surgical site infiltration, did not exceed the maximum recommended dose of Bupivacaine 1.5 - 2 mg/kg.

In the postoperative period, assessments were made for postoperative analgesia after shifting the patient to the postoperative ward (0hr) as a baseline then at 0hr, 2hr, 4hr, 6hr, 8hr,12hr and 24 hrs.

The primary observation was to compare pain using the Visual Analog Scale (VAS) score. The secondary observation was the time at which the rescue analgesia was given; the total dose of rescue analgesia in the first 24 hours postoperatively; and to observe of any adverse effects of wound infiltration with the study drugs like hypotension, bradycardia, nausea, vomiting and pruritus. The observed data during the preoperative period, intraoperative period and postoperative period were tabulated and analysed statistically.

Visual Analogue Scale(VAS) is the most common simple scale used in pain research. It consists of a 10cm line from 0 ‘No pain’ and 10 ‘Worst Pain Imaginable’ that is self-assessed by the patient. The patients were explained to point out the intensity of their perceived pain. The severity of pain was

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measured at 0hrs, 2hrs, 4hrs, 6hrs, 8hrs, 12hrs, and 24 hours by the observer who was unaware of the group the patient belonged to. If the score was 4 or more, rescue analgesia of Inj Diclofenac 75mg IM was given. The time at which 1st rescue analgesic i.e. time to reach a VAS score of ≥ 4, and total doses of rescue analgesia given are recorded.

Data were entered and analysed with the help of MS Excel and SPSS software. Qualitative or categorical data were presented as numbers (proportion) and compared with the Chi-square test. Quantitative or continuous variables were presented as mean ± SD and compared using the student t-test. P < 0.05 was considered statistically significant.

RESULTS

Sixty adult patients of ASA class I and II, who were admitted to the hospital attached to PES Institute of Medical Sciences and Research (PESIMSR), Kuppam, Andhra Pradesh for elective abdominal surgery under spinal anesthesia were included in the study. It was a prospective randomized, double-blind study. Patients were randomly allocated into two groups, Group BT and Group BD.

Both the groups comprised 30 patients each, with the mean age in the BT group being 39.3±12.09 years and in the BD group 38.17± 10.52 years with a p-value of 0.6999(> 0.05) thus the difference between the two groups is statistically insignificant.

The mean weight in the BT group was 66.5± 8.69 kgs, and in the BD group 66.03± 7.93 kgs, with a p-value of 0.8289, there is no statistical significance between these two groups. The mean height of the patients in the BT group was 158.53 ± 5.89 cms and in the BD group 157.87 ± 5.03 cms, with a p-value of 0.6392.

Both the groups were statistically comparable for the demographic profile with a p-value> 0.05, statistically insignificant [Table 1].

The Distribution of diagnosis of the patient studied in the BT group, and the BD group was statistically insignificant p-value 0.698 [Table 2].

The mean duration of surgery in the mean BT group was 111.3 ± 15.75711 min, and in the BD group 117.8667 ± 12.79 min, p-value 0.0861 was statistically insignificant.

There was no significant difference in VAS scores between these two groups until 4 hours with the mean VAS score of group BT versus group BD at 2hrs, and 4hr were 2.00 ± 0.00 vs. 1.97 ± 0.1825 and 2.1 ± 0.305 vs. 2.00 ± 0.00 with p-values 0.3215 and 0.0779 respectively. VAS score was significantly low in the BD group compared to the BT group at 6hrs, 8hrs, and 12hrs with mean VAS scores of 2.27±0.449 vs 2.67±0.479,2.7 ±0.466 vs 3.27±0.691, and 3.3±0.466 vs 3.6±0.498 with a p-value of 0.0015, 0.004 and 0.0192 respectively [Figure 1].

The time to reach VAS ≥4 was significantly longer in the BD group compared to the BT group. The time to give 1st rescue analgesia was 10.6 ± 1.631 hours in the BT group and 13.067 ± 1.574 hours in the BD group, which was a statistically significant p-value< 0.05 [Figure 2].

In group BT, 6 patients required a single dose and 24 patients required two doses of rescue analgesia. In group BD, 21 patients needed one rescue analgesic and nine patients required two doses of rescue analgesia, which was a significant p-value of 0.000. The average mean total dose of Inj.Diclofenac required in 24hrs was significantly low in the BD group compared to the BT group which was 1.3 ± 0.467 and 1.8 ± 0.407 respectively, with a p-value of 0.000 [Table 3].

There were no significant changes in hemodynamic parameters over 24 hrs. In both groups, the mean hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, SpO2, and respiratory rate) at (0,2,4,6,8,12 and 24) hours were comparable and were statistically insignificant. Two patients in group BT had nausea and which is clinically and statistically insignificant, and there were no cases reported with other side effects like hypotension, bradycardia, drowsiness, and pruritus in either of the study groups.

Table 1: Demographic Profile

Parameter	Group BT	Group BD	P-value
Age (years)	39.3 ±12.09	38.17 ± 10.52	0.6999 NS
Sex (male:female)	15:15	15:15	1.000 NS
Height (cms)	158.53 ±5.89	157.87 ± 5.03	0.6392 NS
Weight (kgs)	66.5 ± 8.69	66.03 ± 7.93	0.8289 NS

Table 2: Distribution of Diagnosis of Patient Studied

Type of Diagnosis of Patient	Group BT(N=30)		Group BD(n=30)		$\chi 2$ value	p-value
	No of cases	Percentage	No of cases	Percentage		
Umbelical Hernia	6	20.00	8	26.67	3.8413	0.698NS
Incisional Hernia	2	6.66	1	3.33		
Elective LSCS	3	10.00	6	20.00		
PID/Adenomyosis/Fibroid Uterus	7	23.33	7	23.33		
Acute Appendicits	1	3.33	0	0.00		
Umbelical Sinus	1	3.33	0	0.00		
Inguinal Hernia	10	33.33	8	26.67		
Total	30	100	30	100		

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Table 3: Comparison of total no of rescue analgesia administered over 24 hrs.

No of Rescue Analgesia	0	1	2	≥3	χ2 value	P-value
GROUP – BT	0	6	24	0	15.1515	0.000 S
GROUP – BD	0	21	9	0		

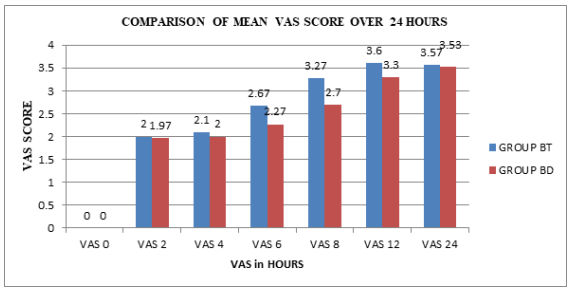

Figure 1: Comparison of Mean Vas Score Over 24 Hours

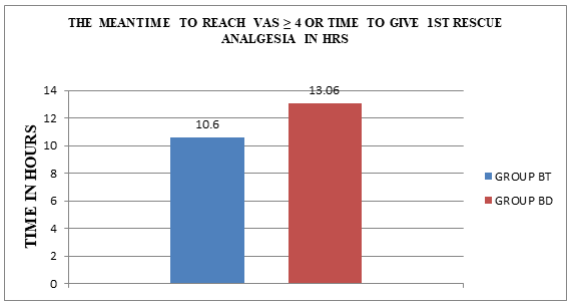

Figure 2: The meantime to reach vas ≥ 4 or time to give 1st rescue analgesia in hrs

DISCUSSION

Postoperative pain relief results in early mobilization of the patient, better hemodynamic stability, and better satisfaction from the patient and family.[2] Wound infiltration at the time of closure had been described as a part of multimodal analgesia and demonstrated to have an analgesic sparing effect and a significant influence on the patient's ability to resume their normal activities of daily living.[3] Due to local application, the transmission of pain from the wound is reduced, and the local inflammatory response to the injury is suppressed. Consequently, the sensitization of nociceptors and the ensuing hyperalgesia may be prevented. Various agents like local anaesthetics, opioids, and NSAIDs have been used for wound infiltration, but with varying results.[3]

Our study was planned to provide postoperative analgesia in patients undergoing abdominal surgeries with a single-shot wound infiltration technique using a combination of bupivacaine with tramadol or bupivacaine with dexmedetomidine and Inj.Diclofenac as a rescue analgesic.

Tramadol is a synthetic 4‐phenyl‐piperidine analogue of codeine. It is a μ receptor agonist. The non‐opioid mechanism is mediated through α2 and the serotonergic pathway. It inhibits the reuptake of norepinephrine and hydroxyl tryptamine from the nerve endings. Various advantages have been described for the subcutaneous administration of drugs, which include avoiding first‐pass metabolism, improved patient comfort, and excellent analgesia. Clinical studies have shown that tramadol has a local anaesthetic effect with minimal sedation and cardiovascular compromise.

Dexmedetomidine, a highly selective α2-adrenoceptor agonist, has a sedative, analgesic and opioid-sparing effect, which is implicated in the management of acute postoperative pain.[4] The peripheral analgesic effect of dexmedetomidine is mediated through α2-adrenoceptor binding and potentiates the action of local anaesthetics. It has got a potent antinociceptive property on peripheral administration. Many studies have concluded that wound infiltration of bupivacaine with dexmedetomidine provides superior pain relief.

Guidelines for postoperative acute pain management specify that "unless contraindicated all patients should receive round the clock regimen of non-steroidal anti-inflammatory drugs NSAIDs, cyclooxygenase-2 inhibitors (COX2) or acetaminophen".[5] The mechanism of action of NSAIDs includes inhibition of the synthesis of prostaglandins both in the spinal cord and at the periphery. Thus it decreases the hyperalgesic state after surgical trauma and reduces the postoperative opioid requirement. Thus in the present study, all patients received an intramuscular injection of Diclofenac 75 mg on reaching VAS score 0f ≥ 4 and at 12 hr intervals after that as a part of the multimodal postoperative analgesia regimen.

In our study, the majority of patients were middle-aged in both groups. In both groups, there was equal sex distribution, and the mean height and meant weight in either group were also identical. The type of surgeries performed were also identical in both groups. These parameters were kept equal in both groups to avoid variations in the intraoperative and postoperative outcomes of patients. None of the patients were excluded from our study.

The primary observation of our study was to compare pain using the VAS score. In our study, the VAS score did not differ significantly between the two groups until 4 hours, but the VAS score was significantly low in the BD group compared to the BT group at 6hrs, 8hrs, and 12hrs with a p-value of 0.0015,0.004 and 0.0192 respectively. Hence wound infiltration with the combination of bupivacaine with dexmedetomidine was superior in reducing pain scores compared to bupivacaine with tramadol. Better pain scores were achieved in the BT group in a few studies like Shekoufch Behdad et al,[3] Roopa Sachidananda et al,[6] and Yavuz Demiraran et al,[7] who compared surgical site infiltration with plain Bupivacaine versus addition of tramadol with bupivacaine. Pain scores were lower in the BD group in a few studies like Jyothi B et al,[2] and Netravathi H et al,[8] who compared surgical site infiltration with

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a Bupivacaine with Dexmedetomidine versus Bupivacaine with Clonidine. Hence wound infiltration with the combination of bupivacaine with dexmedetomidine was superior in reducing pain scores

The secondary observation of our study was the time to reach VAS ≥ 4 that is the time at which 1st rescue analgesia was given was significantly longer in Group BD patients compared to Group BT patients (13.067 ± 1.574 hours in the BD group vs. 10.6 ± 1.631 hours in BT group, P = 0.000)) which was comparable with the study conducted by Netravathi H et al,[8] who studied sixty women posted for abdominal hysterectomy where Group BC received wound infiltration with 30 ml 0.25% bupivacaine with 3µg/kg clonidine, and Group BD received wound infiltration with 30 ml 0.25% bupivacaine with 1µg/kg dexmedetomidine, and this study concluded that Postoperative pain score, duration of effective analgesia (The meantime for the first rescue medication was 662.83 ± 15.63 min. in Group BC and 664.16 ± 15.54 min. in Group BD), number of patients requiring rescue analgesia and side effects were comparable in both the groups (p> 0.05) with equal efficacy and without any significant side effects.

However, there were few studies where the time to reach VAS ≥ 4 was significantly longer compared to our present study like E Niyirera et al,[9] where it was more than 12 hours for the BT group, and in Jyothi B et al,[2] study it was 23.4hrs in levobupivacaine with dexmedetomidine group.

In group BT: There were 6 patients reported to have a single dose of rescue analgesia and 24 patients required two doses of rescue analgesia whereas, In group BD: 21 patients required a single treatment of rescue analgesia and 9 patients required two doses of rescue analgesia. Thus the demand for rescue analgesia consumption was significantly less in the BD group compared to the BT group which was evidenced by The Mean value of total doses of rescue analgesic consumption in 24 hrs (1.3 ± 0.467 in Group BD vs 1.8 ± 0.407 in BT group vs, p-value 0.000 which were comparable with Ayse Ulgey et al,[10] and Kadir Ozyilmaz et al.[11]

There were no significant changes in hemodynamic parameters over 24hrs and the mean hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, SPO2, and respiratory rate) at (0,2,4,6,8,12 and 24) hours In both groups were comparable with a p-value> 0.05, statistically insignificant which were comparable with Shaman Bhardwaj et al,[12] and Netravathi H et al.[8]

There were two patients reported with nausea in group BT, and there are no other side effects like hypotension, bradycardia, drowsiness, and pruritus in either of the study groups which were comparable with a few studies like Shekoufch Behdad et al,[3] Mohammad Ali Sahmeddini et al,[13] and Netravathi H et al,[8] Thus wound infiltration with the combination of bupivacaine with dexmedetomidine and bupivacaine with tramadol was safe and efficient in prolonging the action of bupivacaine, and both drug combinations provide stable hemodynamics with insignificant adverse effects, but the combination of bupivacaine with dexmedetomidine provides superior pain relief compared to bupivacaine with tramadol which was comparable with few studies.

Limitations

The surgeries were conducted by different surgeons, thus causing differences in tissue handling and local anaesthetic infiltration. All of our patients belonged to physical status ASA Grade I and II with no severe underlying disease; therefore, the results of the present study should not be generalized to all the patients. All the VAS measurements were not carried out by a single observer to eliminate any interobserver variability. Different types of surgeries are included in our study, which can alter the type, nature, and duration of pain associated with surgery.

CONCLUSION

The quality of analgesia in this study was evidenced by a reduction in pain scores and decreased rescue analgesic demand, stable hemodynamics, and no significant adverse effects.

Thus, dexmedetomidine and tramadol seem to be an attractive adjuvant to bupivacaine for surgical site infiltration in patients undergoing abdominal surgeries; however, the combination of bupivacaine with dexmedetomidine provides superior pain relief compared to bupivacaine with tramadol.

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