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A comparative study of tramadol suppository and ultrasound guided Transversus Abdominis plane block with bupivacaine versus tramadol suppository alone in providing post-operative analgesia after caesarean section

[1]Nisheed Joseph, [2]Bhagyashree Shivde, [3]Swapna Naik, [4]Gayathri Subhash Banasode

[1,4]Assistant Professor, Department of Anaesthesiology, Kodagu Institute of Medical Sciences, Madikeri, Karnataka, India
[2]Senior Consultant, Department of Anaesthesiology, Deenanath Mangeshkar Hospital & Research Center, Pune, Maharashtra, India
[3]Honorary Consultant, Department of Anaesthesiology, Deenanath Mangeshkar Hospital & Research Center, Pune, Maharashtra, India

Corresponding Author:
Gayathri Subhash Banasode

Abstract

Background: The aim of the study was to compare multi-modal approach with Tramadol suppository and Ultrasound guided Transversus Abdominis Plane (TAP) Block with Bupivacaine versus Tramadol suppository alone in providing adequate post-operative analgesia after Caesarean section.
Method: 158 patients, aged between 18 to 40 years with ASA physical status I-II scheduled for elective caesarean surgery, were enrolled in this prospective randomized comparative study. 79 patients (of Group A) were given Ultrasound guided Transversus Abdominis Plane Block with Bupivacaine and Tramadol suppository as post-operative analgesia. The remaining patients were given only tramadol suppository as post-operative analgesic (Group B). They were observed for 12 hours or till the patient requested for rescue analgesic. Pain (VAS score), satisfaction (Likert scale), sedation (Four-point sedation scale), nausea & vomiting (PONV Impact scale) and adverse effects at 3hours, 6hours, 9hours and 12hours post-operatively were observed and compared in both the study groups.
Results: Both groups were comparable in demographic data. There was a statistically significant difference between the VAS scores and satisfaction scores with a $p < 0.001$ between the two groups. No statistically significant differences in the sedation, PONV or adverse effects were found between the two groups. In our study, Group A patients who received ultrasound guided TAP block remained painless for longer period (23hours) than Group B (6.5hours).
Conclusion: In conclusion, our study suggests that Ultrasound guided TAP block significantly improved postoperative analgesia in women undergoing Caesarean delivery patients.

Keywords: Bupivacaine, tramadol, caesarean section and Transversus Abdominis Plane

Introduction

Perioperative pain control is a major concern and it is still inadequately relieved despite substantial

improvements in the knowledge of the mechanisms and treatment of pain. The International Association for the study of Pain (IASP) defines pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" [1, 2].

Caesarean section is one of the most commonly performed surgical procedures. It is estimated that 15% of births worldwide and 21.1% of those in the developed world occur by Caesarean section [3].

An ideal post-caesarean analgesic regimen must be cost-effective, simple to implement and with minimal impact on staff workload. Drug transfer into breast milk must also be minimal, with no adverse effects on the baby. When questioning parturient women's fears and expectations, pain during and after caesarean section is the greatest concern [4].

Chronic pain, which is defined as pain that persists beyond the usual course of an acute disease or after a reasonable time for healing (this period can vary from 2 to 6 months), is being recognized as a complication of caesarean delivery. Poorly controlled pain in the early post-operative period may contribute to the generation of chronic pain [5].

Many options are available for treatment of acute postoperative pain, including systemic analgesics (opioid and non-opioid) and regional (neuraxial and peripheral) analgesic techniques.

Rectal suppository of tramadol is convenient to use and is the established treatment for post-operative pain in adults. A rectal dose of 1.5-2.0 mg/kg Tramadol is therapeutic and has low incidence of side effects like nausea and vomiting. Tramadol is a weak opioid analgesic with additional serotonin-norepinephrine reuptake-inhibiting effects and its rectal suppository has minimal side effects. It is safe, non-invasive technique accepted in regular routine practice. As a part of a multimodal analgesic regimen, opioids are required initially to achieve effective analgesia. However, opioids are associated with dose dependent side effects including nausea, vomiting, pruritus, sedation and respiratory depression [6, 7, 8].

An important component of pain experienced by patients after abdominal surgery as in caesarean section derives from abdominal wall incision. The nerves that supply the anterior abdominal wall course through the neuro-fascial plane between the internal oblique and Transversus Abdominis muscles [9]. Regional blocks of the anterior abdominal wall can significantly help with postoperative analgesia especially when used as a part of multimodal technique. Hemodynamic effects are minimal as spread of local anaesthetic is limited to the abdominal wall.

The Transversus Abdominis plane (TAP) block, whose popularity is growing, is a relatively new technique. The TAP block is a regional anesthesia technique that provides analgesia to the parietal peritoneum as well as the skin and muscles of the anterior abdominal wall. The TAP block was first described in 2001 by Rafi then known as the Regional Abdominal Field Infiltration (RAFI) technique and was further developed and tested by McDonnell *et al.* in 2007 [10, 11].

More recently, ultrasound techniques have been applied to facilitate performance of these blocks. It allows direct observation of the correct needle placement and spread of local anaesthetic thereby allowing identification of relevant anatomical structures and ensuring complications are kept to a minimum.

An ultrasound guided approach for TAP block was first described in 2007 by Hebbard *et al*. also noted that the "pop" sensations in the classic approach could be imprecise due to anatomic variability, especially in patients with large BMI and as such concluded that real-time visualization of local anaesthetic spread was likely to be a more definitive endpoint, as is often the case with other regional block techniques [12].

Since most of the reviews have shown good analgesic efficacy with Transversus Abdominis plane (TAP) blocks and the use of ultrasound has an increased chance of more precise and accurate localization of the tip of needle and drug injected, our study was designed to hypothesize that a bilateral ultrasound guided TAP block in addition to conventional analgesics may improve pain relief after caesarean delivery.

Objectives

To compare multi-modal approach with Tramadol suppository and Ultrasound guided Transversus Abdominis Plane Block with Bupivacaine versus Tramadol suppository alone in providing adequate

post-operative analgesia after Caesarean section.

Materials and Methods

The Prospective randomized controlled study was done compare the effectiveness of multi-modal approach with Tramadol suppository and Ultrasound guided Transversus Abdominis Plane Block with Bupivacaine and Tramadol suppository alone for postoperative pain relief in patients after Caesarean section by the Department of Anaesthesiology admitted for Caesarean section in Deenanath Mangeshkar Hospital and Research Centre, Erandwane, Pune.
A Total 158 patients [79 in each group].: Based on the data from literature mean VAS score at 6 hours after surgery for patients treated with Tramadol alone is 2.93±1. Sample size of 158 patients (79 in each group) will have 80% power to detect > 15% reduction in VAS score (VAS= 2.48) among patients treated with TAP+ Tramadol, based on a 2-sided test with 0.05 α-level".
The individual study period will be the time period from when Tramadol suppository and/or Ultrasound Guided Transversus Abdominis Block is given to the patient and a follow-up for 12 hours (unless the patient opts out of the study or other analgesia is given) and the total study duration is 12-month period. Those patients who were willing and who satisfied the inclusion criteria, were enrolled into the study; they were randomized to fall into either of two groups of 79 each, by using a computer-generated random number table, by an anesthesiologist not otherwise involved in the study, outside the operating room, namely:
Group A: Tramadol suppository and Ultrasound guided Transversus Abdominis Plane Block with Bupivacaine
Group B: Tramadol suppository.

Inclusion criteria

1. Physical status ASA grade 1 and 2.
2. Age group of 18 to 40 years undergoing elective Caesarean Section under spinal anaesthesia.

Exclusión criteria

1. Patient refusal.
2. History of relevant drug allergy.
3. Coagulation disorders.
4. BMI >35 kg/m2 at initial hospital visit.
5. Pre-eclampsia.
6. Contraindication to neuraxial anaesthesia.
7. Patients who have received other analgesia not in study group.

Pre-operative investigations and assessment

Pre-anaesthetic examination included general examination, systemic examination of cardiovascular system, respiratory system, central nervous system and gastro-intestinal system. Basic investigations like hemogram, random blood sugar, blood urea, serum creatinine and coagulation profile were assessed and verified before including the patients in the study. Demographic data like Age, Sex, and body weight were recorded.
The purpose and procedure of the clinical study was informed to all patients. They were counselled about the intensity of pain normally associated with the surgery and pain relief that could be achieved with the technique employed.
Patients were trained to assess pain using Visual Analogue Scale (VAS) during preoperative evaluation.

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The effectiveness of analgesia was measured by the average pain at rest and on moving over the period of 3, 6, 9 and 12 hours respectively on a graduated 100 mm VAS, effects and possible complications were explained to patients.

Method: Ultrasound-guided TAP block technique (posterior approach) was given to 'Group A' patients as described by Hebbard and colleagues. After covering the surgical site with a dressing, the procedure was performed using aseptic technique (gown, gloves, facemask and protective sheath for the ultrasound probe). The block was performed using the PHILIPS-CX30 ultrasound machine (Model-SG61450041). A 60 mm curved array US probe (2-5 Megahertz) was positioned in transverse plane in the mid-axillary line in the axial plane half-way between the iliac crest and the costal margin (Figure No 14.1). The TAP block was performed only if the views were satisfactory. Views were considered satisfactory if subcutaneous fat, external oblique muscle, internal oblique muscle, Transversus Abdominis muscle, peritoneum and intraperitoneal structures were identified.
A 20G 3.5inch Quincke spinal needle (BD) with 10 cm extension tubing was connected and flushed with 2 ml of saline. The needle was introduced anteriorly in-plane under real-time US guidance to lie between the internal oblique and the Transversus Abdominis muscles with the tip in the mid-axillary line. 2 ml of study drug was used to separate fascial layers to confirm needle location. The calculated volume of 0.25% Bupivacaine was injected on each side in 5 ml increments after aspiration to avoid intravascular placement. An echo-lucent lens-shaped space (*Kayak sign*) between the two muscles was taken as a successful injection same step was repeated on the other side. In Group A patients, Zero hour was considered after the TAP block was administered before shifting to post-anaesthesia care unit (PACU) and in Group B patients, Zero hour was taken as the end of surgery before shifting to PACU.
The patient was observed in the PACU and later in obstetric ward. PACU stay of more than 3 hours if required was noted along with the reason for delay.
Rescue analgesia (Paracetamol 1 gram IV as a bolus dose for body weight > 50 kg or a bolus dose of 15 mg/kg IV for body weight < 50 kg) was given for breakthrough pain. Time to the first rescue analgesic (Paracetamol) was recorded.
The primary observation was pain at rest and pain on movement which is defined as pain on elevation of the head and shoulders from the pillow, lateral tilt and pain on cough. Secondary observation was the proportion of patients who achieved adequate analgesia, satisfaction or sedation.
Patients were assessed at 3, 6, 9 and 12 hours for the following parameters of post-operative pain by Visual Analogue Scale (VAS), Four-point scale sedation score, PONV Impact Scale Score and Satisfaction score (LIKERT SCALE) and whenever patient complains of pain.
Statistical analysis was carried out with the help of SPSS (version 20) for Windows package (SPSS Science, Chicago, IL, USA). The description of the data was done in the form of mean +/- SD for quantitative data while in the form of % proportion for qualitative (categorical) data. *P*-values of < 0.05 was considered significant. For quantitative data Student's t-test was used to test statistical significance of difference between two independent group means. Chi square test (or Fisher's exact test in case of small frequencies in cell) was used to examine the associations between qualitative/quantitative variables.

Results

A total of 79 study subjects were enrolled in each group of the study.

Table 1: Distribution of the study subjects based on age group

		Group A (n=79)	Group B (n=79)	Inter-Group Comparison (P-value) Group A v/s Group B
Age Group (years)	<25	23 (29.1)	19 (24.1)	0.545 (NS)
	25-34	51 (64.6)	57 (72.2)	
	35-44	5 (6.3)	3 (3.8)	

The age distribution did not differ significantly across two intervention groups (P-value>0.05 for comparing Group A v/s Group B). The mean ± SD of age in Group A and Group B was 27.7 ± 4.3 and 27.0 ± 3.4 respectively.

Table 2: The comparison of Pain Scores between the Groups A & B

Pain Score	Group A (n=79)	Group B (n=79)	Inter-Group Comparison (P-value) Group A v/s Group B
3 Hours	0.0 (0 – 2.0)	1.0 (0 – 3.0)	0.001***
6 Hours	0.0 (0 – 2.0)	2.0 (1.0 – 5.0)	0.001***
9 Hours	0.0 (0 – 2.0)	7.0 (5.0 – 8.0)	0.001***
12 Hours	0.0 (0 – 6.0)	--	--

Values are Median (Minimum-Maximum). P-value by Mann-Whitney U test.

The average Pain Score at 3 hours, 6 hours and 9 hours is significantly higher in Group B compared to Group A (P-value<0.001 for both).

Table 3: The comparison of Satisfaction Scores between the Groups A & B

Satisfaction Score	Group A (n=79)	Group B (n=79)	Inter-Group Comparison (P-value) Group A v/s Group B
3 Hours	4.0 (3.0 – 5.0)	4.0 (3.0 – 5.0)	0.999 (NS)
6 Hours	4.0 (3.0 – 5.0)	4.0 (3.0 – 5.0)	0.999 (NS)
9 Hours	4.0 (3.0 – 5.0)	2.0 (1.0 – 4.0)	0.001***
12 Hours	4.0 (2.0 – 5.0)	--	--

Values are Median (Minimum-Maximum). P-value by Mann-Whitney U test.

The average Satisfaction score at 3 hours and 6 hours did not differ significantly across two intervention groups (P-value>0.05 for both). The average Satisfaction score is at 12 hours is significantly higher in Group A compared to Group B (P-value<0.001).

Table 4: The comparison of sedation scores between the Groups A & B

Sedation Score	Group A (n=79)	Group B (n=79)	Inter-Group Comparison (P-value) Group A v/s Group B
3 Hours	0.0 (0 – 0)	0.0 (0 – 0)	0.999 (NS)
6 Hours	0.0 (0 – 0)	0.0 (0 – 0)	0.999 (NS)
9 Hours	0.0 (0 – 0)	0.0 (0 – 0)	0.999 (NS)
12 Hours	0.0 (0 – 0)	--	--

Values are Median (Minimum-Maximum). P-value by Mann-Whitney U test.

The average Sedation Score at 3 hours, 6 hours, 9 hours did not differ significantly across two intervention groups (P-value>0.05 for all).

Table 5: The comparison of PONV Impact scale scores between the Groups A & B

PONV	Group A (n=79)	Group B (n=79)	Inter-Group Comparison (P-value) Group A v/s Group B
3 Hours	0.0 (0 – 0)	0.0 (0 – 0)	0.999 (NS)
6 Hours	0.0 (0 – 1)	0.0 (0 – 1)	0.999 (NS)
9 Hours	0.0 (0 – 0)	0.0 (0 – 0)	0.999 (NS)
12 Hours	0.0 (0 – 0)	--	--

Values are Median (Minimum-Maximum). P-value by Mann-Whitney U test.

The average PONV Impact Scale Score at 3 hours, 6 hours, 9 hours did not differ significantly across two intervention groups (P-value>0.05 for all).The PONV Impact Scale score in both studies were Group A-2.5% (2/79) & Group B-3.7% (3/79).

Table 6: The comparison of Time-to-Rescue Analgesia between the Groups A & B

Time to Rescue Analgesia (hrs)	Group A (n=79)	Group B (n=79)	Inter-Group Comparison (P-value) Group A v/s Group B
Median (Min - Max)	23.0 (10.0-30.0)	6.5 (6.0-8.0)	0.001***

Values are Median (Minimum-Maximum). P-value by Mann-Whitney U test.

The average time to rescue analgesia is significantly higher in Group A compared to Group B (P-value<0.001).

Discussion

Effective pain control is a major concern in the postoperative period in caesarean delivery and has a significant impact on our health care system. Any technique if used for postoperative analgesia should confer certain advantages over the others. The advantage can be in terms of better pain relief or decreased consumption of supplemental analgesics thus allowing early mobilization and rehabilitation of the patient.

Regional blocks of the anterior abdominal wall can significantly contribute to postoperative analgesia especially when used as a part of a multimodal technique. Farragher RA *et al.* [13] observed that the hemodynamic effects are minimal as spread of local anaesthetic is limited to the abdominal wall. It is well recognized that local anaesthetic techniques can improve the quality of postoperative recovery by reducing pain and analgesic requirements. An important component of pain experienced by patients after abdominal surgery, as in caesarean section, derives from abdominal wall incision.

Mishriky BM *et al.* [7] has concluded that women undergoing caesarean delivery who had local anaesthetic infiltration or abdominal nerve block had reduction in the use of postoperative opioids. Given these issues, there is considerable potential for a regional technique such as TAP blockade to be included as effective component of a multimodal regimen for post caesarean delivery analgesia.

In our study, the two groups were well matched demographically with reference to age, weight and ASA grade. There was no statistically significant difference between the groups with respect to the above parameters.

Evidence from various studies [7, 14] using different drug regimens suggests that there is a place for the use of TAP blocks following caesarean section, but its efficacy and side effects are yet to be explored. The TAP block is usually performed bilaterally, aiming to ensure complete sensory blockade of the abdominal wall.

Bupivacaine, an amide type of local anaesthetic, stabilises the neuronal membrane by blocking sodium channels (depolarisation channels) and thereby interrupts the initiation and transmission of nerve impulses. Bupivacaine (0.25%) at a total dose of 2 mg/kg with equally divided dose on each side was used in our study. This accounted to total volume of Bupivacaine of 0.4 X weight (in Kg) of the patient on each side. Mean volume of 23.2ml (for 58 kg) was used on each side in the study. Hebbard P *et al.* [12] observed that TAP block relies on the local anaesthetic spread rather than concentration and therefore is more volume dependant. Hence, we chose the above concentration, volume and dosage. This dose is well within the recommended safe dose range for Bupivacaine.

Tramadol, centrally acting analgesic, is an atypical opioid which relieves pain by opioid receptors as well as inhibiting reuptake of norepinephrine and serotonin, increasing serotonin release, and thus activating monoaminergic spinal inhibition of pain. Tramadol causes less respiratory depression, sedation, constipation, urinary retention and rise in intra-biliary pressure than morphine and it is well tolerated [6, 8].

Our study was comparable with Baaj JM *et al*. [15] as they used ultrasound guided TAP block with 0.25% Bupivacaine (similar to our study) versus saline/placebo. The study by Baaj JM *et al*. concluded that in the bupivacaine group a reduction in total morphine consumption by more than 60%, improved satisfaction with their pain relief over 24 hours after surgery, less nausea, vomiting and better patient's satisfaction. Similarly, our study showed no rescue analgesia requirement, less PONV, and better patient satisfaction in the 12 hours study period.

The study by Kanazi *et al*. [16] was in contrast to our study as they used 0.375% Bupivacaine 20 ml with epinephrine 5µ/ml per side in ultrasound guided TAP block (TAP) versus subarachnoid morphine (SM). Median (range) time to first analgesic request was longer in group SAM than in group TAP [8 (2-36) hours versus 4 (0.5 to 29) hours (p = 0.005)]. Postoperative visceral pain scores at rest and on movement during first 4 hours were lower in group SM than in group TAP, but were not different at any other time period. The incidence of moderate to severe nausea was higher in group SM than in group TAP [13/28 (46%) versus 5/29 (17%) (p=0.02)]. More patients developed pruritus requiring treatment in group SAM than in group TAP [(11/28 (39%) versus none (0%) (p<0.001)]. In our study, the postoperative analgesia given to both groups was tramadol suppository which had less opioid and analgesic effects as compared to morphine and no comparison was done with morphine. And the time to rescue analgesic for TAP block was 23(10-30) hours-this might be because of higher volume (median 23.4ml) of the local anaesthetic we have used in the study. The PONV score was less for TAP block, no sedation, pruritis or adverse effects were noted and showed better patient satisfaction.

McMorrow *et al.* [3] used anatomical approach for TAP block which is considered inferior as compared to ultrasound guided technique which was used in our study. Bupivacaine 2 mg/kg was used similar to our study. The patients were randomized to one of four groups to receive (in addition to spinal anaesthesia) either subarachnoid morphine 100 mg (SM) or saline (SS) and a postoperative bilateral TAP block with either bupivacaine (TLA) 2 mg/kg or saline (TS). The rank order of median pain scores on 100 mm Visual Analogue Scale (VAS) on movement at 6 h was: SM & TLA (20 mm), SM & TS (27.5 mm), SS & TS (51.5 mm), SS & TLA (52.0 mm) (P,0.05, highest vs. lowest). Sedation scores and patient satisfaction did not differ between groups. Anti-emetic use and pruritus were highest in the SM&TLA group. They concluded that Spinal morphine-but not TAP block-improved analgesia after Caesarean section. The addition of TAP block with bupivacaine 2 mg/kg to spinal morphine did not further improve analgesia. In our study VAS scale score at 6hrs was 0 mm in Group A & 1 mm in Group B. compared to this study our analgesia is more effective & prolonged possibly because of more accuracy by ultrasound technique. The short duration of analgesia in Group B is because we used Tramadol which is weak opioid as compared to morphine. There was no sedation in both study groups and satisfaction score was better with TAP block. The PONV score was less in both studies-Group A (2/79) & Group B (3/79).

In study by Eslamian L *et al.* [17] the patients received TAP block with 15 ml each 0.25% bupivacaine on both sides (group T, n=25) or no blockade (group C, n=25) at the end of the caesarean section under general anaesthesia. The pain intensity in the patients was assessed at the time of discharge from recovery and at 6, 12 and 24 hours postoperatively, with a visual analogue scale (VAS) for pain. The women in the TAP block group had significantly lower VAS pain scores at rest and during coughing. There was a significantly longer time to the first request for analgesic in the TAP block group [210 min (0-300) vs. 30 min (10-180) in group C, p=0.0001]. Our study is similar to this study since it showed that TAP block is an effective analgesia prolonging the time for rescue analgesia. In our study the volume of Bupivacaine used was more and tramadol suppository was also used in both groups. So, in our study the time to rescue analgesia was longer and it showed lower VAS scores and longer time for rescue analgesia.

Joshi *et al*. [6] compared the suppositories of Tramadol versus Diclofenac in post-operative analgesia of caesarean delivery and postulated that both are effective for postoperative analgesia in caesarean section & Diclofenac is better alternative than tramadol as it is devoid of nausea and vomiting and have longer duration. Prostaglandins are commonly used as uterotonics. NSAIDs like Diclofenac inhibit prostaglandin biosynthesis by blocking the cyclooxygenase enzyme which catalyses the conversion of arachidonic acid to prostaglandin but Tramadol is devoid of these effects. So, we preferred Tramadol

suppository for our study. Our study is comparable with this study as it is consistent with pharmacology of tramadol.

Conclusion

The present study demonstrated that the addition of ultrasound guided TAP block to tramadol suppository following caesarean section prolonged the time to first rescue analgesic, improved pain scales, provided better patient satisfaction thereby helping the mother to provide better care for the baby. There were no complications due to the block and no added side effects.
In conclusion, our study suggests that TAP block significantly improved postoperative analgesia in women undergoing Caesarean delivery patients and it is therefore recommended.

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