Original Research Paper

Volume - 12 | Issue - 04 | April - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anaesthesiology

NALBUPHINE AS AN ADJUVANT TO BUPIVACAINE IN TRANSVERSUS ABDOMINIS PLANE BLOCK FOR POST-OPERATIVE ANALGESIA IN TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA.- A COMPARATIVE RANDOMIZED SINGLE-BLINDED STUDY.

Dr.Priyanka Nimbalkar* M.D.Anaesthesia,DY Patil Education Society, Kolhapur, Maharashtra, India. *Corresponding Author

Dr.Anupama Sahasrabudhe Associate Professor,Department of Anaesthesiology, DY Patil Education Society, Kolhapur, Maharashtra, India.

ABSTRACT

Background and objectives: Transversus abdominis plane (TAP) block is a type of multimodal analgesia for postoperative pain relief in surgical procedures like abdominal hysterectomy, caesarean section, open appendectomy, inguinal hernia repair, nephrectomy etc .This study evaluated the efficacy of adding nalbuphine to bupivacaine in TAP block in patients who have undergone total abdominal hysterectomy (TAH) with spinal anesthesia.

Methodology: A comparative randomized single-blinded study was carried out in 60 patients posted for elective TAH under spinal anaesthesia in a tertiary care centre during March 2019-October 2020. After completion of surgery, all patients were given TAP block by 2 pop-up technique. Patients of group A (n=30) were administered with 20ml of 0.25% bupivacaine and group B (n=30) with 20ml of 0.25% bupivacaine with 0.5ml of 5mg nalbuphine. Degree and duration of analgesia after TAP block was compared between the two groups. Scores analysed by visual analogue scale (VAS) were used for comparison of the intensity of pain.

Results: At 4 hours and 6 hours after TAP block, mean VAS were significantly lower in patients who were given nalbuphine along with bupivacaine (1.5±0.51 and 3.2±0.76, p<0.001) as compared to patients who were given bupivacaine, alone (2.33±0.55 and 4.43±0.82, p<0.001).Duration of analgesic action of TAP block was clinically longer in patients who were given nalbuphine along with bupivacaine(454±25.81 mins) compared to patients who were given bupivacaine alone (405±42.24 mins,) but was not statistically significant.

Conclusion: Adding nalbuphine as an adjunct to bupivacaine in TAP block lowers the post-operative pain scores with no remarkable side effects. Although, there is no prolongation of postoperative analgesia or the time for first rescue analgesic.

KEYWORDS : Anaesthetic adjuvants, bupivacaine, nalbuphine,transversus abdominis, TAP block, postoperative analgesia

BACKGROUND

Total abdominal hysterectomy (TAH) has been mainly associated with postoperative pain, anaesthesia related complications and wound infections.[1]The pain caused by TAH is due to the somatic pain signals coming from anterior abdominal wall and its sensory afferents that course through the transversus abdominis plane (TAP) superficial to the transversus abdominis muscle.[2] TAP block is a new regional anaesthesia technique that delivers analgesia to the parietal peritoneum along with the skin and muscles of the lower anterior abdominal wall.[3] It was originally introduced by Rafi in 2001 as a breakthrough technique. TAP block is administered through the triangle of Petit to attain a field block that comprises a single shot anaesthetic delivery into a plane between the internal oblique muscle and transversus abdominis muscle.[4]Subsequent studies on TAP block provide evidence for analgesic efficacy of the block with anatomical basis such as neurofascial space, skin, muscles of the anterior abdominal wall, and parietal peritoneum.[5] It is a constituent of multimodal analgesia for postoperative pain in several surgical procedures such as large bowel resection, open appendectomy, retropubic prostatectomy, nephrectomy, hernia repair, laparoscopic cholecystectomy and caesarean section.[6]

Bupivacaine, a local anaesthetic belonging to the amide group of anaesthetic agents, has been generally used for local infiltration, nerve blocks, spinal and epidural anaesthesia.[7] Several adjuvants like tramadol, fentanyl, morphine are being used along with the local anaesthetic bupivacaine to further diminish the negative effects of the local anaesthetic and to extend the period of intraoperative and postoperative analgesia. Nalbuphine is a synthetic opioid with mixture of kappa receptor agonism and partial mu receptor antagonism.Its analgesic effectiveness is analogous to morphine and acts by modulating visceral pain with fewer adverse effects.[1]Nalbuphine is efficacious to provide good intraoperative and postoperative analgesia with decreased incidence and severity of mu receptor sideeffects when added to intrathecal local anesthetics.[8] In this study , an attempt was made to evaluate the effectiveness of adding nalbuphine to bupivacaine in TAP block for post-operative pain control after TAH with spinal anaesthesia.

METHODOLOGY

An interventional, randomized single-blinded clinical study was conducted among patients posted for elective TAH under spinal anaesthesia in a tertiary care centre during March 2019- October 2020.The study was performed with the approval of the Ethics Committee of the Institute (No. DYPMCK/200/2019/IEC).Written informed consent was obtained from patients before starting the study. Patients aged 35-60 years, undergoing elective TAH under spinal anaesthesia, and classified American Society of Anesthesiologists (ASA) grade 1 and 2 were enrolled . Patients were excluded, if they were ASA grade 3 and 4, allergic to local anaesthetic agents, patients having obesity with a body mass index (BMI)>35 kg/m^2 and presented with any contraindications to peripheral nerve block.

The sample size was calculated as follows:

$$n = \frac{2\left(z_{1-\alpha/2} + z_{1-\beta}\right)^2 \sigma^2}{\left(d/\sigma\right)^2}$$

Where, zα/2 is the value corresponding to level of confidence required. z_(1-β)is the value corresponding to power.By assuming effect size as 0.8 (large effect size) with 95% confidence level and 80% power.As per the calculation, minimum sample size required was 25 subjects in each study group.

Patients fulfilling the inclusion criteria were examined and medical history was obtained. Vital parameters of the patients were recorded and classified as per the ASA grading system. Patients were categorized randomly using computer generated codes. Baseline values of noninvasive blood pressure (NIBP), pulse rate (PR) and oxygen saturation (SpO2) were monitored. An intravenous cannula (18-Gauge) was secured for intravenous access. All the subjects were given spinal anesthesia with 0.5% bupivacaine(heavy) in the sitting position under aseptic conditions in the operating room at the L3-L4 level, using a 25-G spinal needle.

After administering spinal anesthesia, standard protocol for intraoperative sedation with injection midazolam 0.04mg/kg and pentazocine 0.6mg/kg was given After completion of surgery, all patients were administered TAP block using 10 cm stimuplex needle by 2-popup method in the midaxillary line at the midpoint between costal margin and the highest point of iliac crest. The drug mixture was prepared and administered by the anaesthesiologist to the patient (who was blinded). Patients of group A (n=30) were administered with 20 ml of 0.25% bupivacaine and group B (n=30) were administered 20ml of 0.25% bupivacaine with 0.5ml of 5mg nalbuphine.

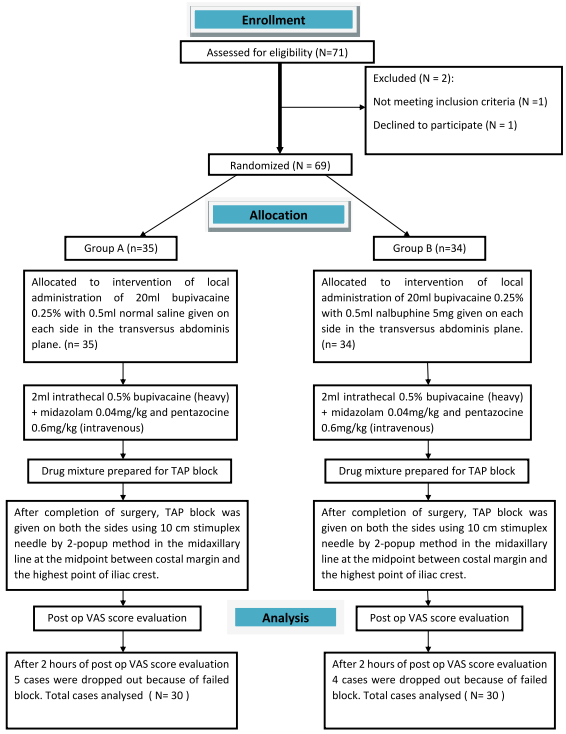
VAS scores were documented at (i) second hour post operatively, to exclude the cases of failed block, and (ii) every 2 hours till patients

themselves complained of pain or asked for rescue analgesic post operatively.

Duration of analgesia of TAP block was calculated by recording the time duration until patient complains of pain and requests for an analgesic. Intravenous injection tramadol 100mg in 100ml of normal saline over 20mins was administered as a rescue analgesic. The patients were further observed for at least one day post-operatively. In addition, they were observed for various adverse effects such as nausea, vomiting, bradycardia (defined as PR<60 bpm), hypotension (mean arterial pressure <60 mmHg), respiratory depression, pruritis etc.

Statistical analysis of the data was performed using the statistical software R(Version 4.0.3). Categorical variables were represented as frequency tables and continuous variables as mean standard deviation (SD).Chi-square test was employed to measure the association between two categorical variables. p-value ≤ 0.05 was measured statistically significant. (Figure 1)

Consort flow chart



RESULTS

The average age of 60 subjects under the study was 47.82 ± 4.45years. It was observed that 93.3% of total patients were aged above 40 years. Table 1 and figure 1 presents the demographic details of patients. No significant association was observed between age group in the two treatement groups (p=0.61) and the distribution of age was not statisticallydifferent in the two groups (p=0.29).Patients of ASA grade 1 and 2 have been included in the study, among them, 61.66%(n=37) were Grade 1 and 38.33% (n=23)were Grade 2.There was no significant association between ASA grades in the two groups (p=0.59) Further, mean BMI of the study population was 26.48 ± 3.6kg/m^2 and no patients were underweight (BMI < 18.5kg/m^2).An ideal BMI (18.5-22.9kg/m^2)was recorded in 16.66% (n=10) and BMI(23 to 24.9 kg/m^2) in 16.66% (n=10), overweight (BMI 25 to 29.9 kg/m^2) in 40% and obese (BMI > 30 kg/m^2) in 26.66% (n=16) of patients.Patients stratified according to BMI were similarly distributed in both the study groups (p = 0.32) (Table 1 and fig 1).

In this study population, fibroid was the most common indication for TAH (n=30, 50%) followed by adenomyosis (n=21, 35%). Dysfunctional uterine bleeding and endometrial polyp were observed only in 6 and 3 patients, respectively.It was observed that both the study groups had a similar distribution of patients according to their indication for undergoing TAH.No significant association was observed between indication for surgery in the two groups (p=0.99) (Table 1).

The distribution of VAS after TAP block at different intervals was significantly different over the treatment groups (p<0.0001)(Table 2 and figure 2).VAS scores after post-TAP block at 2 hours were 0.60 ± 0.72 and 0.37 ± 0.61 in Group A and B, respectively.At 4 hours post TAP block, mean VAS was remarkably lesser in Group B (1.5 ± 0.51) as compared to Group A (2.33 ± 0.55) (p < 0.0001). Continually,at 6 hours post TAP block, VAS was significantly lower in Group B (3.20 ± 0.76) than in Group A (4.43 ± 0.82). Hence, the trend of lower VAS scores continued after 4 hours post TAP block.

Duration of action of TAP block in groups-A and -B were recorded to be 405±42.24 mins and 454 ± 37.8 mins, respectively (Table 3 and figure 3).Group B (bupivacaine + nalbuphine) showed clinically higher duration of action of TAP block in contrast to group A (bupivacaine). However, a statistically significant variance was not observed between two study groups for length of action of TAP block (p value= 0.57).Table and figure 4 describe the likelihood ratio of VAS scores over different factors. Since VAS scores were ordinal in nature, repeated measure was done by fitting cumulative link mixed model. The factors *viz*., group (p <0.0001), time (p <0.0001) and group:time (p=0.0004) have significantly affected the differences in the VAS scores.

DISCUSSION

Nalbuphine, a mixed agonist-antagonist drug when administered intrathecally, binds to kappa receptors in the spinal cord, which are responsible for nociception, producing analgesia and sedation without sideeffects.[8] The present study compared the efficiency of nalbuphine and bupivacaine with bupivacaine monotherapy in inducing analgesia after TAH.

Opioid receptors similar to neuropeptides and other proteins are synthesized in the dorsal root ganglion and then carried into the central and peripheral terminals via axonal transport . Also, the peripheral analgesic effects of exogenous opioids are enhanced under inflammatory conditions.

Patients of both groups , bupivacaine(A) and bupivacaine+nalbuphine (B) were similar with respect to the demographic profile such as age, ASA status, BMI category and indication for surgery (TAH).

Patients who were given bupivacaine monotherapy, reported significantly higher pain scores at 4 hours than patients who were given nalbuphine-bupivacaine combinations as measured byVAS (p<0.001). In an earlier study by Jyothi *et al.*, addition of nalbuphine 0.8 mg to intrathecal bupivacaine 0.5% in caesarean section provided excellent analgesia (VAS 3.4±0.4) than bupivacaine alone(VAS 4.08±0.5) (p< 0.05).[8] Further, Gupta *et al.*studies also reported that pain scores were comparatively lower in study groups treated with nalbuphine as an adjunct to bupivacaine (VAS 5.6) than bupivacaine alone (VAS 1.44)(p< 0.01) in ultrasound guided supraclavicular brachial plexus blockade.[9]

Duration of action of TAP block was higher in 0.25% bupivacaine +5mg nalbuphine (B)combination than in bupivacaine(A) alone clinically but was not statistically significant (p value 0.57). Previously,Jyothi *et al.* revealed that nalbuphine hydrochloride (0.8, 1.6, and 2.4 mg) extends the period of sensory blockade, offers excellent quality and extended period of postoperative analgesia with good sedation and minimal sideeffects when added to 0.5% bupivacaine in lower abdominal and orthopedic surgeries.[8] Further, Gupta *et al.* also reported that a significant increase was seen in the length of analgesia in patients who obtained 10mg nalbuphine as an adjunct to 0.5% bupivacaine (481.53±42.45 min) in contrast to 0.5% bupivacaine alone(341.31±21.42 min)(p< 0.001).[9] These findings on combination of nalbuphine and bupivacaine are comparable to the results of this study.

A meta-analysis of randomized controlled trials exhibited that the analgesic efficiency of nalbuphine is analogous to morphine, however,nalbuphine provides pain control with less incidence of nausea and vomiting, respiratory depression and pruritus.[10] In an other study, addition of 10 mg nalbuphine hydrochloride to levobupivacaine 0.375% solution in supraclavicular brachial plexus block prolonged the period of sensory and motor blockades(P < 0.05)without any appreciable side effects.[11] Also, a small dose of nalbuphine (15µgkg^{-1}ml^{-1}) combined with flurbiprofen(1mg ml^{-1}) showed greater efficacy in aged patients who had undergone gastrointestinal surgery with TAP

block with efficient postoperative analgesia and shortened severity of nausea and vomiting.[1]

This study has a few limitations. The study did not measure the bloodlevel of nalbuphine to detect its route of prolonged postoperative analgesia, whether it is due to local effect or systemic absorption. Adverse effects of the anesthetics have not been recorded. Further studies are necessary to analyse the exact mechanism of action.

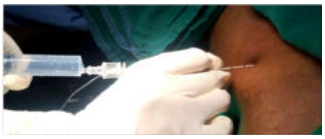


Figure 1

Table 1: Distribution of patients according to their age groups , ASA grade, BMI and indications.

Categorical variables		Bupivacaine (A)	Bupivacaine with nalbuphine (B)	*P*-value
Age groups (Years)	≤40	3 (10)	1 (3.33)	0.61†
	>40	27 (90)	29 (96.66)	
	Total	30 (100)	30 (100)	
	Mean (SD)	47.3 (4.49)	48.33 (4.44)	0.29††
	Median (IQR)	50 (45-50)	50 (47.25-50)	
ASA Grade	I	17 (56.67)	20 (66.67)	0.59†
	II	13 (43.33)	10 (33.33)	
	Total	30 (100)	30 (100)	
BMI category (kg/m^2)	18.5 – 22.9	4 (13.33)	6 (20)	0.32†
	23 – 24.9	3 (10)	7 (23.33)	
	25 – 29.9	15 (50)	9 (30)	
	≥ 30	8 (26.67)	8 (26.67)	
	Total	30 (100)	30 (100)	
	Mean (SD)	27.03 (3.55)	25.93 (3.63)	0.24††
	Median (IQR)	27.5 (25.2529.75)	25.5 (24-29.75)	
Indication for TAH	Adenomyosis	11 (36.67)	10 (33.33)	0.99†
	Dysfunctional uterinebleeding	3 (10)	3 (10)	
	Endometrial polyp	1 (3.33)	2 (6.67)	
	Fibroid	15 (50)	15 (50)	
	Total	30 (100)	30 (100)	

†Chi-square test, ††Mann Whitney U test were used for statistical analyses. All the values are presentd in frequency (percenatge) form except mean and median. ASA, American Society of Anesthesiologists; BMI, body mass index; IQR, interquartile range; SD, standard deviation; TAH, total abdominal hysterectomy.

Table 2: Description of VAS scores after TAP block at different time intervals

Time	Bupivacaine (A)		Bupivacaine with nalbuphine (B)		*P*-value*
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
2 hrs	0.60 (0.72)	1.0 (1 – 2)	0.37 (0.61)	1.0 (1 – 2)	<0.0001
4 hrs	2.33 (0.55)	3.0 (3 – 4)	1.50 (0.51)	2.5 (2 – 3)	<0.0001
6 hrs	4.43 (0.82)	5.5 (5 – 6)	3.20 (0.76)	4.0 (4 – 5)	<0.0001

*Repeated measure ANOVA was used forstatistical analyis. *Statistically signifcant (p<0.05). IQR, interquartile range; SD, standard deviation, TAP, transverse abdominis plane; VAS, visual analog scale*

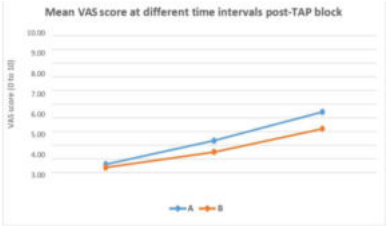


Figure 3: Distribution of VAS after TAP block between two groups

Table 3: Description of duration of action of TAP block (in mins)

Variables	Duration of action of TAP block (in minutes)		*P*-value
	Mean (SD)	Median (IQR)	
Bupivacaine (A)	405 (42.24)	390 (360, 420)	0.57*
Bupivacaine with nalbuphine (B)	454 (37.8)	450 (450, 480)	

*Independent sample t test was done.*Statistically significant; IQR, interquartile range; SD, standard deviation, TAP, transverse abdominis plane*

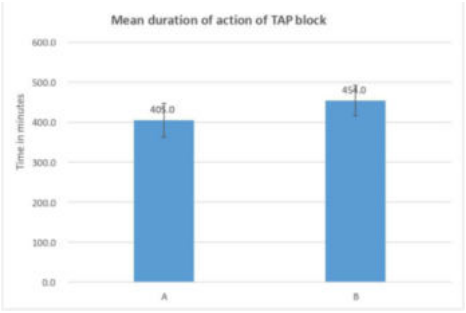


Figure 4: Distribution of Duration of action of TAP block between groups

CONCLUSION

The pain scores were comparatively lower in patients treated with nalbuphine 5mg in addition to bupivacaine 0.25% than bupivacaine 0.25% alone .Further,addition of nalbuphine to bupivacaine showed clinically longer period of action of TAP block in comparison to bupivacaine alone, but the difference was not statistically significant. The results exhibited that addition of nalbuphine to bupivacaine in TAP block lowers the post-operative pain scores and diminishes the requirement for postoperative parenteral analgesic therapy with no remarkable side effects.

REFERENCES

1. Mao, Y., Cao, Y., Mei, B. et al. Efficacy of nalbuphine with flurbiprofen on multimodal analgesia with transverse abdominis plane block in elderly patients undergoing open gastrointestinal surgery: a randomized, controlled, double-blinded trial. Pain Res Manag. 2018;2018(2):1-9.
2. El-Kabariety, R. Tramadol as an adjuvant to levobupivacaine in an ultrasound-guided transversus abdominis plane block in women undergoing abdominal hysterectomy. Ain-Shams J Anaesthesiol. 2013;6(3):304-311.
3. Metwally, A.A., Abo-El-Enin, K.M., Abd Allah, S.I., et al. Ultrasound-guided transversus abdominis plane block for lower abdominal surgeries: bupivacaine alone or combined with fentanyl or epinephrine. Menoufia Medical Journal. 2017;30(2):538.
4. Tsai, H.C., Yoshida, T., Chuang, T.Y., et al. Transversus abdominis plane block: an updated review of anatomy and techniques. Biomed Res Int.2017; 2017:8284363.
5. Petersen, P.L., Mathiesen, O., Torup, H., et al. The transversus abdominis plane block: a valuable option for postoperative analgesia? A topical review. Acta Anaesthesiologica Scandinavica. 2010;54(5):529-535.
6. Bhattacharjee, S., Ray, M., Ghose, T., et al. Analgesic efficacy of transversus abdominis plane block in providing effective perioperative analgesia in patients undergoing total abdominal hysterectomy: A randomized controlled trial. J Anaesthesiol Clin Pharmacol. 2014;30(3):391-396.
7. Chatrath, V., Attri, J. P., Bala, A., et al. Epidural nalbuphine for postoperative analgesia in orthopedic surgery. Anesth Essays Res. 2015;9(3):326-330.
8. Jyothi, B., Gowda, S., and Shaikh, S.I. A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries. Indian J Pain. 2014;28(1):18.
9. Gupta, K., Jain, M., Gupta, P.K., et al. Nalbuphine as an adjuvant to 0.5% bupivacaine for ultrasound-guided supraclavicular brachial plexus blockade. Indian J Pain. 2016;30(3):176.
10. Zeng, Z., Lu, J., Shu, C., et al. A comparison of nalbuphine with morphine for analgesic effects and safety: meta-analysis of randomized controlled trials. Sci Rep. 2015;5(1):1-8.
11. Chiruvella, S., Konkyana, S.K., Nallam, S.R., et al. Supraclavicular brachial plexus block: Comparison of varying doses of nalbuphine combined with levobupivacaine: A prospective, double-blind, randomized trial. Anesth Essays Res. 2018;12(1):135.