Postoperative Analgesic Effect of Morphine Added to Bupivacaine for Transversus Abdominis Plane (TAP) Block in Appendectomy

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ABSTRACT

Background

Transversus abdominis plane (TAP) block with local anaesthetics produces effective pain relief following lower abdominal surgeries. Although opioids have been found to have effects through peripheral receptors also, reports on their effect when used as additive to local anaesthetics for TAP block are lacking.

Objective

To assess the analgesic effect of peripherally administered morphine with bupivacaine for ipsilateral TAP block in patients undergoing emergency appendectomy under general anaesthesia.

Method

Sixty patients undergoing appendectomy were randomized to undergo ipsilateral TAP with 20 ml of 0.5% bupivacaine plus 2 ml of NS (total 22 ml) and 2 ml of intravenous (IV) saline (Group TB) or with 20ml of 0.5% bupivacaine plus 2 mg (2 ml) of morphine (total 22 ml) and 2 ml of NS IV (Group TBM) or with 20 ml of 0.5% bupivacaine plus 2 ml of NS (total 22 ml) and 2 mg (2 ml) IV morphine (Group TB-IVM). Pain severity was measured using Visual Analogue Scale (VAS) preoperatively (Baseline) and at 30 min, 6h, 12 h and 24 h postoperatively. Inj. tramadol 50 mg IV was used as rescue analgesic when postoperative VAS was 4 or more. The duration of analgesia (time to first analgesic) and the postoperative 24 h tramadol requirement was recorded.

Result

The mean duration of analgesia in Group TBM was significantly longer (801.50 ± 74.92 min, p=0.002) than in Group TB (720.00 ± 42.17 min) and Group TB-IVM (712.70 ± 40.94 min). The mean postoperative 24 h tramadol requirement was also less in Group TBM (69.23 ± 25.31mg) than in Groups TB (100.00 ± 38.34 mg) and TB-IVM (95.00 ± 39.40 mg) but did not reach the level of statistical significance (p=0.057). Significantly less ondansetron was required in Group TBM (3.80 ± 2.04 mg) than in Group TB (6.80 ± 2.93 mg) and TB-IVM (6.00 ± 2.75 mg) (p=0.002).

Conclusion

Morphine added to bupivacaine effectively prolongs the analgesic duration of TAP block in appendectomy.

KEY WORDS

Morphine, postoperative analgesia, transversus abdominis plane block, USG guided

INTRODUCTION

Appendectomy is one of the commonest surgical procedures involving significant tissue injury. Patients undergoing appendectomy suffer significant postoperative pain and require effective analgesia.[1] Transversus abdominis plane (TAP) block is one of the new approaches to provide effective postoperative analgesia in patients undergoing surgical procedures involving anterior abdominal wall and is being investigated for its usefulness in different types of surgeries in different settings. TAP block can be performed either by using ultrasound or in an open abdomen or blindly with land mark technique in which local anaesthetic is deposited in the transverses abdominis fascial plane via a regional anaesthesia needle inserted through the lumbar triangle of Petit.[2-4] Different adjuvants have been studied to improve the quality and increase the duration of local anaesthetics during various nerve block techniques.[5-7] Although opioids have been found to have effects through peripheral receptors also, reports on their effect as an additive to local anaesthetic for TAP block are lacking.[8-10] The current study aimed to assess the effectiveness of adding morphine to bupivacaine on the quality and duration of USG guided TAP block for postoperative analgesia in adult patients undergoing appendectomy in a community based hospital setting.

METHODS

The study was carried out from August 2015 to July 2016 in a community based tertiary care hospital of eastern Nepal. Ethical clearance was obtained for the study from the Institutional Review Committee (IRC). Informed written consent was obtained from each patient regarding the participation in the study. During the preoperative assessment, patients were familiarized and explained about Visual Analogue Scale (VAS) score and its use for pain assessment in simple understandable language and baseline VAS was recorded at the same time. We studied adult patients aged 18 years belonging to American Society of Anaesthesiologists Physical Status (ASA PS) I and II, scheduled for emergency open appendectomy. Patients were excluded if they had history of allergy to the drug used in the study, had chronic painful conditions, or were on analgesics on regular basis. Patients with known or suspected pregnancy, bleeding diathesis, morbid obesity and those showing unwillingness to participate in the study were excluded.

A total of 60 patients with 20 in each group were randomly allocated to Group TB, TBM or TB-IVMA as per computer generated random allocation sequence. Group TB patients received ipsilateral USG guided TAP block with 20 ml of 0.5% bupivacaine plus 2 ml of normal saline (NS) (total 22 ml) and 2 ml of NS intravenously (IV), Group TBM received ipsilateral USG guided TAP block with 20 ml of 0.5% bupivacaine plus 2 mg (2 ml) of morphine (total 22 ml) and 2 ml of NS IV and Group TB-IVM received ipsilateral USG guided TAP block with 20 ml of bupivacaine plus 2 ml of NS (total 22 ml) and 2 mg (2 ml) of morphine IV. Group allocation was concealed in sealed opaque envelopes, which were not opened until patient consent was obtained. The patients and the investigator observing the outcome data were kept unaware of the group assignment. Venous access was established (if not in situ) on the dorsum of non-dominant hand with 16 G intravenous (IV) cannula under local anaesthesia and lactated ringer's solution was infused. In the operation theatre, non-invasive blood pressure (NIBP) cuff, electrocardiogram (ECG) leads and pulse oximetry (SpO_2) probe were attached to the patient and baseline NIBP, respiratory rate (RR), heart rate (HR) and SpO_2 were recorded.

All the patients received a standardized rapid sequence induction of anaesthesia. After pre-oxygenation for 3 minutes, anaesthesia was induced with inj. propofol 2 mg/kg IV. Cricoid pressure was applied immediately after induction and inj. succinylcholine 1.5 mg/kg IV was administered for facilitation of laryngoscopy and intubation. The trachea was intubated after 60s of succinylcholine administration. All the patients received inj. fentanyl 1.5 mcg/kg IV before surgical incision. Anaesthesia was maintained using 1-1.5 minimum alveolar concentration of isoflurane in oxygen and inj. vecuronium bromide 0.1 mg/kg IV. After completion of the surgical procedure, the ipsilateral USG guided TAP block was performed using 22 gauge block needle with the drugs as per the random allocation sequence. All the blocks were performed by single anaesthesiologist experienced in the technique.

After the skin closure, the residual effect of the muscle relaxant was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg IV. After emergence from anaesthesia, the patients were transferred to the recovery room. The patients were assessed postoperatively at 30 min in the recovery area; and at 6, 12 and 24 h in the surgical ward. A standard postoperative analgesic regimen consisting of IV paracetamol 15 mg/kg (not exceeding 1 gm) was infused 6 hourly in all the groups. All patients were asked to give scores for their pain at rest and on coughing; and for the degree of nausea at each time point. Pain severity was measured using a 10 cm horizontal VAS scale. Nausea was scored using a categorical scoring system (none- 0, mild-1, moderate-2, and severe-3). Injection ondansetron 4 mg IV was used as rescue antiemetic. If the severity of the pain became more than 4 in the scale or the patient complained of pain and asked for analgesia, injection tramadol 50 mg was given IV slowly as a rescue analgesic and was repeated every 6 h as required. Time of administration of rescue analgesic was noted and total amount of drug required during the study period was also noted.

The time of first administration of initial dose of rescue analgesic was considered as the time of termination of

postoperative analgesic effect of TAP block. The duration of postoperative analgesia (defined as the time duration from the time of performing the block to the time of first administration of rescue analgesic) attained in the study groups was the main outcome variable of the study along with the level of analgesia in VAS experienced by the patients. Other outcome parameters observed included postoperative 24 h tramadol requirement, incidence of postoperative nausea vomiting and the ondansetron use as well as any complication attributable to TAP block. In addition, the patients were also asked whether they were satisfied with the postoperative pain relief or not after 24 h of the block.

For sample size estimation we used the finding of a previous study by Al- Touny et al.[11] where the mean verbal pain score ± standard deviation (at 12 h postoperatively) in the group with TAP block with bupivacaine plus morphine was 0.77 ± 0.42 and without morphine was 1.27 ± 0.46. Using these values and keeping two sided confidence interval of 95% and power of 0.9, it was estimated that a minimum of 17 patients were required per group. For simplifying calculation we elected to recruit 20 patients per group into the study.

Data was entered in excel filtered coded and further analysed by SPSS version 11.5. Mean values were compared using one way analysis of variance (ANOVA). Independent t test was used to compare the mean values between the groups. Paired t test was used to compare the mean values before and after the study drug administered within the same group. Chi-square test was used to compare the non-parametric variables.

RESULTS

All the 60 patients completed the study. The baseline patient characteristics were comparable between and among the groups (Table 1).

Table 1. Baseline patient characteristics

Characteristics		Characteristics			p-value
		TB (n=20)	TBM (n=20)	TB-IVM (n=20)	
Gender	M	12(37.5%)	9(28.1%)	11(34.4%)	0.626
	F	8(28.6%)	11(39.3%)	9(32.1%)	
ASA-PS	I	12(31.6%)	11(28.9%)	15(39.5%)	0.393
	II	8(36.4%)	9(40.9%)	5(22.7%)	
Age (years)		31.85±10.68	33.80±16.36	37.15±14.83	0.493
Height (cm)		158.80±4.34	160.65±9.31	158.55±7.14	0.607
Weight (Kg)		58.55±5.73	57.45±5.86	58.25±5.97	0.829
Duration of operation(min)		73.75±13.65	69.75±14.37	72.75±13.22	0.457

The intensity of pain both at rest and during coughing remained statistically comparable at all the observation time points among the groups (Table 2 and 3; Figure 1 and 2).

Table 2. Comparison of VAS scores for pain at rest before and after administration of block among the groups

Observation time points	Group			p-value
	TB(n=20)	TBM(n=20)	TB-IVM(n=20)	
Baseline (preoperative)	4.20±1.19	4.05±1.05	3.90±0.96	0.680
30 min	1.15±1.18	0.70±0.86	0.70±0.97	0.279*
6 h	2.15±1.08	2.30±0.73	2.15±0.87	0.835
12 h	3.15±0.81	3.15±0.58	3.00±0.64	0.731
24 h	3.40±0.68	3.65±0.48	3.00±0.79	0.011

*Mann- Whitney U test

Table 3. Comparison of VAS score for pain on coughing before and after administration of block among the groups

Observation time points	Group			p-value
	TB(n=20)	TBM(n=20)	TB-IVM(n=20)	
Baseline (preoperative)	5.15±1.18	4.60±1.09	4.95±1.05	0.292
30 min	2.25±1.25	1.70±0.73	1.65±0.87	0.108
6 h	2.70±1.12	2.60±0.75	2.60±0.83	0.927
12 h	3.75±0.71	3.65±0.67	3.45±0.75	0.409
24 h	3.70±0.65	3.85±0.58	3.40±0.68	.0881

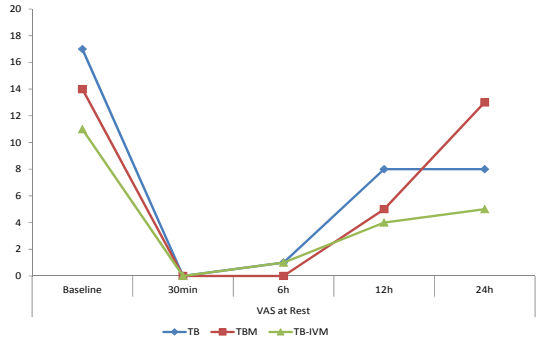

Figure 1. Number of patients with VAS 4 or more at rest before and after administration of block

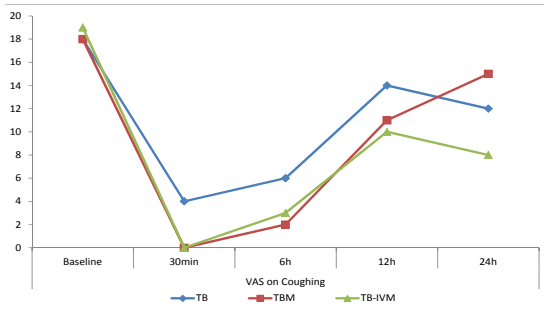

Figure 2. Number of patients with VAS 4 or more on coughing before and after administration of block

The duration of analgesia was significantly longer in TBM group compared to TB and TB-IVM group. The tramadol requirement as rescue analgesic was also less in the same group but not to the level of statistical significance. Similarly total postoperative ondansetron requirement for treating

PONV was also less in TBM group compared to the other two groups. More patients expressed satisfaction with the postoperative analgesia in TBM group and TB-IVM than TB group. (Table 4)

Table 4. Comparison of duration of analgesia, tramadol requirement, ondansetron requirement, patient satisfaction among the groups

Characterstics	Group			p-value
	TB (n=20)	TBM (n=20)	TB-IVM (n=20)	
Duration of analgesia (min)	720.00± 42.17	801.50± 74.92	712.70± 40.94	0.001
Total tramadol requirement (mg)	100.00± 38.34	69.23± 25.31	95.00± 39.40	0.057
Total ondansetron requirement (mg)	6.80± 2.93	3.80± 2.04	6.00± 2.75	0.002
Number of patient satisfied (%)	13(65%)	19(95%)	19(95%)	0.009

All patients received ondansetron when tramadol was administered as rescue analgesic. Four patients in the group TB and 3 patients in the group TB-IVM developed mild to moderate nausea, while patients in group TBM had none or mild nausea.

DISCUSSION

The present study has shown that morphine added to bupivacaine for ipsilateral TAP block significantly prolongs the duration of analgesia following emergency appendicectomy with reduced 24 h postoperative analgesic requirement.

Patient receiving morphine as additive to bupivacaine for TAP block in our study had more than one and half hour duration longer analgesia compared to the patients receiving only bupivacaine for TAP block or those receiving bupivacaine for TAP block and intravenous morphine. This finding is further supported by reduction in tramadol requirement in patient receiving bupivacaine and morphine for TAP block. The precise mechanism of prolonged analgesic effect of local anaesthetics in TAP block is not clear but it is assumed that the TAP is poorly vascularized space and the drug clearance is therefore delayed.[12] None of the patients experienced any unwanted effects of morphine. The duration of analgesia of the other two groups who received only bupivacaine for TAP block was similar to the findings of a previous study.[3]

During our literature review we did not come across any study that assessed the effects of addition of morphine to bupivacaine during TAP block on the duration and quality of postoperative analgesia following appendectomy. In one study published before designing of our study, the TAP block was done with bupivacaine plus 2 mg of morphine following inguinal herniorrhaphy.[11] The investigators observed lower postoperative VAS for pain at all time points assessed both at rest and on movement. They also observed reduced 24 h morphine requirements and a longer time to PCA morphine request compared to TAP block alone. El Sherif et al. compared the effect of with or without addition of morphine to bupivacaine in ultrasound guided transversus abdominis plane block for postoperative analgesia following lower abdominal cancer surgery and found significantly prolonged duration (10.40±4.96 Vs 6.97±3.26 h) of analgesia with TAP block with bupivacaine plus morphine.[13] In contrast to our study, they performed TAP block immediately after the induction of anaesthesia and added larger amount (10 mg) of morphine. The mean duration of surgery in their study was 3.08±0.54 hours. Though, we used only 2 mg of morphine in addition to bupivacaine for TAP block, the mean duration of analgesia in our study and El Sherif and co-workers's study (including the intraoperative period) are comparable. However, it is difficult to compare between our study and their study as the nature of surgeries were different and cancer patients with more extensive surgeries require more analgesics as compared to patients undergoing appendectomies. Requirement of rescue analgesics in the El Sherif et al. study was significantly lower in patients who received morphine along with bupivacaine for TAP block.[13] Addition of morphine to combination of lidocaine/bupivacaine for supraclavicular blocks has been shown to prolong the median duration of analgesia from 11.5 to 21 hours after internal fixation of upper extremity fractures.[14]

Our study showed reduction of opioids requirement in the postoperative period in patients receiving bupivacaine plus morphine for TAP block. Al-Touny et al. also observed reduction in morphine consumption as in the postoperative period in bupivacaine/morphine arm by about 39%.[11] Keskinbora et al. examined the use of bupivacaine versus bupivacaine plus morphine administered via a popliteal catheter for patients with chronic lower extremity pain,[15] the study included a short term single bolus treatment phase where morphine was noted to prolong analgesia by approximately three hours compared to alone.

To improve the efficacy of postoperative analgesia, opioids are injected close to the nerve trunks and nerve endings. The biological basis is the availability of opioid receptors and their endogenous ligands in the peripheral nervous system and their effect in modulation of inflammatory pain.[8,9] At dorsal root ganglions, opioid receptors are synthesized and transferred to the nerve terminals and when the receptors are stimulated, both endogenous and exogenous opioid peptides are activated simultaneously inside inflammatory cells.[10] Nielsen and colleagues in a review article conclude that the analgesic effects of peripherally applied opioids may depend on the presence of preoperative inflammation.[16]

Systemic opioids are regarded effective in managing postoperative pain but are not free of unwanted effects like respiratory distress, nausea-vomiting, pruritus and urinary

retention. So, elderly patients, obese patients with history of obstructive sleep apnea may benefit more with TAP blocks as it provides opioids sparing effects. The incidence of nausea in our study was consistent with the findings of other studies as well.[17,18] However, the occurrence of nausea and vomiting and requirement of ondansetron as rescue antiemetic was clinically more with the patients who received systemic morphine and in patients who received TAP block with bupivacaine only. Seemingly, higher ondansetron requirement in these patients is attributable to their higher requirement of tramadol for postoperative analgesia.

There are some limitations of our study. First, we limited the observation for postoperative analgesic effect of TAP block for 24 h only, however, it has been demonstrated that the clinical analgesic effect of TAP block can last for even 48 h.[19] Second limitation is our small sample size. Third, we were unable to assess serum morphine concentration. Fourth, we used intermittent tramadol as rescue analgesic; the use of PCA pump in the postoperative period would have given better idea in assessing analgesic requirement more precisely.

CONCLUSION

Morphine as an adjunct to bupivacaine in ipsilateral ultrasound guided transversus abdominis plane block as a component of multimodal analgesia provides effective postoperative analgesia with reduced opioid analgesic requirement in patients undergoing appendectomy.

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