

Effects of Morphine Added to Bupivacaine in Ultrasound - guided Transversus Abdominis Plane Block for Inguinal Hernia Repair Under Spinal Anaesthesia: A Randomized Double Blind Study

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Abstract

Background: The transversus abdominis plane (TAP) block is an easy-to-perform and effective peripheral abdominal field block that has gained popularity as part of a multimodal analgesic regimen. The aim of this study was to determine the analgesic effects of morphine added to bupivacaine in a TAP block for inguinal hernia repair.

Methods: Forty adult patients with ASA PS I–II scheduled for elective inguinal hernia surgery under spinal anaesthesia were randomized to undergo ultrasound-guided (USG) TAP block with 20 ml of 0.25% bupivacaine (group B) versus 20 ml of 0.25% bupivacaine with 3 mg morphine (group BM). Patients were followed for 24 hours postoperatively for rescue analgesics consumed, duration of analgesia, NRS scores at rest and on cough, and adverse effects.

Results: The median (IQR) duration of analgesia in minutes of group B {385(248.75-825)} and group BM {761(248.75-1440)} were statistically non-significant ($p > 0.05$). The median (IQR) rescue analgesics tramadol consumed were 50 (50-50) mg in group B and 50 (0-50) mg in group BM ($p > 0.05$). There were no significant differences in NRS scores at rest and on cough at 0 and 4 hour, but were significantly less in group BM than group B at 8 and 24 hour ($p < 0.05$).

Conclusions: The addition of morphine to bupivacaine in USG TAP block failed to show significant analgesic effects than bupivacaine alone in terms of duration of analgesia and total analgesic consumed, but a significantly lower pain score was observed in group BM than group B at 8 and 24 hr.

Keywords: Inguinal hernia; Morphine; Pain; Rescue analgesic; TAP block.

Declarations

Ethics approval and consent to participate: This study was conducted with prior ethical approval from Institutional Review Committee of BPKIHS, Dharan (IRC No. 252/074/075-IRC) and trial registration done at Clinicaltrials.gov (NCT05379374). Informed consent has been obtained from participants prior to the enrolment.

Consent for publication: Informed consent was obtained from the patient for the publication of identifying features along with the manuscript.

Availability of data and materials: The full data set supporting this research is available upon request by the Journal.

Competing interest: The authors declare that they have no

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BACKGROUND

Inguinal hernia repair is a commonly performed surgical procedure worldwide, either by open technique or laparoscopically. Postoperative pain following the open technique may range from moderate to severe and to more intense on the day of surgery if not managed properly. The use of multimodal regimen for postoperative analgesia has gained popularity in recent years worldwide due to multiple benefits such as better patient satisfaction, early hospital discharge, early return of daily activities, and, most importantly, decreased morbidity and mortality [1]. In addition, an association between the intensity of acute postoperative pain and the subsequent development of chronic pain has been demonstrated after inguinal hernia repair, breast surgery, and thoracotomy [2]. Therefore, effective pain control during the postoperative period is essential and should not be ignored.

Transversus abdominis plane (TAP) block is an alternative, easy to perform and effective peripheral abdominal field block that blocks lower intercostal (T7-11), subcostal (T12), ilioinguinal (L1), and iliohypogastric (L1) nerves. The technique involves the injection of a local anaesthetic agent between the transversus abdominis (TA) and the internal oblique (IO) muscles [3] and has been used in various surgical procedures.

The discovery of peripheral opioid receptors has led to growing interest in the use of locally applied opioids (intra-articular, intrapleural, intraperitoneal, and perineural) for managing acute pain [4–6]. Morphine is a commonly used opioid as an adjunct to local anesthetics in neuraxial and peripheral nerve blocks. However, some studies have shown no benefits of perineural injection of opioids alone or with local anesthetics in providing analgesia [7–9].

To date, we could find only one study conducted on the analgesic effects of morphine added to bupivacaine in a TAP block for inguinal hernia surgery [10]. Hence, this study was carried out to identify the analgesic effects of morphine as an adjunct to bupivacaine in UG TAP block in patients undergoing open unilateral inguinal hernia repair.

METHODS

Ethical approval was obtained from the Institutional Review Committee of BPKIHS, Dharan, Nepal (252/074/075-IRC) and registered on Clinicaltrials.gov (NCT05379374). The study adheres to CONSORT guidelines for reporting clinical trials. The study was conducted from August 2018 to January 2020 at B.P. Koirala Institute of Health Sciences. The inclusion criteria

were either sex aged 18 to 65 years with American Society of Anesthesiologists physical status (ASA PS) I-II, planned for elective open unilateral inguinal hernia repair under spinal anesthesia. The exclusion criteria were: (1) patient's refusal (2) Body mass index (BMI) > 35 kg/m² or < 18 kg/m², (3) allergic or contraindication to drugs used in study (4) coagulopathy (5) local site infection (6) spine deformity (7) uncooperative or psychological illness inability to comprehend pain scale (8) drugs not injected in target area. Based on a computer-generated random number table, 40 patients were equally divided into two groups. A total of 40 envelopes with numbers indicating the sequence of the patient on the outside and the allocated group and study drug inside were prepared by an anesthesiologist. The participants and clinicians who were involved in patient assessment and data collection postoperatively were blinded to group assignment.

All the patients were instructed about the assessment of pain by a numeric rating scale preoperatively and were premedicated with oral diazepam 5 mg a night before surgery. Perioperatively, standard monitoring equipment was used. The patient was co-loaded with 10 ml/kg Ringer's Lactate (RL)/ Plasmalyte solutions and inj. Ondansetron 4 mg was administered just before spinal anesthesia. A standardized anesthetic regimen consisting of 2.4 ml of 0.5% hyperbaric bupivacaine with 10 micrograms of fentanyl was administered intrathecally. The patient was kept in the lateral decubitus position with the operative side in the dependent position for 5 minutes. The surgery started when the sensory block reached the level of T10, as detected by the loss of pain sensation from the pinprick. At the end of surgery, all the enrolled patients were given intravenous Paracetamol 1 gm, and then after every 6 hourly for 24 hours.

Once the surgery ended, a TAP block was performed by an experienced anaesthesiologist. The drug required for the TAP block was prepared according to the random number allocation by the anaesthesia assistant. The study groups were divided according to the medications received for the TAP block as follows-

Group B – 0.25% bupivacaine 20 ml

Group BM – 0.25% bupivacaine 20 ml with 3 mg morphine.

Under all aseptic precautions, an ipsilateral lateral approach was used for the TAP block with the patient in the supine position by using a high-frequency ultrasound probe (SonoSite). The probe was placed in the transverse plane to the lateral abdominal wall in the midaxillary line at the level of the umbilicus, between the lower costal margin and the iliac crest. After identification of the internal oblique (IO) and transversus abdominis (TA) muscles, local

infiltration with 1% (2 ml) lignocaine was performed at the site of needle placement. Block was performed with a 88 mm long 22-gauge spinal needle placed in the plane of the ultrasound probe, which was advanced until it reached the plane between the IO and TA muscles. After confirmation of the correct placement of the needle tip between the aponeurosis of the IO and TA muscles, 1 ml of normal saline (NS) was injected after negative aspiration. Once the spread of NS was observed as a dark shadow between the aponeurosis of the IO that moved anteriorly and the TA muscles that pushed the muscle deeper, the study drug was injected in incremental doses after negative aspiration.

Pain was evaluated using a standard numerical rating scale (NRS, 0 = no pain, 1-3 = mild, 4-6 = moderate, and 7-10 = severe pain). Pain at rest and on coughing was assessed using the NRS at 0, 4, 8, and 24 hrs after surgery. The duration of analgesia (time from TAP block to first request of analgesic) and total consumption of analgesics were recorded. During the postoperative period, patient side effects such as nausea, vomiting, and sedation were recorded at 0, 4, 8, and 24 hrs after the end of surgery. A rescue analgesic was given if the NRS score was ≥ 4 or on patient demand. Inj. Tramadol 50 mg was administered intravenously up to four times (200 mg) as a rescue analgesic and inj. Metoclopramide 10 mg up to three times as an antiemetic in 24 hrs.

The primary outcome measures in this study were duration of analgesia and the total rescue analgesics consumed in 24 hours. The secondary outcome measures were the NRS score at rest and on cough, and side effects associated with the TAP block.

The sample size was calculated on the basis of the 24 hour rescue analgesic (Tramadol) consumed in our pilot study. Using the mean dose of tramadol consumed by both groups (group B = 70 mg, group BM = 30 mg) and a combined standard deviation of 42, we calculated 17 patients in each group with consideration of a 95% confidence interval and 80% power of estimate. Further adding 15% for data loss, the sample size came out to be 20 in each group.

Statistical analyses were performed using SPSS software version 23. The data were tested for normality using the Shapiro-Wilk test. The data are presented as mean (standard deviation), median (range), number, and percentage as appropriate. Student's t-test was used for normally distributed continuous data, and the Mann-Whitney U test was used for non-normally distributed data. Categorical data were analyzed using the χ^2 test or Fisher's exact test. A p-value < 0.05 was considered statistically significant.

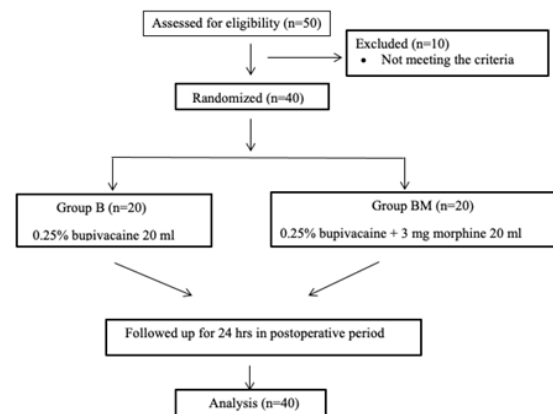


Figure 1: Consort Flow Diagram

RESULTS

Forty patients were enrolled in the study, with 20 in each group. The demographic variables of age, sex, BMI, and duration of surgery between the groups were similar and statistically non-significant (**Table 1**). The median (IQR) duration of analgesia of group B and group BM were 385(248.7-825) vs 761(248.7-1440) min, respectively, with $p > 0.05$ (**Table 2**). Similarly, median (IQR) rescue analgesic consumed by group B and group BM were 50 (50-50) vs 50 (0-50) mg, respectively, with $p > 0.05$ (**Table 2**). However, there were 9 in group BM and 3 in group B who did not receive rescue analgesics.

Table 1: Patient demographics and clinical data

| | Group B (n = 20) | Group BM (n = 20) | p value |
|---------------------------------|----------------------------------|---------------------------------|-----------|
| Age (year) | 53.5 (41.25 - 62.75) α | 46.5 (27.75 - 59.5) α | 0.253* |
| BMI | 23.6 (3.9)+ | 22.6 (3.1)+ | 0.408** |
| Gender (M/F) | 17/3 | 17/3 | 0.99*** |
| ASA (I/II) | 13/7 | 15/5 | 0.490**** |
| Duration of surgery (min) | 63 (51.25 - 84.75) α | 60 (51.25 - 78.75) α | 0.565* |

Data expressed as Mean (SD)+, Median (IQR) α and Number.

*Mann Whitney U test, **Student t test, ***Fisher's Exact test, ****Chi Square test

In group B, one patient received two doses of antiemetics, fifteen received one, and four patients didn't receive any antiemetic. Similarly, in the group BM, two patients received two doses of antiemetic, nine received one, and nine patients didn't receive antiemetic.

There was no significant difference in NRS scores at rest and on cough between the two groups at 0 and 4 hours. However, median (IQR) NRS scores at rest during 8 and 24 hr were 3.5 (3 - 4) and 3 (3 - 3.75), respectively, in group B compared with 2.5 (2 - 3.75) and 2 (2 - 3) in group BM, with statistically significant $p < 0.05$. Likewise, median (IQR) NRS scores on cough during 8 and 24 hr were 6 (6 - 7) and 7 (6 - 7), respectively, in group B compared with 5 (5 - 6) and 6 (5 - 6) in group BM with statistically significant p values of < 0.01 and 0.016 , respectively. (**Table 3**).

There was no significant difference in the incidence of adverse effects like nausea, vomiting, and sedation between the two groups.

Table 2: Postoperative analgesia and antiemetic consumption

| Parameters | Group B (n = 20) | Group BM (n = 20) | p value |
|--------------------------------|--------------------------------|---------------------------------|---------|
| Duration of analgesia (min) | 385 (248.75 - 825) α | 761 (248.75 - 1440) α | 0.188* |
| Total analgesic consumed (mg) | 50(50-50) α | 50(0-50) α | 0.192* |
| Antiemetic use frequency 0/1/2 | 4/15/1 | 9/9/2 | 0.107** |

Data expressed as median (IQR) α and Number.

*Mann-Whitney U, **Fisher's Exact Test

Table 3: Postoperative NRS score

| Time of assessment | Group B (n = 20) | Group BM (n = 20) | p value* |
|--------------------|---------------------|----------------------|----------|
| At rest | | | |
| 0 h | 0 (0 - 0) | 0 (0 - 0) | 0.97 |
| 4 h | 2 (2 - 3) | 2 (2 - 3) | 0.66 |
| 8 h | 3.5 (3 - 4) | 2.5 (2 - 3.75) | 0.02 |
| 24 h | 3 (3 - 3.75) | 2 (2 - 3) | 0.003 |
| On cough | | | |
| 0 h | 0 (0 - 0) | 0 (0 - 0) | 0.62 |
| 4 h | 5 (5 - 6) | 4.5 (3.25 - 5.75) | 0.14 |
| 8 h | 6 (6 - 7) | 5 (5 - 6) | < 0.01 |
| 24 h | 7 (6 - 7) | 6 (5 - 6) | 0.016 |

Data expressed as Median (IQR)

*Mann-Whitney U test for differences between the groups.

DISCUSSION

A multimodal analgesic regimen has been advocated due to its opioid sparing effects, better pain management, early recovery, and eventual minimization of morbidity and mortality. Further, due to the discovery of peripheral opioid receptors, the

use of opioids in peripheral nerve block for managing postoperative pain has gained popularity. However, there have been contradictory results regarding the peripheral use of morphine [9 - 14]. We could find only one study conducted on the analgesic effects of morphine added to bupivacaine in a TAP block for inguinal hernia surgery [10].

The factors that affect the spread of the injectate in TAP might include anatomical variation, choice of approach, injected drug, and the clinician's expertise. Studies have shown that a posterior TAP block provides more effective and prolonged analgesia than the lateral approach for infraumbilical abdominal surgery [15, 16]. However, the lateral approach TAP block has been used for inguinal hernia surgery for postoperative pain, and the results are conflicting.

In our study, we compared the analgesic effects of 20 ml of 0.25% bupivacaine with 3 mg morphine added to 20 ml of 0.25% bupivacaine in a lateral approach TAP block for inguinal hernia surgery. There was no significant difference in postoperative analgesic consumption and duration of analgesia. However, NRS scores at rest and on cough in group BM were significantly lower than group B at 8 and 24 hour. These differences in NRS scores at 8 and 24 hr probably could be due to the delayed effect of morphine in the TAP block. Our results contradict the study done by Atif HM et al [10] in view of the total consumption of analgesics in 24 hr and the first request of analgesia. However, in terms of pain score, similar to our study, their study also found a significantly lower pain score at 24 hr in the morphine group. The difference could have been due to the greater strength of the local anesthetic and the use of the double pop landmark technique TAP block, as opposed to our lesser strength and lateral approach technique. It has been reported that the use of the blind technique TAP block near the Triangle of Petit might lead to the paravertebral spread of local anesthetics from T4 at the highest level to L2 at the lowest level [17], leading to effective analgesia and the possibility of a better effect of low-dose morphine in the vicinity of nerves at this site. However, due to the safety concern, expertise unavailability, and lack of real time needle tip visualization in the target area, the landmark technique has been discouraged [18].

Abdel-Ghaffar et al. [13] compared the analgesic and respiratory effects of bupivacaine alone and two different doses of morphine added to bupivacaine in a UG subcostal TAP block for upper abdominal surgery. They concluded that the addition of morphine (10 mg and 15 mg) to bupivacaine in subcostal TAP block controlled pain and reduced opioid requirements in a dose-dependent manner. Likewise, a study done by R. Likar et al. [19] to identify

whether the analgesic effects of different doses of intra-articular morphine are dose dependent, concluded that increasing doses increases the analgesic effects.

M. Onay et al. [20] investigated the comparison of analgesic effects of TAP block with bupivacaine and morphine vs bupivacaine and intramuscular morphine (IM) in lower abdominal surgery. They found significantly lower morphine consumption at 6, 12, and 24 hr in the TAP group than in the IM group, with no significant difference in VAS score at rest and on movement at different time points.

El Sherif FA et al [21] conducted a study with and without 10 mg morphine added to bupivacaine in the serratus anterior plane block. Duration of analgesia and total consumption of analgesics were significantly lower in the morphine group, which contradicts our study. However, pain scores were significantly lower in the morphine group, similar to our study at 8 and 24 hr. Similarly, Sabana AM et al. [22] also compared with and without 2 mg morphine in bupivacaine for bilateral rectus sheath blocks. The mean total morphine consumption in 24 hr for the morphine group was significantly lower, which was not comparable to our study. The mean VAS on mobilization and at rest in the morphine group during 6, 12, and 18 hr were statistically lower than control group. Our study also showed a lower NRS score at the later time, 8 and 24 hr in the morphine group.

Regarding the rescue antiemetic, four patients in group B and nine patients in group BM didn't receive an

antiemetic. This difference in the antiemetic requirements of group B might be due to the use of more tramadol. We did not encounter any major complications related to the procedure in our study. However, one patient developed slight swelling at the needle insertion site due to multiple attempts.

Overall, in comparison with other studies conducted regarding the peripheral morphine analgesic effects, we were able to detect similar findings of lower pain score in the morphine group in the later period of observation, i.e., after 4 hr of surgery.

There were certain limitations of the study. The sample size was small and may not have been adequate for all of the outcome measures. The lateral approach of the TAP block was used. The effectiveness of the TAP block was not assessed after each block.

CONCLUSION

The addition of morphine to bupivacaine in USG TAP block failed to show significant analgesic effects than bupivacaine alone in terms of duration of analgesia and total rescue analgesics consumed. However, NRS scores at 8 and 24 hour were significantly lower in group BM than group B, which shouldn't be ignored and suggesting analgesic effects of peripheral morphine in reducing pain intensity.

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