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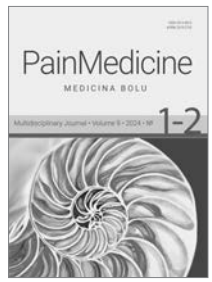

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Comparative Analysis of Ultrasound Guided Transversus Abdominis Plane Block with or without Buprenorphine Following Inguinal Hernia Repair

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Abstract

Background and Aims. *Inguinal hernia is a commonly performed surgical procedure globally, which is often accompanied by significant post-operative pain that peaks on the day of the surgery. The transversus abdominis plane block (TAP) offers better postoperative pain relief for lower abdominal procedures. However, the duration of TAP block is restricted by the effects of given local anaesthetic drugs, necessitating the use of an adjuvant, such as buprenorphine, to improve the quality and duration of analgesia. Hence, we designed the present study to analyse the effect of a TAP block with buprenorphine on the relief of pain after inguinal hernia repair surgery.*

Methods: *A prospective, randomized, double-blinded study was conducted on fifty American Society of Anaesthesiologists Physical Status I and II patients posted for elective unilateral inguinal hernia repair under spinal anaesthesia. At the end of the surgery, group B patients received 20 ml of 0.25 % bupivacaine and group BB patients received 20 ml of 0.25 % bupivacaine along with 300 µg of buprenorphine for ultrasound-guided transversus abdominis plane block. The duration of analgesia, postoperative analgesic consumption and pain scores at rest and during sitting up to 24 h were recorded.*

Results: *Patients who received perineural buprenorphine experienced prolonged duration of analgesia (870.32 ± 27.86 vs. 385.64 ± 27.86 minutes), lower tramadol consumption (135.08 ± 23.05 vs. 246.72 ± 38.8 mg), and decreased pain scores both at rest and during sitting for up to 24 hours post-surgery.*

Conclusion: *The present study shows that the addition of buprenorphine to bupivacaine in TAP block after inguinal hernia repair produces superior postoperative analgesia compared with the control group without any significant side effects.*

Keywords: *Transversus abdominis plane block, ultrasound guided, buprenorphine, inguinal hernia repair, acute postoperative pain*

Introduction

The prevalence of inguinal hernias among abdominal wall hernias is 75 %. Globally, we conduct approximately 20 million inguinal hernia repairs annually, making it one of the most frequently performed surgical procedures [1]. After a hernia surgery, about 60 % of patients have moderate to severe acute postoperative pain (APOP) [2]. Given the large number of patients receiving IHR, the gap in postoperative pain management greatly raises morbidity, affects quality of life, raises the incidence of chronic pain, and burdens society financially.

In order to mitigate pain at its source prior to centrally mediated changes taking place, peripheral regional anesthetic techniques may be a more rational and straightforward approach. And the new guidelines published by Committee on Regional anaesthesia in 2016 also recommend the use of peripheral regional anaesthetic techniques as a component of multimodal analgesia for pain management of inguinal hernia repair (IHR) [3]. To block neural afferents from the anterolateral abdominal wall, particularly the ilioinguinal and iliohypogastric nerves and the lower intercostal nerves T7-T11, which pass between the internal oblique and transversus abdominis muscles, a local anaesthetic (LA) drug is injected in the neurofascial plane between the fascia of the internal oblique and transversus abdominis muscles in the transversus abdominis plane (TAP) block [4]. The duration of analgesia is restricted to the amount of the given local anesthetic, even though ultrasound-guided (USG) transversus abdominis plane (TAP) block provides excellent analgesia with a notable decrease in neuroendocrine stress response.

To extend the efficacy and duration of single-shot peripheral nerve blocks, the addition of perineural adjuvants is an attractive and straightforward alternative; among all the adjuvants used, buprenorphine appears to be the most effective due to its distinctive pharmacological profile. Unlike other adjuvants like dexamethasone, dexmedetomidine, and clonidine, buprenorphine is not widely used for fascial plane blocks, despite its ability to generate a longer duration of analgesia in peripheral nerve blocks [5,6]. The purpose of this study was to assess the effect of buprenorphine added to bupivacaine for ultrasound-guided transversus abdominis plane block in terms ofduration and quality of analgesia, analgesic consumption for a period of 24 hours, and its side effects after inguinal hernia repair.

Materials and Methods

After receiving approval from the Institutional Human Ethics Committee, fifty patients with physical status I and II as defined by the American Society of Anaesthesiologists were chosen to participate in this prospective, randomized, double-blind, controlled study. Males between the ages of 18 and 60 with a body mass index (BMI) of less than 30 kg/m^2 who were scheduled to undergo elective unilateral open inguinal hernia repair at a tertiary care hospital under spinal anesthesia were enrolled.

Patients with complicated hernia, bilateral hernia, and coagulopathy were excluded. Ninety patients who were scheduled to undergo elective unilateral open inguinal hernias were enrolled in this study. Participants were randomized and divided into two groups, in accordance with the flowchart of the Consolidated Standards of Reporting Trials (CONSORT) (Figure 1), subsequent to a thorough evaluation of the inclusion and exclusion criteria and gathering written informed consent. Just prior to the administration of the TAP block, sealed envelopes bearing sequential numbers were unsealed within the operating room to reveal the group allocation. For the TAP block, patients in Group B were administered 20 ml of 0.25 % bupivacaine, while those in Group BB were given the same volume of 0.25 % bupivacaine mixed with 300 μg of buprenorphine.

An anesthesiologist who was not a participant in the study was responsible for the preparation and coding of the study drug. Aside from the patient, the anesthesiologist conducting the TAP block, and the anesthesiologist who contributed to the data collection process were all blinded. Following conclusion of the research, the code was breached. During the preoperative visit conducted on the day before surgery, patient history was recorded and a physical examination and routine laboratory investigations were conducted. The procedure was thoroughly described. Patients were provided with comprehensive information regarding the NRS (0 = no pain, 10 = intolerable pain). Prior to surgery, patients were premedicated orally with 0.25 mg of T. Alprazolam the night before and the morning of the procedure.

Upon arrival in the operating theater, intravenous access was established. Standard monitoring, including pulse oximetry (SPO_2), electrocardiogram (ECG), and non-invasive blood pressure (NIBP), was initiated and continuously monitored throughout the procedure. All patients received hydration with a crystalloid solution at a

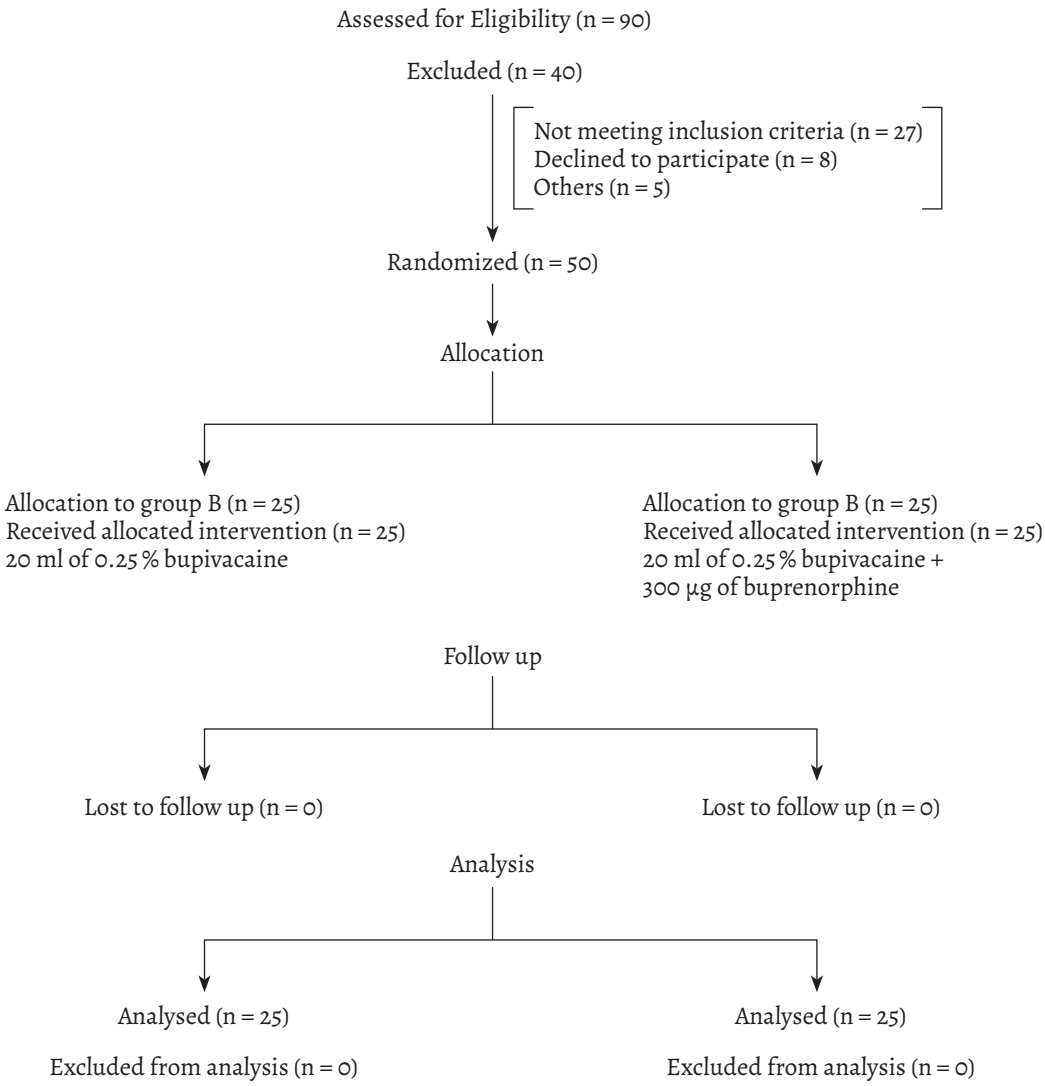

Figure 1. Consolidated Standards of reporting trials (CONSORT) Diagram

rate of 2 ml/kg/h. Following strict aseptic measures, spinal anesthesia was performed using 3 ml of 0.5 % bupivacaine heavy at the L3–4 interspace, employing a 25 Quincke spinal needle while the patient was positioned laterally.

The level of block was assessed after 5 minutes, and surgery commenced with all patients undergoing the Lichtenstein procedure. Upon completion of the surgery, the block level was noted, and an ultrasound-guided TAP block was performed on the corresponding side following a standard sterile protocol. To perform the TAP block, the lower costal margin and iliac crest were identified. A sheathed high-frequency linear ultrasound probe (6–14 MHz) of Sonosite II was positioned in the mid-axillary line to obtain a transverse view of the abdominal layers. Once the abdominal layers were visualized, a 22G 50 mm blunt insulated nerve block needle was inserted 1 cm medial to the probe, utilizing an in-plane technique between the muscle layers of the internal oblique and transversus abdominis. Upon confirming the needle tip placement, 1 ml of normal saline was injected to hydro dissect the tissue. Subsequently, the prepared drug was injected in 5 ml aliquots after confirming negative aspiration.

Following surgery, pain scores were assessed both at rest and in a sitting position using the numeric rating scale (NRS) at intervals of 0, 2, 4, 8, 12, and 24 hours. Heart rate, non-invasive blood pressure (NIBP), and oxygen saturation (SPO_2) were monitored regularly. The primary outcome measure of the study was the duration of analgesia, defined as the time from block administration to the first request for additional analgesia. Additionally, the quality of analgesia and total rescue analge-

sic doses required within 24 hours were recorded. Intravenous tramadol at a dose of 1 mg/kg was administered as rescue analgesia if the NRS at rest exceeded 4 or upon patient request. This was not repeated within a 6-hour interval. If the NRS remained above 4, an additional intravenous injection of diclofenac 50 mg was administered. Patients were monitored for potential adverse effects such as nausea, vomiting, dry mouth, pruritus, sedation, and respiratory depression. Sedation levels were assessed using the Ramsay sedation scale.

A power analysis, relying on a previous study [7] was performed to identify a clinically meaningful difference in the duration of analgesia between the groups. It determined that a sample size of 25 in each group would provide a power of 90 % and a confidence interval of 95%. The alpha error was established at 0.05.

Statistical analyses were conducted utilizing the IBM Statistical Package for the Social Sciences (SPSS 20.0). The mean, median, and standard deviation were computed for all quantitative variables. For normally distributed data, independent samples t-tests were utilized to compare means, while for non-normally distributed data, the Mann –.Whitney U test was applied, with interquartile ranges calculated. Qualitative and categorical variables were presented as frequencies and proportions, and the chi-squared test was employed to compare proportions. A significance level of $P < 0.05$ was considered statistically significant.

Results

This study was conducted on 50 male patients age 18–60 years. There was no exclusion or drop-out and all patients were included in analysis. Both the groups were comparable in terms of demographic characteristics such as age, weight, height, BMI and ASA category and mean duration of surgery (Table 1). All patients were comfortable while performing USG TAP blocks at the end of surgery.

The present study showed that addition of buprenorphine to bupivacaine in TAP block produced longer duration of analgesia compared to control group (870.32 ± 27.86*vs* 385.64 ± 24.20 min) (Figure 1). The buprenorphine group had significantly reduced tramadol consumption compared to control group over 24 h (136.1 ± 21.9 *vs* 247.27 ± 44.27 mg) (Figure 2). There was a significant reduction in pain scores both at rest and sitting for up to 24 h in the buprenorphine group compared to the control group (Figure 3–4). Hemodynamic and respiratory parameters were comparable between the groups for up to 24 h.

The incidence of side effects was comparable between the groups. Five (20 %) patients in group B and 3 (12 %) in group BB experienced nausea. Three (12 %) patients in group B and 2 (8 %) patients in group BB had vomiting (Table 2). One (4 %) patient in group B and 3

Table 1. Demographic and clinical parameters

Parameter	Group B	Group BB	P value
Age (year)	39.56 (12.087)	38.4 (12.74)	0.743[1]
Weight (kg)	72.28 (6.34)	70.24 (7.09)	0. 289[1]
BMI (kg/m^2)	27.36 (1.95)	27.48 (2.41)	0.848[1]
ASA (I/II)	17/8	14/11	0.340[2]
Duration of surgery (min)	79.13 (10.80)	78.83 (10.02)	0.912[3]

Data are presented as mean (SD), absolute number.
BMI — Body Mass Index, ASA — American Society of Anaesthesiologists.
1 — Mann – Whitney U test, 2 — Chi-Squared Test, 3-t Test.

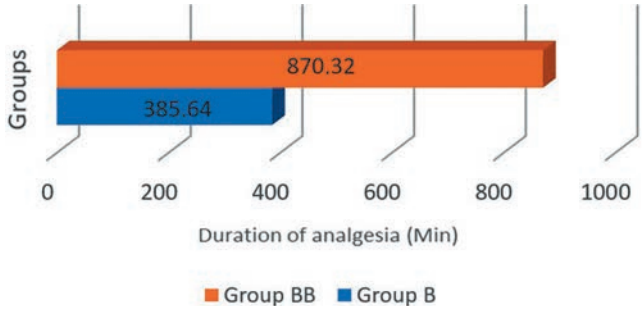

Figure 1. Duration of analgesia

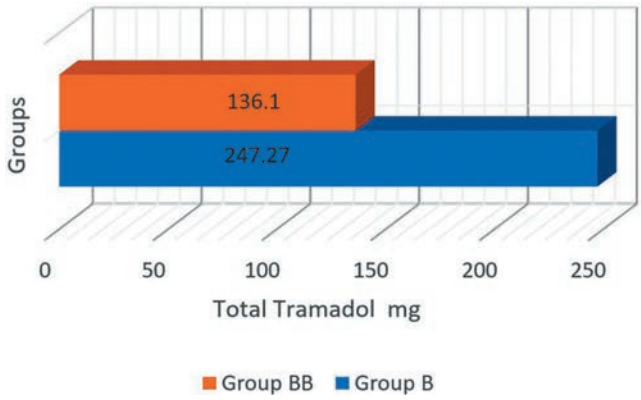

Figure 2. Tramadol consumption

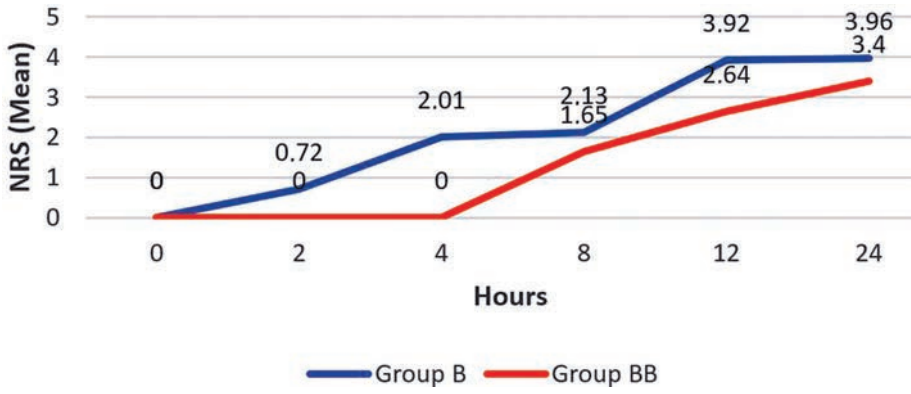

Figure 3. Pain score at rest

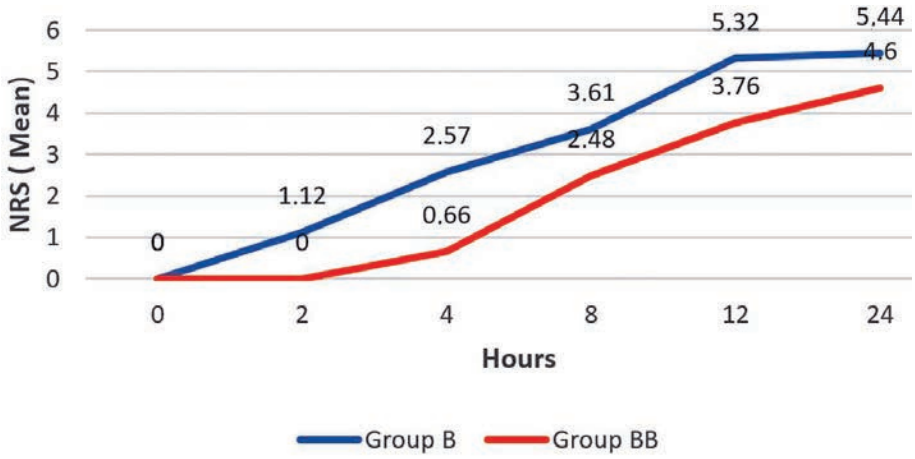

Figure 4. Pain score at sitting

(12 %) patients in group BB had sedation. The Ramsay sedation score was 2 for all patients. Only one patient (4 %) in group BB had dry mouth. All side effects occurred during the first 8 hours postoperatively. No respiratory depression was noted in any groups. No TAP block related complications were noted in any patient.

Discussion

The current study highlights that adding 300 μg of buprenorphine to bupivacaine in the TAP block prolongs the duration of analgesia, decreases tramadol consumption, and lowers pain scores up to 24 hours, both at rest and during sitting, in comparison to the control group. Similar findings of extended analgesia duration were observed in brachial plexus blocks with the adjunct of buprenorphine[5,8]. Patients in both studies did not receive any co-analgesics until reporting their first instance of pain. Moreover, this study demonstrated a 45 % reduction in tramadol consumption in the buprenorphine group compared to the control group, a slightly higher reduction than the 30 % reduction seen in adductor canal block with buprenorphine after total knee arthroplasty [9]. Other studies have also shown extended analgesia duration and reduced pain scores with the addition of buprenorphine in various regional anesthesia tech-

Table 2. Incidence of side effects

Side effects	Group B		Group BB	
	No	%	No	%
Nausea	5	20 %	3	12 %
Vomiting	3	12 %	2	8 %
Sedation	1	4 %	3	12 %
Dry mouth	0	0	1	4 %

Values are expressed as Number and percentage

niques, including perineural infiltration for percutaneous nephrolithotomy, lumbar plexus blocks, and femoral nerve blocks [10–12]. Mechanism of peripheral action.

The prolonged analgesic effect observed may be attributed to buprenorphine's high binding capacity and affinity for μ receptors [13]. Upon receptor binding, it stimulates the inhibitory G protein, leading to the closure of voltage-sensitive calcium channels and activation of potassium channels, consequently reducing cyclic adenosine monophosphate (cAMP) production. This cascade ultimately reduces the transmission of nociceptive impulses [14]. Additionally, peripheral administration of opioids can exert central effects through the centripetal movement of opioids from the periphery to the dorsal horn via binding to opioid-binding proteins [15].

It was also proposed that opioids could diffuse from the brachial plexus sheath to the extradural and subarachnoid spaces, subsequently binding with opioid receptors in the dorsal horn following brachial plexus block with buprenorphine [16]. Nevertheless, studies estimating the concentration of morphine in the spinal fluid after perineural morphine administration around the femoral nerve indicated insufficient levels to directly induce analgesia by acting on the spinal cord. This finding suggests a peripheral rather than central mechanism of action for morphine [17].

Moreover, buprenorphine exerts its analgesic effects by inhibiting the release of the excitatory neuro transmitters substance P and calcitonin gene-related peptide, as well as by diminishing the excitability of primary afferent neurons [18]. Additionally, it has been suggested that opioid receptors in primary afferent neurons undergo axonal transport with exogenous opioids, leading to prolonged analgesia through peripheral action [19]. Inflammatory conditions may enhance axonal transport and the proliferation or activation of opioid receptors [18]. The heightened peripheral opioid actions in inflamed tissue could be clinically advantageous, particularly given that many painful conditions, whether subacute or chronic, are associated with inflammation (e.g., postoperative pain, cancer-related pain, and arthritis) [20].

The most plausible explanation for the peripheral action of buprenorphine is its potent inhibition of the α-subunits of voltage-gated sodium channels. By binding to the intramembranous part of the receptor, buprenorphine triggers a tonic and concentration-dependent blockade of sodium channels, leading to the blockade of electrically induced action potentials at the terminal end of C fibers. Notably, the potency of buprenorphine in blocking sodium channels surpasses that of lidocaine and even exceeds that of the most potent local anesthetic, bupivacaine. Furthermore, research indicates that buprenorphine's potency in inhibiting sodium channels surpasses that of any other opioid [21]. This observation aligns well with buprenorphine's high lipophilicity, with an octanol-water partition ratio ranging from approximately 2000 to 10,000, which serves as the major determinant of the blocking potency of local anesthetics on sodium channels [22].

The extended duration of analgesia achieved with perineural buprenorphine, as compared to intramuscular buprenorphine and the placebo group, has been demonstrated in axillary and interscalene blocks [23, 8]. Furthermore, the peripheral action of perineural opioids is supported by Obara *et al.*, who showed selective blockade of peripheral opioid receptors using the peripheral-selective opioid antagonist naloxone-methiodide in an animal model [24].

The prolonged duration of analgesia achieved with perineural buprenorphine holds significance, as patients often report experiencing intense burning rebound pain once the effects of a single-shot nerve block wear off [25]. This rebound pain is an undesirable clinical outcome of peripheral nerve blocks. By extending the duration of the nerve block beyond the effects of local anesthetics through the addition of adjuvants such as buprenorphine, the incidence of rebound pain can be reduced. This improvement in pain control can increase patient satisfaction and lower the risk of persistent pain by ensuring adequate pain management during the transition from peripheral nerve blocks to oral analgesia.

A prospective study comparing the addition of buprenorphine to 0.25% levobupivacaine with perineural dexamethasone and control groups in TAP block demonstrated reduced analgesic consumption and postoperative pain scores up to 24 hours, with a prolongation of duration of analgesia (DOA) by 1 hour and 5 hours, respectively, after inguinal hernia repair (IHR) [26]. However, in the present study, perineural buprenorphine extended DOA by 8 hours compared to the control group. This prolongation of analgesia duration is particularly beneficial, as the duration of severe pain within the initial 24-hour period, rather than just the intensity of pain, is indicative of the likelihood of developing persistent postoperative pain (PPOP) [27]. Prolonged periods of severe postoperative pain may also contribute to central sensitization, which is a factor in the development of chronic postoper-

ative pain. Notably, each 10 % increase in the percentage of time spent in severe pain after surgery was associated with a 30 % increase in the incidence of chronic postoperative pain, underscoring the significance of postoperative pain duration and the critical role of effective pain control in the postoperative period [27].

The significant reduction in pain scores observed in the buprenorphine group holds importance, as poorly managed postoperative pain stands as one of the leading causes of readmission following day-care surgery [28]. Lower pain scores enable earlier ambulation post-surgery, thereby facilitating enhanced recovery and hastening discharge from the hospital. Additionally, effective postoperative pain management plays a crucial role in decreasing the incidence of chronic pain.

Buprenorphine functions as a μ receptor agonist, eliciting various opioid effects including analgesia, sedation, euphoria, and respiratory depression, albeit to a lesser extent compared to morphine and other opioids. This characteristic enhances its safety profile, augmenting the safety margin in comparison to traditional opioids [16,29]. While some studies have reported a high incidence of vomiting associated with 300 μg perineural buprenorphine, our study did not demonstrate such an occurrence [30].

The current study has several limitations. Firstly, the extent of the block under spinal anesthesia could not be measured, which may be crucial in assessing the block's success. However, the success of the block was confirmed through direct visualization of drug deposition and postoperative evaluation of analgesic effect. Secondly, the study did not measure the plasma concentration of buprenorphine to rule out systemic effects. Nonetheless, previous studies have established the perineural effect of buprenorphine as an adjuvant in regional anesthesia. Future studies are recommended to evaluate the beneficial antihyperalgesic effect of buprenorphine in TAP blocks.

Conclusion

The present study demonstrates that adding buprenorphine to bupivacaine in TAP block following inguinal hernia repair results in superior postoperative analgesia compared to the control group, with no significant side effects observed.

Acknowledgement

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Порівняльний аналіз площинної блокади поперечного м'яза живота під УЗ контролем з використанням бупренорфіну та без нього після операції з приводу пахової грижі

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Анотація

Передумови та мета. *Операція з приводу пахової грижі є однією з найбільш поширених хірургічних процедур у світі, яка часто супроводжується значним післяопераційним болем, що досягає піку в день операції. Площинна блокада поперечного м'яза живота (TAP-block) забезпечує краще післяопераційне знеболення для процедур на нижній частині живота. Однак тривалість TAP-блокади обмежена дією місцевих анестетиків, що вимагає використання ад'ювантів, таких як бупренорфін, для покращення якості та тривалості знеболення. Тому ми провели дослідження, щоб проаналізувати вплив TAP-блокади з бупренорфіном на полегшення болю після операції приводу пахової грижі.*

Методи. *Було проведено проспективне, рандомізоване, подвійне сліпе дослідження за участю п'ятдесяти пацієнтів із фізичним статусом I та II відповідно до Американського товариства анестезіологів, яким була запланована одностороння операція з приводу пахової гриж під спінальною анестезією. Наприкінці операції пацієнти групи B отримували 20 мл 0,25 % бупівакаїну, а пацієнти групи BB отримували 20 мл 0,25 % бупівакаїну разом із 300 мкг бупренорфіну для TAP-блокади під УЗ контролем. Було зафіксовано тривалість знеболення, післяопераційне споживання анальгетиків та оцінку болю в стані спокою і під час сидіння протягом 24 годин.*

Результати. *У пацієнтів, які отримували периневрально бупренорфін, спостерігалась більша тривалість знеболення (870,32 ± 27,86 проти 385,64 ± 27,86 хвилин), зменшення споживання трамадолу (135,08 ± 23,05 проти 246,72 ± 38,8 мг), а також зниження рівня болю як у стані спокою, так і під час сидіння протягом 24 години після операції.*

Висновок. *Це дослідження показує, що додавання бупренорфіну до бупівакаїну в TAP-блокаді після операції з приводу пахової грижі забезпечує краще післяопераційне знеболення порівняно з контрольною групою без суттєвих побічних ефектів.*

Ключові слова: *площинна блокада поперечного м'яза живота, УЗ контроль, бупренорфін, операція з приводу пахової грижі, гострий післяопераційний біль*