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Original contribution

The effect of morphine added to bupivacaine in ultrasound guided transversus abdominis plane (TAP) block for postoperative analgesia following lower abdominal cancer surgery, a randomized controlled study☆,☆☆,☆☆☆,★

Fatma Adel El Sherif *, Sahar Abdel-Baky Mohamed, Shereen Mamdouh Kamal

South Egypt Cancer Institute, Assiut University, Assiut, Egypt

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ABSTRACT

Objectives: Transversus abdominis plane (TAP) block used for management of surgical abdominal pain by injecting local anesthetics into the plane between the internal oblique and transversus abdominis muscles. We aimed to explore the effect of adding morphine to bupivacaine in ultrasound guided TAP-block in patients undergoing lower abdominal cancer surgery.
Study design: Randomized, double-blind, prospective study. Clinical trial identifier: NCT02566096.
Setting: Academic medical center.
Patients: Sixty patients were enrolled in this study after ethical committee approval.
Interventions: Patients divided into 2 groups (30 each): Bupivacaine group (GB): given ultrasound guided TAP-block 20 ml 0.5% bupivacaine diluted in 20 ml saline; Morphine group (GM): given ultrasound guided TAP-block with 20 ml 0.5% bupivacaine + 10 mg morphine sulphate diluted in 20 ml saline.
Measurements: Patients were observed for total morphine consumption, time for first request of rescue analgesia, sedation scores, hemodynamics and side effects for 24 h postoperatively.
Results: Morphine added to bupivacaine in TAP block compared to bupivacaine alone reduced total morphine consumption (5.33 ± 1.28 mg) (10.70 ± 3.09 mg) respectively ($p < 0.001$), prolonged the time to first request of analgesia (10.40 ± 4.96 h) (6.97 ± 3.26 h) respectively ($p < 0.008$), with a statistically significant decrease in (VAS-M) in GM compared with GB at 12 h postoperatively ($p < 0.002$). No significant differences in hemodynamics, respiratory rate, oxygen saturation, sedation score, and side effects except for nausea were observed ($p > 0.05$).
Conclusion: Addition of morphine to bupivacaine in TAP block is effective method for pain management in patients undergoing major abdominal cancer surgery without serious side effects.

1. Introduction

A substantial component of the pain experienced by patients after major abdominal surgery is derived from the abdominal wall incision. The abdominal wall consists of three muscle layers, the external oblique, the internal oblique and the transversus abdominis, and their associated fascial sheaths. This muscular wall is innervated by nerve afferents that course through the transversus abdominis neuro-fascial plane [1].

Transversus abdominis plane (TAP) block, first described by Kuppuvelumani et al. [2], and formally documented by Rafi [3] it is used for the management of surgical abdominal pain by injecting local anesthesia into the plane between the internal oblique and transversus abdominis muscles [3,4].

TAP-block has been shown to be a safe and effective postoperative analgesia method in a variety of general [5], gynecological, urological, plastic and pediatric surgeries, and it is suggested as part of the multimodal anesthetic approach to enhance recovery after lower abdominal surgeries [6].

Opioids exert a local analgesic effect as based on several observations. Nociceptive afferent nerve fibers contain peripheral opioid

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* Corresponding author.
E-mail address: fatma_anesthesia@aun.edu.eg (F.A. El Sherif).

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receptors which are silent except in the presence of local inflammation. An effective topical opioid analgesic that could be applied to inflamed or open skin lesions would be a useful option for some patients where other options for pain relief have been exhausted [7].

Morphine and its metabolites are largely undetected systemically when applied topically to skin ulcers, suggesting the analgesic effect is local. Intra-articular morphine injections for local analgesia after knee surgery have been found to be effective in several trials [7].

Brachial plexus studies mostly fail to demonstrate compelling reasons to add opioids to anesthetizing solutions, most often finding was no significant differences in the onset, duration, block quality, or pain scores [8–10]. A systematic review which studied the role of opioids in peripheral nerve block concluded that their anesthetic and analgesic effects are not clinically relevant [11].

Our aim was to explore efficacy and safety of morphine added to bupivacaine in ultrasound guided TAP-block in patients undergoing lower abdominal cancer surgery.

2. Patients and methods

2.1. Study design

This randomized, double-blind, controlled study was approved by the local ethics committee of South Egypt Cancer Institute, Assuit University, Egypt. After written informed consent 60 ASA I–II patients (age 18–60 years, weight 50–89 kg), were scheduled for lower abdominal cancer surgery (abdominal hysterectomy and radical cystectomy) were enrolled in the study. Patients with a known allergy to the study drugs, significant cardiac, respiratory, renal or hepatic diseases, bleeding diathesis and those with psychiatric illnesses that would interfere with perception and assessment of pain were excluded from this study. Preoperatively, patients were taught how to evaluate their own pain intensity using the visual analog scale (VAS), scored from 0 to10 (where 0 = no pain and 10 = worst pain imaginable) and how to use PCA machine.

2.2. Randomization and blinding

Patients were randomly divided using an online research randomizer (www.randomized.org) into two groups (30 patients each):

Bupivacaine group (GB): patients were given ultrasound guided TAP-block with 20 ml of 0.5% bupivacaine hydrochloride (Markyrene® Sigma-Tec, Egypt) diluted in 20 ml saline (total volume 40 ml); 20 ml on each side of the abdominal wall.

Morphine group (GM): patients were given ultrasound guided TAP-block with 20 ml of 0.5% bupivacaine + 10 mg morphine sulphate (morphine SO_4® Misr CO, Egypt) diluted in 20 ml saline (total volume 40 ml); 20 ml on each side of the abdominal wall. Investigated drugs were prepared in a sterile syringe by hospital pharmacy and given to the investigator who was blinded to the identity of drugs. Also the observer was masked to treatment-group assignment.

2.3. Anesthesia regimen

Oral diazepam (5 mg) was given the night before surgery. On arrival to the operating room, an intravenous line was inserted. Monitoring included electrocardiography (ECG), non-invasive blood pressure (NIBP), arterial oxygen saturation (SAO_2) and end-tidal carbon- dioxide ($ETCO_2$) were applied.

Anesthesia was induced for all participating patients with 2 μg/kg fentanyl, 2–3 mg/kg propofol and 1.5 mg/kg lidocaine. Endotracheal intubation was facilitated by 0.15 mg/kg cisatracurium. Anesthesia was maintained by 1–1.5 MAC isoflurane in 50% oxygen/air mixture and 0.03 mg/kg cisatracurium respectively in ventilation parameters to maintain $ETCO_2$ of approximately 35–40 mm Hg. Two anesthetists experienced in the technique, under ultrasound guidance had performed the blockade under the direct supervision of the study investigator. Ultrasound guided TAP block performed immediately after induction of anesthesia and about 15 min before skin incision.

The ultrasound-guided (US) bilateral TAP block was performed with a high frequency linear ultrasound probe (Sonosite®, Inc. U.S.A.) and an in-plane 100 mm 20 G needle (Pajunk® SonoPlex Stim cannula U.S.A.) guidance techniques. The ultrasound probe was placed transverse to the abdomen (horizontal plane) in the mid-axillary line between the costal margin and the iliac crest, piercing the 2 in. cephalad to the iliac crest. Three muscle layers are clearly seen in the image. The needle is inserted in a sagittal plane approximately 3–4 cm medial to the ultrasound probe, the needle tip was directed into the plane below the internal oblique and above the transversus abdominis muscle. After negative aspiration to exclude vascular puncture, a test dose of (1 ml of saline) was seen to open the plane between the two muscles and followed by insertion of the full dose of local anesthetic. If the 1 ml dose appears to be within muscle rather than between them, needle reposition was required and test repeated.

Intra-operative systolic and diastolic blood pressure, heart rate, oxygen saturation were monitored before the block (baseline), 10, 20, 30, 60, 90 and 120 min after the block. At the end of the operation, intravenous neostigmine 50 μg/kg and atropine 20 μg/kg were administered to reverse muscle paralysis. After extubation; successful block was confirmed in the recovery room as loss of cold sensation over all the skin incisions for the ports. Patients transferred to surgical intensive care unit (SICU) where they were followed for 24 h. All patients connected to intravenous patient-controlled analgesia (IV-PCA) for postoperative pain management. The IV-PCA solution contained 100 mg morphine in 100 ml 0.9% normal saline (1 mg/ml). The IV-PCA program consisted of an initial morphine bolus of 0.1 mg/kg once pain expressed by the patient or if VAS ≥ 3 followed by 1 mg boluses with a lockout period of 5 min with no background infusion was allowed.

2.4. Postoperative follow up

Postoperative hemodynamic assessments included: heart rate, non-invasive systolic and diastolic blood pressure, respiratory rate and oxygen saturation recorded immediately postoperative, 2 h, 4 h, 6 h, 8 h, 12 h, 18 h and 24 h postoperatively. Pain intensity was evaluated by the visual analog pain scale at rest (VAS-R) and during movement (on coughing) (VAS-M) were assessed at the same time points. The time to first request for analgesia and the total analgesic consumption in the first 24 h were recorded. Postoperative sedation was assessed at the same time points using sedation score (awake and alert = 0, quietly awake = 1, asleep but easily roused = 2, deep sleep = 3). Postoperative side effects such as (nausea, vomiting, itching, hypotension, bradycardia and respiratory depression) were recorded and treated.

3. Statistical analysis

The primary endpoint was the total dose of IV PCA morphine consumption in the first 24 h postoperative. The secondary end-points were the postoperative VAS score, first request of analgesia, safety profile of the study drugs in terms of predefined adverse cardiovascular events, respiratory depression, nausea, vomiting, and level of sedation during the study period. Our aim was to obtain a 20% decrease in IV PCA morphine consumption after TAP with bupivacaine plus morphine in comparison to the other group. A calculated sample size of 28 would have an 80% power of detecting a difference at a 0.05 level of significance using a confidence interval of 95%. Qualitative data was described by numbers and percentages, where quantitative data were described using mean and standard deviation. Chi-square test was used to test the relationship between qualitative variables and independent samples *t*-test was used to compare between 2 groups of quantitative data. $p < 0.05$ was considered significant.