

Adding Sufentanil to TAP Block Hyperbaric Bupivacaine Decreases Post-Cesarean Delivery Morphine Consumption

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Abstract- Pain management is crucially important in the postoperative period as it increases patient comfort and satisfaction. The primary outcome of present study was to evaluate the effect of sufentanil added to hyperbaric bupivacaine solution 0.25% in transversus abdominis plane (TAP) block, on postoperative analgesic consumption. Fifty ASA physical status I–II term primiparous single-tone pregnant women aged 20–40 years scheduled for elective cesarean delivery with Pfannenstiel incision under general anaesthesia were enrolled in this randomized, double-blind, placebo-controlled trial. Ultrasound guided TAP block was performed at the end of surgery. Patients were randomly enrolled into two groups. Patients in the study group received 20 ml of hyperbaric bupivacaine 0.25% plus 1mL of sufentanil on either side while patients in the placebo group were administered 20 ml of hyperbaric bupivacaine 0.25% along with 1mL of placebo. Post-cesarean delivery visual analogue scale (VAS) for pain and morphine usage were measured and recorded. The morphine consumption was significantly less in the study group (37.2 ± 16.1 mg) than the control group (52.8 ± 16.7 mg, $P=0.002$). The VAS for pain both in rest and coughing were same in groups. Sufentanil added to 0.25% hyperbaric bupivacaine in TAP block decreases post cesarean delivery morphine consumption.

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Introduction

Pain management is crucially important in the postoperative period as it increases patient comfort and satisfaction and decreases side effects (1). Pain management in women who undergo cesarean delivery has even greater importance as babies need a painless and comfortable mother beside them as soon as possible (2). Except for opioids, other analgesics could not provide sufficient pain relief in most moderate to severe post-operative pain (3). Opioids administered by any route can produce some side effects such as nausea, vomiting, urinary retention, and itching (4).

Multimodal analgesia technique is currently suggested for effective post-operative pain control. A multimodal combination of regional anesthetic techniques and systemic administration of analgesic agents results in better pain control (5-6).

Previously it was demonstrated that in elective cesarean delivery performed under general anaesthesia

with a Pfannenstiel incision, bilateral TAP blockade with 30 mL 0.25% bupivacaine (15 mL in each side) could decrease 24 h postoperative pain intensity and analgesic consumption (7).

In the present study, it was hypothesized that adding sufentanil to TAP block hyperbaric bupivacaine solution can reduce post-cesarean delivery morphine consumption and pain intensity.

The primary outcome of this study was to evaluate the effect of sufentanil added to hyperbaric bupivacaine solution in TAP block on postoperative analgesic consumption. The severity of postoperative pain and incidence of nausea and vomiting were considered as the secondary outcomes.

Materials and Methods

The study proposal was accepted by the Institutional Ethics Committee and registration of the clinical trial (NCT 01516268) an informed written consent was

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achieved by the participants. Fifty ASA physical status I–II term primiparous single-tone pregnant mothers aged between 20–40 years scheduled for elective cesarean delivery with Pfannenstiel incision under general anaesthesia were registered in this randomized, double-blind, placebo-controlled trial.

Patients with a history of addiction (including opioids and benzodiazepines), known protocol drug's allergy or prescribed analgesics, psychological disorders, coagulopathy, and any surgical complications, infection of the block injection site or any other contraindications for TAP block, and those receiving any drugs within 48 hours of surgery (except for the study protocol drugs), obese patients with a BMI >40 were not recruited in the study.

Prior to general anaesthesia, all the required drugs were made ready by an anesthetist who was not either collaborated in the management or observation of the patients. All TAP blocks were completed by an anesthesiologist, who did not participate in the data gathering, and patients got their block when they were under general anaesthesia; thus, both the anesthesiologist and the patients were unaware of group assignment, so the study was double blinded. The prepared syringes contained either 40 ml of hyperbaric Bupivacaine 0.25% plus 2mL normal saline for placebo group or 40 mL of hyperbaric bupivacaine 0.25% plus 2mL of sufentanil for the study group.

Visual analogue scale (VAS) was used to assess pain intensity. VAS scale for pain was explained thoroughly to the participants at the night before surgery in the perioperative visit by a trained physician. The severity of postoperative pain was measured and recorded using a 10-cm scale, where 0=no pain and 10=the worst possible pain.

On arrival in the operating room, by a computer produced randomization list, patients were assigned to the study group (Group A, n=25) or the control group (Group B, n=25).

All women were monitored with an electrocardiogram (ECG), noninvasive blood pressure and pulse oximetry. An 18-gauge cannula was put in a vein on the dorsum of the non-dominant hand and lactated ringer solution 7 ml kg⁻¹ was infused. All patients received rapid sequence induction of anaesthesia. Anaesthesia was induced with sufentanil 5 ug and thiopental sodium 5 mg/kg, and the tracheal intubation was facilitated by administration of succinylcholine 1.5 mg/kg. Following tracheal intubation, anaesthesia was maintained with isoflurane 0.8%, N₂O 50%, and 0.3 mg/kg atracurium. After the

delivery of the neonate, 0.2 ug/kg sufentanil was administered. Ventilation was adjusted to maintain normocapnia (end-tidal carbon dioxide partial pressure 4.7–5.3 kPa). Patients were actively warmed to keep core temperature normothermic. At the end of the surgical procedure and wound dressing, the skin was prepared with 2% chlorhexidine solution. A high-frequency linear ultrasound probe (6–13 MHz) is placed transverse to the abdominal wall between the costal margin and iliac crest on the midaxillary line. The satisfactory image was aimed to visualize the subcutaneous fat, external oblique muscle, internal oblique muscle, transversus abdominis muscle, peritoneum, and intraperitoneal cavity. The needle was introduced in the plane of the ultrasound probe directly under the probe and advanced until it reaches the plane between the internal oblique and transversus abdominis muscles. Upon reaching the plane, 21mL of prepared solution was injected on each side. The transversus abdominis plane is visualized expanding with the injection.

Subsequently, the anesthetic administration was stopped, and neuromuscular blockade was antagonized by IV administration of 2.5 mg of neostigmine along with 1.0 mg atropine. Patients were considered awake when they opened their eyes on command or after gentle tactile stimulation; they were extubated soon thereafter.

In the recovery room, the patients were attached to a patient controlled analgesia (PCA) device. The PCA device was programmed to achieve each patient's desired level of comfort via delivery on demand. The device contained 30 mg of morphine in 30 ml saline 9% (1 mg/ml). First, a 40 ug/kg loading dose of IV morphine was administered; next, a bolus dose of 1 mg of morphine with lockout at 8-min intervals with no preset of maximum dose was set.

Patients were requested to score the pain both at rest and during coughing, in the time of discharge from recovery and 6, 12, and 24 h later.

It was assessed that a least of 22 patients in every group would be obligatory to have a 90% power of identifying three scores diff, considering SD=15 at a significance level of 0.05. This number was raised to 25 in each group to allow a predicted drop-out of almost 10%.

The distribution of age, weight, surgery time, morphine consumption was checked by using the Kolmogorov–Smirnov test, and it was found that these factors followed a normal distribution. Student's t-test was used for independent groups to compare between both groups for measurable variables, i.e. age, BMI,

weight, height, morphine consumptions, and visual analogue score.

Results

Patients' characteristics

Fifty patients were enrolled in the study. There was no study protocol violation and all the patients' data were analyzed. The patients' demographic characteristics, surgery time and ASA physical status classes were alike in groups (Table 1).

Primary Outcome

The patients who received 40 ml of hyperbaric bupivacaine 0.25% plus 10ug of sufentanil (study group, n=25, 37.2 ± 16.1 mg) consumed less morphine

during 24 h following surgery compared to the control group, (n=25, 52.8 ± 16.7 mg, independent t-test, $P=0.002$). The mean difference in morphine consumption between the study and control group was 15.6 mg in the first 24 hours postoperatively.

Secondary Outcome

The VAS score for pain both at rest and on coughing was not significantly different in groups. (Repeated measure analysis of variance, between subjects effect), yet there was statistically meaningful differences in VAS for pain (rest and coughing) scores in different measured times in each group (repeated measure analysis of variance, within subjects effect, $P<0.05$ (Table 2).

Table 1. Patient's characteristics

	Study Group (n=25)	Control Group (n=25)
Age(year) *	28.9±3.4	29.9± 5.9
Weight(kg)*	75.8±11.9	81.3±15.3
Height(cm)*	164.5±6.6	163.1±5.7
Surgery time(min)*	57.6±4	53.0±2
ASA physical status class (I/II)	(14/11)	(12/13)

*Values are expressed as mean±sd.

**There were no significant differences between the groups

Table 2. Post-cesarean delivery VAS score in each measured times

	Study Group (n=25)	Control group (n=25)
Recovery Time		
Coughing	5.1 ± 3.1	6.1 ± 2.8
Rest	2.6 ± 1.9	3.0 ± 1.8
2h the following Surgery		
Coughing	4.6 ± 2.3	5.0 ± 2.8
Rest	1.8 ± 2.1	2.1 ± 1.6
6h the following Surgery		
Coughing	3.7 ± 2.2	4.3 ± 2.6
Rest	1.6 ± 1.1	1.9 ± 1.0
12h following Surgery		
Coughing	2.6 ± 1.4	2.8 ± 1.9
Rest	1.3 ± 1.1	1.8 ± 1.1
24h following Surgery		
Coughing	2.8 ± 2.2	2.9 ± 1.9
Rest	1.2 ± 1.0	1.1 ± 1.0

*Data are expressed as mean ± SD

** There was no significant difference. Repeated measure analysis of variance, between subjects effect

There was significant difference, repeated measure analysis of variance, within subjects effect, $P<0.05$

Three patients in group C had complaints of post-cesarean delivery nausea and vomiting compared to one

patient in other groups. There was no statistically significant difference.

Discussion

The present study indicated that adding sufentanil to the 0.25% hyperbaric bupivacaine solution in ultrasound-guided bilateral TAP block reduces post cesarean delivery morphine consumption.

Considering the high prevalence and increasing rate of cesarean delivery worldwide, the suitable post-operative pain management in mothers becomes a serious challenge for anesthesiologists (8-10). It is imperative to point out that although spinal anaesthesia is usually the first choice, a large number of patients prefer general anaesthesia for cesarean delivery (11).

A variety of agents and techniques such as opioids, non-steroidal anti-inflammatory drugs and regional nerve blocks have been used to reduce postcesarean delivery pain; each one with their cons and pros (12-14)

Opioids are undoubtedly the core of every analgesia technique. However, side effects such as nausea, vomiting, pruritus, sedation, and respiratory depression limit their use. Therefore, a multimodal analgesic technique to decrease opioid requirements clearly has many benefits.

TAP block is a regional anesthetic technique that blocks the abdominal wall neural afferents by introducing local anesthetic into the neurofascial plane between the internal oblique and transversus abdominis muscles (15). Since transversus abdominis plane block with the aim of anaesthetizing nerve supplies to the anterior abdominal wall was first described in 2001 by Rafi (16), its use in post-operative pain management has gained popularity.

Previously, it was showed that two-sided TAP block with 0.25% bupivacaine in parturients who undergo cesarean section with a Pfannenstiel incision under general anaesthesia can decrease postoperative pain and analgesic consumption (7).

A meta-analysis to study the efficacy of TAP block shows that it reduces the need for postoperative opioid, the time for the first request for further analgesia, provides more effective pain relief, and reduces opioid-associated side-effects (17).

Considering the mentioned points, there is substantial potential for TAP block to be part of an effective multimodal regimen for postcesarean section analgesia.

Adding adjuvants to various peripheral nerve blocks has been studied previously. It has been shown that adding epinephrine to levobupivacaine reduces its peak plasma concentration after unilateral TAP blocks, with no remarkable effects on block characteristics or

duration (18). Also, adding clonidine to a TAP block with bupivacaine did not affect wound hyperalgesia index and it did not improve short-term or long-term pain scores in women undergoing elective cesarean delivery (19). The addition of fentanyl to local anesthetics improved the quality and prolonged the duration of cervical plexus block (20). Buprenorphine may enhance and prolong the analgesic effect of bupivacaine when used for sciatic nerve blocks in patients undergoing foot and ankle surgery under general anaesthesia (21).

To our knowledge, the effect of adding opioids to TAP block on postoperative morphine consumption has not been previously studied. We believe that by adding sufentanil to bupivacaine solution in TAP block, we could achieve more comfort and less opioid consumption in mothers undergoing cesarean delivery under general anaesthesia.

Although TAP block is a safe procedure, few side effects have been reported previously.

TAP blocks can result in elevated plasma ropivacaine concentrations in patients undergoing a cesarean section, which may be associated with neurotoxicity (22). In one report, TAP block led to hepatic trauma (23). Colon puncture or hematoma formations are other potential side effects of TAP block (24).

Opioids' analgesic effect through the central nervous system (CNS) has been studied previously thoroughly. However, evidence exists that opioid antinociception can be initiated by activation of opioid receptors located outside the CNS; one of the earliest reports was that of Wood (25). Previous studies indicate that a large amount of the analgesic effects produced by systemically administered opioids can be mediated by peripheral opioid receptors (26-29). Without a doubt, opioid agonists acting peripherally would be most attractive for their lack of central side effects and typical adverse effects of non-steroidal anti-inflammatory drugs. The significance of the peripheral action of the opioid system needs to be transferred to the clinical situation.

There were some limitations in the present study. First, as in our center, all women candidates for cesarean delivery had bladder catheter and the evaluation of the incidence of urinary retention was not possible. Furthermore, the power of this study was not sufficient to show any differences in the incidence of opioids' side effects. Conducting a study with more power is necessary to evaluate the incidence of side effects of opioids.

In conclusion, sufentanil added to a bilateral TAP

block with 0.25% bupivacaine reduces post- elective cesarean delivery morphine consumption.

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