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Ultrasound-guided bilateral quadratus lumborum block vs. intrathecal morphine for postoperative analgesia after cesarean section: a randomized controlled trial

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Background: Adequate pain control after cesarean section (CS) is crucial for mothers caring for newborns, and early ambulation to avoid thromboembolism and chronic abdominal and pelvic pain. This randomized controlled trial compared the efficacy of quadratus lumborum block (QLB) and intrathecal morphine (ITM) for analgesia after CS.
Methods: Ninety women at ≥ 37 weeks pregnancy scheduled for elective CS were enrolled. All patients received spinal anesthesia and post-operative QLB. They were randomly allocated to Control (anesthesia: 0.1 ml saline, QLB: 24 ml saline), ITM (anesthesia: 0.1 mg morphine, QLB: 24 ml saline), or QLB groups (anesthesia: 0.1 ml saline, QLB: 24 ml 0.375% ropivacaine). Integrated analgesia score (IAS) and numerical rating scale (NRS) scores at rest and during movement, morphine requirements in the first 48 h, time to first morphine dose and morphine-related side effects were recorded.
Results: IASs and NRS scores at rest and during movement were significantly lower in QLB and ITM group than in Control group. Moreover, IASs and NRS scores at rest and during movement were lower in QLB group than in ITM group. Time to first morphine dose was significantly longer in QLB group than in ITM and Control group. Furthermore, morphine requirements in the first 48 h were significantly lower in QLB group than ITM and Control group. Incidence of morphine-related side effects was significantly higher in ITM group than in QLB and Control group.
Conclusions: QLB and ITM are effective analgesic regimens after CS. However, QLB provides better long-lasting analgesia and reduced total postoperative morphine consumption.

Keywords: Analgesia; Cesarean section; Morphine; Quadratus lumborum; Spinal.

Introduction

Cesarean section (CS) is the most frequently performed surgical procedure in obstetrics and gynecology. It represents 27.2% of births in the most developed regions and 21.1% of those worldwide with a projection of further increase [1,2]. Adequate pain management after CS is vital to help new mothers feed and care for the newborn [3,4]. Furthermore, effective analgesia is crucial for early ambulation of parturients to avoid the risk of thromboembolism and development of chronic pain in the abdomen and pelvis [5].

Most CSs are performed under spinal anesthesia and opioids are still considered a cornerstone for postoperative analgesia that is systemic, spinal, or both [6,7]. However, it is

associated with undesirable side effects including delayed maternal respiratory depression, nausea, vomiting, and pruritis causing a reduction in overall patient satisfaction. Hence, alternative, opioid-free analgesic approaches are necessary [6,8].

Transversus abdominis plane (TAP) block is currently the most popular regional analgesic technique used for postoperative analgesia after CS. However, TAP block is inferior to intrathecal morphine (ITM) and of little benefit if used as a part of a multimodal regimen that includes ITM [6,8]. Acute pain after CS has both somatic and visceral components that result from surgical cutting of the abdominal wall and uterus. TAP block, as a part of a multimodal analgesic regimen after CS, provides effective analgesia for somatic pain at the abdominal wall [9].

Ultrasonographic research into a new approach to TAP block has yielded the quadratus lumborum block (QLB). QLB was first reported at the annual European Society of Regional Anesthesia congress in 2007 (QLB I). In 2015, the QLB technique was modified by shifting the injection point from the anterolateral border of the quadratus lumborum to the posterior border (QLB II) [10]. QLB inhibits the dual pain components (somatic and visceral) as a result of local anesthetic spreading to the paravertebral space [9,10]. The analgesic efficacy of QLB II and its superiority over TAP block after CS were proved by Blanco [10,11]. The aim of this double-blind randomized controlled trial was to study the efficacy of QLB and ITM and compare the two treatment techniques for postoperative analgesia after CS.

Materials and Methods

After approval of the Research Ethical Committee of our hospital (Ethical Committee No. 31982/09/17) on 12 September 2017 and obtaining a written informed consent from all patients, 90 parturients were enrolled in this double-blind randomized placebo-controlled study between October 2017 and August 2018. The inclusion criteria were parturients with an American Society of Anesthesiologist physical status of II, those aged between 19 and 40 years, and scheduled for elective CS via a Pfannenstiel incision under spinal anesthesia. The exclusion criteria were a history of allergy to any of the study drugs, a body mass index (BMI) ≥ 35 kg/m^2, coagulopathy, local infection, pregnancy-induced hypertension, gestation diabetes mellitus, and opioid abuse. The study was registered at www.pactr.org (ID: PACTR201809600342881).

Based on numbers randomly generated by allocation software (QuickCalcs; GraphPad Software Inc., USA) in sealed opaque envelops, parturients were allocated randomly into one of three groups: the Control group (n = 30), QLB group (n = 30), and ITM group (n = 30).

Oral ranitidine (150 mg) was administered to all patients at night and again 2 h before surgery. Before the patient was transferred to the operating room, an 18-gauge intravenous cannula was inserted into the nondominant arm or hand and 500 ml of hydroxyethyl starch (6% solution) was infused. In the operating room, standard monitoring was applied, including peripheral pulse oximetry, electrocardiography, and noninvasive arterial blood pressure.

Spinal anesthesia was performed under ultrasonographic guidance at levels of L2 to 3 or L3 to 4 intervertebral spaces, using a 27-gauge pencil point needle (Portex RapID™ Spinal Needle Set Pencil Point Spinal Needle, Smiths Medical International Ltd., UK) with 12.5 mg of hyperbaric bupivacaine 0.5% (Astrazeneca Pharmaceuticals, UK) and 10 μg of fentanyl (Martindale Pharmaceuticals, UK) combined with 0.1 mg of preservative-free morphine (0.1 ml) in the ITM group, and with 0.1 ml of 0.9% saline in the Control and the QLB groups. Subsequently, the partu-rients adopted the supine position with left uterine displacement of 15–20° and a facemask was applied to deliver oxygen at a rate of 6 L/min

Five minutes after the spinal injection, the spinal anesthesia level was assessed by a pinprick and considered successful if a bilateral sensory blockade at T4-T6 was established. Anesthesia and surgical management were performed as per the hospital protocol.

After skin closure and the covering of the wound with a dressing, patients received intravenous paracetamol (1 g) and rectal diclofenac (100 mg). Ultrasound-guided QLB was then performed through the posterior approach, using the technique described by Blanco et al. [11], while the patients were still in the supine position and fully monitored.

A convex (5–8 MHz) ultrasound probe (SonoScape, China) with a protective sheath was used after imaging depth and gain was adjusted. The procedure was performed under complete aseptic conditions (including a facemask, gown, and gloves). After the abdominal skin was cleaned with an antiseptic solution, the probe was positioned transversely at the level of the anterosuperior iliac spine and then advanced in the cranial direction to visualize the three muscle layers of the abdominal wall. Following the external oblique muscle posterolaterally, its posterior border was identified (hook sign) with the internal oblique muscle below it displayed as a roof above the quadratus lumborum. The transducer was then tilted down to visualize the middle layer of the thoracolumbar fascia as a bright hyperechoic line. A 21-gauge Stimuplex® A 100-mm needle (B. Braun Melsungen AG, Germany) was inserted in-plane under real-time ultrasound guidance in the anterolateral-to-posteromedial direction via the abdominal wall. Two milliliters of 0.9% saline was injected to visualize the solution

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spread (hydrodissection) to determine the optimal point of injection over the lumbar interfacial triangle. In the QLB group, 24 ml of 0.375% ropivacaine was then slowly injected on each side after negative aspiration in 4 ml aliquots (total dose, 180 mg), whereas in the Control and the ITM groups, patients received the same volume of 0.9% saline (placebo). Spread of the study solution was observed during the injection, revealing a tendency to difuse posteromedially rather than anterolaterally.

After the patients were transferred to the postanesthesia recovery unit, intravenous morphine was started via a patient-controlled analgesia (PCA) pump adjusted to deliver a bolus of 1 mg with a 5 min lockout period, a 4 h maximum dose of 48 mg, and no background infusion for the next 48 h (study period). The intensity of pain was assessed at rest and during movement (knee flexion) using the numerical rating scale (NRS) ranging from 0 to 10 (0 indicating no pain and 10 indicating severe intractable pain) at 2 h, 6 h, 12 h, 24 h, 36 h, and 48 h by nursing staff, and 1 g of paracetamol was administered intravenously if the NRS score was > 3, with a maximum dose of 4 g/24 h. All treating staff and outcome assessors were blinded to the study group allocation.

Patients were evaluated for their level of sedation using the Pasero Opioid-induced Sedation Scale [12], incidence of pruritis, and severity of postoperative nausea and vomiting (PONV), using a 4-point rating (4 = severe, 3 = moderate, 2 = mild, and 1 = absent), at 6 h, 12 h, 24 h, and 48 h. Patients were also monitored for respiratory depression, which was defined as a respiratory rate of ≤ 8 breaths/min In addition, time to first postoperative morphine dose and time to first postoperative ambulation were recorded.

Intravenous ondansetron (4 mg) was administered to treat PONV and diphenhydramine (25 mg) was administered to treat pruritis. At the end of the study period, patients were asked to rate their satisfaction with the pain control regimen using a 3-point scale (1 = highly satisfied, 2 = satisfied, or 3 = dissatisfied).

The integrated analgesia score (IAS) was calculated at all NRS pain scores measurement time points using the following formula: $(NRS + 1) \times (1 + M / 10)$, where M indicates morphine dosage in milligrams 2 h before recording time of NRS. The basic formula of $(PI \times [1 + M/10])$ [13], where PI is pain intensity, was modified by replacing PI with NRS + 1 to avoid a zero result when NRS = 0.

The primary outcome measure of this clinical study was the IAS at rest and during movement, and the secondary outcome measures were morphine consumption in the first 48 h, NRS pain scores at rest and during movement, time to first morphine dose, time to first ambulation, patient satisfaction, and morphine-related adverse effects including pruritis, nausea and vomiting, respiratory depression, and sedation.

Based on similar investigations [9,14], a sample size of 26 patients was calculated for an alpha error of 0.05, beta error of 0.1, probability (power) of 90%, and anticipated effect size of 0.40 using sample size software (G*Power Version 3.00.10, Franz Faul, Universität Kiel, Germany). Therefore, we included 30 patients per group to allow for any missing data or dropouts. Statistical analyses were performed using the Statistical Package for Social Sciences version 20 (SPSS Inc., USA). The Shapiro–Wilk test was first used to test the data for normality. Data were expressed as the mean ± SD, median (range), or frequency and percentage as appropriate. A one-way analysis of variance was used for analysis of normally distributed continuous data. The Kruskall–Wallis test was used for analysis of non-normally distributed continuous data. The chi-square test was used for pair-wise comparison of qualitative parameters among the groups after Bonferroni adjustment. A P value of < 0.05 was considered statistically significant.

Results

A total of 118 patients were eligible, among whom only 90 patients were enrolled in the study and randomized into three groups. No patient was excluded from the study thereafter because of deviation from the study protocol (Fig. 1). The three groups were comparable regarding the baseline maternity characteristics (Table 1). IASs and NRS scores at rest and during movement were significantly lower in the ITM and QLB groups than in the Control group at the various measurement time points. Moreover, the QLB group had lower IASs and NRS scores at rest and during movement in comparison to the ITM group (Figs. 2A, 2B, 3A, and 3B). Table 2 shows that time to first morphine dose was significantly longer in the QLB and ITM groups in comparison to the Control group it was also significantly longer in the QLB group than in the ITM group. Total PCA morphine consumption during the first postoperative 48 h was significantly lower in the QLB and ITM groups in comparison to the Control group it was also significantly lower in the QLB group than in the ITM group (Table 2). The three groups were comparable regarding the time to first ambulation ($P > 0.05$) (Table 2). A significantly higher number of patients had pruritis in the ITM group than the Control and the QLB groups at 6 h. Moreover, the incidence of PONV was significantly higher in the ITM group at 12 h. Patient satisfaction with the assigned treatment regimen was significantly higher in the QLB group than in the Control and the ITM groups (Table 3). Sedation scale scores did not differ among the three groups, with no clinically detectable respiratory depression in any of the study patients (data not shown).

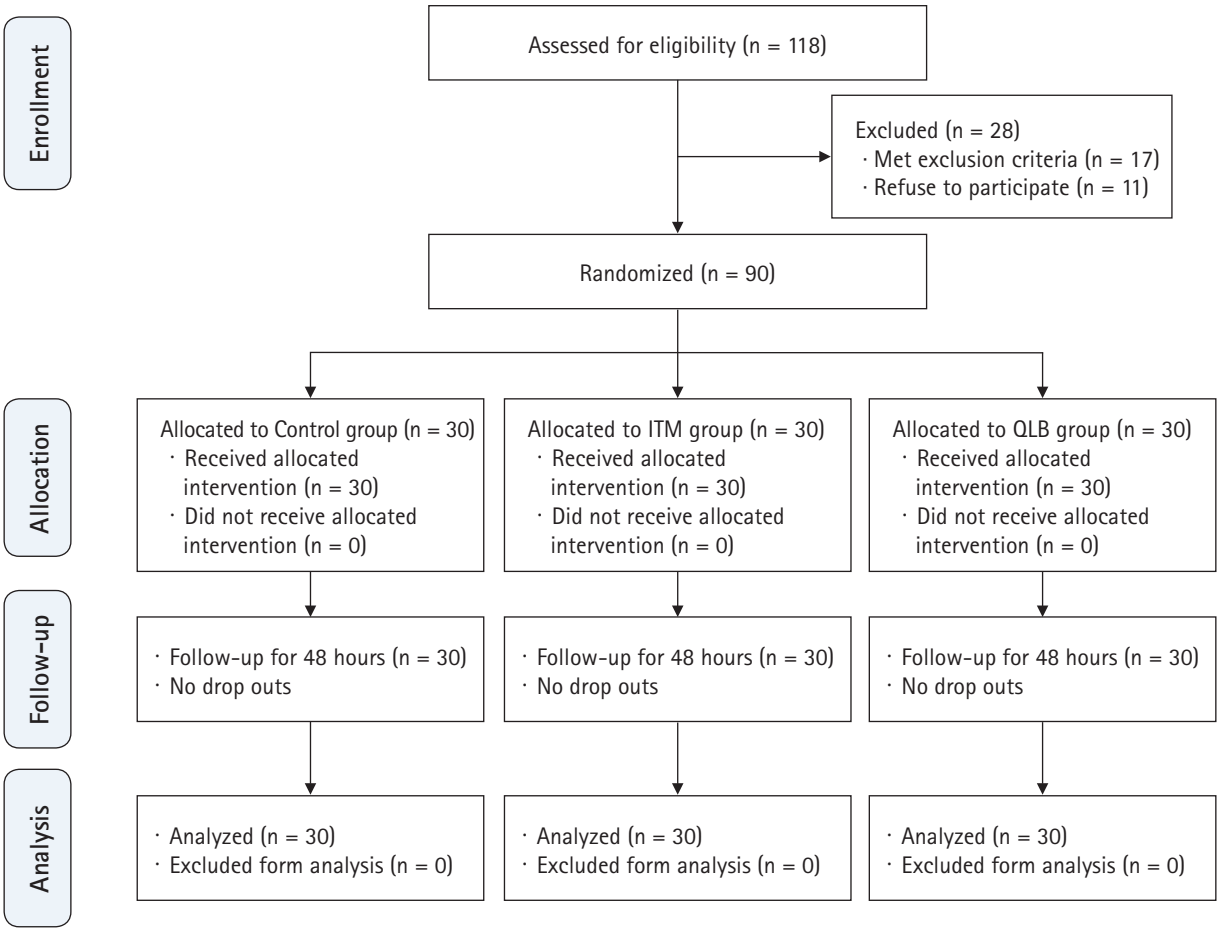

Fig. 1. CONSORT-flow diagram of participants in the study. ITM: intrathecal morphine, QLB: quadratus lumborum block.

Table 1. Maternity Characteristics

Variable	Control group (n = 30)	ITM group (n = 30)	QLB group (n = 30)
Age (yr)	32.5 ± 6.6	29.9 ± 7.5	31.1 ± 5.9
Weight (kg)	81.7 ± 11.3	78.9 ± 13.6	79.8 ± 12.6
Height (cm)	166.7 ± 14.6	165.4 ± 15.6	164.7 ± 12.9
BMI (kg/m^2)	29.6 ± 6.7	28.5 ± 5.9	29.2 ± 6.2
Gestation age (weeks)	38.6 ± 1.4	39.2 ± 1.1	38.9 ± 1.8
Parity	1.5 ± 0.6	1.6 ± 0.6	1.6 ± 0.5

Values are presented as mean ± SD and were compared with Fisher's exact test. ITM: intrathecal morphine, QLB: quadratus lumborum block, BMI: body mass index. No significant differences were seen among the three groups.

Table 2. Patient-controlled Analgesia Morphine Requirements

Variable	Control group (n = 30)	ITM group (n = 30)	QLB group (n = 30)	P value
Morphine requirement (mg) at 48 h	61 ± 12.9	42.8 ± 10.4	18.2 ± 9.6	< 0.05*
Time to first morphine dose (h)	2 (0.5–4)	8 (3–24)	17 (6–36)	< 0.05†
Time to first ambulation (h)	11.7 ± 1.9	12.9 ± 1.6	13.4 ± 1.8	> 0.05

Values are presented as mean ± SD or median (range). ITM: intrathecal morphine, QLB: quadratus lumborum block. *P values: ITM vs. Control = 0.001, QLB vs. Control = 0.001, QLB vs. ITM = 0.001. †P values: ITM vs Control = 0.008, QLB vs. Control = 0.001, QLB vs. ITM = 0.002.

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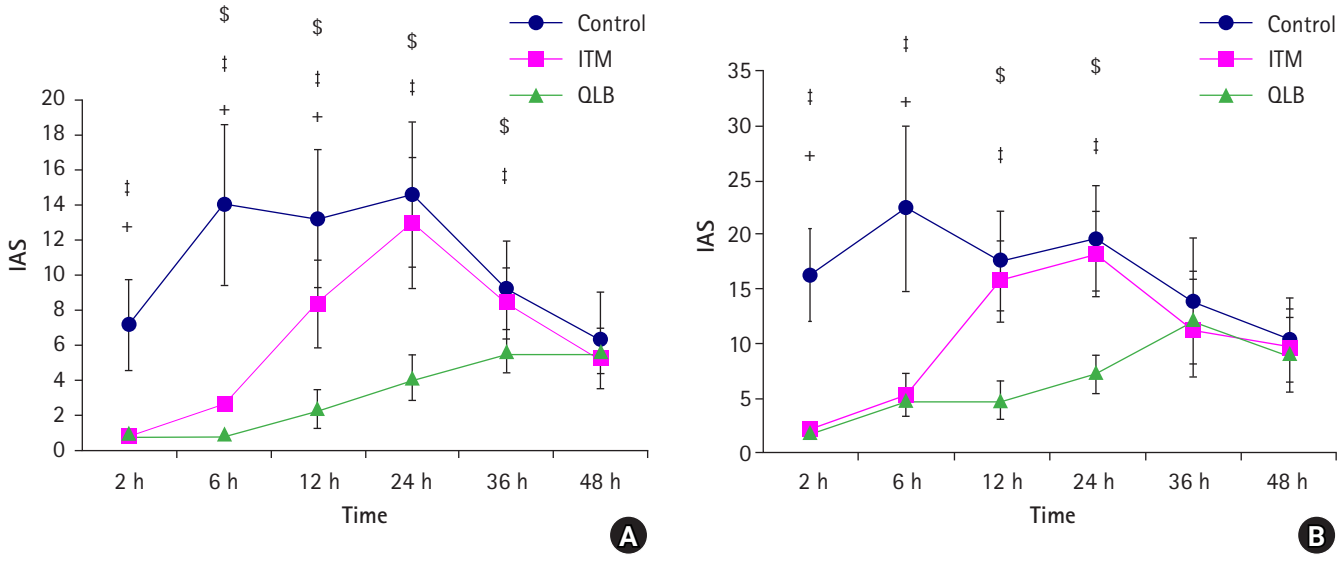

Fig. 2. (A) Comparison of IAS at rest among the three groups. (B) Comparison of IAS during movement among the three groups. Values are presented as mean ± SD. ITM: intrathecal morphine, QLB: quadratus lumborum block, IAS: integrated analgesia score. *P values < 0.05 ITM vs. Control, †P values < 0.05 QLB vs. Control, ‡P values < 0.05 QLB vs. ITM.

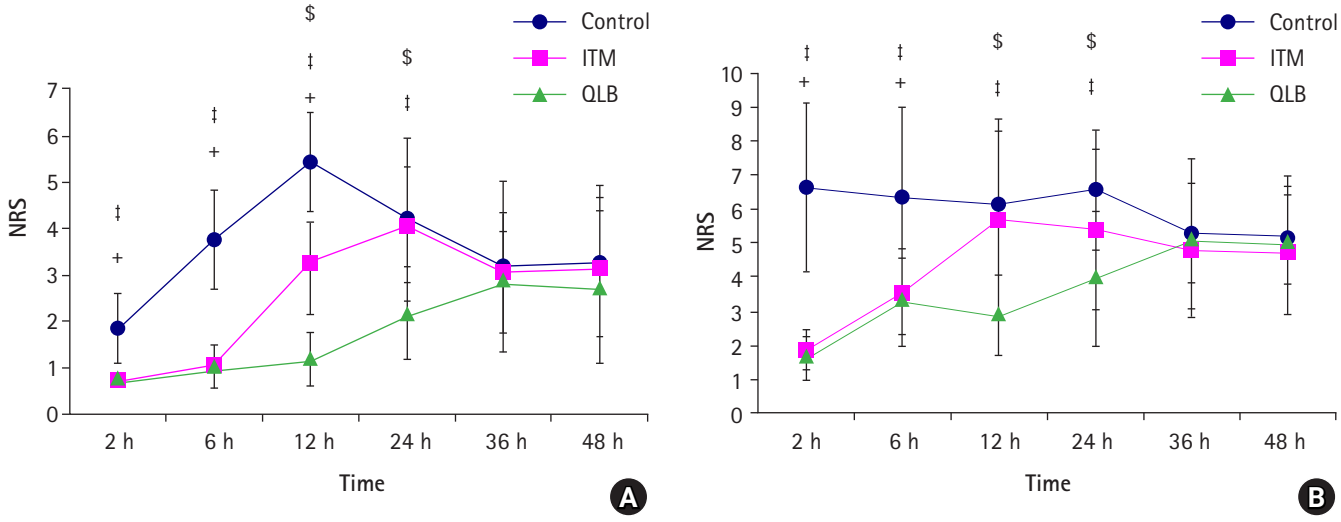

Fig. 3. (A) Comparison of NRS Scores at rest among the three groups. (B) Comparison of NRS Scores during movement among the three groups. Values are presented as mean ± SD. ITM: intrathecal morphine, QLB: quadratus lumborum block, IAS: integrated analgesia score, NRS: numerical rating scale. *P values < 0.05 ITM vs. Control, †P values < 0.05 QLB vs. Control, ‡P values < 0.05 QLB vs. ITM.

Discussion

Our results demonstrated that both QLB and ITM are effective postoperative analgesic regimens after CS; however, QLB provides longer-lasting analgesia with lower postoperative morphine requirements.

In our study, IASs and NRS scores were significantly lower in the ITM group for up to 12 and 6 h at rest and during movement, respectively, in comparison to the Control group. In addition, IASs and NRS scores during movement were significantly lower in the QLB group for up to 24 h in comparison to the Control and the ITM groups.

The overall benefits provided by any proposed analgesic technique may not be clearly identified when analgesic requirements and pain scores are used as isolated parameters [15]. Hence, we adopted the IAS described by Silverman et al. [13] as the primary outcome measure of the current study. The IAS provides a global end point based on a unique formula integrating pain intensity

Table 3. Morphine Related Side Effects and Patient Satisfaction

Variable			Control group (n = 30)	ITM group (n = 30)	QLB group (n = 30)	P value
Pruritus	6 h		5 (16.7%)	12 (40%)	4 (13.3%)	< 0.05*
	12 h		6 (20%)	9 (30%)	7 (23.3%)	> 0.05
	24 h		7 (23.3%)	6 (20%)	7 (23.3%)	> 0.05
	48 h		0 (0%)	3 (10%)	2 (6.7%)	> 0.05
PONV	6 h	absent	12	5	14	
		mild	14	22	13	> 0.05
		moderate	4	2	3	
		severe	0	1	0	
	12 h	absent	18	4	20	
		mild	10	18	9	< 0.05†
		moderate	2	7	1	
		severe	0	1	0	
	24 h	absent	19	9	17	
		mild	8	17	10	> 0.05
		moderate	1	3	3	
		severe	2	1	0	
	48 h	absent	24	22	25	
		mild	4	6	4	> 0.05
		moderate	2	2	1	
		severe	0	0	0	
Satisfaction	highly satisfied		11 (36.7%)	5 (16.7%)	28 (93.3%)	
	satisfied		14 (46.7%)	16 (53.3%)	2 (6.7%)	< 0.05‡
	dissatisfied		5 (16.6%)	9 (30%)	0 (0%)	

Values are presented as number (%) or number only. ITM: intrathecal morphine, QLB: quadratus lumborum block, PONV: postoperative nausea and vomiting. *P values: ITM vs. Control = 0.045, QLB vs. Control = 0.602, QLB vs. ITM = 0.020, †P values: ITM vs. Control = 0.002, QLB vs. Control = 0.782, QLB vs. ITM = 0.001, ‡P values: ITM vs. Control = 0.172, QLB vs. Control = 0.001, QLB vs. ITM = 0.001.

and morphine consumption rather than a specific end point such as pain scores or analgesic requirements. We believe that the IAS improves sensitivity in assessing different treatment techniques. In our study, the IAS clarified the extended analgesic action of QLB during rest for up to 36 h, with a significantly lower IAS in comparison to the Control and the ITM groups. however, this was not noted when NRS scores were used as a pain intensity measurement tool at rest to compare QLB with ITM or placebos because NRS scores at rest were significantly lower in the QLB group in comparison to the Control and the ITM group. until 24 h.

Our results also revealed that compared with the Control group, QLB provided an opioid-sparing effect of 70% during the first 48 h. By contrast, only a 30% reduction in morphine consumption was recorded in the ITM group. Furthermore, time to first morphine dose was significantly longer in the QLB group than in the ITM and the Control groups; it was also significantly longer in the ITM group than in the Control group.

ITM was previously the gold standard treatment for pain management after CS [16]. In a systemic review and meta-analysis, Mishriky et al. [17] found that ITM had greater analgesic efficacy in comparison to TAP block but was associated with a high incidence of morphine-related side effects. TAP block is an infiltration of local anesthetic solution in the anterior abdominal wall, as proved by Carney et al. [18] through magnetic resonance imaging of the chest and abdomen. In another systemic review and meta-analysis conducted by Champaneria et al. [19], TAP block was confirmed to have no additional benefits if combined with ITM. However, other studies found no differences between the two treatment techniques [16].

Our results are in concurrence with previous studies that have reported QLB as a successful postoperative pain control regimen after different types of surgery [20–23]. Moreover, our results are also in concurrence with those of Blanco et al. [10], who initially investigated QLB for pain control after CS by injecting 0.2 ml/kg of bupivacaine at 1.25 mg/ml on the posterior margin of the quadratus lumborum, resulting in a significant decrease in visual analogue pain scores and morphine consumption in the first 48 h. A year later, the same author group investigated QLB in comparison

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to TAP block and proved that QLB had a significantly superior analgesic efficacy for up to 48 h [11]. However, to our knowledge, no previous studies have investigated and compared the analgesic efficacy of QLB and ITM for postoperative pain relief after CS.

QLB is a superficial posterior abdominal wall block that is technically easy to perform. It targets a very bright hyperechoic and easily dissected fascial plane. QLB level extends from T7 to T12 compared with T10 to T12 dermatomal distribution after TAP block [10]. This can be explained by two main theories: the spread of local anesthetic to the sympathetic nerve network in the thoracolumbar plane, and the spread of local anesthetic into the paravertebral space. These two theories can also explain the prolonged blockage effect and visceral pain control achieved by QLB but not by TAP block [11]. Hence, QLB is a safe, effective, and reliable analgesic option for postoperative pain control after abdominal surgeries [23–26].

In our study, compared with the other 2 groups, patients in the QLB group had no significant tendency for delay in ambulation. Weakness of the iliacus, quadriceps, and psoas muscles can result from the spread of local anesthetic after QLB, causing lumbar plexus block, as described by Wikner [27] in a case report.

Nausea, vomiting, pruritis, and respiratory depression are the major adverse effects of ITM. Nausea and vomiting are the most frequent adverse effects, occurring in approximately 30% of patients, whereas the incidence of pruritus ranges from 0% to 100% [28]. In our study, the incidence of pruritus was significantly higher in the ITM group at 6 h, whereas that of PONV was significantly higher in the ITM group at 12 h in comparison to the Control and the QLB groups. which led to the significantly lower number of patients who were satisfied with the treatment regimen in the ITM group compared to the QLB group.

In our study, sensory testing for evaluating block success was lacking because of efforts to preserve the blinding of group allocation. Obese patients with a BMI of ≥ 35 kg/m^2 were excluded from the study to ensure similar patient groups. Therefore, further investigation of QLB in this patient category is recommended to assess its efficacy. Furthermore, morphine might be used by the parturients through PCA pumps to control nonsurgical pain; however, they were instructed before starting the study to avoid the use of PCA pumps for such purposes. The optimal dose of local anesthetic in the case of QLB has not yet been determined and our study could not reveal any data about the ideal dose; hence, further research is warranted. The evaluation of pain scores and requirements of analgesia in pain control studies remains challenging. Hence, a combined outcome measure with improved validity was introduced in the form of the IAS, which is more consistent and informative. However, studying differences in treatment consequences still represents a major challenge and constitutes a limiting factor.

In conclusion, QLB and ITM are effective analgesic regimens after CS. However, QLB provides longer-lasting analgesia, reduced total postoperative morphine consumption, and improved patient satisfaction.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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