Midazolam as an Adjuvant to Bupivacaine in Quadratus Lumborum Block after Caesarean Section: Does It Improve Postoperative Pain Control? A Randomized Double-Blind Clinical Trial

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Abstract:

Background: The Quadratus Lumborum Block (QLB) effectively provides postoperative analgesia. In this study, we sought to demonstrate the impact of adding Midazolam to the Quadratus Lumborum Block on the 24-hour total dosage of ketorolac, 1st VAS in the first 24 hours, initial analgesia required, and duration of analgesia after cesarean section [1, 2].

Methods: Forty-two female patients who underwent cesarean sections were included in this research.

The study group got 41 ml (40 ml bupivacaine 0.25% with 5 mg midazolam in 1 ml) divided on each side.

We assessed the amount of ketorolac consumed over 24 hours, the VAS score, and the time for the first analgesia request (for ketorolac).

Results:

Forty-two participants participated in this double-blinded, prospective, controlled randomized clinical study.

Compared to the control group, the study group's VAS decreased significantly at rest and during movement (2,4,8, and 12 hours) with a *p*-value < 0.0001. Compared to the control group (10.43 ± 1.75) hours, the study group had a substantial delay in their initial analgesic demand (15.48 ± 1.75) hours. The ketorolac dosages were significantly lower in the midazolam group (35.45 ± 11.8 mg) compared to the control group (55.7 ± 10.7mg).

Discussion:

Posterior QLB reduces postoperative pain following cesarean surgery. Midazolam reduces ketorolac dosages, the VAS score, and the initial rescue analgesia when added to PQLB.

Keywords: VAS, ketorolac, Quadratus Lumborum Block (QLB).

Introduction

QLB was first used in 2007; it became more popular in 2013 when ultrasound-guided methods were introduced [3].

QLB is a fascial plane block where a local anesthetic is injected next to the quadratus lumborum muscle. QLB has four techniques: anterior, lateral, posterior, and intermuscular. It has significantly improved the management of pain following surgery [4].

Since its 1957 discovery, bupivacaine, a long-acting local anesthetic, has been

extensively used because of its effectiveness in producing extended sensory and motor anesthesia [5].

Bupivacaine has a variety of adjuvants added to increase the analgesic duration and reduce the need for postoperative analgesics. Among these adjuvants, short-acting benzodiazepine midazolam has drawn interest because Midazolam is thought to interact with GABA receptors at the site of action when administered as an adjuvant to local anesthetics, potentially boosting the effects of the local anesthetic. Long-term sensory and motor blockage may result from this interaction [7].

This study assumes that Midazolam as an adjuvant to bupivacaine in post-QLB could improve postoperative pain quality in C.S. with the least side effects.

Our Primary outcome included the total dose of rescue analgesia. The time to rescue analgesia in the postoperative period is 24 hours.

The secondary outcome included the Visual analog scale during the 1st 24 hours, patient satisfaction, and side effects of drugs or block.

Ethical Considerations:

Upon approval from the medical ethics committee of the Faculty of Medicine at Assiut University, Assiut, Egypt, a double-blinded, prospective controlled randomized clinical trial involving 42 female patients undergoing elective caesarean section was carried out in the hospital (Protocol ID: IRB 17101682, date: 3/2022). Registration in ClinicalTrials.gov (Identifier: NCT05261672)

Inclusion criteria:

- Age: 18-40 years.
- ASA physical status: I and II.
- Single pregnancy.

Exclusion criteria:

- Patient refusal.
- Coagulopathy.
- Maternal anatomic abnormalities of the abdomen.
- Allergy to local anesthetics.
- Localized infection at the procedure site.
- Women who were incapable of comprehending or using the Verbal rating pain scoring system
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- History of chronic pain or regular opioid use.
- Abuse of opioids or alcohol.
- Gestational age below 36 weeks.

Randomization

Two 50 ml syringes were prepared, one labeled as "Drug-X" with a 50 ml syringe containing 40 ml of bupivacaine 0.25% (in total 100 mg)+1 ml saline, and the other labeled as "Drug-Y" with a 50 ml syringe containing 40 ml of bupivacaine 0.25% (in total 100 mg)+5 mg of Midazolam in 1 ml. The groups were sealed before the study began and opened before anesthesia by a physician who prepared the anesthetic solution.

Patients were randomly assigned to 2 groups:

- QLB I (Bupivacaine): Patients got 40 ml of bupivacaine, 0.25% (100 mg), and +1 ml saline, divided on both sides.
- QLB II (bupivacaine + midazolam): Patients got 40 ml of bupivacaine 0.25% (in total 100 mg)+5 mg of Midazolam in 1 ml, divided on both sides.

Patients and Methods:

Each patient had an intravenous cannula introduced into the arm throughout the procedure, and they were all observed using peripheral pulse oximetry, non-invasive arterial blood pressure monitoring, and electrocardiograms. Without the use of an extra opioid, patients received 12.5 mg 0.5% hyperbaric bupivacaine for spinal anesthesia while seated in the L3-L4 interspace. Subsequently, the parturient was positioned supine with a 15-degree left uterine displacement. Their sensory level was assessed, and C.S. was initiated upon reaching T6.

Patients received an IV infusion of ecbolic after delivery, and a prophylactic antiemetic was administered.

The patient was positioned in a lateral posture following wound closure. An antiseptic solution was used to sterilize the skin. The linear probe was positioned on the lateral abdomen, somewhat cephalad to the iliac crest. After observing the quadratus lumborum muscle, the probe was gently rotated toward the caudal direction to highlight the muscle's great size. A 20-G needle was positioned 1 centimeter ventral to the probe in a plane. The needle tip moved forward until it entered the quadratus lumborum muscle's fascia. After that, a tiny quantity of saline was injected to ensure the tip was placed correctly. Each side of the QLB patients got 20.5 ml of the previously prepared fluid. Following aspiration, 4 ml increments of this solution were administered. On the opposite side, the same method was applied. Following the surgery, the patients were moved to the PACU, where their peripheral pulse oximetry, heart rate, non-invasive arterial blood pressure, and breathing rate were monitored.

Next, using a VAS scale of 0 to 10, where 0 represents no pain and 10 represents the greatest pain, the freshly delivered moms' pain intensity was assessed at rest and when moving.

Depending on their level of pain (VAS>5), the patients received 30 mg of ketorolac intravenously as needed. The VAS was assessed at rest, during movement, and after 2, 4, 8, 12, and 24 hours. The following parameters were measured: the Ramsay sedation score [8] was divided into six categories: 0 for awake and oriented; 1 for agitated and anxious; 2 for awake and cooperative; 3 for sleeping but cooperative; 4 for deep sedation and quick response to pain stimuli; 5 for deep sedation and slow response to deep stimuli; 6 for deep sedation and no response to pain stimuli; nausea, vomiting, side effects of QLB (infection, hematoma), and signs of local anesthetic toxicity. Five points were used to evaluate the patient's satisfaction at the time of discharge. The satisfaction scale is a Likert scale, with one denoting extremely displeased, two unsatisfied, three neither satisfied nor dissatisfied, four satisfied, and five strongly satisfied.

In this clinical investigation, the intake of ketorolac for 24 hours was our primary outcome. Secondary outcome measures were the VAS score before the first request for ketorolac.

Statistical Analysis:

To achieve 90% research power and detect a difference of 0.35 effect size in time to rescue analgesia in 24 24-hour postoperative periods between the two groups at the 5% level of significance, and with the use of G* power, a minimum of 21 patients per group were needed in each group.

IBM Corp., Armonk, NY, USA, provided SPSS, version 20.0, to analyze the collected data. The Shapiro-Wilk test was used to determine if the data distribution was normal. Depending on the data type, it was displayed as a percentage, mean ± SD, or median (range). Parametric data was analyzed using an unpaired t-test, nonparametric data was analyzed using the Mann-Whitney U test, and between-percentage data was analyzed using the $\chi 2$ test. It was determined that a *P*-value of less than 0.05 was statistically significant.

Results:

Eight instances were removed from the current study (five did not match the inclusion criteria, and three declined to participate), leaving 42 cases included. No patients were lost to follow-up. Twenty-one cases from group 1 (control group: bupivacaine only) and twenty-one cases from group 2 (bupivacaine plus Midazolam) were analyzed.

CONSORT 2010 Flow Diagram of patients and study design

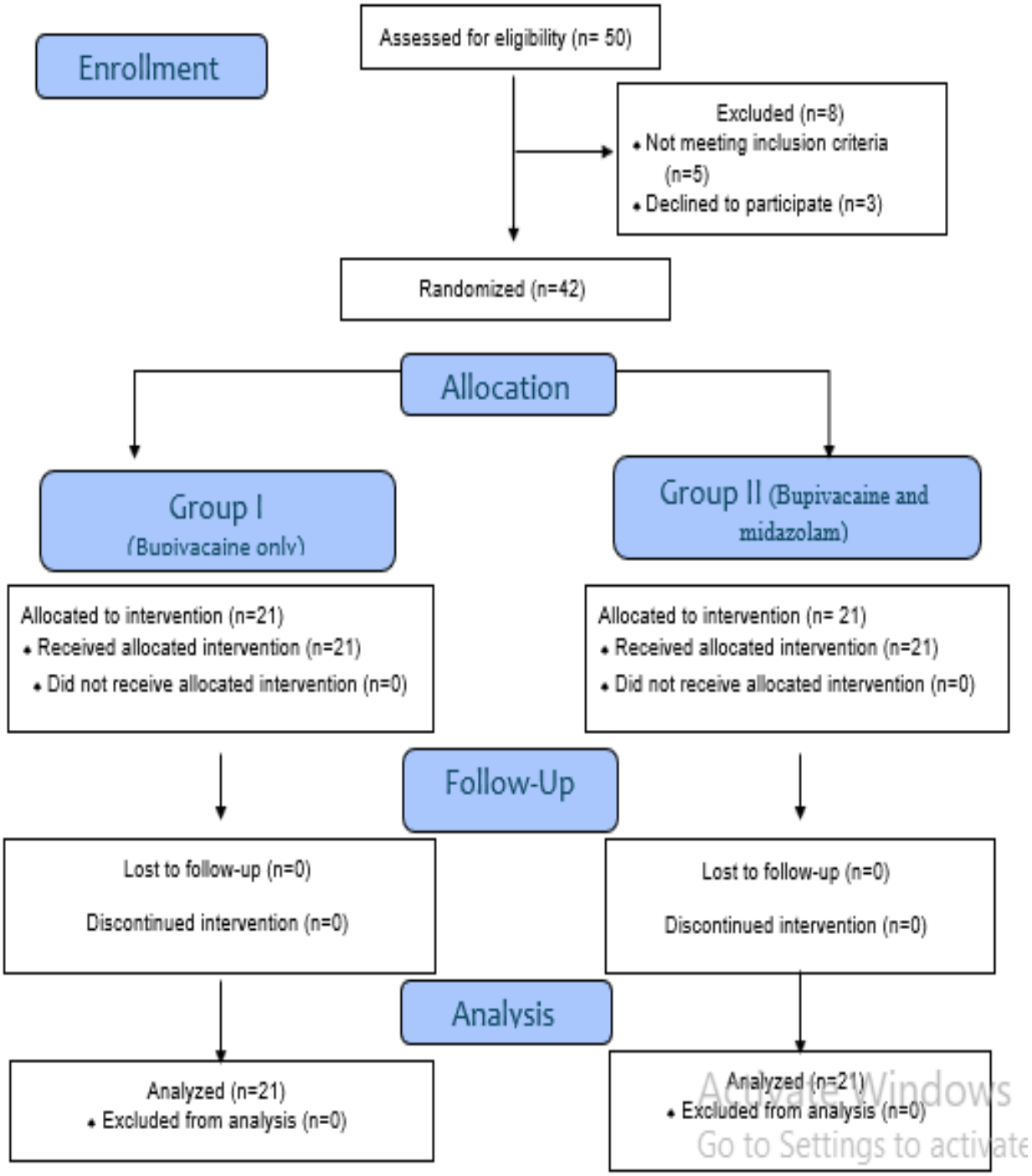
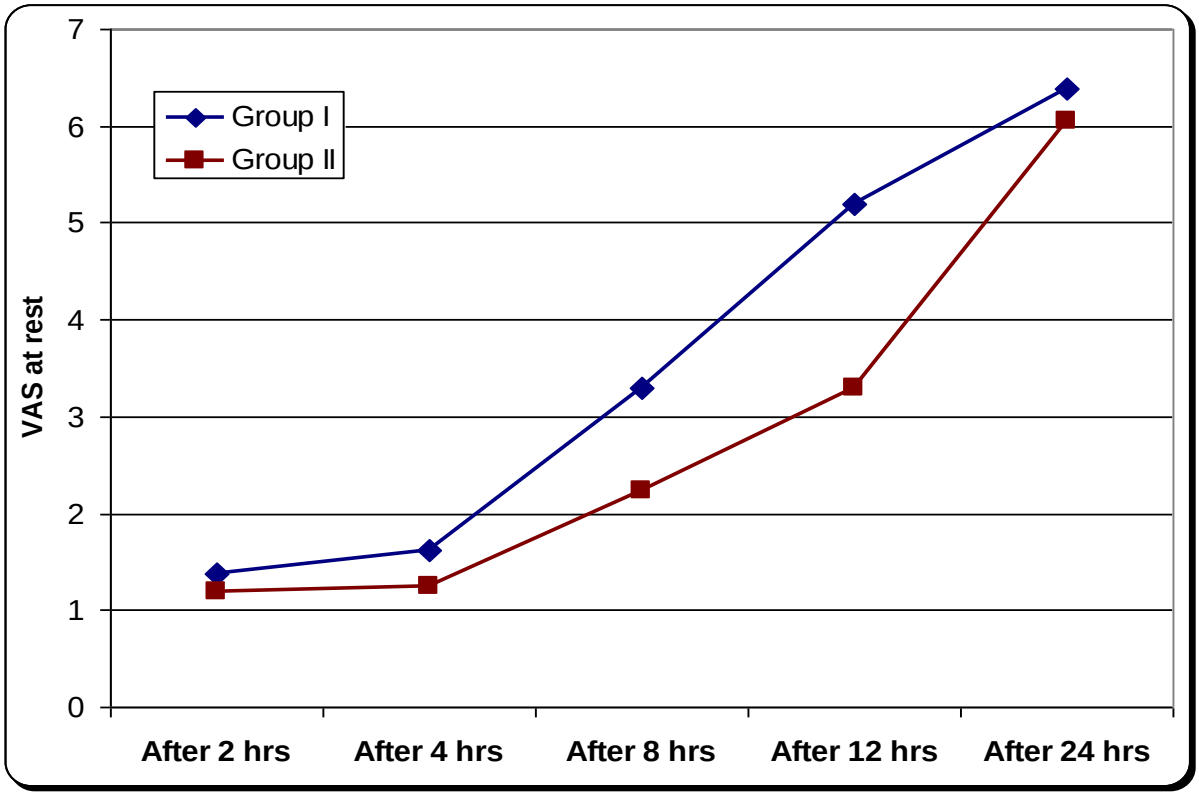


Table (1): Personal data of the studied groups

Personal data	Group I (n= 21)	Group II (n= 21)	P-value
Age: (years)			
Mean ± SD	27.76 ± 3.19	27.90 ± 2.68	0.876
Range	23.0-36.0	23.0-33.0	
Weight:			
Mean ± SD	78.48 ± 9.68	82.10 ± 7.63	0.186
Range	65.0-100.0	70.0-97.0	
Height:			
Mean ± SD	164.52 ± 5.90	163.57 ± 6.35	0.617
Range	155.0-175.0	155.0-175.0	
ASA:			
I	17 (81.0%)	15 (71.4%)	0.469
II	4 (19.0%)	6 (28.6%)	

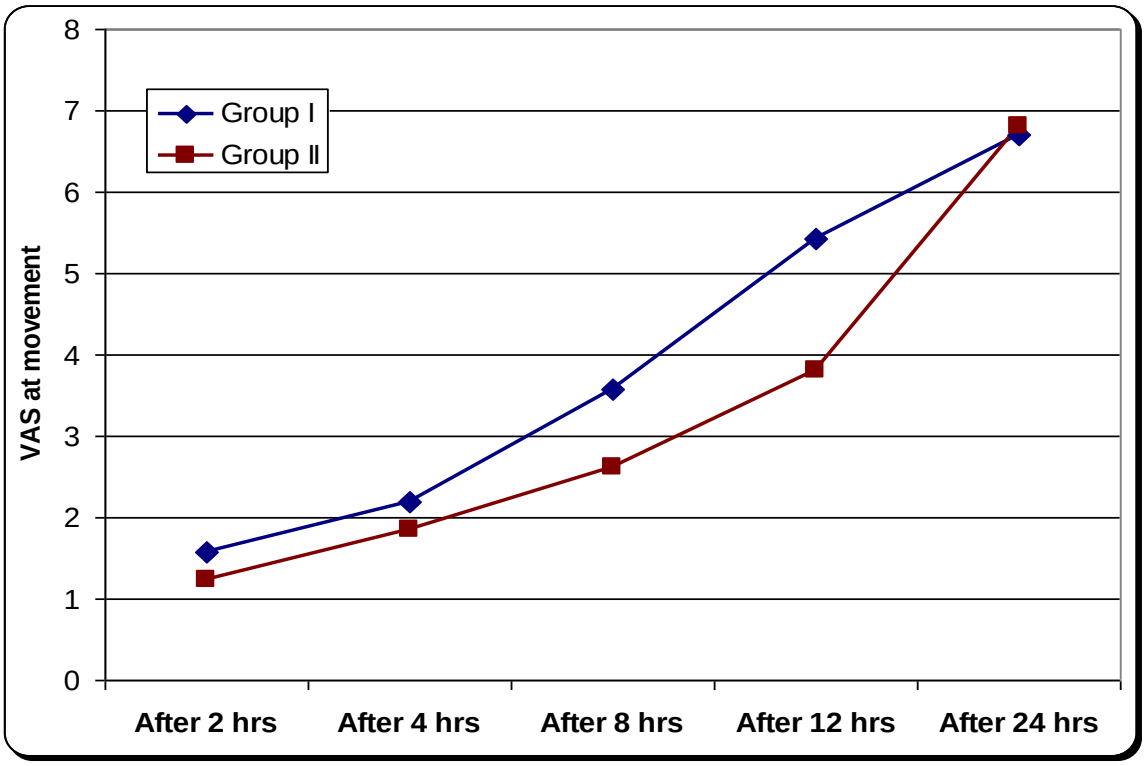
There's no significant difference between the two groups in age, height, and weight.

Figure (1): VAS score at rest



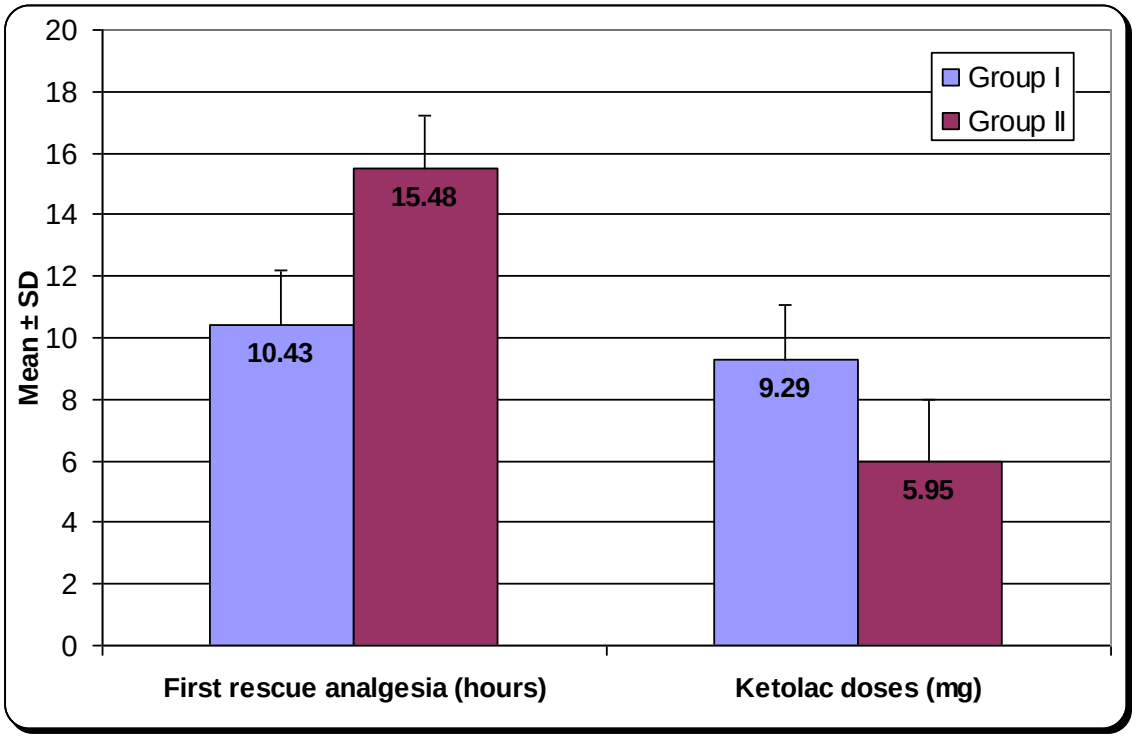
There's a significant difference between the control group (bupivacaine only) and the study group (bupivacaine and Midazolam) at pain during rest at 4,8,12, and there's no significant difference at 2 hr and after 24 hr.

Figure (2): VAS score at movement



There's a significant difference between the control group (bupivacaine only) and the study group (bupivacaine and Midazolam) at pain during rest at2,8,12, and there's no significant difference at 4 hr and after 24 hr.

Figure(3): First rescue analgesia and ketorolac doses



A highly significant difference exists between groups I and II at first rescue analgesia and ketorolac doses.

The first analgesic requirement was late in group II and early in group I. Doses of ketorolac are higher in group I than in group II.

Table (2): Sedation score
There's no significant difference between the two groups in sedation score

Sedation score	Group I (n= 21)	Group II (n= 21)	P-value
Mean ± SD	2.14 ± 1.28	2.24 ± 1.04	0.978
Median (Range)	2.0 (0.0-4.0)	2.0 (0.0-4.0)	

Discussion:

The quadratus lumborum block in the Cesarean section, our investigation demonstrated that the addition of Midazolam to bupivacaine resulted in much lower doses of ketorolac used (35.45 ± 11.8) mg, longer time for first rescue analgesia (15.48 ± 1.75) hr, and better VAS score in the first 12 hours during movement and during rest and better satisficed without significant side effects.

Zhao et al. (2021) [9] conducted a meta-analysis of randomized controlled trials to assess the effectiveness of Quadratus lumborum block and its various approaches for postoperative analgesia following cesarean surgery. The 13 randomized controlled studies involved 1269 patients, 632 of whom received QLB and 637 received systemic analgesia alone. This meta-analysis indicates that QLB can reduce the total intravenous morphine needed in the 24 and 48 hours after C.S. This study demonstrated that QLB reduced the incidence of complications, extended the time until the first analgesic was needed, and enhanced pain management at 2, 6, 12, 24, and 48 hours after surgery.

A randomized controlled experiment was conducted by **Ammar and Mahmoud (2012)[10]** to assess the impact of combining Midazolam with bupivacaine during rectus sheath block. In his trial, 50 patients were randomly assigned to one of two groups: one received 0.25% bupivacaine in 2 milliliters of saline (0.9%), while the other group received 0.25% bupivacaine plus 50 mic/kg of Midazolam in 2 milliliters of saline (0.9%). As demonstrated by a statistically significant reduction in morphine consumption in the postoperative 48 hours [11.2 (5.3–18.3) vs. 25.9 (15.2–31.0) mg, P = 0.002], a longer duration of analgesia, a lower VAS during the postoperative 48 hours, a lower incidence of postoperative nausea and vomiting PONV, pruritus, and somnolence, the study found that adding Midazolam to bupivacaine for Rectus Sheath block provided good analgesia **[10]**.

Esa et al. (2020)[11] described a case series of eight patients treated with a continuous local anesthetic infusion via bilateral posterior QL catheter infusion block for analgesia after abdominal surgeries. They found that the median opioid consumption over the first postoperative 72 h was 110 mg of morphine equivalents. The bilateral continuous posterior QL block is a feasible analgesic intervention.

Ahmad et al. (2024)[12] study showed that posterior quadratus lumborum versus caudal epidural block for perioperative an2algesia in pediatric patients undergoing upper abdominal surgeries.

Fifty-two pediatric patients scheduled for upper abdominal surgeries under general anesthesia were assigned randomly to undergo CEB or ultrasound-guided QLB 2. QLB type 2 can provide perioperative analgesia to pediatric patients; it provides more stable intraoperative hemodynamics[12].

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