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The Analgesic Effect of Ultrasound-Guided Quadratus Lumborum Block After Cesarean Delivery: A Randomized Clinical Trial

Anders Krohg, MD,* Kyrre Ullensvang, MD,* Leiv Arne Rosseland, PhD, MD,†‡ Eldrid Langesæter, PhD, MD,* and Axel R. Sauter, PhD, MD†§

BACKGROUND: Landmark and ultrasound-guided transversus abdominis plane blocks have demonstrated an opioid-sparing effect postoperatively after cesarean delivery. The more posterior quadratus lumborum (QL) might provide superior local anesthetic spread to the thoracolumbar fascia and paravertebral space. The aim of our study was to evaluate the efficacy of the QL block after cesarean delivery.

METHODS: A randomized, double-blind, controlled trial was performed. Forty parturients undergoing cesarean delivery received bilateral ultrasound-guided QL blocks with either 2 mg/mL ropivacaine or saline postoperatively. All patients received spinal anesthesia with bupivacaine and sufentanil and a postoperative analgesic regimen of paracetamol, ibuprofen, and ketobemidone administered by a patient-controlled analgesic pump. The ketobemidone consumption and time of each dose administered were recorded. The primary outcome was ketobemidone consumption during the first 24 hours postoperatively. Secondary and exploratory analyses compared repeated measures of pain scores, nausea, and fatigue, and total differences in time until patients were able to stand and able to walk 5 m, and the interaction between the effective analgesic score and time.

RESULTS: All 40 patients completed the trial, 20 in each group. The cumulative ketobemidone consumption in 24 hours was reduced in the active group compared with the control group ($P = .04$; ratio of means = 0.60; 95% confidence interval, 0.37–0.97). The effective analgesic scores were significantly better in the treatment group compared with the placebo group both at rest ($P < .01$) and during coughing ($P < .01$).

CONCLUSIONS: QL block with ropivacaine reduces the postoperative ketobemidone consumption and pain intensity as a part of a multimodal analgesic regimen that excludes neuraxial morphine. (Anesth Analg 2018;126:559–65)

KEY POINTS

- **Question:** Does quadratus lumborum block improve pain treatment after cesarean delivery?
- **Findings:** Opioid consumption in 24 hours was reduced, and the effective analgesic scores were significantly better in an active treatment group compared with the control group.
- **Meaning:** Quadratus lumborum block reduces the postoperative opioid consumption and pain intensity as a part of a multimodal analgesic regimen.

Pain treatment after cesarean delivery is important for early mobilization and to enable the mother to care for the newborn child.

Ultrasound (US)-guided transversus abdominis plane (TAP) blocks are now widely used for postoperative analgesia after surgery with incision in the inferior part of the abdominal wall.[1] However, standard TAP blocks provide inferior analgesia to neuraxial morphine and little benefit when added to a multimodal regimen that includes neuraxial morphine.[2] The quadratus lumborum (QL) block, an US-guided abdominal wall block, was presented by Raphael Blanco as an abstract at the annual European Society of Regional Anaesthesia (ESRA) congress in 2007. A similar technique was later published as transversalis fascia plane block by Hebbard.[3] In 2015, Blanco et al[2] introduced a modified QL block technique with an injection site at the posterior border of the QL muscle. Theoretically, QL blocks might give better and longer lasting analgesia compared to the US-guided anterior TAP block due to a spread

From the *Division of Emergencies and Critical Care, Department of Anesthesiology, Oslo University Hospital Rikshospitalet, Oslo, Norway; †Division of Emergencies and Critical Care, Department of Research and Development, Oslo University Hospital, Oslo, Norway; ‡Faculty of Medicine, Institute of Clinical Medicine, University of Oslo, Oslo, Norway; and §Department of Anesthesiology and Pain Medicine Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland.

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Address correspondence to Anders Krohg, MD, Division of Emergencies and Critical Care, Department of Anesthesiology, Oslo University Hospital Rikshospitalet, Sognsvannsveien 20, 0372, Oslo, Norway. Address e-mail to andkro@ous-hf.no.

to the thoracic paravertebral space and sympathetic nerves in the thoracolumbar fascia.

The aim of our study was to evaluate the postcesarean analgesic effect of the US-guided lateral QL block.[4] We tested the primary hypothesis that bilateral QL block with ropivacaine reduces cumulative ketobemidone consumption during the first 24 hours after QL block, when compared with bilateral placebo injection with saline. Secondary and exploratory analyses compared additional measures of analgesic quality and side effects between groups.

METHODS

Ethical approval for this study was provided by the Committee for Medical Research Ethics, Region South East, Oslo, Norway, on June 25, 2013 (Ethical Committee Number 2013/1293-1; Document-id: 392062). The study was registered with a clinical trial registry (ClinicalTrials.gov identifier: NCT02036749). Good Clinical Practice guidelines were followed. The trial was conducted and reported according to the Consolidating Standards of Reporting Trials (CONSORT) 2010 statement.[5] Study design was randomized, placebo-controlled, and double blind, with parallel-group comparison.

The study was conducted at the Department of Anesthesiology, Division of Emergency and Critical Care, Oslo University Hospital, Rikshospitalet, between March 2014 and April 2015. The study was funded by the Department of Anesthesiology. The Birth Clinic at Rikshospitalet is a tertiary care center, but the majority of the laboring women are healthy and reflect the general population in Southeast Norway. Forty healthy parturients scheduled for cesarean delivery via a Pfannenstiel incision gave written informed consent to participate in the study. Patients in American Society of Anesthesiologists classification II or stable American Society of Anesthesiologists III were included. Exclusion criteria were as follows: body mass index >32, chronic pain, neuropathy, age <18 or >45 years old, allergy to local anesthetic (LA), inadequate Norwegian language skills, or inability to operate a patient-controlled analgesia (PCA) pump.

All patients had spinal anesthesia with 10 mg of isobaric bupivacaine with 4 μg of sufentanil. Postoperatively both groups received a basic analgesic regimen of oral paracetamol 1 g and ibuprofen 400 mg, dosed together 4 times daily. A CADD-Legacy (Smith Medical MD, Inc, St Paul, MN) PCA pump with ketobemidone 1 mg/mL was programmed with a 1-mg demand dose, a lockout of 8 minutes, and a maximum dose of 7 mg/h. Patients were instructed to administer PCA boluses to achieve acceptable pain control not exceeding a pain level at rest of 3 on a numeric rating scale (NRS). Ketobemidone is regarded as equianalgesic to morphine.[6,7]

The QL blocks were performed in the postoperative care unit within the first hour after cesarean delivery, before the patients experienced any postoperative pain or pain during the QL block procedure. Routine monitoring included electrocardiogram, pulse oximetry, and noninvasive arterial blood pressure. Three consultant anesthesiologists experienced in US-guided regional anesthesia (A.K., K.U., and A.R.S.) performed the blocks.

QL Block Performance

A modified technique combining the techniques described by Blanco et al[2] and Hebbard[3] were used for the blocks. A

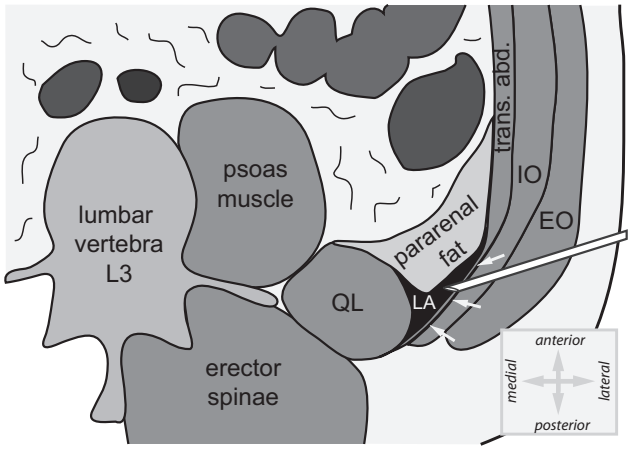

Figure 1. QL block technique: an injection needle is advanced in-plane under US guidance in anteroposterior direction through the muscle layers of the abdominal wall to the transversus aponeurosis (white arrows). The needle tip is positioned superficial to the pararenal fat and lateral to the border of the QL muscle. EO indicates external oblique muscle; IO, internal oblique muscle; trans. abd., transversus abdominis muscle; LA, local anesthetic; QL, quadratus lumborum.

SonoSite Edge ultrasound unit (SonoSite, Bothell, WA) with a HFL50, 6–15-MHz linear transducer was used. The patients were in the supine position. The side to be blocked was slightly elevated by pillows underneath the hip and shoulder. The transducer was placed in the transverse plane on the flank of the patient cranially to the iliac crest, at the level of the umbilicus (Supplemental Digital Content 1, Figure 1, http://links.lww.com/AA/C136). The muscle layers of the abdominal wall were identified. The transducer was then moved posteriorly to visualize the aponeurosis of the transversus abdominis muscle. The pararenal fat and the QL muscle were imaged medial to the aponeurosis (Figure 1). A Vygon Echoplex 21G 100-mm needle (Vygon SA, Ecouen, France) was advanced in-plane under US guidance in anteroposterior direction through the muscle layers of the abdominal wall. The needle tip was advanced to the transversus aponeurosis and positioned superficial to the pararenal fat and lateral to the border of the QL muscle. Two milliliters of the study medicine (ropivacaine 2 mg/mL or saline 9 mg/mL) were injected to verify the needle position. If necessary, the needle was repositioned. On each side, volume of 0.4 mL/kg study solution with a maximum of 30 mL was then injected under repeated aspiration for every fifth milliliter injected. Hence, for the bilateral procedures in the active group, a total amount of 1.6 mg/kg ropivacaine with a maximum of 120 mg was used.

The exact time of each ketobemidone bolus was recorded in the internal memory of the PCA pumps and extracted to a computer with CADD-Sentry Medication Delivery Manager software package (Smith Medical MD, Inc, St Paul, MN) The patients registered pain severity at rest and when coughing 2, 4, 6, 12, 24, and 48 hours after the QL block using NRS scales (0 = no pain, 10 = worst pain imaginable). Nausea and fatigue were also registered by the patients using NRS scales at the same time intervals. In addition, the patients registered the first time standing on their feet and when they walked 5 m.

Outcome Variables

The primary outcome was ketobemidone consumption during the first 24 hours after QL block. Secondary outcomes

were ketobemidone consumption during 12, 36, and 48 hours, pain intensity (PI) (NRS) scores, the integrated scores for pain, nausea, and fatigue, and time to mobilization. All other comparisons were exploratory.

Randomization and Blinding

Patients were randomly assigned to either QL block with ropivacaine 2 mg/mL (n = 20) or saline 9 mg/mL (placebo) (n = 20). A person not involved in the data collection or in patient care randomly assigned the patients in blocks of 8 or 6, into 2 groups of equal size using a list of random numbers,[8] according to the Moses–Oakford algorithm.[9] The block size (8 or 6) was also randomized using a list of random numbers. Block size and randomization codes were not revealed to the investigators until all measurements and calculations had been entered into the database for all patients. Each patient, the investigators, and all medical caregivers were blinded to group allocation.

One hour before the QL block procedure of an enrolled patient, a nurse, not otherwise participating in the study, opened a sealed opaque envelope containing group allocation. The nurse then filled 4 syringes (2 × 20 mL and 2 × 10 mL) labeled "study medicine" with the allocated solution, either ropivacaine 2 mg/mL or saline.

All data were entered in the database before entering the randomization codes. The principles for intention-to-treat analysis were followed.

Statistics

All the statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 22 (IBM Corp, Armonk, NY).

Histograms, box plots, Q-Q plots, and the Kolmogorov–Smirnov test were used to assess whether the variables and the residuals were normally distributed.

The primary hypothesis was that the main cumulative ketobemidone consumption after 24 hours (primary outcome variable) was less in the active treatment group compared with the control group. Data for this primary outcome variable ketobemidone consumption was estimated as log-normal distributed. Therefore *t* tests for independent samples were used with log-transformed data. The data are given as ratio of means and confidence intervals (CIs).

PI (NRS) and ketobemidone consumption were integrated in an effective analgesic score (EAS), both secondary outcomes of the study. EAS was calculated using the formula: (NRS + 1) × (1 − K/10), where K indicates doses (mg) of ketobemidone consumption 2 hours before registration time point of NRS.[10] The original formula has been modified as NRS + 1 replaces PI to avoid a zero product in case of NRS = 0. The modified EAS score represents an integration of both pain and analgesic consumption at every time point, even if pain score is zero.

Oxycodone was converted into ketobemidone equivalents and added to cumulative ketobemidone consumption (5 mg of short-acting oxycodone was considered equivalent to 3.3 mg of intravenous ketobemidone distributed over 4 consecutive hours; 10 mg of long-acting oxycodone was considered equivalent to 6.7 mg of intravenous ketobemidone distributed over 12 consecutive hours).

Cumulative consumption of ketobemidone at 24 hours was the primary end point of our study. Given statistically significant group difference in the primary end point (level of significance $P < .05$), analyses of secondary end points were performed. Differences in EAS at rest (EAS rest) and during coughing (EAS evoked) at 2, 4, 6, 12, 24, and 48 hours were analyzed in the 2 treatment groups. We used the linear mixed model in SPSS to test if the development of EAS over time differed between the 2 treatment groups; that is, an interaction effect (type III test of fixed effects, *F* test). Baseline (time point 2 hours after study drug injection) was used as reference point. Level of significance in the secondary outcome analyses was $P < .01$ to account for multiple comparisons. The residuals were checked for normality, and the assumption was found satisfied.

For nonparametrical data including NRS scores for fatigue and nausea (secondary outcomes), 2-sample Wilcoxon rank sum tests were used.

Sample Size

Sample size calculation was performed using SPSS SamplePower (IBM Corp, Armonk, NY). Our primary hypothesis was that opioid consumption after 24 hours was less in the active treatment group. We considered a 40% reduction in cumulative opioid consumption as clinically relevant. Based on previous studies on opioid consumption, a standard deviation (SD) of 40% was estimated. A sample size of 17 patients in each group would give 80% power to detect a 40% reduction in opioid consumption, using *t* tests with $\alpha = .05$. Estimating a mean cumulative ketobemidone consumption of 50 mg (SD, 20 mg), a reduction of 20 mg could be detected. Forty patients were included in the study to allow missing data or dropouts.

RESULTS

Sixty-one patients were considered eligible; of these 40 patients were randomly assigned and included in analysis (Figure 2). Baseline characteristics are shown in Table 1. The mean age showed a statistically significant difference of 2 years. Other baseline characteristics did not show significant differences. Three patients (1 in the active group and 2 in the control group) received oral oxycodone at 30, 32, and 33 hours, respectively, after the QL block.

Primary Outcome

Patients receiving the active QL block had lower cumulative ketobemidone consumption at 24 hours, compared with the control group ($P = .04$; ratio of means = 0.60; 95% CI, 0.37–0.97). Figure 3 shows the cumulative ketobemidone consumption per hour in both study groups.

Secondary Outcomes

At 12 hours, the cumulative ketobemidone consumption was significantly lower in the active group compared with the control group ($P < .01$; ratio of means = 0.52; 95% CI, 0.35–0.79). No statistically significant differences were found at 36 hours ($P = .13$; ratio of means = 0.71; 95% CI, 0.45–1.12) or at 48 hours ($P = .20$; ratio of means = 0.74; 95% CI, 0.47–1.18).

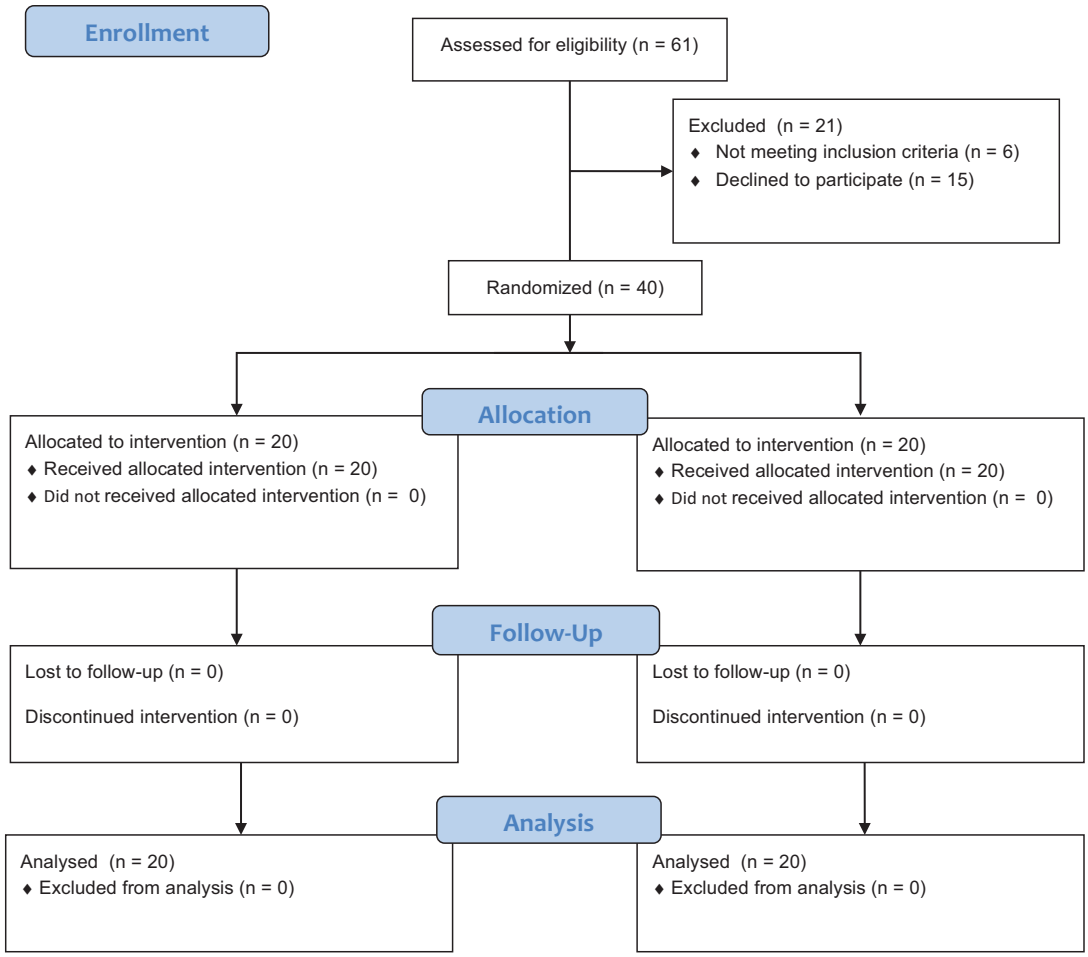

Figure 2. Study flowchart.

Table 1. Baseline Characteristics

Variable	Active Group	Control Group	*P*
Age (y)	34 ± 4	36 ± 4	.03
Weight (kg)	74 ± 7	79 ± 9	n.s.
Height (cm)	169 ± 5	168 ± 5	n.s.
ASA (1/2/3)	0/16/4	0/14/6	n.s.
BMI (kg/m^2)	26 ± 3	28 ± 3	n.s.
Total dose of study medicine (mg)	114 ± 8	114 ± 14	n.s.

Data are presented as mean ± SD and counts.
Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; n.s., not significant.

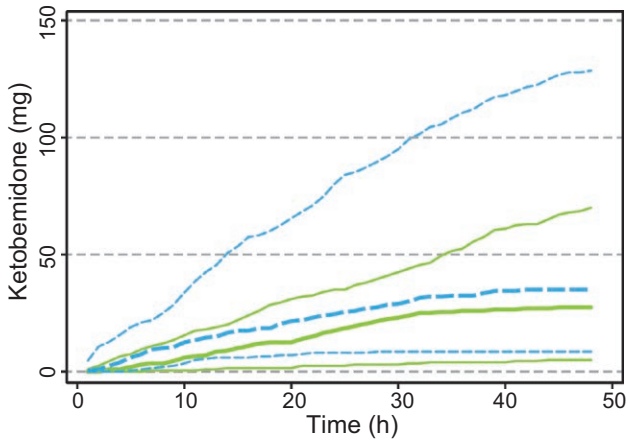

Figure 3. Cumulative ketobemidone consumption (mg) per hour for the patients treated with QL block (thick green line) with 95% percentiles (thin green lines) and for the patients in the control group (dashed blue thick line) with 95% percentiles (dashed blue thin lines). QL indicates quadratus lumborum.

The analyses of the interactions between time (0–48 hours) and treatment showed statistically significant group differences in PI at rest ($P < .01$) and when the patients were coughing ($P < .01$) (Figure 4A, B). The interactions between time (0–48 hours) and treatment analyses showed statistically significant differences in EAS at rest ($P < .01$) and when the patients were coughing ($P < .01$) (Figure 4C, D). The PI at rest and during coughing and the estimated analgesic score at rest and during coughing are presented in Table 2 (mean difference and 95% CI).

The patients' experience of fatigue was similar in both groups. Median NRS scores for nausea were 0 at all measurement time points in both groups, and no significant difference could be found (Supplemental Digital Content 2, Table 1, http://links.lww.com/AA/C137).

Patients in the active group were able to stand 14.5 hours (SD, 1.6) after QL block, while patients in the control group were able to stand after 13.5 hours (SD, 1.5) ($P = .66$; difference

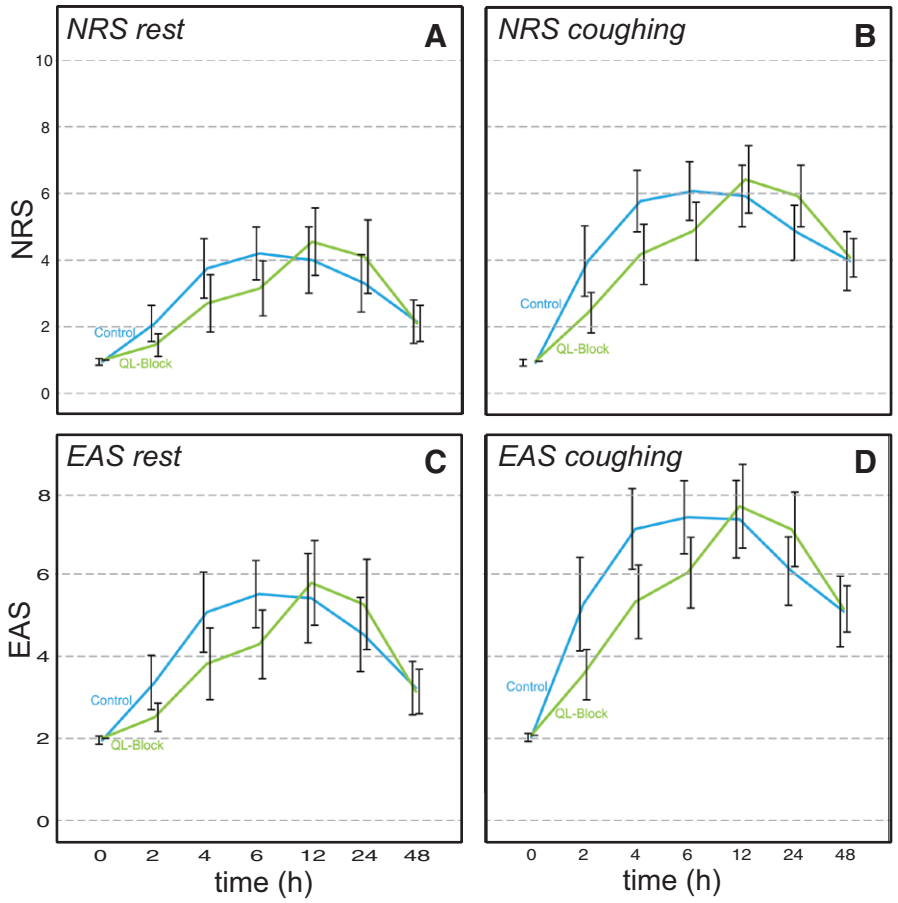

Figure 4. Pain intensity (NRS, 0–10) at rest (A) and during coughing (B) presented as mean (± 2 SEM), and EAS (= [NRS + 1] × [1 + K/10], where K = mg of ketobemidone the 2 h before registration) at rest (C) and during coughing (D) presented as mean (± 2 SEM). EAS indicates estimated analgesic score; NRS, numeric rating scale.

of mean = −1.00; 95% CI, −5.48 to 3.49). In the active group, patients were walking at least 5 m after 19.1 hours (SD, 1.8), while patients in the control group were walking 5 m or more after 17.2 hours (SD, 1.8) (P = .44; difference of mean = −1.97; 95% CI, −7.13 to 3.18).

There were no complications or adverse events.

DISCUSSION

Our randomized controlled trial demonstrated a 41% opioid-sparing effect of the QL block during the first 24 hours postoperatively after cesarean delivery, when administered with multimodal analgesia in the absence of neuraxial morphine.

In 2008, McDonnell et al[11] described the TAP block to anesthetize the lower anterior abdominal wall after cesarean delivery. Patients receiving active TAP blocks had a morphine-sparing effect of 70% compared to the control group. The LA doses used by McDonnell et al[11] were 150 mg of ropivacaine, compared to the maximum dose of 60 mg each side in our study. A higher dose of LA may increase the efficacy and/or the duration of the QL block and may also produce high serum concentrations of local anesthetic, leading to both a systemic analgesic effect[12] and risk for systemic side effects and toxicity.[13]

In systematic review published by Abdallah et al[1] in 2012, only 3 of 6 randomized controlled studies showed a reduction of morphine consumption when therapeutic TAP block is performed after cesarean delivery. In 2016, Champaneria et al[14] published a meta-analysis of 20 studies that confirmed TAP blocks can be effective for acute pain relive after cesarean delivery. However, TAP blocks did not confer additional analgesia when intrathecal hydrophilic opioids were used.

Blanco et al[2] published the first study investigating the analgesic effect of QL block after cesarean delivery, in which 0.2 mL/kg 0.125% bupivacaine was injected on the posterolateral border of the QL muscle. A significant reduction in the morphine consumption and visual analogue scores scores was found during 48 hours after QL block administration.[2] In a second trial, this group compared QL block with TAP block and found a significantly superior effect of the QL block lasting from 6 to 48 hours.[15]

Two theories explain why injection at the posterolateral border of the QL muscle may achieve superior pain relief when compared with standard anterior TAP blocks. First, the QL block may facilitate spread of LA into the paravertebral space, theoretically prolonging the block and achieving visceral pain relief. Alternatively, Blanco et al[2] posit that LA spread to a network of sympathetic nerves in the thoracolumbar fascia can explain the long-lasting analgesic effect.[15]

During pilot studies, our group of anesthetists was unable to consistently establish sensory blockades when injecting LA at the posterior border of the QL muscle. The QL block technique that was used in our study (Figure 1) is similar to the methods originally described by Raphael Blanco as an abstract at the annual ESRA congress in 2007 and the "fascia transversalis sheath block" published by Hebbard.[3] When

Table 2. Pain Intensity and Estimated Analgesic Scores

Time (h)	Mean Difference (Control – Ropivacaine)	99% CI
Pain intensity (NRS) at rest (h)		
2	0.65	−0.30 to 1.61
4	1.05	−0.81 to 2.91
6	1.05	−0.66 to 2.76
12	−0.55	−2.67 to 1.58
24	−0.80	−2.90 to 1.30
48	0.05	−1.22 to 1.32
Pain intensity (NRS) during coughing (evoked pain) (h)		
2	1.55	−0.28 to 3.38
4	1.60	−0.34 to 3.54
6	1.20	−0.66 to 3.06
12	−0.50	−2.55 to 1.55
24	−1.10	−2.96 to 0.76
48	−0.10	−1.68 to 1.48
EAS at rest (h)		
2	0.85	−0.27 to 1.97
4	1.26	−0.70 to 3.22
6	1.23	−0.54 to 2.99
12	−0.38	−2.63 to 1.88
24	−0.74	−2.87 to 1.40
48	0.85	−1.19 to 1.36
EAS during coughing (evoked) (h)		
2	1.75	−0.23 to 3.72
4	1.81	−0.22 to 3.84
6	1.38	−0.52 to 3.27
12	−0.33	−2.45 to 1.80
24	−1.04	−2.92 to 0.85
48	−0.65	−1.64 to 1.51

The table presents the results of the linear mixed-model analyses of pain intensity measured as NRS 0–10 and the integrated pain intensity + analgesic consumption variable EAS. Pairwise comparisons are presented as group differences, 99% CI.

Abbreviations: CI, confidence interval; EAS, estimated analgesic score; NRS, numeric rating scale.

injecting between the transversus aponeurosis and the pararenal fat lateral to the QL muscle, a slow reabsorption of LA may lead to prolonged analgesic effect of a single injection.

In contrast to Hebbard,[3] we did not try to identify the very thin fascia transversalis medially to the transversus aponeurosis by US. We therefore do not know if the LA was injected medial or lateral to the fascia transversalis. When dissecting the abdominal wall in cadavers, the anterior abdominal branches of L1 could be found within the fascia transversalis on the medial side of the transversus aponeurosis (unpublished data). When the aponeurosis turns into the transversus abdominis muscle, the nerves regularly enter the TAP plane (unpublished results). We expect that LA injected medial to the aponeurosis can reach the nerves from either side of the thin fascia transversalis layer.

We did not find a clinically relevant opioid-sparing effect of the QL block in the 24–48-hour period. Catheter-based QL blocks might prolong the analgesic effect.

Compared with the control group, the patients with QL block had a nonsignificant trend toward a delay in ambulation. Theoretically, a spread to the lumbar plexus can cause weakness of the psoas, iliacus, and quadriceps muscles as described in a case report by Wikner.[16] However, no obvious effects of a lumbar plexus block have been observed in our patients.

Limitations

US-guided needle placement is an operator-dependent technique. In our study, we wanted to ensure correct placements by having a second investigator confirm the correct needle placement as imaged by US. We did not assess block success by sensory testing in our study. The lack of a sensory test was chosen to preserve blinding of group allocation. The optimal dose of LA for QL blocks is not known, and our study cannot provide information on the adequate dose. A higher dose of ropivacaine may have improved and prolonged the analgesic effect. We excluded patients with body mass index >32 to ensure homogeneous patient groups. We therefore do not know if QL blocks are as effective in obese patients.

Postoperative ibuprofen and paracetamol were administered in addition to PCA ketobemidone. Despite this multimodal analgesic regime, which may have obscured some of the effects of the QL blockade, the study was adequately powered to identify an opioid-sparing effect in the first 24 hours. Patients were instructed to use their PCA pumps to achieve a NRS at 3 or less. This instruction may limit the value of examining the difference in PI between the groups. However, patient-reported PI was lower in the first 12 hours in the active group, and the analyses of EAS—integrating PI and PCA opioid consumption—supported the observation of clinically and statistically significant group differences.

The assessment of PI and analgesic consumption in clinical pain trials is challenging. The introduction of an estimated analgesic score enables the researchers to present a combined outcome measure of improved validity. Presenting PI, analgesic consumption, and the integration of both is informative, but the analyses of potential differences in treatment effects are still challenging and represent a limiting factor.

The study included pregnant women scheduled for planned cesarean delivery under standard anesthesia, and the postcesarean pain treatment was only slightly modified compared to the standard practice in the department. The sample is representative for the population at our birth clinic, and a majority of the screened patients were eligible for participation. However, generalizability is limited to those institutions and clinical contexts in which neuraxial morphine is not available.

CONCLUSIONS

Ropivacaine US-guided QL block reduced postoperative ketobemidone consumption and pain after cesarean delivery. The patients received small doses of ropivacaine, and further trials must be conducted to evaluate the ideal dose, volume, and injection site. Future studies should compare the analgesic efficacy with a multimodal regimen that includes neuraxial morphine; analgesic outcomes of QL block and more traditional US-guided TAP block should be directly compared.

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DISCLOSURES

Name: Anders Krohg, MD.
Contribution: This author helped design and conduct the study; collect, analyze, and interpret the data; and write the manuscript.
Conflicts of Interest: None.
Name: Kyrre Ullensvang, MD.
Contribution: This author helped design and conduct the study; interpret the data; and write the manuscript.
Conflicts of Interest: None.
Name: Leiv Arne Rosseland, PhD, MD.
Contribution: This author helped design the study; analyze and interpret the data; and write the manuscript.
Conflicts of Interest: None.
Name: Eldrid Langesæter, PhD, MD.
Contribution: This author helped design the study, interpret the data, and write the manuscript.
Conflicts of Interest: None.
Name: Axel R. Sauter, PhD, MD.
Contribution: This author helped design and conduct the study; collect, analyze, and interpret the data; and write the manuscript.
Conflicts of Interest: A. R. Sauter has advised B. Braun concerning regional anesthesia. He served as a consultant for Philips and received compensation for these services. He has received speaker fees by Siemens.
This manuscript was handled by: Jill M. Mhyre, MD.

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