

Original Article

Posterior quadratus lumborum block (QLB2): 0.2ml/kg vs 0.4ml/kg of 0.25% levobupivacaine in pediatric laparoscopic abdominal surgery. A comparative study

Aamir Abdullah Khadaied¹, Shereen Tang Suet Ping², Raha Abdul Rahman¹, Azarinah Izaham¹, Maryam Budiman¹, Rufinah Teo¹.

¹Department of Anesthesiology & Intensive Care, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia.

²Department of Surgery, Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman, Kuala Lumpur, Malaysia.

Corresponding author: Rufinah Teo, Department of Anesthesiology and Intensive Care, Universiti Kebangsaan Malaysia Medical Centre, 56000 Cheras, Kuala Lumpur, Malaysia. Email: rufinah@ppukm.ukm.edu.my

Keypoints

- 1) The quadratus lumborum block (QLB), which was developed from the established transversus abdominis plane (TAP) block is increasingly in favor due to its longer duration of action and wider distribution of local anesthetics (LA) when compared to TAP block.
- 2) The general recommended volumes of local anesthetics LA described were mostly based on studies in the adult population and data obtained from the pediatric patients have been limited.
- 3) This study will provide some preliminary insights on the minimum effective dose of LAs required for the QLB in laparoscopic surgeries.

Abstract

Introduction

The Quadratus Lumborum Block (QLB) which is a truncal plane block, is increasing in favor as part of multimodal analgesia for abdominal surgeries due to its analgesic effect which gives a good coverage for visceral pain as compared to oral and intravenous analgesics. The QLB being a plane block, depends on volume of local anesthetic (LA) for its efficacy. However, to date there are no consensus for the lowest effective volume of LA for the QLB in both adult and pediatric groups. The pediatric age group particularly are sensitive to small changes in drug doses, which is more important to ascertain the lowest effective volume. Hence, we conducted a prospective, randomized, double blinded study to compare the effects of two volumes of LA in the QLB in pediatric patients undergoing laparoscopic abdominal surgeries.

Material and Methods

A total of 52 American Society of Anesthesiologist physical status I or II patients, aged 1-12 years old were recruited and randomized into two groups, A & B. A standard general anesthesia protocol was conducted. Group A patients received 0.2 ml/kg of levobupivacaine 0.25% and Group B patients received 0.4 ml/kg of levobupivacaine 0.25% for the QLB2 that was done. Postoperatively patients were reviewed for FLACC and VAS pain scores and side effects up to 24 hours.

Results

The result showed that Group A was non-inferior compared to Group B in mean difference of pain scores, pain score severity (p value of 1.000), mean pain scores across 24-hour time line, requirement of rescue analgesia (p value of 0.569) and patients' parents' satisfaction scores (p value of 0.664).

Discussion and Conclusion

In conclusion, a volume of 0.2 ml/kg which is further away from the LA toxic dose, was proven to be non-inferior to 0.4 ml/kg of levobupivacaine for QLB2 done in pediatric laparoscopic abdominal surgeries. However larger and multi-centered studies, employing different types of surgeries and possibly lower volumes of LA need to be done to further ascertain the lowest effective volume for the QLB in pediatric surgery.

Keywords

pediatrics, anaesthetics, local anesthetics, levobupivacaine, laparoscopy, minimally invasive surgical procedures

Introduction

Pain after laparoscopic surgery is due to rapid distension of peritoneum, visceral manipulation, irritation and traction of vessels and phrenic nerves, presence of residual gas and inflammatory mediators.^{1,2} A study by Koivusalo et al in 2015 concluded that the median pain score in pediatric laparoscopic hernia repair was significantly higher than its open procedure counterpart.^{3,4}

Quadratus lumborum block (QLB) which was first described by Blanco in 2007, is one of the ultrasound guided truncal blocks that was recently discovered and developed to be part of multimodal analgesia technique in adult abdominal surgeries.⁵

Developed from the established transversus abdominis plane block (TAPB), the QLB aims to infiltrate LA beyond the distribution of what the TAPB can achieve, reaching deep into the paravertebral space.^{6,7} The analgesic effect of QLB is longer, up to 48 hours compared to TAPB, due to the spread of the block which infiltrates the thoracolumbar fascia, reaching the paravertebral space and is superior compared to TAPB.^{7,8} The QLB have a few approaches and nomenclatures, the QLB1 (lateral QLB) which is given at the anterolateral border of the quadratus lumborum muscle, QLB2 (posterior QLB) which is given at the posterior aspect of the muscle, QLB3 (trans-muscular or anterior QLB) which is given at the anterior aspect of the muscle, and intramuscular

Khadaied et al. Posterior quadratus lumborum block

QLB (IQLB) which is given in the quadratus lumborum (QL) muscle itself.⁶⁻¹⁰

Amongst the various types of QLB, QLB1 has an analgesic spread similar to that of QLB2, covering the dermatome levels T7 to L1.¹⁰ As the lateral border of the quadratus lumborum muscle occurs at the point where the internal oblique and transversus abdominis muscles taper off, QLB1 is technically easiest among all QLB as it is most superficial and anterior in its approach.¹¹ However, QLB2 and QLB3 have potentially wider paravertebral levels spread due to its more posterior approach. This may explain why the QLB1 has fallen out of favor in the recent time.¹¹

Preference for QLB2 were attributable to higher success rates in the pediatric population due to its accessibility in both the supine and lateral positions using the linear ultrasound probe, a more superficial point of injection that confers better ultrasound image resolution and a predictable spread of local anesthetics. Furthermore, the needle tip is separated from the peritoneum by the quadratus lumborum muscle, hence reducing the risk of intraperitoneal injection and bowel injury.⁶⁻⁸ Furthermore, it also results in lower plasma levels of local anesthetic when compared to TAPB. This is thought to be due to the spread of LA into the paravertebral space which is filled with adipose tissue that has low tissue perfusion.^{8,12}

The QLB which was first described about 13 years ago, had only gained increasingly popular in the pediatric population in about 7 years ago. The first to describe the use of QLB in the paediatric population was Visoiu and Yakovleva in a case report in 2013, where they used a unilateral quadratus lumborum catheter for analgesia following colostomy closure, as an alternative for TAPB which is usually suboptimal. They concluded that the quadratus lumborum block provided adequate analgesia outcome, which is low pain scores and minimal use of rescue analgesia.¹³

Subsequently, more studies were done involving the pediatric population, describing the efficacy of QLB. Cakraborty et al in 2015 reported a case of continuous

QLB for postoperative analgesia in a pediatric patient undergoing left radical nephrectomy for Wilms tumor. The result was excellent postoperative analgesia and minimal requirement for rescue analgesics.¹⁴ Baidya et al in the same year described that QLB provided very good postoperative analgesia in children undergoing lumpectomy and pyeloplasty.¹⁵ In an RCT done by Oksuz et al in 2017 which compared TAPB and QLB in children undergoing lower abdominal surgeries, they concluded that QLB provided longer and more effective postoperative analgesia compared to TAPB.⁸ And the latest, Hussein in 2018 compared QLB3 and IQLB, and concluded that patients in the QLB3 group required less rescue analgesia, had lower pain scores and more stable hemodynamics compared to patients in the IQLB group.¹⁶

The QLB is a plane block which depends on the volume of LA to determine the block distribution. Generally, the recommended volumes of LA described in literatures are between 0.2 ml/kg to 0.4 ml/kg, 10, 11, 16 which are mostly based on studies done in adults. In the pediatric population, this general recommendation is adopted. However, Oksuz et al and Baidya et al used 0.5 ml/kg of 0.2% ropivacaine and levobupivacaine in their studies respectively.^{8, 15} There is minimal understanding regarding the lowest effective volume of LA in the pediatric population, hence the vast difference in practices, and to date, there are no consensus as to the volumes which are recommended for the block. By utilizing QLB to provide improved quality of analgesia, this study is designed to compare the lowest effective volumes of local anesthetic in QLB for pediatric laparoscopic surgeries.

Material and methods

This prospective, randomized, double-blinded study was conducted in the general operation theatre, following approval from the Research Committee of the Department of Anesthesiology & Intensive Care, and the Medical Research and Ethics Committee, UKMMC (Research code: FF-2019-204). This study was conducted by a single operator, who performed at least ten QLB2 supervised by an anesthetist prior to data collection. The patient and

anesthetic doctors in charge of the operation theatre were blinded in this study.

A total of 52 patients aged 1 – 12 years old, American Society of Anesthesiologist (ASA) physical status I or II scheduled for laparoscopic abdominal surgery under general anesthesia were recruited in this study. Patients with known allergy to LA and contraindications to block performance were excluded.

Following written informed consent, patients were randomized into two groups using computer generated random numbers. All patients received bilateral QLB2 with different volumes, where Group A received 0.2 ml/kg and Group B 0.4 ml/kg of 0.25% levobupivacaine.

Patients were fasted for at least six hours prior to surgery. No premedication was given to the patients. The LA used for the study was prepared by the investigator. Baseline vital signs of at least oxygen saturation (SpO₂), heart rate (HR) and non-invasive blood pressure (NIBP) was recorded. If the patient had an intravenous (IV) cannula, induction was performed using 1 mcg/kg fentanyl and 3 mg/kg propofol. If the patient did not have an IV cannula, general anesthesia was induced with a face mask primed with 8% sevoflurane and 100% oxygen. An appropriately chosen size IV cannula was set and 1 mcg/kg of fentanyl was given. An appropriately chosen size ProSeal™ laryngeal mask airway (Intavent-Orthofix, Maidenhead, United Kingdom) based on body weight was inserted for all patients.

The block was done under aseptic technique, in lateral position with the side intended to block side up. A high frequency (6 – 14 MHz) ultrasound (Mindray DC-70, Shenzhen, China) linear probe covered in sterile sheath was placed anterior and superior to the iliac crest. (Figure 1). The three anterior abdominal muscles were visualized. The external oblique muscle was followed posterolaterally until its posterior border was identified. Subsequently, the probe was tilted towards the attachment site of both the internal and external oblique muscles over the quadratus QL muscle until the midline of the thoracolumbar fascia was seen as a bright hyperechogenic line,

located between the posterior border of the quadratus lumborum muscle and the middle thoracolumbar fascia (anterior to latissimus dorsi and erector spinae muscles) (Figure. 2). A 22-gauge Facet-tip SonoPlex needle of appropriate length estimated from the depth and length of required needle trajectory during scout scanning (Pajunk®, Geisingen, Germany) was inserted via in-plane technique. The needle was directed from anterolateral to posteromedial after making a negative aspiration test with aliquots of 0.5 ml saline to confirm hydrodissection in the lumbar interfascial triangle (LIFT) between the QL muscle and middle thoracolumbar fascia. An injection of LA was given according to the group allocated. Aliquots of LA with intermittent aspiration during injection was performed in the desired confirmed space as per group allocation.

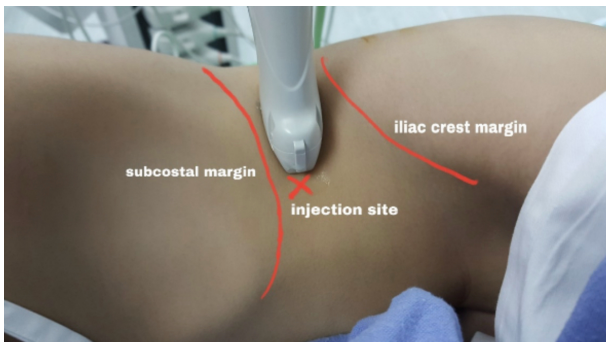


Figure. 1: Surface anatomy (anterior view) for QL.

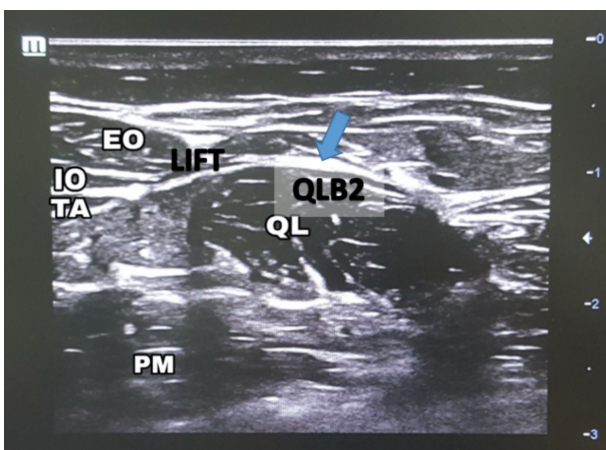


Figure. 2: Sonoanatomy of QL B2.

EO, external oblique; *IO*, internal oblique; *TA*, transversus abdominis; *QL*, quadratus lumborum; *QLB2*, quadratus lumborum block 2; *PM*, psoas muscle; *LIFT*, lumbar interfascial triangle.

Surgery was commenced following the completion of the block. Hemodynamic parameters (NIBP, HR, SpO₂) was monitored and recorded at; pre-induction (T0), pre-block (T1) and at 5-minute intervals (T5, T10, T15 until T60) subsequently until end of surgery. All patients received suppository paracetamol 30mg/kg (maximum of 1 gram in total) before surgery started. Anesthesia was maintained with Sevoflurane 2% with 50:50 oxygen air mixture to achieve minimum alveolar concentration of 1.0. Patient was kept hydrated during surgery with IV fluids which accounts for the pre-operative deficit and maintenance. Pneumoperitoneum in laparoscopic procedure was achieved by carbon dioxide insufflation with intra-abdominal pressure of <14mmHg. Complete exsufflation of surgical pneumoperitoneum was done prior to standard emergence and extubation of the patient.

Assessment of pain was done using FLACC (Face, Legs, Activity, Cry, Consolability) score for children aged up to 7 years old and numerical rating scale (NRS) in older children by the anesthetic trainee in-charge of the post anesthetic care unit. The assessment was conducted upon arrival and at 30 minutes in the recovery (P0). Patients with pain scores of more than 4 were given rescue therapy with fentanyl up to 2 mcg/kg. Patients were discharged to the wards when their pain score was less than 4 and have a modified Bromage score of 0 (0 = free movement of leg and feet with the ability to raise extended leg; 1 = inability to raise extended leg and knee flexion decreased; 2 = inability to raise or flex knees; 3 = inability to raise leg, flex knee or ankle, move toes). Any lower limb weakness was recorded including the dermatome level, sides either unilateral or bilateral and duration of the weakness was also noted. The FLACC and NRS scores were taught to the patients' parents and a follow-up call was done to attain pain scores at the given intervals for daycare patients and inpatients who were discharged less than 24 hours.

In the ward, the FLACC or NRS as appropriate was used to assess postoperative pain at 1, 4, 8, 12 and 24 hours (P1, P4, P8, P12, P24) by Acute Pain Service team. Oral suspension of paracetamol 15mg/kg was given to patients

with a score of greater than 4 for both scores, on a per needed basis, and regular doses up to four times daily as per recommended dose for weight were given, not exceeding maximum dose of 1g/dose or 4 g/day. Parents' satisfaction with the perioperative analgesic regime was assessed using a Likert scale from 1 to 5 (1 = very satisfied; 2 = satisfied; 3 = neutral; 4 = dissatisfied; 5 = very dissatisfied) at the end of 24 hours post-operatively. Ability to sleep well overnight was also assessed as part of the post-operative parameter using a dichotomous 'Yes' or 'No' response on post-operative nights day 1. Other adverse effects such as allergic reaction, inflammation or signs of infection over the injection site(s), and the uncommon signs of dysrhythmias, agitation, restlessness, muscle twitching, seizures and unconsciousness was also noted if any occurred.

Sample size was calculated with pain as primary endpoint using FLACC scale and VAS scale. Assuming one-sided type I error rate 2.5% and 80% power, the standard deviation is anticipated to be 3 and true mean difference between the treatments is thought to be zero.¹⁷ Therefore, 23 subjects per group were needed for this study with non-inferiority limit (dNI) of 2.5, power of 80% and an estimated 10% dropout rate.

All data were analyzed using SPSS version 25 (IBM Corp, New York, USA) and Dr. Daniel Soper's online Calculator for Effect Size (Cohen's d) for a Student t-Test (<https://www.danielsoper.com/statcalc/calculator.aspx?id=48>). Independent t-test was used for continuous data as appropriate. The qualitative data were analyzed using Chi-square test. Pearson Chi-square and Fisher's Exact Test were used to determine correlation between variables. A P value of < 0.05 was considered as statistically significant. The non-inferiority limit set during sample size calculation was 2.5, where a difference of 2 – 3 in pain scores is deemed clinically significant. Thus, a mean difference of < 2.5 between the two groups would mean non-inferiority between the treatment groups. Effect size of ≤ 0.2 is considered as small effect size, 0.5 – 0.7 is considered as medium effect size, and ≥ 0.8 is considered

as large effect size. This means that if two groups' means do not differ by 0.2 standard deviations or more, the difference is trivial, even if it is statistically significant.

Results

A total of 52 patients were recruited and no patients were dropped out in this study. The demographic characteristic of the patients, type of surgery and duration of surgery were presented in Table 1. There was no statistically significant difference between the two groups.

	Group A (n = 26)	Group B (n = 26)	P value
Age (years)**	3.00 (1.75 – 4.00)	3.00 (2.00 – 4.00)	0.402
Gender			
Male	18 [34.60]	19 [36.50]	1.000
Female	8 [15.40]	7 [13.50]	
ASA			
I	24 [46.20]	21 [40.20]	0.419
II	2 [3.80]	5 [9.6]	
Weight (kg)**	11.00 (10.00 – 15.25)	12.00 (10.00 – 16.00)	0.573
Hernia Repair			
Unilateral	23 [44.20]	18 [34.60]	0.140
Bilateral	2 [3.80]	7 [13.50]	
Others	1 [1.90]	1 [1.90]	
Volume of LA (ml)***			
1 – 10 kg	3.70±0.414	7.82±0.352	0.000
10.1 – 20 kg	5.22±1.063	11.01±1.763	0.000
20.1 – 30 kg	10.00±1.050	17.60±0.000	0.002
>30 kg	-	32.00±7.919	-
Duration of anesthesia (minutes)**	40.00 (35.00 – 40.00)	40.00 (35.00 – 40.00)	0.984

Table 1. Demographic data, type of surgery, duration of surgery and mean volume of LA given according to weight. Values were expressed as median (IQR), numbers [percentages], and mean±SD where appropriate. *P < 0.05 is considered as statistically significant. Variables marked with ** are represented as median (IQR). Variables marked with *** are represented as mean±SD.

In this study, the mean difference of pain scores from t-Test for equality of means and effect size (Cohen's d) was used to prove non-inferiority of 0.2 ml/kg as compared to 0.4 ml/kg in each time interval where pain is assessed (as in Table 2).

Time Interval (hours)	Mean ± SD and (95% CI)		Mean Difference	Effect Size (Cohen's d)
	Group A (n=26)	Group B (n=26)		
P ₀	0.70±0.827 (0.389-0.543)	0.65±0.846 (0.389-0.543)	0.770	0.095
P ₁	1.00±0.800 (0.661-0.353)	1.15±1.008 (0.661-0.354)	-0.154	0.164
P ₄	1.15±0.925 (0.645-0.491)	1.23±1.107 (0.645-0.492)	-0.077	0.078
P ₈	1.58±1.301 (0.895-0.664)	1.69±1.490 (0.895-0.664)	-0.115	0.078
P ₁₂	1.27±1.151 (0.710-0.633)	1.31±1.258 (0.710-0.633)	-0.038	0.033
P ₂₄	0.73±0.874 (0.487-0.487)	0.73±0.874 (0.487-0.487)	0.000	0.000

Table 2. Mean±SD and 95% CI, mean difference and effect size (Cohen's d) reference values for pain scores at given intervals. * Effect size of ≤ 0.2 is considered as small effect size, 0.5 – 0.7 is considered as medium effect size, and ≥ 0.8 is considered as large effect size.

There was no significant difference in the severity of pain between the two groups at the time intervals of which pain was assessed.

There was no significant difference between the two groups when pain scores were compared across the 24-hour time line using General Linear Model, Repeated Measures (Figure. 3).

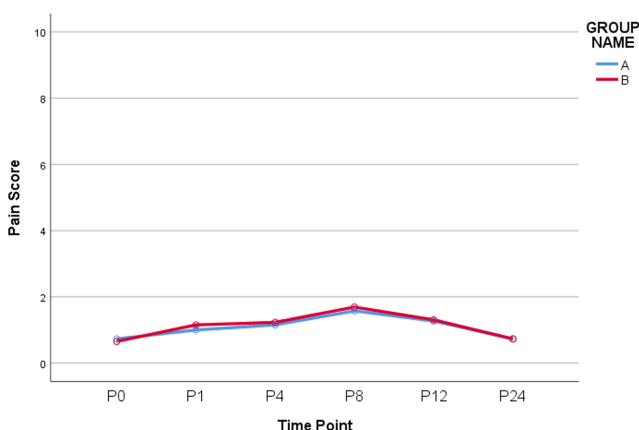


Figure 3. Mean pain scores over 24-hour time line in both Group A and Group B.

There was no statistical significance in the hemodynamic parameters that were monitored between the two groups.

Group B required more rescue analgesia during the peri-operative period, however it is not statistically significant. There was no significant difference in satisfaction scores given by the patient's parents for the QLB given in both groups. There were no adverse effects observed in this study.

Discussion

The idea of incorporating QLB as part of multimodal postoperative analgesia approach is to minimize the use of opioids, encourage early ambulation and hospital discharge especially in the pediatric population. This idea was inspired by several studies which showed good post-operative analgesic outcome in the pediatric population. For example, Oksuz et al in 2017 in their study found that the number of patients who required analgesia in the first 24 hours postoperatively was significantly lower in the QLB group compared to the TAPB group, as well as lower FLACC scores and higher parents' satisfaction scores.⁸ Due to limited studies in the pediatric population, the consideration of the other aspects of efficacy of the QLB such as postoperative opioid consumption was also taken from adult studies. In a study by Blanco et al in the adult obstetric population, it has been shown that the QLB can significantly reduce the cumulative morphine consumption postoperatively.⁷

Multiple studies have demonstrated similar good postoperative analgesia in adult patients undergoing abdominal surgery when US-guided QLB is employed. The expected replication of QLB2 block success in pediatric patients may be explained by a few factors. The LA distribution in QLB is more similar to paravertebral block than a TAP block, when studied by imaging.¹⁴ QLB also provides analgesia not only in the abdominal muscle plane but also at the visceral level.¹⁴ This can be explained by the understanding of the surrounding anatomy of the QLB.

The parietal peritoneum is innervated by somatic and visceral afferent nerves and receives sensitive branches from the lower intercostal nerves and from the upper lumbar nerves. Though the visceral peritoneum itself is not

innervated, but the sub-mesothelial tissue is innervated by the autonomic nervous system, vagal nerve and spinal nerves.¹⁸ This knowledge of the anatomy is in keeping with the spread of LA injectate in QLB. Elsharkawy et al in 2018 described that LA will spread to the thoracic paravertebral space, posterior to the medial and lateral arcuate ligaments of the diaphragm, along the endothoracic fascia to block the somatic nerves and thoracic sympathetic trunk of the lower thoracic levels.¹⁹ In addition, the iliohyogastric and ilioinguinal nerves exit through the proximal and lateral aspect of the psoas major muscle and travel through the ventral surface of the QL, which explains dermatomal sensory blockade for levels T12 – L2.¹⁹

Quadratus lumborum block is a plane block, thus the volume given is an important factor for the block success. Hesham Elsharkawy and Akerman et al in 2017 and 2018 respectively, described in their articles that a volume of 0.2 to 0.4 ml/kg unilaterally are usually recommended, with taking into consideration the weight of the patient as not to exceed the toxic dose.^{11,16} Taking a 75 kg adult as an example, the range of volume will be translated to 15 – 30 mls of LA, which is the volume which is generally accepted for a unilateral QLB in the average weighted adult population. Interesting to note that in our study, we managed to get the mean volumes given for both the 0.2 ml/kg and 0.4 ml/kg groups according to corresponding weight groups. Larger sample size studies can be done to ascertain the generally accepted volumes of LA for weight group, and possibly be further translated into proper guidelines.

Generally, in plane blocks, it is thought that the more volume is given, the better the block will be due to more spread of the LA to the site of interest. However, we theorize that this might not be accurate. Plane blocks depend on the LA travelling through a fascia. Fascia are potential spaces with certain capacities, of which a certain volume will be adequate to fill up the space and cause the LA given to spread to the desired site. Unfortunately, there

are no studies done to date which examine this aspect of plane blocks.

The pediatric population in particular are sensitive to slight changes in drug doses, thus the importance of finding the lowest effective volume of LA in a block such as the QLB, to avoid any complications from LA administration. To date, there is no consensus for the volume of LA in the pediatric population which is effective for the block. To our knowledge, this is the first double-blind, randomized, prospective study comparing two volumes of QLB for postoperative pain relief after laparoscopic abdominal surgery in the pediatric population.

We postulated that a volume of 0.2 ml/kg of LA is non-inferior to 0.4 ml/kg, and was later proven when mean difference of pain scores and effect size (Cohen's d) were compared at all the interval time up to 24 hours postoperatively.

There have been little data available on the pharmacokinetics of the drug in truncal plane block specifically in the pediatric population. Burlacu and Buggy described in a study that the onset of levobupivacaine took between 6 – 10 minutes for brachial plexus nerve blocks and 25 – 30 minutes for sciatic nerve blocks.²⁰ We did not find any literature describing the onset of truncal plane blocks such as the QLB. Although not statistically significant, we found that those who need rescue analgesia were highest during the first ten minutes post-block. This may be related to the onset of levobupivacaine which takes time before it exerts its analgesic effect. Even with prior knowledge regarding onset of LA to work, in the pediatric age group, it is not feasible to perform a block pre-GA. This in turn becomes a setback point in performing block in the pediatric population.

In our study, the highest mean pain score in both groups were at the eighth hour postoperatively, which might explain the start of the offset of the QLB, which have yet to be described by any study, though it is reported that the analgesic effects of QLB last up to 48 hours.^{7,8} Probably in the future, studies employing the time of which the first

dose of oral analgesia is given, may further support the suggested time of offset for the QLB.

Comparing the mean pain scores across the 24-hour timeline, there is no significant difference in the pain scores for both groups. Parent's satisfaction scores were comparable in both groups, and the majority of them were very satisfied with the regimen employed. There were no side effects reported in this study. A larger sample size may be able to detect undesired and rare side effects.

In conclusion, this study found that 0.2 ml/kg of 0.25% levobupivacaine is non-inferior to 0.4 ml/kg in QLB2 for pediatric laparoscopic abdominal surgeries. Parents' satisfaction scores were also comparable in both groups.

Disclosure/Acknowledgement

This study was approved by Research Ethics Committee, The National University of Malaysia (Ref no: UKM PPI.800-1/1/5/JEP-2019-132) and received the UKM Fundamental Grant (Project Code: FF-2019-204). All authors declared there is no conflict of interest in this study.

References

1. Gupta, R., & Singh, S. (2009). Challenges in Paediatric Laparoscopic Surgeries. *Indian Journal of Anaesthesia*, 53(5), 560–566.
2. Wiryana, M., Sinardja, I. K., Kurniyanta, P., Senapati, T. G., Widnyana, I. M., I Gusti Agung Gede Utara Hartawan, Pradhana A.P. (2017). Anesthesia on Pediatric Laparoscopy. *Bali Journal of Anesthesiology*, 1(1), 1.3.
3. Raveenthiran, V. (2010). Pediatric laparoscopy: Facts and factitious claims. *Journal of Indian Association of Pediatric Surgeons*, 15(4), 122–128.
4. Koivusalo, A. I., Korpela, R., Wirtavuori, K., Piiparinen, S., Rintala, R. J., & Pakarinen, M. P. (2009). A Single-Blinded, Randomized Comparison of Laparoscopic Versus Open Hernia Repair in Children. *Pediatrics*, 123(1), 332–337.
5. Blanco R. TAP block under ultrasound guidance: The description of a 'nonpopstechnique' *Reg Anaesth Pain Med*. 2007;32(Suppl 1):130.

6. Blanco, R., Ansari, T., & Girgis, E. (2015). Quadratus lumborum block for postoperative pain after caesarean section. *European Journal of Anaesthesiology*, 32(11), 812-818.
7. Blanco, R., Ansari, T., Riad, W., & Shetty, N. (2017). Quadratus Lumborum Block Versus Transversus Abdominis Plane Block for Postoperative Pain After Cesarean Delivery. *Obstetric Anesthesia Digest*, 37(3), 164-165.
8. Öksüz, G., Bilal, B., Gürkan, Y., Urfalioğlu, A., Arslan, M., Gişi, G., & Öksüz, H. (2017). Quadratus Lumborum Block Versus Transversus Abdominis Plane Block in Children Undergoing Low Abdominal Surgery. *Regional Anesthesia and Pain Medicine*, 42(5), 674-679.
9. El-Boghdadly, K., Elsharkawy, H., Short, A., & Chin, K. J. (2016). Quadratus Lumborum Block Nomenclature and Anatomical Considerations. *Regional Anesthesia and Pain Medicine*, 41(4), 548-549.
10. Ueshima, H., Otake, H., & Lin, J. (2017). Ultrasound-Guided Quadratus Lumborum Block: An Updated Review of Anatomy and Techniques. *BioMed Research International*, 2017, 1-7.
11. Elsharkawy, H. (2019). Quadratus Lumborum Blocks. *Atlas of Ultrasound-Guided Regional Anesthesia*, 277-285.
12. Murouchi, T., Iwasaki, S., & Yamakage, M. (2016). Quadratus Lumborum Block. *Regional Anesthesia and Pain Medicine*, 41(2), 146-150.
13. Visoiu, M., & Yakovleva, N. (2013). Continuous postoperative analgesia via quadratus lumborum block - an alternative to transversus abdominis plane block. *Pediatric Anesthesia*, 23(10), 959-961.
14. Chakraborty, A., Goswami, J., & Patro, V. (2015). Ultrasound-Guided Continuous Quadratus Lumborum Block for Postoperative Analgesia in a Pediatric Patient. *A & A Case Reports*, 4(3), 34-36.

15. Baidya, D. K., Maitra, S., Arora, M. K., & Agarwal, A. (2015). Quadratus lumborum block: An effective method of perioperative analgesia in children undergoing pyeloplasty. *Journal of Clinical Anesthesia*, 27(8), 694-696.
16. Akerman, M., Pejčić, N., & Veličković, I. (2018). A Review of the Quadratus Lumborum Block and ERAS. *Frontiers in Medicine*, 5.
17. Flight, L & Julious, S.A. 2016. Practical guide to sample size calculation: non-inferiority and equivalence trials. *Pharmaceutical Statistics*, 15: 80-89.
18. Baidya, D. K., Maitra, S., Arora, M. K., & Agarwal, A. (2015). Quadratus lumborum block: An effective method of perioperative analgesia in children undergoing pyeloplasty. *Journal of Clinical Anesthesia*, 27(8), 694-696.
19. Elsharkawy, H., El-Boghdady, K., & Barrington, M. (2019). Quadratus Lumborum Block. *Anesthesiology*, 130(2), 322-335.
20. Burlacu, C. L. (2008). Update on local anesthetics: Focus on levobupivacaine. *Therapeutics and Clinical Risk Management*, Volume 4, 381-392.