Effect of ultrasound-guided quadratus lumborum block on neuroendocrine stress response and postoperative analgesia in paediatric patients undergoing elective open pyeloplasty - A randomised clinical trial

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ABSTRACT

Background and Aims: Quadratus lumborum block (QLB) is a compartmental block of the anterior abdominal wall. Surgical trauma produces neuroendocrine surgical stress responses, which are modified by anaesthetic blocks. The aim of this study was to evaluate the effect of ultrasound (US)-guided QLB on analgesia and surgical neuroendocrine stress response in paediatric patients undergoing pyeloplasty. Methods: A randomised trial was conducted in 60 children aged 1-7 years undergoing elective open pyeloplasty. Patients were randomised into Group QLB [US-guided QLB with 0.5 ml/kg of 0.25% ropivacaine after induction of general anaesthesia (GA)], and Group GA, which received only GA. Perioperative haemodynamic parameters, serum cortisol, blood glucose, analgesic consumption and postoperative FLACC scores were recorded. Unpaired t-test, Wilcoxon rank-sum test or Mann-Whitney U test was used to compare variables between the two groups. Two-way analysis of variance or the Friedmann test was used to compare quantitative variables at various points within a group. Results: A decrease in serum cortisol and blood glucose values was observed in Group QLB at 30 min after surgical incision and 24 h after surgery compared to the preoperative value and compared to Group GA (P < 0.05). The quality of analgesia assessed by the FLACC scale was significantly better in group QLB. Dose of fentanyl consumption (µg/kg) was higher in Group GA compared to Group QLB in the intraoperative and postoperative period (P < 0.05). Conclusion: QLB is effective as part of multimodal analgesia and attenuates the neuroendocrine stress in paediatric patients undergoing open pyeloplasty.

Keywords: Analgesia, cortisol, glucose, neuroendocrine surgical stress, pain, pyeloplasty, quadratus lumborum block, regional block

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> Submitted: 27-Jun-2023 Revised: 02-Mar-2024 Accepted: 05-Mar-2024 Published: 12-Apr-2024

Access	this article online
Website	e: https://journals.lww. com/ijaweb
DOI: 10	.4103/ija.ija 608 23

Quick response code



INTRODUCTION

Pyeloplasty is a standard surgical procedure performed for ureteropelvic junction obstruction in children and is associated with significant postoperative pain.^[1] Neuraxial analgesia and peripheral nerve blockade techniques provide superior analgesia compared to systemic opioids and non-steroidal anti-inflammatory drugs.^[2] Ultrasound (US)-guided quadratus lumborum block (QLB) has been described as a newer modality This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

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How to cite this article: Rathod PR, Bhoi D, Kumar A, Ray BR, Mohan VK, Kashyap L. Effect of ultrasound-guided quadratus lumborum block on neuroendocrine stress response and postoperative analgesia in paediatric patients undergoing elective open pyeloplasty – A randomised clinical trial. Indian J Anaesth 2024;68:467-72.

truncal block in paediatrics for providing somatic and visceral pain relief after abdominal surgery in both the upper and lower abdomen.^[3,4]

Surgical stress contributes to postoperative morbidity and mortality, associated with extreme catecholamine response, which may worsen the outcome. Surgical stress produces sympathetic activation, resulting in immunological, haematological, metabolic and endocrine reactions. Secretion of endogenous catecholamines, glucocorticoids and inflammatory mediators is increased by hypothalamic–pituitary– adrenal axis activation following surgical stress.^[5] The neuroendocrine stress response is obtunded by epidural, spinal and peripheral nerve blocks.^[6]

The current study hypothesises that the US-guided QLB will provide effective analgesia and attenuate the neuroendocrine response of surgical trauma in paediatric open pyeloplasties. The primary outcome was to assess US-guided QLB's effect on modifying the surgical neuroendocrine stress response by measuring serum cortisol and blood glucose levels. The secondary outcomes were the haemodynamic changes in the intraoperative and postoperative period, intraoperative total fentanyl requirement, Face, Legs, Activity, Cry, Consolability (FLACC) scores and total fentanyl requirement in the first 24-h postoperative period and incidence of block-related complications.

METHODS

Following approval by the institutional ethics committee for postgraduate research, All India Institute of Medical Sciences, New Delhi (vide approval number IECPG-283/07.09.2017; dated 28/09/2017) and registration at the Clinical Trials Registry-India (vide registration number CTRI/2017/11/010406; http://ctri. nic.in), this randomised, single-blinded interventional study was conducted from October 2017 to May 2019. This study was carried out in accordance with the principles of the Declaration of Helsinki of 1975, revised in 2013, and good clinical practice.

Before enrolment in the study, informed written consent was obtained from the parents of the children or their guardians for their children to participate in the study and for the child's data to be used for research and educational purposes. Sixty patients of the American Society of Anesthesiologists (ASA) physical status I or II, aged 1–7 years, of either gender, undergoing open pyeloplasty under general anaesthesia (GA) were included. Exclusion criteria were refusal to give consent, distorted anatomy and infection at the site of block and children with metabolic abnormalities, cardiac disease, sepsis, coagulopathic disorder or hypersensitivity to relevant drugs.

The included patients were randomly allocated using permuted block randomisation into two groups of 30 children each, in which a computer-generated random number list was used to randomise the patients into the following groups based on treatment: Group QLB (n = 30): US-guided QLB with 0.5 ml/kg of 0.25% ropivacaine after induction of GA and Group GA (n = 30): only GA. The random allocation sequence was concealed in sequentially numbered, opaque, sealed envelopes. Once an eligible patient consented, the respective envelope was opened by an anaesthesiologist who was not a part of the study to include the patient in the marked group.

All surgeries were performed in the morning hours to equalise circadian changes in the stress hormone level. On the day of surgery, all children who were >6 months old were premedicated with intravenous (IV) midazolam 0.05-0.1 mg/kg, 20-30 min before the anticipated time of induction. About 2 ml of the blood sample was taken in a serum separating tube for serum cortisol measurement, and blood glucose level was also measured. Patients were given GA as per the standard protocol. The baseline haemodynamic parameters were noted. In Group QLB, the block was administered 15 min before the start of surgery, in lateral decubitus position, and 0.5 ml/kg of 0.25% ropivacaine was deposited in the fascial plane between the quadratus lumborum muscle and the psoas major muscle [Figure 1]. Non-invasive blood pressure, mean arterial pressure, heart rate, end-tidal carbon dioxide and oxygen saturation were monitored intraoperatively every 5 min and recorded after endotracheal tube intubation, after skin incision, 15 min and 30 min after skin incision and at the end of surgery. A change of more than 20% in haemodynamic parameters in the intraoperative period was considered inadequate analgesia and treated with $0.5 \ \mu g/kg$ IV fentanyl. Also, the number of fentanyl IV boluses was recorded. Again, 2 ml of the blood sample was taken in a serum separating tube for serum cortisol and blood glucose level measurement 30 min after surgical incision.

All the patients were extubated at the end of surgery; 0.1 mg/kg IV ondansetron was administered for antiemetic prophylaxis, and 7.5–15 mg/kg IV



Figure 1: Transmuscular quadratus lumborum block showing LA spread between PM and QLM. Ant = anterior, EO and TA = external oblique and transverse abdominis muscle, ESM = erector spinae muscle, LA = point of local anaesthetic injection, LDM = latissimus dorsi muscle, PC = peritoneal cavity, PM = psoas major muscle, Post = posterior, QLM = quadratus lumborum muscle, TP = tip of transverse process of L4, VB = vertebral body of L4

paracetamol was administered before extubation and continued sixth hourly in the postoperative period for analgesia. Patients were shifted to post-anaesthesia care unit (PACU), where the FLACC scores and haemodynamic parameters were noted at 1/2, 1st, 2nd, 4^{th} , 8^{th} , 12^{th} , 16^{th} , and 24^{th} hour. If the FLACC score was more than 4, rescue analgesia with $0.5 \mu g/kg$ IV fentanyl was administered. The block was considered a failure when rescue analgesia was needed within the first 2 h after surgery. The time to first rescue analgesia, the number of fentanyl IV boluses and the total amount of IV fentanyl required were recorded. Complications such as postoperative nausea, vomiting, urinary retention, motor weakness, respiratory distress and block site haematoma formation were also noted. In the postoperative period, serum cortisol and blood glucose levels were measured 30 min and 24 h after surgery.

The calculated based sample size was on attenuation of neuroendocrine the stress response to surgery. Considering the results of parameters (cortisol and glucose) from the earlier published study,^[7] that is, serum cortisol level was significantly lower in group transversus abdominis plane (TAP) compared to group GA intraoperatively [17.73 (1.51) vs. 21.80 (2.22) µg/dl] and 30 min postoperatively [15.03 (1.56) vs. 18.30 (1.53) µg/dl] and blood glucose level was significantly lower in group TAP compared to group GA intraoperatively [107.57 (3.77) vs. 115.40 (6.30) mg/ dl] and 30 min postoperatively [104.13 (3.78) vs.

110.73 (4.83) mg/dl] at 95% confidence interval and 90% power of the study, the required minimum sample size was very small (eight in each group). Therefore, to derive valid results on considered outcomes between the groups, statistically large number of patients, at least 30 patients, were taken in each group.

Qualitative variables were described as frequency and percentage. A Chi-squared test/Fisher's exact test was used to compare qualitative variables (gender, ASA class) between the two groups. The quantitative variables (serum cortisol, blood glucose, weight, heart rate, blood pressure, total dose of fentanyl requirement, number of IV fentanyl boluses, FLACC score) were described as mean (standard deviation) and/or median (first guartile-third guartile). Unpaired t-test, Wilcoxon rank-sum test or Mann-Whitney U test was used to compare quantitative variables between the two groups. However, to compare quantitative variables within a group at two points in time, a paired *t*-test or Wilcoxon signed-rank test was used. If quantitative variables (serum cortisol, blood glucose, heart rate, blood pressure) at a basal point between two groups were comparable (i.e. not significant), they were compared at successive points straightaway. Otherwise, the differences in basal values between the two groups were compared. Two-way analysis of variance or the Friedmann test was used to compare quantitative variables (serum cortisol, blood glucose) at various points within a group. The result was considered statistically significant at a 5% level of significance (P < 0.05). The statistical data were analysed using STRATA 14.0 version and Statistical Package for the Social Sciences 20.0 version software (Armonk, NY: IBM Corp, USA).

RESULTS

We assessed 70 patients for eligibility for possible inclusion in our study. Of these, 60 were included and randomised into two groups, and the study protocol was completed [Figure 2]. Demographic data and baseline characteristics between the two groups were comparable with respect to age, weight, gender and duration of anaesthesia [Table 1]. All patients in both groups belonged to ASA physical status I.

There was a significant decrease in serum cortisol and blood glucose values in Group QLB at 30 min after surgical incision and also at 30 min and 24 h post surgery compared to the preoperative value and in comparison to Group GA [Table 2]. Rathod, et al.: Paediatric QLB on analgesia and stress response



Figure 2: Consolidated Standards of Reporting Trials (CONSORT) diagram showing patient progress through the study phases. GA = general anaesthesia, QLB = quadratus lumborum block

Table 1: Demographic data							
	Group QLB (<i>n</i> =30)	Group GA (<i>n</i> =30)					
Age (years)	3.59 (2.18)	4.16 (2.26)					
Gender (male/female)	27/3	26/4					
Weight (kg)	14.80 (5.82)	14.86 (5.60)					
Duration of anaesthesia (min)	112.83 (17.65)	120.33 (22.2)					

Data expressed as mean (standard deviation) or numbers. GA=general anaesthesia, QLB=quadratus lumborum block

The median number of fentanyl boluses (0.5 μ g/kg) required in the intraoperative period was 3 (2–3) and 0 (0–0) and in the postoperative period was 2 (1–2) and 0 (0–0) in Group GA and Group QLB, respectively (P = 0.001). The median doses of fentanyl consumption (μ g/kg) required in the intraoperative period were 1.74 (1.27–2.13) and 0 (0–0) and in the postoperative period were 1 (0.76–1.33) and 0 (0–0) in Group GA and Group QLB, respectively (P = 0.001) [Table 3].

There was a decrease in systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate in Group QLB compared to the baseline value following surgical incision in the intraoperative period and at 2, 4, 8, 12, 16 and 24 h in the postoperative period [Figure 3]. Mean FLACC scores in Group GA were higher compared to Group QLB in the entire postoperative period [Figure 4]. There were no complications such as postoperative nausea and vomiting, urinary retention, motor weakness, respiratory distress or block site haematoma formation in any of the subjects.

DISCUSSION

We observed very good analgesia with US-guided QLB with stable haemodynamics and neuroendocrine response. No incision response in the block group correlated with serum cortisol and blood glucose levels, and the effect extended to the postoperative period.

The blunting of the neuroendocrine stress response and blunting of activation of the hypothalamic– pituitary–adrenal axis was observed with US-guided QLB.^[8] Thus, we observed that QLB provides effective adjuvant analgesia.^[9,10]

Nerve blocks significantly suppress the neuroendocrine stress response in the perioperative period.^[5,8]US-guided TAP block has been found to provide adequate perioperative analgesia and blunt neuroendocrine

Table 2: Serum cortisol level and blood glucose level							
	Group QLB (n=30)	Group GA (<i>n</i> =30)	<i>P</i> 1	P 2	P 3	P 4	
Serum cortisol (nmol/l)							
C1 – Before induction of anaesthesia	1056.60 (712.15–1541.71)	485.29 (285.76–1041.60)	0.003				
C2 – 30 min after surgical incision	932.83 (476.72–1360.71)	1190.80 (701.32–1954.10)	0.035	<0.001	<0.001	<0.001	
C3 – 30 min after surgery	668.37 (437.91–1126.63)	1952.22 (1174.41–2711.31)	< 0.001	<0.001	< 0.001	<0.001	
C4 – 24 h after surgery	899.29 (508.60-1273.99)	807.42 (479.58–1152.21)	0.727	<0.001	< 0.001	<0.001	
Blood glucose (mg/dl)							
G1 – Before induction of anaesthesia	110.87 (8.59)	102.13 (13.71)	0.004				
G2 – 30 min after surgical incision	110.90 (10.30)	150.60 (17.69)	< 0.001	>0.05	<0.001	<0.001	
G3 – 30 min after surgery	109.00 (12.00)	181.60 (18.09)	<0.001	>0.05	<0.001	<0.001	
G4 – 24 h after surgery	105.73 (7.05)	107.73 (10.00)	0.374	<0.001	<0.001	<0.001	

Data expressed as median (Q1–Q3) or mean (standard deviation). P1 – Comparison between two groups. P2 – Comparison within Group QLB with the preoperative value within Group QLB, C1 is significantly different from C2, C3, C4 (P<0.05) within Group QLB, G1 is significantly different from G2, C3, C4 (P<0.05) within Group QLB, G1 is significantly different from G4 (P<0.001). P3 – Comparison within Group GA with the preoperative value within Group GA, C1 is significantly different from C2, C3, C4 (P<0.05) within Group GA, G1 is significantly different from G2, G3, G4 (P<0.05). P4 – Comparison of changes in value with the preoperative value between the two groups. GA=general anaesthesia, QLB=quadratus lumborum block



Figure 3: Patient mean arterial BP (mmHg) in the intraoperative period. P < 0.05 at induction, surgical incision, 30 min after surgical incision, end of surgery and extubation. BP = blood pressure, GA = general anaesthesia, QLB = quadratus lumborum block

stress response in paediatric patients undergoing elective open inguinal hernia repair.^[7] However, in pyeloplasty, there is more visceral component of pain, so QLB was preferred over TAP block.^[11]

The analgesic efficacy of QLB was also observed in a case series, wherein US-guided QLB with 0.5 ml/kg of 0.2% ropivacaine provided good analgesia in the postoperative period in children undergoing open pyeloplasty.^[3] They used the Wong–Baker Faces scale for pain assessment and administered IV morphine in increments of 50 μ g/kg in the postoperative period for rescue analgesia. We obtained similar results and found a decrease in IV fentanyl consumption.

USG-guided QLB was compared with caudal epidural using 1 ml/kg of 0.2% ropivacaine with



Figure 4: Patient mean FLACC score trends between the two groups in the postoperative period. P < 0.05 at extubation, 0.5, 2, 4, 8 and 12 h after the surgery. FLACC = Face, Legs, Activity, Cry and Consolability, GA = general anaesthesia, QLB = quadratus lumborum block

0.03 mg/kg morphine for vesicoureteral reflux surgery in paediatric patients. The authors concluded that QLB was more effective than the caudal epidural in decreasing the need for rescue analgesia during the 24-h postoperative period.^[12]

Complications like quadriceps weakness, haematoma associated with allodynia, hyperalgesia and back pain have been reported following QLB in the postoperative period.^[13] However, none of our study participants had haematoma, muscle weakness, significant Postoperative nausea and vomiting, urinary retention or respiratory depression.

A few limitations of our study include the following. Due to the nature of interventions, the anaesthesiologist taking intraoperative care of patients in Group GA could not be blinded. Other indicators of stress response, such as serum catecholamine and cytokine levels, were not evaluated. The control group could have received another alternative mode of analgesia, like a caudal block or a placebo. The use of a continuous catheter technique and the use of additives

Table 3: Fentanyl consu	umption intraoperat	ively and postoperatively I	petween the groups	
Parameter		Group QLB (<i>n</i> =30) Median (Q1–Q3)	Group GA (<i>n</i> =30) Median (Q1–Q3)	Р
Number of fentanyl boluses (0.5 µg/kg)	Intraoperative	0 (0–0)	3 (2–3)	0.001
	Postoperative	0 (0–0)	2 (1–2)	0.001
Total dose of fentanyl consumption (µg/kg)	Intraoperative	0 (0–0)	1.74 (1.27–2.13)	0.001
	Postoperative	0 (0–0)	1 (0.76–1.33)	0.001

GA=general anaesthesia, QLB=quadratus lumborum block

would have increased the duration of analgesia. Future studies may be directed towards redo surgery or more complex pyeloplasty surgery with extensive dissection to prove the analgesic efficacy of QLB.

CONCLUSION

Ultrasound-guided quadratus lumborum block with general anaesthesia is a safe and effective alternative mode of analgesia as a component of multimodal analgesia, and it blunts the haemodynamic and neuroendocrine stress response following surgery in children undergoing open pyeloplasty.

Study data availability

De-identified data may be requested with reasonable justification from the authors (email to the corresponding author). After approval, they shall be shared upon request as per the author's institution policy.

Acknowledgement

We acknowledge Dr. Sadanand Dwivedi, Professor, Department of Biostatistics, AIIMS, New Delhi, Dr. Archana Singh, Assistant professor, Department of Biochemistry, AIIMS, New Delhi and Dr. Devendra Kumar Yadav, Associate Professor, Department of Paediatric surgery, AIIMS, New Delhi, for helping us in conducting this study.

Financial support and sponsorship Nil.

Conflicts of interest

There are no conflicts of interest.

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