Transversus Abdominis Plane Block in Children: A Multicenter Safety Analysis of 1994 Cases from the PRAN (Pediatric Regional Anesthesia Network) Database

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BACKGROUND: Currently, there is not enough evidence to support the safety of the transversus abdominis plane (TAP) block when used to ameliorate postoperative pain in children. Safety concerns have been repeatedly mentioned as a major barrier to performing large randomized trials in children. The main objective of the current investigation was to determine the incidence of overall and specific complications resulting from the performance of the TAP block in children. In addition, we evaluated patterns of local anesthetic dosage selection in the same population.
METHODS: This was an observational study using the Pediatric Regional Anesthesia Network database. A complication from the TAP block was defined by the presence of at least one of the following intraoperative and/or postoperative factors: puncture of the peritoneum or organs, vascular puncture, cardiovascular, pulmonary and/or neurological symptoms/signs, hematoma, and infection. Additional analyses were performed to identify patterns of local anesthetic dosage.
RESULTS: One thousand nine hundred ninety-four children receiving a TAP block were included in the analysis. Only 2 complications were reported: a vascular aspiration of blood before local anesthetic injection and a peritoneal puncture resulting in an overall incidence of complications (95% CI) of 0.1% (0.02%–0.3%) and a specific incidence of complications (vascular aspiration or peritoneal puncture) of 0.05% (0.0054%–0.2000%). Neither of these complications resulted in additional interventions or sequelae. The median (95% range) for the local anesthetic dose per weight for bilateral TAP blocks was 1.0 (0.47–2.29) mg of bupivacaine equivalents per kilogram; however, subjects' weights were not sufficient to explain much of the variability in dose. One hundred thirty-five of 1944 (6.9%; 95% CI, 5.8%–8.1%) subjects received doses that could be potentially toxic. Subjects who received potentially toxic doses were younger than subjects who did not receive potentially toxic doses, 64 (19–100) months and 108 (45–158) months, respectively ($P < 0.001$).
CONCLUSIONS: The upper incidence of overall complications associated with the TAP block in children was 0.3%. More important, complications were very minor and did not require any additional interventions. In contrast, the large variability of local anesthetic dosage used can not only minimize potential analgesic benefits of the TAP block but also result in local anesthetic toxicity. Safety concerns should not be a major barrier to performing randomized trials to test the efficacy of the TAP block in children as long as appropriate local anesthetic dose regimens are selected. (Anesth Analg 2014;119:395–9)

Postoperative pain has been associated with increased morbidity in surgical patients, but recent studies suggest that pain remains suboptimally controlled.[1–3] Scientific evidence on the efficacy of strategies to minimize postoperative pain in pediatric patients is often very limited and various barriers to conduct large randomized trials in children have been identified.[4–6] Among those barriers, the unproven safety of a tested intervention can not only decrease patient recruitment but also question the ethics of performing a randomized trial in a vulnerable population.[7,8]

Transversus abdominis plane (TAP) block has been shown to minimize postsurgical pain in adults undergoing specific procedures.[9–11] In contrast, very few and small randomized trials have examined the efficacy of TAP block to minimize postoperative pain in children.[12,13] The potential complications of TAP block reported in adults are a major barrier to conduct more randomized trials in children.[14,15] The safety of TAP block in children remains to be determined. If proven to have acceptable safety, more randomized studies will be performed to evaluate TAP block efficacy for specific surgical procedures in children.

The major objective of the current investigation was to evaluate the safety of TAP block in pediatric surgical patients. Specifically, we sought to determine the estimated incidence of overall and individual complications related to the performance of TAP block in that patient population. In addition, we evaluated patterns of local anesthetic dosage selection for TAP block placement in children.

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METHODS

The study was performed using data obtained from the Pediatric Regional Anesthesia Network (PRAN) database. Study approval was obtained from the Ann & Robert H. Lurie Children's Hospital of Chicago IRB. Approval for data collection was obtained from individual sites. All centers granted waiver of informed consent by their IRBs because the data had no patient historical information identifiers, and there were absolutely no changes in patient care. Eligible subjects were pediatric patients (<18 years) undergoing surgery who also received a TAP block for postoperative pain control. The data were collected from April 16, 2007, until December 19, 2012. The data collection form for the current study followed the same variables established by the PRAN group and has been described in detail.[16] In brief, the database and data collection instruments were performed with guidance from Axio Research, LLC (Seattle, WA). Data collection started on April 1, 2007, and was performed in 5 centers constituting the steering committee centers (Children's Hospital Colorado, Aurora, CO; Seattle Children's Hospital; Ann & Robert H. Lurie Children's Hospital of Chicago; Lucile Packard Children's Hospital at Stanford University, Palo Alto, CA; and Children's Hospital at Dartmouth-Hitchcock Medical Center, Lebanon, NH). Currently, 22 pediatric hospitals nationwide contribute data to the network database (Appendix). Data from each center is entered in a single database supported by Axio Research, LLC. The Web site maximizes data entry efficiency and minimizes errors. The database has been audited multiple times to ensure completeness and accuracy of the data. Incomplete cases are marked and listed in the individual sites' homepages until full completion of data per each case is achieved. Demographic characteristics included subjects' age, weight, ASA physical status, and gender. Data on the block performance included patient consciousness status during block performance (awake, sedated, and anesthetized) and the technique used to perform the block (landmark or ultrasound-guided). In addition, the local anesthetic type, dose, volume, and the use of adjuncts were recorded.

A complication from TAP was defined by the presence of at least one of the following intraoperative and/or postoperative factors: inadvertent puncture of the peritoneum, inadvertent puncture of abdominal organs (liver and bowel), vascular puncture (defined by the presence of a blood aspirate), cardiovascular (arrhythmias, hypotension, and cardiac arrest), pulmonary (pneumothorax), neurological (seizure or paresthesia), hematoma, and infection. If a complication was noted, the need for interventions (such as computed tomography, different specialty consultation, and medications) was recorded. In addition, the complication was coded for the time required for resolution and the presence of temporary or permanent sequelae.

Normally distributed interval data are reported as mean (SD). Nonnormally distributed interval and ordinal data are reported as median (range or interquartile range [IQR]), and it was evaluated using Mann-Whitney *U* test.[17,18] Categorical variables are presented as counts and were evaluated using the Fisher exact test. The 95% binomial confidence interval for the incidence of TAP block complications was calculated using the Jeffreys method. The coverage properties of that method are similar to that of others, but it has the advantage of being equal-tailed (e.g., for a 95% confidence interval, the probabilities of the interval lying above or below the true value are both close to 2.5%).[19] Because not enough information is available on the dosage of local anesthetics used in TAP block for children and our group has previously demonstrated an association between dose and postoperative pain outcomes,[20] an exploratory analysis was also performed to identify patterns of local anesthetic dose and patient demographic characteristic. Simple linear regression was performed using the total local anesthetic dose as a dependent variable and patient characteristics (age and weight as independent variables) for bilateral TAP blocks. When the block was performed using ropivacaine, equipotent doses of ropivacaine were converted to bupivacaine (0.7 mg of bupivacaine = 1 mg of ropivacaine).[21,22] A 2-tailed *P* value of <0.05 was used to reject the null hypothesis.

RESULTS

One thousand nine hundred ninety-four children receiving TAP block were included in the current analysis. Demographic and block characteristics of subjects are presented in Table 1. Before the year 2010, 7 of 151 (5%) blocks were not performed with ultrasound compared to 42 of 1736 (2.5%) in the subsequent years ($P = 0.11$). Subjects who had their TAP block performed while awake and/or sedated were older than subjects who had TAP block performed under general anesthesia, median (IQR) of 172 (129–192) months and 93 (26–156) months, respectively ($P = 0.002$). Only 2 complications were reported: vascular aspiration of blood before local anesthetic injection and peritoneal puncture resulting in an overall incidence of

Table 1. Demographic and Block Characteristics

	Subjects (*n* = 1994)
Age (mo)	95 (27–156)
Gender	
Male	1099
Female	895
Weight (kg)	26.4 (12.9–48.3)
ASA physical status class	
I	723
II	711
III	517
IV	43
Calendar year of block performance	
2007	4
2008	32
2009	130
2010	449
2011	739
2012	640
Anesthetic technique used with the block	
None (awake)	7
Sedation	11
General anesthesia without muscle paralysis	883
General anesthesia with muscle paralysis	1093
Ultrasound	
Yes	1887
No	49
Not determined	58
Local anesthetic type	
Bupivacaine	1448
Ropivacaine	546

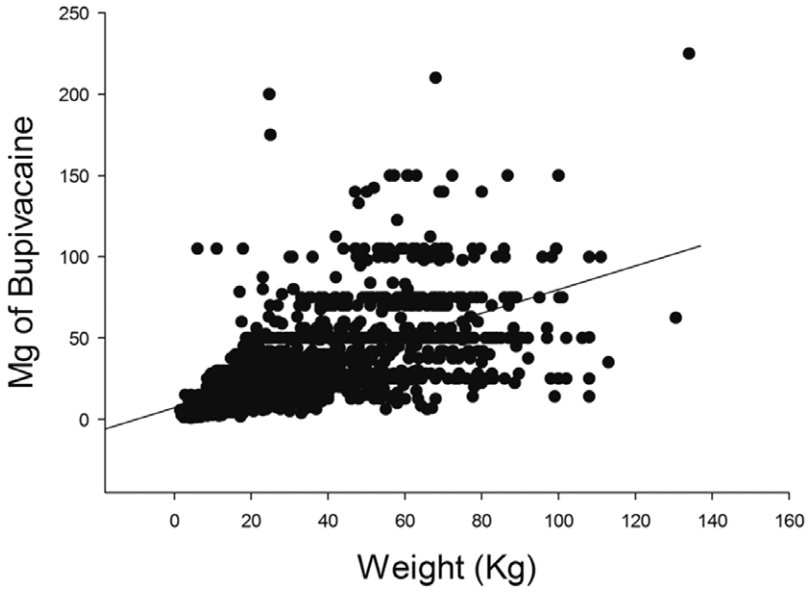

Figure 1. Scatter plot and regression analysis demonstrating a direct relationship between local anesthetic dose (milligram of bupivacaine equivalents) and weight in pediatric patients receiving a transversus abdominis plane (TAP) block. Slope of regression line 7.31 ± 0.76, goodness of fit R^2 = 0.41, and slope significantly different from 0 (P < 0.0001).

complications (95% CI) of 0.1% (0.02%–0.3%) and a specific incidence of complications (vascular aspiration or peritoneal puncture) of 0.05% (0.0054%–0.2%). Both complications did not result in any additional interventions or any subsequent sequelae.

The median (95% range) for the local anesthetic dose per weight for bilateral TAP blocks was 1.0 (0.47–2.29) mg of bupivacaine equivalents per kilogram representing a large variation in clinical practice. There was a direct linear relationship between the total local anesthetic dose and patients' weights; however, subjects' weights were not sufficient to explain much of the variability in dose (Fig. 1). Variation in the local anesthetic dose was not explained by age (P = 0.01, R^2 = 0.007) or gender (P = 0.34).

The median (IQR) local anesthetic dose/weight was greater when epinephrine was used as a block adjunct compared to that when no epinephrine was used, 1.4 (0.81–1.56) and 1.0 (0.51–1.40) mg of bupivacaine equivalents per kilogram, respectively (P = 0.0001). The weight-based dose in unilateral blocks was significantly lower compared with that of the bilateral doses (0.62 [0.32–0.71] mg of bupivacaine per kilogram and 1.03 [0.72–1.46], P = 0.002), but the analysis was limited by the low number of unilateral cases (n = 7). The absolute dose of local anesthetics was larger in TAP blocks performed with ropivacaine, median (IQR) of 1.27 (0.83–1.97) mg/kg, compared to that in the bupivacaine group, 0.97 (0.64–1.33) mg/kg. In contrast, when adjusting for different local anesthetic potencies, the ropivacaine group, median (IQR) of 0.89 (0.58–1.38) mg of bupivacaine equivalents/kg, received a lower, although not statistically significant, dose than the bupivacaine group, 0.97 (0.64–1.33), P = 0.06.

One hundred thirty-five of 1944 (6.9%; 95% CI, 5.8%–8.1%) subjects received larger doses than commonly used in adults (2 mg of bupivacaine per kilogram) that could be potentially unsafe.[23] Subjects who received doses larger than the maximum safe local anesthetic doses were younger than subjects who did not receive potentially unsafe doses, 64 (19–100) months and 108 (45–158) months, respectively (P < 0.001).

DISCUSSION

The most important finding of the current investigation was the lack of clinically significant complications when TAP blocks were performed in >1900 children. In the current study, we were able to estimate an upper incidence of overall complications of 0.3% that is consistent with other commonly performed regional anesthesia techniques.[24–26] More importantly, none of the identified complications had long-term consequences to patients or resulted in additional interventions. Based on our findings, safety concerns should not be a major barrier to the performance of TAP block in children undergoing surgical procedures.

Our results are important due to the lack of enough randomized studies demonstrating the efficacy of regional anesthesia techniques to ameliorate postoperative pain in children.[27] The safety of proposed interventions has been repeatedly shown to be a major barrier to the performance of randomized studies in children.[7,8] Only few randomized clinical studies have specifically evaluated the efficacy of TAP block to ameliorate pain after pediatric surgery, and safety data originating from those studies were limited by the small number of cases included in those studies.[12,13] To the best of our knowledge, the current study is the largest to report on the safety of TAP block in children.

Both complications observed due to the performance of TAP block, that is, a vascular aspiration of blood before local anesthetic injection and a peritoneal puncture, were recognized by the anesthesia provider, which likely resulted in an even lower rate of potential serious complications. The recognition of peritoneal puncture prevents further manipulation of the needle in the peritoneal cavity and potential bowel puncture or lacerations. Similarly, the detection of intravascular placement of the block needle by aspiration avoids intravascular injection of local anesthetics and systemic toxicity.

Another important finding of the current investigation was an almost 5-fold local anesthetic dosage variation used in the performance of TAP block. Our group has previously detected a relationship between local anesthetic dosage and better analgesic outcomes for adults receiving TAP block for laparoscopic

surgery.[20] It is, therefore, likely that lower doses might not be as effective as commonly used dose regimens (1–2 mg/kg bupivacaine equivalents).[20] Clinical practitioners should avoid suboptimal local anesthetic dosage regimens to obtain better postoperative pain when using TAP block in children.

It was also interesting to note that a substantial number of children had received larger doses than what has been reported to be associated with local anesthetic toxic levels in adults.[14] It seems that patients who receive bilateral blocks are at greatest risk, but our analysis was limited by the small number of unilateral cases. In addition, subjects' weights were not sufficient to explain much of the variability in dose and younger patients were more likely to receive potentially unsafe dosages. Because we do not have access to individual site data, it is important that each clinical site reexamine their practice to avoid significant deviations from current clinical practice that can minimize risks to patients.

Our study should only be interpreted in the context of its limitations. The PRAN database does not offer information on surgical procedures, and we could not evaluate the role of different types of surgeries on local anesthetic dosage variations. Because each site has different postoperative analgesic protocols, we could not reliably evaluate the efficacy of TAP block on postoperative pain outcomes. In addition, we did not measure blood levels of local anesthetics in our study population. Because pharmacokinetic drug profiles can be unique in children,[28–30] future studies evaluating local anesthetic pharmacokinetic profiles after TAP block are needed.

In summary, we evaluated the safety of TAP block in children. The upper incidence of overall complications was 0.3%. More importantly, complications were very minor and did not require any additional interventions. In contrast, the large variability of local anesthetic dosage currently used in clinical practice can not only minimize potential analgesic benefits of TAP block but also result in potential local anesthetic toxicity. Safety concerns should not be a major barrier to performing randomized trials to test the efficacy of TAP block in children as long as appropriate local anesthetic dose regimens are selected.

APPENDIX

1	Seattle Children's
2	The Children's Hospital of Colorado
3	Hitchcock Medical Center—Dartmouth
4	Lurie Children's Hospital of Chicago
5	Lucile Packard Children's Hospital of Stanford
6	University of Puerto Rico
7	Children's Medical Center Dallas
8	Columbia University
9	The Cleveland Clinic
10	Children's Memorial Hermann Hospital/UT Houston
11	University Hospital Rijeka
12	Boston Children's Hospital
13	University of New Mexico
14	Texas Children's
15	Oregon Health Sciences University
16	Nationwide Children's Hospital
17	Hospital Municipal Jesus—Rio de Janeiro
18	American Family Children's Hospital—University of Wisconsin
19	Amplatz Children's Hospital—University of Minnesota
20	Riley Hospital for Children at IU Health
21	University of Mississippi Medical Center

DISCLOSURES

Name: Justin B. Long, MD.
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Attestation: Justin B. Long approved the final manuscript. Justin B. Long attests to the integrity of the original data and the analysis reported in this manuscript.
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