Segmental distribution of high volume caudal anesthesia in neonates, infants and toddlers as assessed by ultrasonography.

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Pediatric Anesthesia

Segmental distribution of high volume caudal anesthesia in neonates, infants and toddlers as assessed by ultrasonography.

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Key Words:	Measurement, regional < Ultrasound, local anesthetics < Drugs, child < Age, infant < Age, neonate < Age

Stockholm 2010-10-11

Dear Editor,

Thank you for allowing us to address the issues raised by the reviewers. Our answers are given in a point-by-point matter below. Alterations are made in red text. Original text pertinent to our response is in blue text.

We hope that you agree with our response and modifications and that the manuscript now is better suited for potential publication in *Pediatric Anesthesia*.

Yours sincerely,

Märit Lundblad MD

For Peer Review

Reviewer No 1:

1. Point taken. The comment regarding cranial spread on page 11 has been deleted.
2. Point taken. Text on page 6 has been modified according to the reviewers comment.

Reviewer No 2:

1. We agree with the reviewer that the mechanism of action of epidurally injected local anesthetics is interesting and important. However, we do believe that this issue is outside the focus of our study and to address this properly would need a very extensive text, in fact it could in our opinion be the focus of a completely separate review article. Thus, we do not believe that such a discussion point would add to the manuscript. No action taken.
2. We appreciate the comment with regards to spread over time. In fact, we are currently undertaking such a study. No further action taken.
3. Point taken. Sub-headings have been provided as suggested.
4. The reviewers comment has been addressed by adding a sentence with regards to the Schulte-Steinberg equation/publication on page 10.
5. The reviewer is absolutely right- this was a mistake on our behalf. The patient at hand was in fact 14 months old and not 11 as previously stated. Appropriate alterations have now been performed in Table 1, with the youngest patient in group III being 13 months old.
6. In the vast majority of cases we used 3 mg/kg of propofol with immediate insertion of the LMA after loss of consciousness. This is our standard practice and works well. However, we do agree with the reviewer that if you wait, even for a very brief period of time, the insertion of the LMA is frequently not possible. No action taken.
7. Point taken. The length of the Epican needle is now corrected.
8. We completely agree with the reviewer regarding this point. However, we believe that we already in the original version of the manuscript have addressed this, page 11 blue text. No further action taken.
9. The requested reference has now been included as reference No 13.
10. The age of the patient is now given as requested in the Figure legend text (Figure 1).
11. Point taken. The number of patients in each point is now given as a corresponding number. We hope that this does clarify the situation in an acceptable manner. The figure legend has also been changed accordingly.

Reviewer No 3:

1. The reviewer adequately points out the intraspinal component of spread (posterior compartment/ anterior compartment). To clarify this point we have added text on page 13 that we hope is sufficient to address this point raised by the reviewer.
2. Abstract; Background. A change according to the suggestion made by the reviewer has been performed.
3. Ropivacaine 0.2 % is now used at the appropriate places in the abstract as suggested.
4. All the other language alterations suggested by reviewer No 3 have now been changed.
5. Comment regarding Reviewers own comment No 8. A smaller volume could obviously have been used in these patients but due to the standardization of the study it was chosen from the outset of the study to use the same volume in all patients, even though this would represent a somewhat excessive volume for more distal surgery.

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There were no objections to this part of the study design by the Ethics Committee. No action taken.

For Peer Review

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Date: 2010 08 23 Contributor name: MÄRIT LUNDBLAD
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 Manuscript number (if known): _____
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Segmental distribution of high volume caudal anesthesia in neonates, infants and toddlers as assessed by ultrasonography.

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Running title:

Caudal anesthesia assessed by ultrasonography

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Abstract

Background: The aim of this prospective, age-stratified, observational study was to determine the cranial extent of spread of a large volume (1.5ml/kg, ropivacaine 0.2 %), single-shot caudal epidural injection using real-time ultrasonography.

Methods: 50 ASA I-III children were included in the study, stratified in three age groups; neonates, infants (1-12 months) and toddlers (1-4 yrs). The caudal blocks were performed during ultrasonographic observation of the spread of local anaesthetic (LA) in the epidural space.

Results: A significant inverse relationship was found between age, weight and height and the maximal cranial level reached by 1.5 ml/kg of LA. In neonates, 93 % of the blocks reached a cranial level of $\geq$ Th12 vs 73 % and 25 % in infants and toddlers, respectively. Based on our data a predictive equation of segmental spread was generated: $\text{Dose (ml/spinal segment)} = 0.1539 \cdot (\text{BW in kg}) - 0.0937$

Conclusions: This study found an inverse relationship between age, weight and height and the number of segments covered by a caudal injection of 1.5 ml/kg of ropivacaine 0.2 % in children 0-4 years of age. However, the cranial spread of local anesthetics within the spinal canal as assessed by immediate ultrasound visualization was found to be in poor agreement with previously published predictive equations that are based on actual cutaneous dermatomal testing.

Keywords: caudal; anesthesia; ultrasound; children

Introduction

Caudal block is the most widely used regional anesthesia method in neonates and small children. Despite being the most common pediatric regional anesthetic block there are still certain issues that remain unclear. One such issue is the relationship between the injected volume of local anesthetics and the resultant spread of the local anesthetic solution within the spinal canal.

Various patient related factors have been used to determine predictive equations regarding the cranial extension of a caudal block (e.g. Schulte-Steinberg, Takasaki, Busoni). (1-3) The methodology to determine the cranial extension of the block has also varied considerably between publications; reaction to surgical stimulation, pin-prick or pinching, injection of radio-opaque dye with subsequent X-ray visualization or cadaver studies. (1-5) However, none of these methods allow real-time visualization of the spread within the spinal canal.

Due to the incomplete ossification of the sacrum and the vertebrae in young children it has been shown that the spread of local anesthetics inside the spinal canal can be visualized by the use of real-time high frequency ultrasound. (6-7) However, no published data so far describe the relationship between injected volume and cranial segmental spread as assessed by this new methodology. Thus, the aim of this prospective, age-stratified, observational study was to determine the cranial spread of a large volume (1.5 ml/kg) of local anesthetic as determined by real-time ultrasonography.

Material and methods

Following Ethics Committee approval and written parental informed consent, children 0-4 years of age (ASA physical status I - III) were enrolled in the study. Patients scheduled for elective subumbilical surgical procedures (e.g. urogenital, anal, foot and inguinal surgery), were eligible for study inclusion. Known contraindications to regional anesthesia (e.g. coagulation disorders, allergy to amide local anesthetics or local infection at the planned injection site) or anatomical abnormalities of the lumbosacral spine were defined as exclusion criteria.

The study patients were stratified according to age and divided into three different age groups; Group I: preterm and neonatal babies younger than 1 month (≤ 45 gestational weeks), Group II: infants 1-12 months, and Group III: toddlers 1-4 years of age (maximum weight 25 kg). A total of 45 patients were planned to be included ($n = 15$ per study group).

Biometric data

According to established clinical routine the children were weighed on admission. Patient height was measured with the patient lying supine on the operating table after induction of anesthesia, using a regular measuring tape. Body mass index (BMI) was subsequently calculated according to standard practice [$\text{weight (kg)} / \text{height}^2 (\text{m}^2)$].

Anesthetic protocol

A peripheral venous cannula was inserted already on the general pediatric ward after prior EMLA cream application. General anesthesia was induced by IV atropine (10 mcg/kg) and propofol (2-3 mg/kg), subsequently followed by insertion of a laryngeal mask airway to secure the airway. Anesthesia was thereafter maintained by sevoflurane-oxygen-air (FiO_2 0.3)

with the patient breathing spontaneously. Standard monitoring devices (ECG, pulse oximetry, end-tidal CO₂ and non-invasive arterial blood pressure) were used throughout the anesthetic.

Haemodynamic data

Heart rate and NIBP was recorded immediately before turning the patient to the left lateral decubitus position for insertion of the caudal block (baseline) and also immediately after surgical skin incision (to determine block success/failure).

Ultrasound investigation and caudal block procedure

After induction of anesthesia the child was positioned in the left lateral decubitus position. By manual palpation the lumbo-sacral junction was determined and the spinous process of L5 was thereby identified. The lumbar spinal processes were thereafter palpated and counted in a rostral fashion to identify the 12th thoracic spinous process. The 12th rib was subsequently identified by ultrasound visualization and followed medially to further verify that the spinous process of Th 12 had been correctly identified. The skin overlying the spinous process of Th 12 was then marked using a skin marking pen.

The ultrasound equipment used for the study was a portable Sonosite M-Turbo software 3.4.1 (Sonosite Inc.Bothell, WA, USA) with a 38 mm wide 7-13 MHz linear array probe. An initial longitudinal paramedian ultrasonographic investigation was performed to identify the epidural space, the conus medullaris, cauda equina and the termination of the dural sac.

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After sterile preparation of the injection site, the sacral cornuae and sacro-coccygeal membrane were palpated. The caudal space was subsequently cannulated using a pediatric 30 mm 25G caudal needle (Epican®, B Braun, Melsungen, Germany) attached to an extension tubing (BD Connecta™, Becton, Dickinson & Co, NJ, USA) An aspiration test was performed to exclude inadvertent intravascular placement, where after the local anesthetic solution was manually injected at a rate of approximately 0.5 ml/s. A total volume of 1.5 ml/kg of 0.2 % ropivacaine (Narop®, AstraZeneca, Södertälje, Sweden) was used, representing the upper limit of safe dosage (3 mg/kg) as described by Bosenberg. (8)

During the injection the ultrasound probe was maintained in the previously determined optimum paramedian position (see above) in order to visualize the cranial spread of the local anesthetic within the caudal/epidural space. The probe was moved cranially as needed in order to follow the advancement of the front of the local anesthetic bulk flow within the epidural space, as evidenced by an anterior displacement of the dura mater, resulting in a reduction of the antero-posterior diameter of the intrathecal space (Figure 1).

For a caudal block to be effective in patients undergoing inguinal hernia repair, the most frequent surgical procedure performed in this age group, a level of at least Th12 needs to be reached by the LA. Thus Th12 was used as an end point target level. When the local anesthetic reached the Th 12 level (the front of the local anesthetic having been identified as reaching the Th 12 skin mark), the volume so far injected was noted and the injection continued until the full total volume of 1.5 ml/kg had been injected.

After the injection of 1.5 ml/kg of local anesthetic the front of the epidural local anesthetic was identified and was positioned in the middle of the ultrasound picture. A skin mark was made corresponding to the middle of the ultrasound probe and the level reached was determined by counting the spinous processes from the previously indicated Th 12 spinous

process. If the ultrasonographic front of the local anesthetic was “hidden” behind the bone shadow of the vertebral lamina the front was approximated to the middle of the corresponding bone shadow.

The caudal block was performed by the attending anesthetist. Ultrasound scans were performed by two of the authors (ML, PAL).

Following the ultrasound examination the child was again placed in the supine position and prepared for surgery. Skin incision was not performed earlier than 15 minutes after the performance of the caudal block.

The caudal block was considered a failure if one or more of the following was noted: 1) movement of the limbs in association with skin incision, 2) an increase in heart rate and/or NIBP of >15% compared to baseline in association with skin incision, 3) intraoperative need for supplemental administration of fentanyl (1 mcg/kg), as judged by the attending anesthetist or anesthetic nurse.

Statistics

The two main study parameters were maximal cranial segmental spread and the number of patients in each age group where the local anesthetic was identified to have reached the target level of Th 12.

Associations between two variables were established by the Spearman rank correlation test. Kruskal-Wallis Test (non-parametric ANOVA) and the Mann-Whitney U-test was used for comparison of percentage of blocks reaching the target level Th12 in the three age groups.

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Based on weight and the resulting number of segments covered by the caudally injected LA a predictive equation was derived.

For Peer Review

Results

A total of 50 children were enrolled in the study. Three of these patients had to be excluded due to study protocol violations ($n = 2$) or inadvertent vascular puncture ($n = 1$), leaving 47 subjects to be included in the final analysis (Group I, $n = 15$; Group II, $n = 16$; Group III, $n = 16$).

Demographic data are presented in Table 1. All 47 blocks were judged to be clinically successful.

An inverse relationship was observed between the different age groups and maximal ultrasonography assessed cranial spread (Figure 2).

An inverse relationship was also observed with regards to individual age ($r_s = -0.5325$; $p=0.0001$), weight ($r_s = -0.5104$; $p = 0.0002$) and height ($r_s = -0.5326$; $p = 0.0001$) (Figure 3A, B, C).

The percentage of patients where the volume of 1.5 ml/kg of local anesthetic did reach the target level of Th12 was significantly different in the three age groups (Table 2, Figure 4). In Group I the target of Th 12 was reached in 93 % of patients, whereas the corresponding values were 73 % and 25 % of patients in Groups II and III, respectively.

The relationship between volume of local anesthetic per covered segment vs. biometric patient data (age, weight and height) is shown in Figure 5ABC. Compared to the predictive

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Takasaki equation, (2) ultrasound assessment overestimated the volume per segment relationship by a factor of approximately 2.5 (median 2.4; range 1.9-3.0) (**Figure 5B**).

If compared to the Schulte-Steinberg equation, which is age-based, ultrasound assessment overestimated the volume per segment relationship by a factor of more than three (Figure 5A).

A predictive equation based on our observed data is given below:

$$\text{Dose (ml/spinal segment)} = 0.1539 \cdot (\text{BW in kg}) - 0.0937$$

Discussion

The main finding of the current study was an inverse relationship between age and the number of segments covered by a caudal injection of 1.5 ml/kg of local anesthetic in children 0-4 years of age. A significantly higher proportion of blocks did reach the Th 12 level in newborns (93 %) as compared to infants (73 %) and toddlers (25 %).

Study design issues

Before commenting on the study results we would like to draw the readers' attention to two design features of the study. The first relates to the accuracy of the ultrasonography assessed segmental distribution. Due to the limited ossification of the sacrum and the vertebrae the ultrasonographic visualization of the intraspinal space is relatively easy in neonates and young infants but as ossification progress the visualization will gradually become more difficult. (7,9,10) Thus, the determination of the actual cranial extension of the injected volume was slightly more difficult to assess in the older age group in our study.

Secondly, a segmental determination based on cutaneous stimulation should ideally have been included in the study protocol to allow for comparison versus the ultrasound assessed levels. However, currently there does not exist any validated method or consensus view on how to perform such a cutaneous stimulation-based assessment of segmental spread in anaesthetized children. Furthermore, to be adequate such cutaneous testing must be performed approximately 20 minutes after the injection of the local anesthetic to allow for a reasonable onset time, something that for logistical reasons is not possible in many institutions due to case load and through-put demands. Deleted text.

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Correlation between cranial spread and patient characteristics

An inverse relationship between age (as well as weight and height) and the maximal cranial segmental spread could be identified in this study (**Figures 2 and 3**). A reflection of this fact was that almost all blocks in the neonatal age group did at least reach the level of Th 12 whereas only a minority of blocks in the oldest age group managed to reach this level (**Table 2, Figure 4**). The absence of the normal spinal curvatures in non-walking children, a difference in the amount of and the characteristics of epidural fat and various other factors may explain why a standardized injected volume reached more cephalad in neonates and infants as compared to toddlers. However, we believe that an important factor that may explain the inverse relationship found in this study is the pressure generated within the spinal canal during the injection of the local anesthetic. Usubiaga have previously described that spread within the epidural space in adults is directly correlated to the pressure generated by the injection. (11) In our study we chose to use a fixed injection rate regardless of the age/size of the patient. This fact **may** result in a higher end-injection pressure within the caudal-epidural space in neonates as compared to toddlers and may, thus, explain the more cranial levels reached in younger children. If the injection rates had been normalized to patient age/size (equating to the use of progressively higher injection rates with increasing age/size) the results of the study may well have been different. This points to the need for further studies addressing the relative influence of pressure on the cranial extension of caudal blocks in children.

Cranial extension assessed by ultrasound vs. previously published predictive equations

Contrary to our expectations, the agreement between the cranial level of the injectate determined by ultrasonography and the calculated levels based on previously published predictive equations (1-3) was very poor (**Figure 5A,B**). The use of the equations consistently

predicted approximately twice the number of blocked segments per volume of local anesthetic as compared to what could be observed by ultrasound. The poor correlation between ultrasound assessment and the predictive equations cannot be explained by the study data but we would like to put forward two different potential explanations for this lack of agreement. First, the end point of the studies that has generated the predictive equations differs considerably from the end point used in this study. Thus, in the previous studies the extension of the caudal block was determined by cutaneous stimulation (e.g. pin-prick or pinching) in children under light halothane anesthesia, whereas the end-point of the current study was the visualized front of the local anesthetic within the posterior compartment of the spinal canal. This situation obviously ends up in an “apple and pear” comparison that can explain the discrepancy between ultrasound assessment and the predictive equations. Second, there is also an important difference in the timing of the assessments of segmental spread. When using different objective visualization techniques, e.g. ultrasound assessment or radio-opaque dye injection, the determination of cranial block extension will be assessed almost immediately after the completion of the injection. This situation substantially differs compared to assessment by means of cutaneous stimulation that regularly is performed about 20 minutes after the injection of the local anesthetic. (1-4) Thus, the result generated by actual cutaneous testing will allow for a certain degree of redistribution of the local anesthetic within the spinal canal (e.g. later spread to the anterior compartment), which is quite different compared to the immediate snapshot produced by ultrasound visualization. Koo have recently provided support for this line of reasoning by showing that also immediate radiographic visualization of local anesthetics mixed with radio-opaque dye (volumes ranging 0.5-1.25 ml/kg) usually fails to reach higher than the thoraco-lumbar junction (Th10-L2) (12), corroborating previously published results from the same group (13). Similar observations following the injection of radio opaque dye has also been found by Thomas & Howard (personal communication, to be

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submitted). Thus, both immediate ultrasound assessment and early radiographic determination using radio-opaque dye will generate comparable results that both differ considerably from results generated by use of the predictive equations based on cutaneous testing.

The above raises the question whether ultrasound visualization of caudal blockade is clinically useful and should be incorporated as standard procedure in daily practice. As pointed out by previous authors, (6,7,9) ultrasound visualization of the spread of local anesthetics within the caudal/epidural space provides objective evidence that the injection is made in the proper anatomical space, thereby providing an almost complete guarantee that an appropriate block will develop if an adequate volume is used and a proper onset time is allowed. In this regard there is no alternative that currently can compete with ultrasound visualization and it is the authors' opinion that the use of ultrasound for this purpose should be encouraged.

However, due to the poor agreement with previously published predictive equations, that in fact are based on actual segmental cutaneous testing after a period of adequate onset time, it can be questioned whether an immediate snapshot ultrasound assessment of the cranial extension is of any major clinical value when trying to predict the final analgesic spread of a caudal block.

Conclusion

In conclusion, the current study found an inverse relationship between age and the number of segments covered by a caudal injection of 1.5 ml/kg of local anesthetic in children 0-4 years of age. However, the cranial spread of local anesthetics within the spinal canal as assessed by immediate ultrasound visualization was found to be in poor agreement with

previously published predictive equations that are based on actual cutaneous dermatomal testing.

For Peer Review

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Figure Legends;

Figure 1: Ultrasound image of intraspinal local anesthetic spread in a 4 kg neonate. The large-size arrow indicates the front of the local anesthetic bulk flow, the smaller arrows point at the dura mater.

Figure 2: Maximal cranial level in neonates (group I), infants (group II) and toddlers (group III). The solid bars indicate median values.

Figure 3:

A. Maximal cranial level in relation to age with regression line ($r_s = -0.5325$; $p = 0.0001$)

● Group I ○ Group II ▲ Group III. The numbers adjacent to some of the points in the graph refer to the number of patients represented in each point.

B. Maximal cranial level in relation to weight with regression line ($r_s = -0.5104$; $p = 0.0002$)

● Group I ○ Group II ▲ Group III.

C. Maximal cranial level in relation to height with regression line ($r_s = -0.5326$; $p = 0.0001$).

● Group I ○ Group II ▲ Group III.

Figure 4: Percentage of blocks reaching the target level Th12.

Figure 5:

A. Volume of local anesthetic per covered segment in relation to age with regression line ($r_s = 0.8371$; $p < 0.0001$). Dotted line represents the Schulte-Steinberg equation ¹.

B. Volume of local anesthetic per covered segment in relation to weight with regression line ($r_s = 0.9852$; $p < 0.0001$). Dotted line represents the Takasaki equation ².

C. Volume of local anesthetic per covered segment in relation to height with regression line ($r_s = 0.9662$; $p < 0.0001$).

Table 1: Patient data; median (range).

	Group I < 1 month	Group II 1 mo-1 year	Group III 1-4 years
Number of patients	15	16	16
Age (gestational weeks)	41.6 (35-45)		
Age (months)	≤ 1	4.75 (2-10)	18.0 (13-40)
Weight (kg)	3.2 (2.23-4.9)	7.8 (4.5-10.9)	11.9 (8.5-14.5)
Height (cm)	52 (47-58)	66 (55-77)	83.5 (73-100)
BMI kg/m ²	12.7 (11.8-16.2)	17.0 (14.3-21.0)	16.1 (13.7-20.0)

Table 2: Segmental spread

	Group I < 1 month	Group II 1 mo-1 year	Group III 1-4 years
Maximal cranial level; median (range)	Th 12 (L 1-Th 9)	Th12 (L 2- Th 10)	L1 (L 2 – Th 11)
Maximal level $\geq$ Th12, No of patients (%)	14 (93 %)	11 (73 %)	4 (25 %)
Volume of LA needed to reach Th12 level (ml/kg); median (range)	1.38 (0.67-1.5)	1.41 (0.85-1.5)	1.38 (1.2-1.5)

Figure 1: Ultrasound image of intraspinal local anesthetic spread in a 4 kg neonate. The large-size arrow indicates the front of the local anesthetic bulk flow, the smaller arrows point at the dura mater.
216x164mm (600 x 600 DPI)

Figure 2: Maximal cranial level in neonates (group I), infants (group II) and toddlers (group III).
The solid bars indicate median values.
66x39mm (600 x 600 DPI)

Figure 3A: Maximal cranial level in relation to age with regression line ($r_s = -0.5325$; $p = 0.0001$)
 ● Group I ○ Group II ▲ Group III. The numbers adjacent to some of the points in the graph refer to the number of patients represented in each point.

72x46mm (600 x 600 DPI)

Figure 3 B:Maximal cranial level in relation to weight with regression line ($r_s = -0.5104$; $p = 0.0002$)
● Group I ○ Group II ▲ Group III.
72x45mm (600 x 600 DPI)

Figure 3 C: Maximal cranial level in relation to height with regression line ($r_s = -0.5326$; $p = 0.0001$). • Group I ○ Group II ▲ Group III.
72x46mm (600 x 600 DPI)

Figure 4:Percentage of blocks reaching the target level Th12.
79x56mm (600 x 600 DPI)

Figure 5 B. Volume of local anesthetic per covered segment in relation to weight with regression line ($r_s = 0.9852$; $p < 0.0001$). Dotted line represents the Takasaki equation ².
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Figure 5 C:Volume of local anesthetic per covered segment in relation to height with regression line ($r_s = 0.9662$; $p < 0.0001$).

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