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The Association between Caudal Anesthesia and Increased Risk of Postoperative Surgical Complications in Boys Undergoing Hypospadias Repair

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Abstract

Introduction—Recent reports have suggested that caudal anesthesia may be associated with an increased risk of postoperative surgical complications. We examined our experience with caudal anesthesia in hypospadias repair to evaluate for increased risk of urethrocuteaneous fistula or glanular dehiscence.

Methods—All hypospadias repairs performed by a single surgeon in 2001-2014 were reviewed. Staged or revision surgeries were excluded. Patient age, weight, hypospadias severity, surgery duration, month and year of surgery, caudal anesthesia use and postoperative complications were recorded. Bivariate and multivariate statistical analyses were performed.

Results—We identified 395 single-stage primary hypospadias repairs. Mean age was 15.6 months; 326 patients had distal (83%) and 69 had proximal (17%) hypospadias. Caudal anesthetics were used in 230 (58%) cases; 165 patients (42%) underwent local penile block at the discretion of the surgeon and/or anesthesiologist. Complications of urethrocuteaneous fistula or glanular dehiscence occurred in 22 patients (5.6%) and were associated with caudal anesthetic use (OR 16.5, 95% CI 2.2-123.8, $p=0.007$), proximal hypospadias (OR 8.2, 95% CI 3.3-20.0, $p<0.001$), increased surgical duration (OR 1.01, 95% CI 1.01-1.02, $p<0.001$) and earlier year of practice (OR 3.0, 95% CI 1.2-7.9, $p=0.03$ for trend). After adjusting for confounding variables via multivariable logistic regression, both caudal anesthetic use (OR 13.4, 95% CI 1.8-101.8, $p=0.01$) and proximal hypospadias (OR 6.8, 95% CI 2.7-16.9, $p<0.001$) remained highly associated with postoperative complications.

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Ethics approval: Local Institutional Review Board oversight and exemption was sought and obtained (Duke University # 00060905). This work complies with the ethics policy of this journal.

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Conclusions—In our experience, caudal anesthesia was associated with an over 13-fold increase in the odds of developing postoperative surgical complications in boys undergoing hypospadias repair even after adjusting for urethral meatus location. Until further investigation occurs, clinicians should carefully consider the use of caudal anesthesia for children undergoing hypospadias repair.

Keywords

Regional anesthesia; Caudal anesthesia; Pediatrics; Hypospadias; Surgical Complications; Urethrocuteaneous fistula

Introduction

Hypospadias repair is one of the most frequently performed urologic procedures in boys. The incidence of surgical complications after operative repair is generally <10% for distal hypospadias but may range significantly higher in the setting of proximal hypospadias.(1-3) In studying surgical outcomes following hypospadias repair, most published reports have focused primarily on severity of the congenital defect (i.e., the pre- or intraoperative location of the urethral meatus) in addition to differences in surgical technique.(2-4) The impact of anesthetic technique has generally not been considered.

Caudal epidural anesthesia is frequently utilized as an adjunct to general anesthesia in pediatric groin/genital surgery. Reviews from several large studies have demonstrated the safety of caudal anesthesia.(5-7) Serious anesthesia-related complications of caudal anesthesia, such as intravascular or intrathecal injection of local anesthetic, are considered unusual. Long-term complications such as nerve damage or paralysis are very rare.

The impact of caudal anesthesia on the incidence of surgical complications is unknown. In a recent study by Kundra *et al* comparing penile nerve blockade to caudal anesthesia for repair of hypospadias, it was incidentally noted that there was a higher incidence of postoperative urethrocuteaneous fistula in patients who had received caudal anesthesia.(8) This unintended finding prompted a review of our own institutional experience with caudal anesthesia for hypospadias repair. Prior to reporting our own findings, 2 groups (9, 10) reported a significant increase in the rate of urethrocuteaneous fistulae after hypospadias repair in patients receiving caudal anesthesia. Conversely, such association was not confirmed by two other studies.(11, 12) There remains a need to answer this important question regarding any association of caudal anesthetic technique and postoperative surgical complications.

Methods

Patient Population

Institutional Review Board approval was obtained prior to chart review or data analysis. All charts on children having hypospadias repairs performed by one surgeon (JSW) at a single center between 2001 and 2014 were reviewed. Potential study candidates were identified from an institutional billing database using surgical codes for hypospadias repair. Each clinic chart and operative/anesthesia record was then individually reviewed by a fellowship-trained pediatric urologist (JCR) and fellowship-trained pediatric anesthesiologists (BMT, AKR,

JBE). Inclusion criteria were primary, single-stage hypospadias repairs performed at our institution. Exclusion criteria included planned 2-stage repairs, revision surgeries, and follow-up of less than 6 months (based on reports showing that the majority of complications present within 6 months of surgery).(13, 14)

Surgical and Anesthetic Considerations

Surgical and anesthetic techniques overall did not change over the study period with few exceptions. All patients received urethral stenting, though a change was made in catheter brand and size (7 French to 6 French). Over time, there was increased emphasis on universal creation of dartos flap coverage of the urethroplasty. Suture materials remained the same. Arterial tourniquet was performed in almost all cases, more to prevent bleeding from the glans during creation of wings and during the urethroplasty and approximation of the glans over the urethra. Surgical penile nerve block was performed with 0.25% bupivacaine in the early period, switching to 0.2% ropivacaine later due to hospital system changes based on safety data. A circumferential ring block was occasionally performed in the distal cases with normal proximal shaft. The dose did not exceed 1 ml/kg. Most cases had 0.5 – 1 ml of 1% lidocaine with 1:100,000 epinephrine injected in the glans for hemostasis. Caudal anesthesia was performed with either bupivacaine 0.25% or ropivacaine 0.2% throughout the study period. The dose typically varied between 2 to 3 mg/kg.

Clinical Data and Outcomes

Demographic and clinical data were extracted and included the following: patient age (in months); patient weight (in kilograms); position of the urethral meatus (defined intraoperatively as distal [glanular, coronal, or distal shaft] or proximal [mid-shaft, proximal shaft, penoscrotal, scrotal, or perineal]); duration of surgery (in minutes, from incision to drapes down); and month/year of surgery (for assessment of years of practice of the pediatric urologic surgeon). The principal predictor of interest was whether or not caudal anesthesia was performed perioperatively. The principal outcome was whether or not the complication of urethrocuteaneous fistulae and/or glanular dehiscence occurred in the postoperative period. Other complications were not specifically analyzed.

Statistical Analysis

Descriptive statistics and 95% confidence intervals (95% CI) were calculated; the primary outcome measure was Odds Ratios (OR). Statistical testing was performed using Fisher's exact test for categorical variables and Wilcoxon rank sum test for continuous variables. Multivariable logistic regression was used to adjust for the effect of confounding variables. Due to the relatively small number of events, only two covariates per model were used. The best-fitting model was selected by comparing the Akaike's Information Criteria and log likelihood tests of sequential models. The final model included the severity of hypospadias (distal vs. proximal as defined above) and whether or not caudal anesthesia was performed. Of note, severity of hypospadias was strongly associated with surgical duration, implying that both should not be considered in the same model in order to avoid collinearity problems. Despite the relatively small number of covariates, this model had a reasonable fit ($c=0.810$). All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). All tests were two-sided and p-values less than 0.05 were considered statistically significant.

Results

Cohort Characteristics

During the study period, 395 primary single-stage hypospadias repairs were performed that met all inclusion and exclusion criteria (Table 1). Mean patient age was 15.6 months (median 12, IQR 9-16), mean weight was 10.4 kg (median 9.6, IQR 8.7-11.1) and mean surgical duration was 139.7 minutes (median 134, IQR 108-164). 326 (82%) patients had distal hypospadias.

Anesthetic and Perioperative Factors

Of the 395 hypospadias repairs, caudal anesthetics were performed in 230 (58%) of the cases; the remaining 165 (42%) underwent local penile block at the mutual discretion of the surgeon and anesthesiologist. Of the 230 patients who received caudal anesthesia, bupivacaine was used in 34 (15%), ropivacaine in 186 (81%) and 10 patients had an unknown (not properly recorded) local anesthetic (4%).

In addition to the local anesthetics that were delivered in the caudal space, adjuncts included epinephrine that was used in 153 (67%) and clonidine that was used in 171 (74%). In the patients who received caudal anesthesia, intravenous dexamethasone was administered in 15 (7%), and intravenous ketorolac in 23 (10%). All patients were prescribed oral acetaminophen and ibuprofen for postoperative pain management.

There was no significant association between the development of perioperative complications and local anesthetics, adjuncts or perioperative medications (all $p>0.05$, Table 2).

Postoperative Outcomes

Urethrocutaneous fistula or glans dehiscence occurred in 22 patients (5.6% total; $n=9$, 2.8% for distal hypospadias; $n=13$, 18.8% for proximal hypospadias). Of these, 21 (95% of fistulae, 9% of caudal anesthetics) received a caudal anesthetic. On bivariate analysis, patients who received caudal anesthetics were significantly more likely to develop complications than those who did not (Table 3; OR 16.5, 95% CI 2.2-123.8, $p=0.007$). Similarly, complications were associated with severity of hypospadias (OR 8.2, 95% CI 3.3-20.0, $p<0.001$), increased surgical duration (OR 1.01, 95% CI 1.01-1.02, $p<0.001$) and earlier year of practice (OR 3.0, 95% CI 1.2-7.9, $p=0.03$ for trend). However, complications were not associated with patient weight (OR 1.01, 95% CI 0.88-1.15, $p=0.51$) or patient age (OR 0.99, 95% CI 0.94-1.03, $p=0.72$).

After adjusting for confounding effects via multivariable logistic regression (Table 3), both caudal anesthetic use (OR 13.4, 95% CI 1.8-101.8, $p=0.01$) and proximal hypospadias (OR 6.8, 95% CI 2.7-16.9, $p<0.001$) were each independently associated with development of postoperative complications (Figure 1).

Discussion

In this single-surgeon series of primary hypospadias repairs, we found increased odds of urethrocuteaneous fistula and glanular dehiscence among children who received caudal anesthesia, even after adjusting for hypospadias severity as defined by the position of the urethral meatus. This finding suggests an important potential implication for the use of caudal anesthesia in boys undergoing hypospadias repair since caudal anesthesia is often utilized for this procedure. We are actively investigating potential mechanisms for this finding and are organizing larger, multi-center studies in order to more definitively answer this question.

Our study is the largest reported series to date that suggests an association between caudal anesthesia and the incidence of surgical complications in children. Kundra *et al*(8) reported the association of caudal anesthesia and development of urethrocuteaneous fistula as an incidental finding in their study, although the authors note that the original aim of that study was to compare efficacy of penile nerve block with caudal anesthesia in 54 children (ages 4-12) undergoing distal hypospadias repair. Saavedra-Belaunde *et al*.(10) found a higher risk of surgical complications in their 192 patients who had undergone distal hypospadias repair when caudal anesthesia was used compared with penile block. Of the 11 children (6%) who developed urethrocuteaneous fistulae requiring further intervention in that study, 9 (81%) had received caudal anesthesia.(10) Kim *et al*.(9) found complications in 25% of their 342 patients having tubularized incised plate urethroplasty hypospadias repair undergoing a caudal block compared to 15% of those not receiving a caudal block. In contrast, Zaidi *et al*. (12) investigated the incidence of urethrocuteaneous fistula formation and its association with caudal anesthesia and found that the location of the urethral opening (proximal > mid > distal shaft) was strongly associated with fistula development. However, no association between fistula formation and use of caudal anesthesia was noted; instead, this group found that the use of subcutaneous epinephrine was instead associated with an increased risk of urethrocuteaneous fistula formation.(12) Because this latter datum was not captured by our surgical database in any consistent or meaningful way, we are unable to comment on whether it may have played a role in our findings (e.g., if subcutaneous epinephrine was used more consistently among patients who also happened to receive caudal anesthesia). Similar to what they report, our surgeon routinely injected lidocaine with epinephrine in the glans during all repairs except the most minimal glanular cases including those with and without caudal anesthetics. Finally, Braga *et al*.(11) found a statistically significant association between fistula development or glans dehiscence and pre-operative use of testosterone, proximal hypospadias, and use of caudal block on univariate analysis; however, the association was only significant for proximal hypospadias on multivariate analysis. Therefore, they concluded, as did Zaidi *et al*.(12) that the association between complications and caudal block was only a confounder and that the severity of the hypospadias was the only predictor of complications.

Caudal anesthesia in pediatric patients undergoing groin and genital surgery is a well-established regional anesthetic technique with a long history of safety.(6, 7) The benefits of this technique include decreased need for postoperative pain medication, decreased stress hormone response and increased overall patient/parent satisfaction.(5) For simple

circumcision, there is no significant difference in postoperative use of analgesic medication or outcomes between pediatric patients receiving caudal anesthesia, penile block, or systemic analgesia.(5) In contrast, hypospadias repair is more likely to result in the need for postoperative analgesia compared to circumcision, and the use of caudal anesthesia is therefore often considered a desirable technique for the repair of these more complicated penile surgeries.(15) Our practice of deciding between employing a caudal technique was likely based on several factors. The first was the presence or absence of a resident or fellow assigned to the case that would correlate with an increased incidence to perform a caudal for teaching purposes. Likewise, the move to the Ambulatory Surgical Center for many of these cases and rapid turnover with CRNA coverage may have played a role in decreased caudal use. Finally, another factor would be the expected severity of repair and anticipated surgical duration. A limitation to any retrospective review is that these factors and the decision making at the time were not recorded.

While the mechanism by which caudal anesthesia increases the risk of postoperative surgical complication remains unclear, it is hypothesized that changes related to blood flow may play a role. It is well established that central neural blockade (e.g., caudal anesthesia) may result in a decrease in sympathetic nervous system activity when the anesthetic block extends to the levels of T5-L1.(5) With 75% of the blood volume in the venous system, this decrease in vascular tone may result in venous pooling in the lower body, including the perineum and penis. Although epinephrine (often used as a test marker for intravascular injection in the local anesthetic solution with caudal anesthesia) may cause vasomotor dilatation due to its beta-adrenergic effects, it was not significantly associated with surgical dehiscence in our study. Increased venous pooling would perhaps explain Kundra's finding of increased penile engorgement in 27% of boys receiving a caudal block at 10 minutes after local anesthetic injection in children undergoing caudal anesthesia.(8) Penile engorgement from the vasodilatory effect of caudal anesthesia could influence the quality of intraoperative surgical repair or result in impaired postoperative wound healing, thus increasing the risk of postoperative complications. A prospective study controlling for timing and technique of caudal anesthesia, including choice of local anesthetics, anesthetic concentrations, injection volumes, and use of epidural adjuncts (such as epinephrine or clonidine) as well as circulatory parameters could help to better define the possible mechanism and true incidence of surgical complications related to caudal anesthesia for hypospadias repair. In addition, the practice of using epinephrine directly to the glans must be controlled and precisely recorded. We are actively planning research projects to further evaluate the relationship between caudal anesthesia and hypospadias complications, including incidence and mechanisms and would be interested in supporting future multicenter projects on this topic.

Our findings should be considered in the context of this study's limitations. First, our report is retrospective and reviews the outcomes from one surgeon at one medical center over a 13-year period. It is possible that our findings are unique to our practice and are not necessarily generalizable to other centers. We, however, believe that limiting our study to patients from a single surgeon is a strength of our study in comparison to others because it removes a potential confounding variable of multiple surgeons. Although patients were followed for a minimum of 6 months, it is possible that we missed postoperative complications that occurred beyond that timeframe. Published data suggest that this is unlikely, however, given

that the majority of significant postoperative issues usually occur within 6 months.(13, 14) It is worth noting that Saavedra-Belaunde *et al.* had a mean 3-year follow up for their boys following hypospadias repair, and there was no evidence that this increased duration of surveillance resulted in additional findings.(10) Furthermore, the purported mechanism of action of caudal anesthesia on hypospadias complications would intuitively seem to be more likely to occur over a short-term window such as 6 months rather than a longer-term period. Lastly, although caudal anesthesia might have been used in patients more likely to develop complications (*i.e.*, those with more severe hypospadias whose repairs would have had a longer surgical duration), we corrected for potential bias and confounding variables in our statistical analysis, though the analysis was limited by the sample size. By including both caudal anesthesia use and hypospadias severity in the multivariable analysis, we were able to conclude that, in our experience, both factors were independently associated with the development of these postoperative complications.

Conclusions

In our experience, after correcting for other factors, caudal anesthesia was associated with a significant increase in the odds of postoperative surgical complications, namely urethrocuteaneous fistula and glans dehiscence, in children undergoing hypospadias repair. A randomized control trial or multicenter prospective study would further clarify associated risk factors.

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Research Report

What is already known

Urethrocutaneous fistula is a known complication of hypospadias surgery. Recent reports have suggested that caudal anesthesia may be associated with an increased risk of fistula formation.

What this article adds

Our study reviewed 395 repairs performed by a single surgeon over 13 years. In our experience, caudal anesthesia was associated with an over 13-fold increase in the odds of developing postoperative surgical complications in boys undergoing hypospadias repair even after adjusting for urethral meatus location.

Figure 1. Complication rates for distal (left) and proximal (right) hypospadias repairs with and without caudal anesthesia.

Table 1
Patient Demographics

	No Complications (n=373)	Fistula or Dehiscence (n=22)	Odds Ratio (95% CI)	P-Value
Age in Months (Mean, SD):	15.7 (12.6)	14.3 (9.2)	0.99 (0.94-1.03)	0.72 *
Weight in kg (Mean, SD):	10.4 (3.2)	10.2 (4.6)	1.01 (0.88-1.15)	0.51 *
Caudal Anesthesia Used:				
Yes	209 (91%)	21 (9%)	16.5 (2.2-123.7)	<0.001 ^
No	164 (99.4%)	1 (0.6%)		
Severity of Hypospadias:				
Glanular	108 (99%)	1 (1%)	1.8 (1.5-2.3)	<0.001 ^
Coronal	183 (97%)	5 (3%)		
Distal Shaft	26 (90%)	3 (10%)		
Mid-Shaft	24 (100%)	0 (0%)		
Proximal Shaft	12 (75%)	4 (25%)		
Penoscrotal	12 (57%)	9 (43%)		
Scrotal/Perineal	8 (100%)	0 (0%)		
Surgery Performed Before 2008				
Yes	175 (92%)	16 (8%)	3.0 (1.2-7.9)	0.03 ^
No	198 (97%)	6 (3%)		
Surgery Duration in Minutes (Mean, SD)	137.1 (55.3)	188.2 (47.9)	1.01 (1.006-1.02)	<0.001 *
Total Intraoperative Fluid(ml/kg/hour anesthesia) (Mean, SD)	11.8 (5.1)	11.4 (3.7)	0.87 (0.37-2.05)	0.99 *
Total Perioperative Fentanyl (mcg/kg) (Mean, SD)	2.36 (2.0)	2.34 (1.9)	0.99 (0.80-1.25)	0.83 *

* = Wilcoxon rank-sum test

^ = Fisher's exact test

Table 2
Bivariate comparison of caudal and perioperative medications and hypospadias complications among patients receiving caudal anesthesia

	No Complications (n=209)	Fistula or Dehiscence (n=21)	Odds Ratio (95% CI)	P-value [^]
Local				
Unknown	9 (90%)	1 (10%)	0.59 (0.07- 5.16)	0.34
Ropivacaine	171 (92%)	15 (8%)		
Bupivacaine	29 (85%)	5 (15%)		
Epinephrine				
Yes	142 (93%)	11 (7%)	0.52 (0.21-1.3)	0.15
No	67 (87%)	10 (13%)		
Clonidine				
Yes	156 (91%)	15 (9%)	0.85 (0.31-2.30)	0.79
No	53 (90%)	6 (10%)		
Ketorolac				
Yes	20 (87%)	3 (13%)	1.57 (0.43- 5.82)	0.45
No	189 (91%)	18 (9%)		
Dexamethasone				
Yes	14 (93%)	1 (7%)	0.69 (0.09- 5.58)	0.99
No	195 (91%)	20 (9%)		

[^]
 = Fisher's exact test

Table 3
Bivariate and Multivariate Logistic Regression Analysis of Hypospadias Complications

	OR	95% CI	P-Value	Adjusted OR	95% CI	P-Value
Severity (Proximal vs. distal)	8.2	3.3-20.0	<0.0001	6.8	2.7-16.9	<0.0001
Caudal Anesthesia (Yes vs. No)	16.5	2.2-123.8	0.0065	13.4	1.8-101.8	0.01
Surgical Duration (> vs. < 150 minutes)	3.5	1.4-8.5	0.005	-	-	-
Surgery Year (2001-07 vs. 2008-14)	3.0	1.2-7.9	0.03	-	-	-