Analysis of preoperative antibiotic prophylaxis in stented, distal hypospadias repair

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Introduction: *Surgical site infection [SSI] is a risk for any surgical procedure, including hypospadias repair. Prophylactic antibiotic therapy for patients having surgery is often effective in preventing SSIs, but with increasing rates of antibiotic resistance, this practice has been questioned. The objectives of this study are 1) to assess the incidence of SSIs in patients following stented, distal hypospadias repair and 2) to observe for any potential difference in the incidence of SSIs for patients with and without preoperative antibiotic utilization in this setting.*
Materials and methods: *We retrospectively reviewed consecutive patients treated with stented, distal hypospadias repair from 2011 to 2014 by three surgeons and compared two groups: patients who received preoperative antibiotics and patients who did not. Patients with a history of previous hypospadias repair were excluded from the study.*
Results: *Two hundred twenty-four subjects were identified. Group 1 (135) received preoperative antibiotic and Group 2 (89) did not receive preoperative antibiotics. There was no statistically significant difference in SSI prevalence with 0 patients in Group 1 and 1 patient in Group 2 having a SSI.*
Conclusion: *Although prophylactic antibiotics prior to hypospadias repair are most often used by pediatric urologists, this study demonstrates further evidence that antibiotics prior to this procedure do not appear to lower the rate of SSI. This study is limited by its retrospective nature and disparate mean follow up in the two cohorts. Surgical site infection does not appear to be decreased by prophylactic antibiotic therapy before distal hypospadias repair.*

Key Words: hypospadias, surgical site infection, prophylactic antibiotics

Introduction

Hypospadias is a common problem in boys, affecting 1/300 live male births,[1] and most often is corrected early in life. Surgical site infection [SSI] is a risk for any surgical procedure, including hypospadias repair, with SSIs comprising the second most common cause of nosocomial infection. Almost 5% of clean extra-abdominal operations can be complicated by SSIs.[2,3] Prophylactic antibiotic therapy for patients having surgery is often effective in preventing SSIs, but with increasing rates of antibiotic resistance, this practice has been questioned.

The American Urological Association [AUA] has recently redefined the role of prophylactic antibiotics in adult urologic surgery,[4] but no such guidelines exist for urologic surgery in children. Ellett et al recently

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retrospectively evaluated their data on the prevalence of SSI for all non-endoscopic pediatric urologic procedures and found a low prevalence of SSI in surgical wound class 1 with a higher rate of SSI in patients in wound class 2.[5] Currently, the mainstay for management of hypospadias repair to prevent SSIs and other types of infections is to use both prophylactic antibiotics preoperatively and postoperatively following stented, distal hypospadias repairs.[6,7] In a recent survey of members of the Society of Pediatric Urology, preoperative antibiotics were used by 76.6% of pediatric urologists before distal hypospadias repair utilizing a postoperative urethral stent.[8,9] However, scant evidence exists demonstrating effectiveness for preoperative antibiotics in reducing the prevalence rate of SSIs.

Baillargeon et al recently reviewed their series of 150 patients with a history of hypospadias repair and analyzed the impact of both preoperative and postoperative antibiotic therapy upon outcomes. This retrospective review demonstrated no benefit in reduction of wound infections for patients receiving preoperative antibiotic therapy as compared to those who did not.[10] Although this report provides some evidence against utilization of antibiotic therapy in this setting, significant variation exists in the technique for repair and the utilization of postoperative urethral stenting with both primary and re-operative repairs included in the series. This lack of uniformity of data dilutes the potential impact of this study.

Variability in utilization of preoperative antibiotic therapy prior to hypospadias repair existed at our institution with two surgeons utilizing preoperative antibiotics while a third surgeon has not done so. With this disparity in antibiotic utilization, we recognized an opportunity to build upon the preliminary findings of Baillargeon and colleagues. Therefore, the aims of this study are 1) to assess the incidence of SSIs in patients following stented, distal hypospadias repair and 2) to observe for any potential difference in the incidence of SSIs for patients with and without preoperative antibiotic utilization in this setting.

Materials and methods

After ethics board approval, we retrospectively reviewed the Division of Urology Hypospadias Database for all patients treated with stented, distal hypospadias repair from 2011 to 2014 by three surgeons at Arkansas Children's Hospital [ACH] in Little Rock, AR, USA. The database was stored in REDCap (Research Electonic Data Capture: 1UL1RR029884) managed by the AR Children's Hospital Research Institute in partnership with the UAMS Translational Research Institute.[11] Consecutive patients with distal penile, subcoronal, coronal, and glanular hypospadias treated with hypospadias repair with urethral stent drainage were included. Patients with a history of previous hypospadias repair were excluded from the study.

Utilization of preoperative antibiotic therapy for distal, stented hypospadias repair at our institution is based upon the surgeon preference. Two of the three surgeons used antibiotics in this setting. Patients were placed into two groups for this review. Group 1 included patients that received the standard preoperative antibiotic cefazolin 30 mg/kg intravenously or clindamycin 10 mg/kg for patients with a penicillin allergy. Group 2 included patients having surgery with no prophylactic antibiotics. Also, the standard practice for all three surgeons at our institution was to utilize postoperative antibiotic therapy (sulfamethoxazole/trimethoprim (2 mg/kg)) during the urethral stenting period.

Patient characteristics recorded include patient age at surgery (months), location of urethral meatus, the type of hypospadias repair technique utilized, and the length of follow up after surgery. The primary outcome evaluated for the two groups was the presence or absence of postoperative SSI defined by the presence of postoperative penile erythema and/or purulent drainage treated with therapeutic antibiotics. The secondary outcome is the incidence of post-surgical complications such as: urethrocuteanous fistula, meatal stenosis, wound dehiscence, and urethral diverticulum. Comparisons of several other outcomes including cost of antibiotics also were performed between Groups 1 and Group 2.

Follow up for hypospadias repair at our institution typically consists of urethral stent removal approximately 1 week after surgery and subsequent reevaluation 3-4 months later with additional evaluations as needed. At the time of urethral stent removal, each patient was evaluated by our nurse practitioner or one of the surgeons on our team for signs of SSI or any complications of hypospadias surgery.

Statistical analysis

Descriptive statistics such as mean and standard deviation for continuous variables, counts and percentages for categorical variables were summarized. Between-group comparisons were carried out using two-sample t-test with unequal variance and Fisher's Exact Test for continuous and categorical variables, respectively. All p values less than 0.05 were considered to indicate statistical significance. The analyses were finished in Stata 14.0 (College Station, TX, USA).

Results

We queried the clinical hypospadias database with 224 consecutive patients identified in these two groups. Group 1 consisted of 135 (60.3%) patients given preoperative antibiotics, and Group 2 had 89 (39.7%) patients who received no preoperative antibiotics. Additionally, 209 patients received postoperative antibiotic therapy during the urethral stenting period with a subset of 15 patients treated without postoperative antibiotics: 10 in Group 1 (7.41% of Group 1) and 5 in Group 2 (5.62% of Group 2).

The median age at surgery was 15.96 months and 15.72 months in Group 1 and Group 2, respectively, Table 1. Of the collective 224 patients identified, 38.39% had a subcoronal hypospadias defects and 21.88% had distal shaft hypospadias. Comparison of meatus location between the two groups demonstrated a statistical significance with Group 1 having a slightly more proximal meatal location on average as compared to Group 2 ($p < 0.01$). Collectively, the most common type of hypospadias repairs performed were tubularized incised plate [TIP] urethroplasty (57.14%), TIP with preputial inlay (18.30%), Thiersch-Duplay technique (18.30%), and other miscellaneous techniques (< 10%). There was no statistical difference in the operative techniques utilized for Groups 1 and 2.

There was no statistically significant difference in prevalence of postoperative SSI observed for Groups 1 and Group 2 with 0 patients in Group 1 and only 1 patient in Group 2 found to have had a SSI ($p = 0.4$), Table 2. The only patient found to have a SSI in the study had a subcoronal hypospadias defect that received no preoperative or postoperative antibiotic therapy and had been repaired with TIP with preputial inlay grafting. This patient was treated with antibiotic therapy with successful resolution. No patients in the study required surgical drainage of their wound.

Collectively, there were 13 (5.80%) secondary outcomes of urethrocutaneous fistula, meatal stenosis, urethral diverticulum, and wound dehiscence for the two groups. No significant difference was observed in the rate of complications in Group 1 (5.19%) versus Group 2 (6.74% ($p = 0.77$)), Table 2. The relative urethrocutaneous fistula rates were 6 (4.44%) and 5 (5.62%) for Groups 1 and 2, respectively ($p = 0.76$). The average length of follow up was 2.14 and 2.68 years for Groups 1 and 2, respectively ($p < 0.01$).

The cost for utilization of antibiotic therapy was $9.93 per administration. The total cost for the utilization of antibiotic therapy for Group 1 was $1,340.55.

TABLE 1. **Preoperative comparison of groups**

	Group 1 preoperative ABX	**Group 2 no preoperative ABX**	**p value**
Number of patients (n = 224)	135 (60.3%)	89 (39.7%)	---
Median age at surgery (months)	15.96 ± 1.92	15.72 ± 0.72	0.87
Meatus location			< 0.01
Glanular (n = 40)	24	16	
Coronal (n = 49)	13	36	
Subcoronal (n = 86)	54	32	
Distal shaft (n = 49)	44	5	
Type of repair			0.17
TIP (n = 128)	78	50	
Thiersch-duplay (n = 41)	23	18	
Preputial inlay graft w/TIP (n = 41)	21	20	
MAGPI (n = 9)	8	1	
Barcatt (n = 2)	2	0	
GAP (n = 3)	3	0	
Use of postop ABX			0.79
Postop ABX used (n = 209)	125	84	
No postop ABX used (n = 15)	10	5	

ABX = antibiotics; TIP = tubularized incised plate; MAGPI = meatal advancement and glanduloplasty; GAP = glans approximation procedure

TABLE 2. **Complications noted by group**

	Group 1 preoperative ABX	Group 2 no preoperative ABX	p value
SSI Noted	0/135	1/89 (1.1%)	0.41
Secondary outcomes	7/135 (5.19%)	6/89 (6.74%)	0.77
Urethrocutaneous fistula	6	5*	0.76
Meatal stenosis	1	1*	0.99
Uretrhal diverticulum	0	1	0.41
Wound dehiscence	0	0	----

*one case had both meatal stenosis and urethrocutaneous fistula
ABX = antibiotics; SSI = surgical site infection

Discussion

Prophylactic antibiotic use has been standard practice following stented, distal hypospadias repair for most pediatric urologists. In fact, a 2010 survey of members of the Society of Pediatric Urology revealed that more than 75% of the members preferred to use preoperative prophylactic antibiotics, and 91% of these surgeons also use postoperative antibiotics as well.[8] However, the incidence of postoperative SSIs following distal hypospadias repair appears to be very uncommon with Baillargeon et al noting 2/150 (1.3%)[10] and the present study noting 1/224 (0.4%) SSI prevalence rate. Furthermore, both studies challenged the need for preoperative antibiotic prophylaxis with neither study demonstrating any benefit for prophylactic antibiotic therapy in prevention of SSI after distal hypospadias repair.

In contrast, Ellett et al strongly encouraged the utilization of preoperative antibiotic therapy in patients having wound class 2 surgical procedures, including children with hypospadias repair.[5] Their study evaluated a total of 1185 unique patients who had undergone non-endoscopic urologic surgical repair with 10 total SSIs observed (overall infection rate of 0.83%). Seven hundred five patients had penile surgery with the total number of hypospadias repairs not reported. Three of 6 patients with SSIs in the study had undergone hypospadias repair and classified as wound class 2. Based upon a higher rate of post-surgical infections for wound class 1 (0.34%) as compared to wound class 2 (2.28%), the authors concluded that "perioperative antibiotics are strongly indicated in these patients (surgical wound class 2 repair) due to their significantly higher risk." However, all patients with hypospadias repair and post-surgical infections received preoperative antibiotic therapy in the study by Ellett et al with no control group of patients without preoperative antibiotics. No further subgroup analysis of hypospadias repair was reported in this study.

The study of Baillargeon et al consisted of 150 patients retrospectively analyzed with 62 having received preoperative antibiotics and 88 with no preoperative antibiotics. Baillargeon et al observed no reduction in SSIs with a single patient noted to have an SSI in each group.[10] However, only 135 (90%) patients in their study had primary hypospadias repair, and only 97 patients (65%) utilized a urethral stent following hypospadias repair. In the preoperative antibiotic group, 87% of patients received postoperative antibiotics, while 56% of patients in the non-preoperative antibiotic group also received postoperative antibiotics ($p < 0.05$). Relative to the series of Baillargeon et al, all patients in our database with non-stented and re-operative hypospadias repair were excluded from the analysis in order to optimize the uniformity of the patients studied. Our study population consisted primarily of patients undergoing primary TIP or TIP with inlay repair (169 patients, 75.4%). No significant difference existed in complications of hypospadias rates in the two cohorts and the length of follow up was significantly longer in Group 2 (2.68 years) as compared to Group 1 (2.14 years) ($p = < 0.01$).

While the purpose of postoperative antibiotic usage after stented, distal hypospadias repair is the reduction of postoperative UTIs,[9] the impact of these antibiotics on the prevalence of SSIs is unknown. In the effort to lower the incidence of postoperative UTIs while having a urethral stent in place, it is plausible that antibiotics use for this purpose may in fact impact the rates of SSIs after surgery as well. Sulfamethoxazole/trimethoprim, for instance, is active against gram-positive bacteria such as staphylococci and streptococci, common skin flora

causing SSI. None of the prospective analyses evaluating patients following stented hypospadias repair have included an arm without antibiotics both pre and post hypospadias repair. Five patients in the current study did not receive antibiotic therapy before or after hypospadias surgery. These findings coupled with other evidence in the literature challenging the need for antibiotic therapy after distal hypospadias surgery prompted our division to begin an institutional randomized study that is well under way testing the need for postoperative antibiotic therapy versus no antibiotic therapy with no preoperative antibiotic prophylaxis in either group. It also is worth noting that patients who elect not to participate in the randomized trial are now typically not treated with preoperative or postoperative antibiotics with distal hypospadias repair any longer.

Although the cefazolin is not an expensive intravenous antibiotic medication, utilization of this drug lead in the setting of distal hypospadias repair amounted to an additional total cost of $1,340.55 for the 135 patients in Group 1. While this cost is not large, the similar outcomes in prevalence of SSIs and hypospadias outcomes for Groups 1 and 2 calls into question the benefit of this additional cost for patients undergoing this procedure.

The limitations of our research include small sample size without large enough power for evaluation of the rarity of the end points studied. In order to make more conclusions on the necessity for preoperative antibiotics, a prospective randomized control study has been started at our institution. Recall bias and inadequate charting are additional limitations in a retrospective chart review that may cause misinterpretation. Because the use of preoperative antibiotics was based on surgeon preference, this study is subject to selection bias as well. This study may be limited by the fact that patients may have presented to an outside facility for a SSI that was not reported to our institution. Lastly, a statistical difference in the location of the hypospadic meatus is another limitation although this may be due to subjective difference in categorizing distal and subcoronal hypospadias.

Conclusion

The incidence of surgical site infections in patients treated with stented, distal hypospadias repair observed was very low. We also observed no difference in the rate of surgical site infections for the two groups treated with or without preoperative antibiotic therapy. Based upon our findings and other retrospective series, a randomized controlled prospective study is being conducted to evaluate the need for antibiotics in patients with distal hypospadias repairs. □

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