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Urinary tract infection in boys with hypospadias

Abstract

The aim of this study was to evaluate the frequency of urinary tract infections (UTI) in boys with hypospadias pre- peri- and post-operatively in order to determine whether antibiotic prophylaxis for UTI is warranted when they undergo a reconstructive surgery for hypospadias. Included in the study group were 174boys undergoing reconstructions for hypospadias. The control group comprised 204 boys operated on for an inguinal hernia. The main outcome measure was the documented finding of a urinary tract infection verified by a positive bacteria culture. The results revealed a significant difference in the findings of a positive urinary culture between the boys undergoing hypospadias surgery, 7.5%, and those operated on for an inguinal hernia, 1.5%, (p=0.0044). The difference between the groups was not significant in the pre- and peri-operative periods. A higher incidence of infections was noted in boys who had other congenital malformations in addition to hypospadias (P=0.02).

Thus, the boys with hypospadias are more likely to incur a urinary tract infection. Since the results did not show a higher incidence of symptomatic urinary tract infections shortly after the surgery, it may not be advantageous to administer prophylactic antibiotics to decrease the number of urinary tract infections. However, comparison of subgroups consisting of the hypospadias without and with prophylactic antibiotics remains to be conducted.

Keywords: hypospadias repair, outcome, complications, urinary tract infections

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Introduction

Hypospadias surgery is hampered with complications. This problem has been addressed by several different methods of reconstructive surgery. More than 300 different procedures have been described in the literature for the treatment of this condition.[1] This considerable number of different operative interventions reflects the frustration of surgeons facing the high rate of complications that result from hypospadias surgery. Furthermore, the complication rate has been addressed by questioning the need for reconstruction in all boys with hypospadias suggesting that operative interventions should only be used for those with preoperative symptoms such as stenosis, curvature, or both.[2] This is further supported by a recent study of long-term complications after hypospadias surgery that does not correlate with preoperative symptoms of the boys.[3]

Another approach to the problem of frequent complications with hypospadias surgery is the use of antibiotic prophylaxis and postoperative treatment. Therefore, surgeons often administer prophylactic antibiotics, which entail administering one dose of antibiotics preoperatively. This is done in order to reduce the risk of a possible urinary tract infection (UTI) or wound infection related to the surgery or the malformation.[4] Previous studies regarding the use of prophylactic antibiotics after hypospadias repair show a difference of opinion.[4–8] Due to increasing prevalence of antibiotic resistance it is important to investigate whether the incidence of UTIs is higher in hypospadias patients and what actions should be taken regarding the antibiotic use associated with the operation.[9]

The aim of this study was to evaluate the frequency of urinary tract infections in boys with hypospadias pre- peri- and post-operatively in order to determine whether antibiotic prophylaxis is warranted for those undergoing a reconstructive surgery for their hypospadias. We are not aware of any similar studies that were focused on determining the frequency of UTI in boys with hypospadias undergoing reconstructive surgery.

Materials and methods

Settings and patients

All patients were treated at a tertiary center of pediatric surgery, which conducts approximately 50% of hypospadias procedures in a region with a population of around 1.8million inhabitants and the birth of 22,000 newborns every year. As healthcare is free in the region, noncompliance due to socioeconomic factors is unlikely. Data was retrospectively collected from medical records and surgical records. The study group comprised boys who underwent a primary surgery for urethral reconstruction. All primary urethral reconstructions during this period were included. The senior hypospadias surgeon at the hospital, or a surgeon trained by him, performed the reconstructions. The surgeon who performed the operation was also responsible for the preoperative evaluation and work-up, as well as follow-up. The study group of hypospadias patients was compared to a control group of 204boys, age 1-5years, operated on for an inguinal hernia. The control group was selected based on age and gender, in order to correspond approximately to the hypospadias group in regard to age at operation and the duration of follow-up.

The surgical methods

Tabularised incised plate repair (TIP): When a TIP repair[10] is performed a U-shaped skin incision is made along the edges of the urethral plate and the penis is degloved. The urethral plate is widened by a midline incision along its length and then tabularised over a stent. A pedicle of subcutaneous tissue is dissected from the ventral or dorsal penile skin and used to cover the neourethra. Finally, the glanular wings, mucosal collar and ventral penile skin are closed in the midline.

Mathieu and "V" Incision sutured meatoplasty (MAVIS): During a MAVIS[11] repair a Mathieu procedure[12] is first performed, that is a skin flap based towards the meatus is turned 180 degrees and sutured

into incision on both sides of the glanular groove and along the tip. Curvature is corrected when present. An outer cover is achieved by partially dividing and mobilising the prepuce to create an outer layer. Then a "V"-incision is made and excised at the apex of the flap and the sides of the "V" are sutured to the glans flaps. The purpose of the "V"-incision is to achieve a vertical slit meatus.

Duckett reconstruction: When a Duckett reconstruction[13] is performed a straightening procedure is firstly done. Then the ventral preputial flap is fanned out and the urethra outlined as a rectangle that is then incised and rolled into a tube over a catheter. An island flap is developed by dissection of subcutaneous tissue from the dorsal penile skin. A glans channel is created with scissors in a plane just above the corpora and all glans tissue is removed from the channel. The island flap urethra is spiralled ventrally, anastomosed to the proximal urethra and delivered to the tip of the glans. Finally, Byars flaps, composed of dorsal penile skin, are transpositioned to the midline.

Modified Byars two-stage reconstruction: Using the Byars technique[14] one starts with a straightening up procedure. A circumferential incision is made proximal to the coronal sulcus, the curvature is corrected and the penile shaft is degloved. Penile straightening and full removal of tension creating structures must be confirmed by means of the artificial erection test. The glans is either divided deeply in the midline to the tip or, if the mucosal groove is deep, this is preserved and incisions are made just lateral to the groove on each side. The dorsal foreskin is unfolded carefully and divided in the midline. The most distal portion of the foreskin is rotated into the glanular cleft and sutured to the mucosa of the glans. A midline closure is performed, and the midline sutures catch a small portion of Buck's fascia. The bladder is drained with an 8-F Silastic Foley catheter for approximately 5-7days.

The second stage of the procedure is carried out 6-12months later, when the tissues have usually softened sufficiently and healing is complete. The previously transferred preputial skin is used to reconstruct the glans and urethra. A-16 mm-diameter strip is measured, extending to the tip of the glans. The strip is tabularised with a running subcuticular stitch all the way to the tip of the glans. The lateral skin edges are mobilized and the remaining tissue is closed over the repair in at least two layers. A strip of skin (3-5mm wide) is then de-epithelialized on one side to provide a raw surface of deep dermis. The medial edge of the shaved flap is brought across the buried uretheroplasty and sutured to fascial tissue beneath the other flap.

Study design

The information collected from the hypospadias patients and the control group was: age, surgery date, number of and the date of UTIs, if a urine culture was taken, and if positive, the microorganism. In order to investigate the number of urinary tract infections in each group, a regional database of bacteriological cultures was used to confirm infection in the urine cultures. Positive bacteria cultures before, during, and after the primary operation were included in this study. All infections that occurred from birth until the primary urethral reconstruction were deemed preoperative, while a perioperative UTI was defined as one confirmed at the day of the operation and within 30 days after the operation. Postoperative infections included infections that occurred after 30days from the surgery date up until the end of this study (May 2015). For the hypospadias patients the following data was also registered: the use of prophylactic antibiotics, other congenital abnormalities of the genitourinary tract, and the degree of hypospadias.

Literature review

The Pub Med database was searched using the following key words: "hypospadias urinary tract infection" (06-05-15). "Bacteria resistance urinary tract" (11-05-15), and "asymptomatic UTI antibiotics children" (01-06-15). Ten articles met the study criteria and were used for background and discussion purposes. The references used were found reliable and relevant for the purpose of this study.

Statistical analysis

Sample size calculation was performed; it provided a sample size of 71 for both samples based on:

The value expected from the study group was 8% and that expected from the control group was 2%.

i. The alpha error level or confidence level was 5%, corresponding to a 95% confidence interval (probability of incorrectly rejecting the null hypothesis that there is no difference in the percentage values).

ii. Beta error level or statistical power (1-beta) was 50% (probability of incorrectly failing to reject the null hypothesis that there is NO difference in the percentage values-assuming no difference when a real difference exists).

Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences). Fisher's exact probability test (two tailed) was used for dichotomous variables and the Mann-Whitney U-test was used for continuous results. $P<0.05$ was considered statistically significant.

Ethical considerations

This study was performed according to the Helsinki declaration and approved by the Regional Ethical Review Board (registration number 2010/49). The study protocol was designed to meet the legislative documentation required by the country of origin. The data were anonymized prior to calculations, and are presented in such a manner that it is impossible to identify or link to any specific individual. Therefore, it was not necessary to obtain approval from the individual patient's guardians. Since this data was retrospectively collected, the treatment plan of each patient was not altered. All evaluations, treatments, and procedures described in this report met the standard of care and were conducted at a tertiary center for pediatric surgery. No protocols were exercised that would have required appropriate informed consent or approval of an institutional review board. The risk of harming the patients in this study in a physical, social or psychological manner was nonexistent.

Results

The results of the data collection on the study group of 174boys who underwent primary hypospadias surgery in regard to degree, other congenital malformations of the urogenital tract, and prophylactic antibiotics are summarized in (Table 1). The most common characteristics were second degree, midshaft, hypospadias (63%), not having other congenital urogenital malformations in addition to hypospadias (83%), and receiving prophylactic antibiotics (67%). Of the boys who suffered a UTI, 77% had other congenital

malformations of the genitourinary tract (P=0.02), either hydrocele or undescended testis.

Table 1 Data on 174 boys who underwent hypospadias surgery in regard to degree, other congenital urogenital malformations, and prophylactic antibiotics

	Hypospadias patients (N=174)
Degree of Hypospadias	
1 (distal)	44(25%)
2 (midshaft)	109(63%)
3(proximal	18(10%)
No degree recorded	3(2%)
Other Congenital Urogenital Malformations	
Yes	29(17%)
No	145(83%)
Prophylactic Antibiotics	
Yes	116(67%)
No	58(33%)

N, number of patients; n (%), Values are presented as the absolute number and percentage of patients

The study group comprised 174boys who underwent primary surgical urethral reconstruction due to hypospadias. The control group comprised 204boys who underwent inguinal hernia repair. The median age at operation and the duration of follow up did not differ between the groups, (Table 2). No patients were excluded from the study.

There were significantly more boys with UTIs in the hypospadias group, compared with the controls, Table 2. Among the hypospadias patients, three of the UTIs were contracted preoperatively, and nine postoperatively (P=0.139; (Table 2).

UTIs were contracted preoperatively in three boys in the hypospadias group (2%), compared to two in the control group (1%). The UTIs contracted peri-operatively and up to 30days postoperatively did not differ between the study group and the control group. This finding of no difference in the 30day postoperative period was true even after excluding the boys receiving preoperative antibiotic prophylaxis. When reviewing the postoperative data, after the 30day postoperative period, nine UTIs occurred. Patients: 5%; control group: 0.5%; P=0.0266; (Table 2).

Table 2 Number of boys with urinary tract infections (UTIs) in the study group of 174 boys operated on for hypospadias compared with a control group of 204 boys who underwent inguinal hernia repair

Surgery for	Study goup: hypospadias(N=174)	Control group: inguinal hernia(N=204)	P-value
Age (years)	4(1-8)	3(1-5)	0.0812*
Follow-up (years)	5(0.5-15)	4(1-8)	0.7324*
Urinary Tract Infection, n (%)	13(7.5%) ****	3(1.5%)	0.0044**
-Preoperatively	3(2%)	2(1%)	0.6649**
-Perioperative***	1(1%)	0	0.0966**
-Postoperatively*****	9(5%)	1(0.5%)	0.0266**

n (%), Values are presented as median (range), and as the absolute number and percentage of patients; n, numbers of patients. *Mann-Whitney U-Test; ** Fisher's exact test (two tailed); ***within 30days postoperative; ****Ten patients with one or more other congenital urogenital malformation; *****From the date of surgery until May 2015. Statistical power: 81%; 19 Confidence level 0.95

Discussion

The results reveal significantly more urinary tract infections in a group of boys with hypospadias undergoing reconstructive surgery compared with a control group of boys operated on for an inguinal hernia. Many of the boys with hypospadias and positive urine cultures, regardless of when the infection occurred, also had another congenital urogenital malformation. Whether the other congenital malformations do have any impact on the frequency of UTI remains to be studied. If boys with hypospadias and associated congenital anomaly are more prone to be hit by UTI cannot be explained by the results of this study and has to be further examined.

The physiological characteristics of children with UTI are quite different from adults. Young children with UTIs may have a fever, poor appetite, vomiting, or no symptoms at all. Besides, the children have problems expressing themselves. To determine that the symptomatic UTIs really exist urinary bacteriological culture is necessary as performed in our study.

In this study, we choose to collect the control group from a cohort of boys undergoing an operative intervention for inguinal hernia. One might argue that a population-based control group would be more appropriate. However, we considered that a group of boys also undergoing an operative intervention at the same hospital to be the most appropriate control group to address the aim of this study. Manipulation of urinary tract is likely to cause UTI and incidence depends of local condition of operating theater and wards. Therefore, it was necessary to select a control group undergoing a surgical intervention in the same operating unit and wards.

The frequency of UTI in this study has to be compared with that in the general population. It has been estimated that 1% of prepubertal boys are diagnosed with urinary tract infections.[15] Using that figure in comparison with the hypospadias boys, instead of using the boys undergoing an inguinal hernia operation, would not change the conclusions in this study. The issue of whether boys with hypospadias have a higher incidence of urinary tract infections has been debated. Wehbi et al.[7] Stated that the incidence of recurrent UTIs

in hypospadias patients is higher over time (1.9%) than that of boys without this malformation (0.1-0.2%), with a median follow-up time of 6.5years.[7] This is in accordance with our postoperative results. Our study focused both on UTIs occurring near the surgery date, where the use of prophylactic antibiotics can have an impact, as well as over a longer duration.

Previous studies have also investigated whether prophylactic antibiotics should be given in conjunction with urethral reconstruction in hypospadias patients. The opinions vary among the different studies, in which some encourage[8,16] the use of this prophylactic treatment while others[4,17] find it unnecessary. Two studies suggest that prophylactic antibiotics should be given to patients operated on for hypospadias.[8,16] Both of these studies are case-control-studies, where one group received prophylactic antibiotics and the other did not. Urine cultures were performed regularly on all patients, regardless of whether symptoms of an infection were present. The results showed a higher incidence of UTIs in the group where no prophylactic antibiotics were given; thus, the use of prophylaxis was recommended.[8,16] On the contrary, two newer case-control-studies, disagreed with the use of antibiotics in conjunction with urethral reconstruction. In these studies, the urine cultures were only performed when the patient presented with symptoms, such as high fever, irritability, or pain while voiding. They could not identify a difference in the incidence of symptomatic UTIs between their two groups, regardless of whether the patients received prophylactic antibiotics. Therefore, the use of prophylaxis was opposed because it did not decrease the number of infections related to the hypospadias procedure.[4,17]

We only registered symptomatic UTIs confirmed by positive urine cultures. Therefore, our study design is more similar to the latter two studies mentioned above.[4,17] Also similar to these studies, our results suggest the same approach towards the use of prophylactic antibiotics. However, if urine cultures had been performed routinely on all our hypospadias patients, as in the first two papers[8,16] cited above, we may have diagnosed a higher number of UTIs. If so, this would, in contrast to those studies, support the use of prophylaxis in conjunction with the surgery. In order to proceed with this issue, one needs to decide whether asymptomatic UTIs should be classified as equally severe as symptomatic ones. Previous studies state that patients with asymptomatic bacteriuria should not be treated with antibiotics, except for pregnant women and patients undergoing urologic interventions.[18] According to these guidelines, standardized urine cultures should be introduced for all hypospadias patients in order to diagnose and treat these asymptomatic infections.

Our results show that there was no statistically significant difference in the number of UTIs between the hypospadias group and the control group within 30days of surgery. This may be due to the preoperative antibiotics prophylaxis used in some of the boys undergoing hypospadias surgery. Conversely, the results show that the one boy who incurred a UTI had been treated with prophylactic antibiotics. When comparing the incidence of UTIs over a longer period of time, it was significantly higher in the group of hypospadias boys than in the control group. Since no significant difference was found in close relation to the procedure, the use of prophylactic antibiotics in order to lower the rate of urinary tract infections do not appear to be warranted.

The frequency of wound infections, which may cause fistula formation during the postoperative course, is an issue that was not the subject of this study. The higher incidence of UTIs found in the total group makes us consider what the actual causes of these urinary tract infections were. There are several possible reasons why these patients have a higher risk of incurring a UTI. Based on our results, we suggest that the primary operation itself is not the source of the increased number of infections. Since many complications can occur in association with this procedure, a single urethral reconstruction is not always adequate to restore full function in all hypospadias patients. Therefore, they often need further surgery and treatment during their childhood; thus, inflicting trauma to the urinary tract and promoting the development of scar tissue that may play a role in the boys' vulnerability to a UTI. We suggest that this could explain the higher frequency of UTIs even several years after the primary surgery.

Other congenital urogenital malformations were evident in 17% of the hypospadias patients (Table 2), and of the boys with UTIs, 77% had another urogenital malformation. This data shows that the numbers of UTIs are not evenly distributed between those with and those without other malformations. It raises the question of whether there can be a connection between infections and these additional malformations. This would be an interesting topic to investigate in a future study that would determine whether these patients should be treated differently in regard to prophylactic antibiotics.

When reviewing the use of prophylactic antibiotics in the hypospadias patients, we determined that 67% of them did receive this treatment. Therefore, it is uncertain whether the outcome was affected by this administration, and if these patients would have contracted an UTI without prophylaxis. On the contrary, the boy who contracted a UTI from birth until 30 days after the surgery did actually receive prophylactic antibiotics. It raises the question of whether this treatment can prevent an infection of the urinary tract. However, antibiotics are not only given to decrease the number of UTIs in relation to the procedure but also in an attempt to avoid other complications including wound infections leading to rupture of the wound and fistula formation. Since this study only investigated the incidence of UTIs, it would have been preferable if prophylactic antibiotics had been given either to all or none of the hypospadias patients. In our case, when comparing to a control group where no patients received prophylaxis, we could have chosen to exclude the hypospadias patients who did receive antibiotics. Excluding the boys receiving antibiotic prophylaxis during their hypospadias surgery revealed no difference in the frequency of UTIs compared with the control group. We believe that this data would have given a more accurate indication on the incidence of infections, and clarify which approach should be used regarding prophylactic antibiotics for UTIs in relation to urethral reconstructions.

Another limitation regarding the prophylactic antibiotics was that the administration was done in a subjective manner, decided by the surgeon in charge at the operation. Also, some infections might have been missed, because only patients with typical symptoms of UTIs were cultured. This could have occurred due to vague symptoms or unawareness by either hospital personnel or patients/parents. Since all patients were not operated on at the same time point, the follow-up time varied from months to years. This difference was found both between the control group and the hypospadias group, as well as inside the hypospadias group itself. This limitation is hard to avoid, but could have affected the final result. A way to improve this study

could be to include a greater number of patients, for example on a national level, and therefore, decrease the number of limitations associated with a small study group.

We suggest that potential noncompliant patients do not need to be considered as limitations in this study. This is due to the fact that healthcare is free in the region, compared to previous studies done in other regions where this might have affected the number of patients who sought care. Also, since all laboratory results regarding urine cultures are registered automatically, inadequate charting does not need to be considered as a limitation of this study.

Conclusion

We suggest that patients undergoing primary urethral reconstruction should not receive prophylactic antibiotics in order to decrease the number of urinary tract infections, since we could not find a higher incidence of these infections among hypospadias patients during the initial perioperative period. The results show that boys with hypospadias are more prone to incur a UTI during the postoperative period, compared to a control group. This may be due to damage to the urethra leading to postoperative consequences due to urethral scarring. Thus, this factor is of importance when the boys undergo repeat operative interventions. There are, however, other reasons to administer antibiotic prophylaxis to the boys undergoing hypospadias surgery because minor wound infections leading to rupture of the wound and development of a fistula can occur. Thus, the findings reported here should influence the decision of whether to administer antibiotics.

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Conflict of interest

The author declares no conflict of interest.

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