

Preputial bacterial colonisation in uncircumcised male children: Is it related to phimosis?

Lokman Irkilata,¹ Hasan Riza Aydin,² Mustafa Aydin,³ Selim Gorgun,⁴ Huseyin Cihan Demirel,⁵ Senol Adanur,⁶ Ebubekir Akgunes,⁷ Aynur Atilla,⁸ Mustafa Kemal Atilla⁹

Abstract

Objective: To evaluate the presence of uropathogens in the periurethral skin and the effect of phimosis on bacterial colonisation.

Methods: The observational cohort study was conducted in Samsun Research and Training Hospital, Samsun, Turkey from June to December, 2014, and comprised patients undergoing circumcision. Before circumcision, all children were examined in the operating room and the presence of phimosis was recorded. All patients had circumcision performed by the same surgical team under general anaesthesia. Before the procedure, samples were taken from preputial skin of all patients by swab before cleansing with polyvidone-iodine. The samples were inoculated on 5% sheep blood agar and eosin-methylene blue agar.

Results: The median age of the 117 children was 5 years (range: 1-12). Of the total, 19(16.2%) children had complete phimosis, and 72(61.5%) had partial phimosis. In all, 91(77.7%) children had phimosis and 26(22.3%) had no phimosis. Of the 91 patients with different degrees of phimosis, 52(57.1%) had clinically significant uropathogenic bacterial colonisation $\geq 100,000$ colony-forming units per millilitre [cfu/ml]. Of the 26 patients without phimosis, 13(50%) had clinically significant colonisation. Thus, there was no effect of the presence of phimosis on bacteria colonisation ($p=0.655$).

Conclusions: Important uropathogens colonise the preputium in uncircumcised male children. There was no effect of phimosis on colonisation.

Keywords: Circumcision, Male, Child, Phimosis, Bacterial colonisation. (JPMA 66: 312; 2016)

Introduction

Urinary tract infection (UTI) is one of the most common infections in childhood and may cause severe morbidity.^{1,2} Potentially life-threatening complications, such as urosepsis, and complications that may result in chronic renal impairment in the long term, such as renal scarring, are observed. As a result, efforts to protect children from recurrent urinary system infections are matched by those used in treating UTIs. Circumcision of male children, which is performed for ethnic, religious and medical reasons, is one such effort around the world. Many studies have shown a relationship between UTI and circumcision in male children, including a reduced risk of infection.³⁻⁵ There is no reasonable biological mechanism to explain the protective effect of circumcision. However, different studies have shown that periurethral colonisation by UTI-causing microorganisms is reduced

by circumcision, and this situation continues into adulthood.⁶⁻⁸ This protective effect may be one reason that circumcision reduces the risk of infection. Another important topic is whether periurethral colonisation is related to the degree of phimosis. Although there are studies showing that the presence of phimosis increases periurethral pathogenic bacteria colonisation, there are also studies showing the opposite.^{9,10}

The current study was planned to prospectively evaluate the presence of uropathogens in the periurethral skin and the effect of phimosis on bacterial colonisation.

Patients and Methods

The observational cohort study was conducted in the Department of Urology, Samsun Research and Training Hospital, Samsun, Turkey from June to December, 2014, and comprised 117 patients undergoing circumcision. None of the patients had findings of paraphimosis or balanoposthitis on examination. All the surgeries were elective, and were performed for ethnic, religious or cultural reasons. The patients had no histories of previous UTI, and routine preoperative laboratory investigations found no signs of urinary infections. Before circumcision, each child was examined in the operating room and the

.....
^{1,3,5,7,9}Department of Urology, ⁴Department of Microbiology, ⁸Department of Infections Diseases, Samsun Training and Research Hospital, Samsun, ²Department of Urology, Recep Tayyip Erdogan University, Rize, ⁶Department of Urology, Ataturk University, Erzurum, Turkey.

Correspondence: Lokman Irkilata. Email: irkilatamd@gmail.com

presence of phimosis was recorded. If the preputium skin could not be retracted or less than half of the glans penis was visible, complete phimosis was recorded. If more than half of the glans penis was visible but could not be fully revealed, partial phimosis was recorded. If the preputium skin could be fully retracted and the whole glans penis made visible without applying force, absence of phimosis was recorded.

Each patient had circumcision performed by the same surgical team under general anaesthesia. Before the surgical procedure, each patient with phimosis had the phimosis gently opened. During this procedure, care was taken to prevent external contamination. Before antiseptic cleaning, a swab was used to take a sample by circumnavigating the glans from proximal to the urethral meatus. The sterile cotton swabs were placed in sterile tubes containing 1cc saline solution and were then transferred to the laboratory. In the laboratory, the solutions were inoculated onto 5% sheep blood and eosin-methylene blue (EMB) agars. The plates were incubated at 37°C for 48h. Later, the colonies of different bacteria were counted. The cultured bacterial colonies were described using morphology, gram staining and standard techniques for biochemical characteristics. The presence of 100,000 cfu/ml was accepted as clinically significant colonisation.

SPSS 20 was used for the statistical analysis. The results of the descriptive analyses were given as mean±standard deviation or median (range). Analyses for patient groups were performed using Fisher's exact test. $P < 0.05$ was considered statistically significant.

Results

The median age of the 117 children in the study was 5 years (range: 1-12 years). Of the total, 19(16.2%) children had complete phimosis and 72 (61.5%) had partial phimosis, totalling up to 91 (77.7%) with differing degrees of phimosis. The remaining 26 (22.3%) had no phimosis.

Of the 91 patients with different degrees of phimosis, 52 (57.1%) had clinically significant uropathogenic bacterial colonisation (100,000 cfu/ml): enterococcus, 23(44%), coagulase-negative staphylococcus 16(31%), staphylococcus aureus 6(11.5%), proteusmirabilis 2(3.8%), and e. coli 5(9.6%) (Table).

In the 26 patients without phimosis, 13(50%) had clinically significant colonisation enterococcus, 7(54%), coagulase-negative staphylococcus 5(38.5%), and e.coli 1(3.8%). There was no effect of the presence of phimosis on bacteria colonisation ($p=0.655$). Among all 117 patients, 65(55.5%) had clinically significant colonisation identified.

Table: Microorganisms isolated from the periurethral areas of 117 male children with and without phimosis.

	With phimosis	Without phimosis
N	91	26
Enterococcus (%)	23 (25.3%)	7 (27%)
Coagulase-negative Staphylococcus (%)	16 (17.6%)	5 (19.2%)
Staphylococcus aureus (%)	6 (6.6%)	-
E. coli (%)	5 (5.5%)	1 (3.8%)
Proteus mirabilis (%)	2 (2.2%)	-
Commensals/no growth (%)	39 (42.8%)	13 (50%)

Of the other 52(44.4%) patients, 20(38.5%) had streptococcus haemolyticus and 8(15.4%) had diphtheroid. These findings were accepted as harmless skin commensals. No pathogens were found in 24(46%) patients. Within the whole patient group, the clinically significant pathogens were found at the following rates: enterococcus 51(46.2%), coagulase-negative staphylococcus 38(32.3%), staphylococcus aureus 12(9.2%), e.coli 12(9.2%) and proteusmirabilis 4(3.1%).

Discussion

UTIs are observed at a rate of 1-2% in the first 10 years of the lives of male children.^{11,12} Many studies in the past have claimed that UTI is more commonly seen in uncircumcised male children. As a result, phimosis and urinary infection prophylaxis are the most frequent indications for circumcision, apart from ethnic, religious and cultural reasons. Recent studies comparing uncircumcised male children with circumcised male children have accepted that the UTI risk is only higher for the first 3 months of life.⁴ Though there is no clear biological mechanism to explain the protective effect of circumcision of male children for UTI in the first months of life, the effect of periurethral uropathogen colonisation may be an important factor. Whether periurethral colonisation is more severe in uncircumcised male children is controversial. Balat et al. found that in spite of an increase in Langerhans cells, CD4 cells were less common in the perivascular regions and they also showed that the lack of CD8 cells in the preputium could promote uropathogen colonisation.¹³ Whatever the reason, it is known that periurethral colonisation of uropathogens is more intense in uncircumcised males.^{6,7} As UTIs generally occur due to uropathogens in the ascending pathway, periurethral colonisation becomes more important.^{10,14,15} However, after the first months of life though bacterial colonisation continues, the opinion that there is no protective effect of circumcision for UTIs has gained significance. The American Urological Association (AUA) 2010 vesico-ureteral reflux guidelines

do not recommend circumcision as a preventative choice inspite of the presence of vesico-ureteral reflux.¹⁶

Even if bacteria colonisation of the preputial sac continues, how the UTI risk reduces with age to the same rate as circumcised children has not been clearly explained.

The most frequent pathogen-causing UTIs in children is e.coli.^{15,17} E. coli and other uropathogens generally colonise the inner preputium rather than the outer surface of the skin.^{18,19} Especially in the early years of life, e.coli is the dominant microorganism in the preputial sac.^{6,19,20,21} Some studies have reported that gram-negative microorganisms rapidly reduce with age and are almost never found on children over age 5.^{12,15,22,23} While the dominant microorganism in our patient group (median age 5 years) was enterococcus, e. coli was the fourth most frequently identified pathogen with a low rate of 9.2%. However, all patients with e.coli in our study were above the age of 5. The results of our study are not fully consistent with literature. However, it is worth noting that e. coli was found at a higher rate in the patient group with phimosis in our study.

In addition to e.coli, enterococcus, proteus mirabilis, coagulase-negative staphylococcus, and staphylococcus aureus were found in our patient group. Klebsiella, which was identified in different studies on this topic, was not isolated in any of our patients.^{18,22}

Whereas enterococcus was the most frequently isolated pathogen in our patient group with a rate of 46.2%, proteus mirabilis was the least isolated pathogen at 3.1%. Different studies have observed enterococcus as the most frequently isolated uropathogen.^{9,17,23} The rate for proteus mirabilis in uncircumcised male children is reported to be between 6.6-22%.^{7,23} Tokgöz et al. did not isolate proteus in their study.⁹ In our patient group, the rate of staphylococci types, which may be a factor in significant nosocomial infection, was 41.5% (coagulase-negative staphylococcus 32.3% and ataphylococcus aureus 9.2%). This rate is higher than other results in literature cited above. Though there are differences in the rates of identification of microorganisms between the literature and our study, two important points attract attention. The first is that enterococcus is generally the most frequently identified uropathogen. The second is that the identified microorganisms are potentially dangerous pathogens that may cause nosocomial and opportunistic infections (staphylococcus species), may be multidrug resistant (enterococcus) and may have lithogenic effects (proteus).^{15,24,25} However, without underlying risk

factors, lack of circumcision alone does not increase the risk of UTI from these pathogens. While our patient group had clinically important uropathogens at a rate of 55.5%, none of our patients had known history of UTI. This result renders the clinical importance of bacteria colonisation of the preputial sac controversial.

Another topic is related to the effect of phimosis on uropathogen colonisation. In a 32-patient series, cTokgöz et al. reported uropathogen identification rate of 100% for the patient group with phimosis.⁹ However, the uropathogen identification rate for patients without phimosis was 48.1%. Whereas Tokgöz et al. presented phimosis as a factor increasing uropathogen colonisation, Hallett et al. found no difference in uropathogen colonisation between patient groups with and without phimosis.¹⁰ With uropathogen identification rates of 57.1% and 50% in the groups with and without phimosis respectively, our study results are similar to those of Hallett et al. The different results from the study by Tokgöz et al. may be due to the low number of patients with phimosis (5 male patients) in the 32-case series.

Conclusion

Though the benefits and application are still debated, there are important studies showing that circumcision reduces the risk of urinary infection in male children below the age of 1 year, as well as affecting rates of penile inflammatory disease, important dermatoses and sexually-transmitted infections (STI) in adults. The underlying reasons for these positive effects are unclear. However, it is a known fact that the preputial sac of male children is a favourable environment for periurethral colonisation of uropathogens. In our study, more than half of our patients had significant periurethral uropathogens. Our results show that phimosis has no effect on colonisation. Though debates about circumcision performed without medical indications have increased in recent years, this situation does not change the reality that the preputial sac forms an ideal environment for colonisation by uropathogens. Circumcision should be debated first in medical terms, before economic and political aspects are considered, and it is necessary to support medical research related to this topic.

Acknowledgements

We are grateful to expert statistician Naci Murat for re-evaluating our study data.

References

1. Ma?rild S, Jodal U. Incidence rate of first-time symptomatic urinary tract infection in children under 6 years of age. *Acta Paediatr* 1998; 87: 549-52.
2. O'Brien K, Stanton N, Edwards A, Hood K, Butler CC. Prevalence of

- urinary tract infection (UTI) in sequential acutely unwell children presenting in primary care: exploratory study. *Scand J Prim Health Care* 2011; 29: 19-22.
3. Saphiro E. American Academy of Pediatrics policy statements on circumcision and urinary tract infection. *Rev Urol* 1999; 1: 154-6.
 4. Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: a meta analysis. *Pediatr Infect Dis J* 2008; 27: 302-8.
 5. Wiswell TE, Hachey WE. Urinary tract infections and the uncircumcised state: an update. *Clin Pediatr* 1993; 32: 130-4.
 6. Wiswell TE, Miller GM, Gelston HM, Jones SK, Clemmings AF. Effect of circumcision status on periurethral bacterial flora during the first year of life. *J Pediatr* 1988; 113: 442-6.
 7. Glennon J, Ryan PJ, Keane CT, Rees JP. Circumcision and periurethral carriage of *Proteus mirabilis* in boys. *Arch Dis Child* 1988; 63: 556-7.
 8. Serour F, Samra Z, Kushel Z, Gorenstein A, Dan M. Comparative periurethral bacteriology of uncircumcised and circumcised males. *Genitourin Med* 1997; 73: 288-90.
 9. Tokgöz H, Polat F, Tan MO, Sipahi B, Sultan N, Bozkirlii. Preputial bacterial colonisation in preschool and primary school children. *Int Urol Nephrol* 2005; 37: 101-5.
 10. Hallett RJ, Pead L, Maskell R. Urinary infection in boys: a three year prospective study. *Lancet* 1976; 2: 1107-10.
 11. Hellström A, Hanson E, Hansson S, Hjalmas K, Jodal U. Association between urinary symptoms at 7 years old and previous urinary tract infection. *Arch Dis Child* 1991; 66: 232-4.
 12. Winberg J, Andersen HJ, Bergström T, Jacobsson B, Larson H, Lincoln K. Epidemiology of symptomatic urinary tract infection in childhood. *Acta Paediatr Scand Suppl* 1974; 252: 1-20.
 13. Balat A, Karakok M, Guler E, Ucaner N, Kibar Y. Local defence system in the prepuce. *Scand J Urol Nephrol* 2008; 42: 63-5.
 14. Bollgren I, Winberg J. The periurethral aerobic bacterial flora in healthy boys and girls. *Acta Paediatr Scand* 1976; 65: 74-80.
 15. Schlager TA. Urinary tract infections in children younger than 5 years of age: epidemiology, diagnosis, treatment, outcomes and prevention. *Paediatr Drugs* 2001; 3: 219-27.
 16. Peters CA, Skoog SJ, Arant BS Jr, Copp HL, Elder JS, Hudson RG, et al. Summary of the AUA Guideline on Management of Primary Vesicoureteral Reflux in Children. *J Urol* 2010; 184: 1134-44.
 17. Wijesinha SS, Atkins BL, Dudley NE, Tam PK. Does circumcision alter the periurethral bacterial flora? *Pediatr Surg Int* 1998; 13: 146-8.
 18. Roberts JA. Circumcision and urinary tract infections. Presented at the annual meeting of the American Academy of Pediatrics, New Orleans, USA: Nov 3, 1987.
 19. Fussell EN, Kaack MB, Cherry R, Roberts JA. Adherence of bacteria to human foreskins. *J Urol* 1998; 140: 997-1001.
 20. Cascio S, Colhoun E, Puri P. Bacterial colonisation of prepuce in boys with vesicoureteral reflux who receive antibiotic prophylaxis. *J Pediatr* 2001; 139: 160-2.
 21. Savas C, Cakmak M, Yorgancigil B, Bezir M. Comparison of preputial sac and urine cultures in healthy children. *Int Urol Nephrol* 2000; 32: 85-7.
 22. Laway MA, Wani ML, Patnaik R, Kakru D, Ismail S, Shera AH, et al. Does circumcision alter the periurethral uropathogenic bacterial flora. *Afr J Paediatr Surg* 2012; 9: 109-12.
 23. Tarhan H, Akarken I, Koca O, Ozgü I, Zorlu F. Effect of preputial type on bacterial colonization and wound healing in boys undergoing circumcision. *Korean J Urol* 2012; 53: 431-4.
 24. Guirguitzova B, Chankova D, Zozikov B, Minkov N. Enterococci as uropathogens. Frequency of isolation and sensitivity to antibacterial agents. *Ann Urol* 1998; 32: 15-9.
 25. Kumari N, Rai A, Jaiswal CP, Xess A, Shahi SK. Coagulase negative staphylococci as causative agents of urinary tract infections-prevalence and resistance status in IGIMS, Patna. *Indian J Pathol Microbiol* 2001; 44: 415-9.
-