PhD thesis

Treatment options for lichen sclerosus, hypospadias and their complications in paediatric urology practice

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INTRODUCTION

In general paediatric urology practice operation due to phimosis is the most frequent procedure. However, the fact that the background of this frequent, „simple” malformation can be a severe disorder, which can lead to complications observed later in life, is not obvious for all specialists. The main reason for this is that at most occasions no histological analysis is performed after circumcisions. New research data show that lichen sclerosus (LS) may appear in childhood as phimosis and can cause severe malformations of the urethral orifice and/or urethral stricture and it can also be associated with later development of penile carcinoma. In urology the expression of balanitis xerotica obliterans (BXO) is used for penile LS. Although the importance of BXO is accepted, the precise incidence of childhood penile LS is not known and there are unmet needs in its treatment.

Until 1962 balanitis xerotica obliterans had been considered to be exclusively an adult disorder. After publication of the first confirmed childhood case only a few case reports and some population studies with very low subject numbers have been published. The authors of these studies suggested that the incidence of this disease is 10-19%. Recently, several authors have indicated that the real incidence of the disease is likely higher, but due to the lack of information based on larger patient group these assumptions have not been confirmed.

In recent years, low potency topical steroid ointments have been used to treat phimosis with success rates varying between 67-95 %. In these series, however, circumcision followed only unsuccessful treatment and the histological diagnosis is known only in these cases. Whether any of those successfully treated had BXO is therefore unknown. Therefore we conducted a double blind placebo controlled study on the effectiveness of local corticosteroid treatment in BXO.

While the surgical treatment of phimosis is usually simple, surgical correction of hypospadias is one of the greatest challenges for paediatric urologists. Despite the several known surgical approaches, better functional and aesthetic results can only be achieved by continuous improvement of currently available methods or development of newer techniques. The most frequent complication of hypospadias repair is the urethral fistula. All urologists know the feeling, which appears when
preparing to close a fistula which developed after a “good” surgical correction of the disorder. In these cases tissues from sources which are not regularly used for fistula closure may be considered as a possibility.

Numerous surgical procedures have been attempted for correction of distal hypospadias, including the perimeatal based flap urethroplasty (Mathieu), which is commonly used for primary repair. Mathieu reported his procedure for repair of hypospadias in 1932. As a result of increasing experience with the technique and the use of some modifications scattered reports in the literature attest to the success of this procedure. Although the Mathieu repair provides good function and satisfactory cosmetic results, there is an increased risk of meatal and urethral stenosis, because the blood flow in the distal part of the neourethral skin flap is reduced. Because of this problem and to improve the cosmetic appearance different modifications were described.

In 1994 Snodgrass described a technique for correcting distal hypospadias by tubularizing the urethral plate combined with a deep longitudinal incision of the groove. The advantage of this procedure is the provision of a generously mobile plate to form the neourethra and also to create a functional neourethra with a vertical, slit-like meatus.

Urethrocutaneous fistula is the most common problem of hypospadias repair and many techniques have been described for its correction. When good penile skin is available the simple closure of a fistula is technically easy, but overlying suture lines form potential risk for recurrence. A paucity of local tissue and subsequent skin coverage is a problem in many cases. In these cases extragenital tissue, split thickness and full-thickness skin grafts as well as bladder mucosa has been proposed as an alternative donor site. Buccal mucosa has been used with good results in complex urethral reconstruction and bulbar urethral strictures for more than 10 years, but only a case report and a review suggest that this tissue may be used for fistula closure.

AIMS

In the first part of my work I investigated the incidence, clinical and histological appearance of childhood BXO and studied the effect of local corticosteroid treatment
in the care of this disorder. We performed a 10 years long prospective study to investigate the incidence, clinical and histological appearance of BXO in randomised paediatric population. Furthermore, I evaluated the effectiveness of topical steroid treatment on BXO in a double-blind placebo controlled study.

In the second part of my studies I studied the surgical correction methods of the repair of hypospadias and its complications. By using and combining two known techniques I have developed a new method. We introduced a modification of the Mathieu technique by the incision of the urethral plate, as described in the Snodgrass method. We assumed that this step would help to avoid blood flow reduction to the graft and to improve functional and cosmetic results of the repair. For the closure of big, recurrent urethral fistulas I have used free buccal mucosa graft, which has not been used previously with this purpose.
Methods

To determine the incidence of BXO we studied 1178 children in 10 years period, from who in 674 cases secondary phimosis (acquired phimosis after at least 6 month period of freely retractable foreskin).

To assess the effect of topical steroid treatment on BXO 40 boys with clinically diagnosed and graded BXO were randomized into the study to receive topical application of mometasone furoate 0.05% or of placebo. After five weeks the severity of phimosis was reevaluated and then all patients were circumcised. Surgical specimens were histologically typed as early, intermediate or late forms of BXO. Seven patients were withdrawn from the study with different reasons.

The Mathieu and Snodgrass repair for hypospadias was combined by using the following steps: A total of 19 consecutive boys aged 20 months to 5 years (mean age 3.2 years) underwent primary repair of distal hypospadias. The Mathieu technique was applied similarly in all cases. A traction suture was placed in the dorsal glans and a ventral perimeatal based skin flap was outlined. A small silicone stent was then inserted in the urethra for protection. Two paramedian balanic incision were outlined forming the distal urethral plate. The plate was then incised in the midline from the meatus to the tip of the glans (Figure 1). This incision was carried deeply, dividing all transverse webs and exposing the underlying corporeal bodies. The skin flap was elevated to preserve the vascular supply, and anastomosed to the distal urethral plate with a layer of 7-zero polyglycolic absorbable suture. The lateral glans flaps were approximated over the neourethra. The penile shaft was covered by the available penile skin, maintaining a midline ventral closure when possible. Finally a transparent permeable dressing was applied around the penis. The neourethra was stented for 6 or 7 days and a suprapubic diversion was used to drain the bladder for the same period. All patients were maintained on antibiotic prophylaxis and anticholinergic medication to control bladder spasm, until the stent was removed.
Figure 1. Combination of the Mathieu and Snodgrass repair, forming the ventral part of neourethra after a deep midline incision of the urethral plate.

To improve methods of closure of large urethrocystic fistulas buccal grafts were applied. During the last 3 years 7 boys (main age 4.8 years, range 3.6-8.5) with urethrocystic fistula developing after hypospadias reconstruction underwent a fistula closure using free graft of buccal mucosa from the inner aspect of the lower lip. The original technique used for hypospadias correction in all patients was Snodgrass urethroplasty.

Results

In our study on the incidence of childhood BXO among phimosis histological examination demonstrated BXO in 471 cases (40%). The average age in BXO patients was 8.7 years, and the incidence of BXO in the patient group of 9-11 years old children was significantly higher (76%) than in younger age groups. The youngest patient with BXO was 2 years old. Histological examination showed 91 (19%) early, 280 (60%) intermediate and 100 (21%) late form of BXO. There was no statistical relation between the clinical appearance of phimosis and the histological stages of BXO.

In the study assessing the use of steroid treatment in BXO the following results were obtained: in the steroid group 7 boys showed clinical improvement and 10 did not change (Figure 2). Histologically, five cases exhibited early, 5 intermediate
and 7 late forms of BXO. Among the clinically improving cases, 5 were of the histologically early and 2 of the intermediate types. In the placebo group 5 cases worsened clinically and 11 did not change. Histologically, 3 early, 7 intermediate and 6 late forms of BXO were found in this group. From the five worsening cases histologically 2 were in the early, 2 in the intermediate and one in the late groups.

![Figure 2. Effect of steroid and place on the clinical severity of BXO. ***: p=0.0004](image)

Combining the Mathieu and Snodgrass repair excellent cosmetic and functional results were obtained in 18 cases. All patients voided spontaneously after stent removal. One patient had a pinpoint urethrocutaneous fistula which required subsequent operation. The mean follow-up period was 12 months (range 6 to 20 months). Uroflowmetry has been performed in all cases after 6 months of surgery. We have not observed any sign of obstruction or asymptomatic strictures.

The repair of large fistulas using buccal mucosa graft was successful in 6 out of 7 cases, and in these cases the urinary stream was good after the removal of the catheter. The unsuccessful case was the coronal one, but in this case the diameter of the fistula became significantly smaller (from 4.5mm to 1 mm) offering good opportunity for subsequent closure.
Summary of new research results

1. Investigating large number of patients we found that balanitis xerotica obliterans is present in 40% of childhood phimosis cases, which is larger as previously assumed. Because of the potential of complications and later development of penile malignancy on the base of BXO histological examination of tissue after circumcision is strongly recommended and the long term follow-up of BXO cases is suggested.

2. We investigated the effect of topical corticosteroid treatment on BXO in a double-blind placebo-controlled study. Our results showed that after 5 weeks of steroid treatment clinical symptoms of BXO improved significantly in 41% of patients and did not change in the rest of them. Histologically the improved cases belonged to the early or intermediate type of the disease. In the placebo group there was no improvement and symptoms worsened in the majority of patients. Our data suggest that topical steroid administration is effective in the treatment of BXO patients, likely in those whom no irreversible tissue changes are present.

3. We developed a new method for hypospadias repair. Our modification uses the combination of the Mathieu and the Snodgrass methods (using a deep midline incision of the urethral plate to help to form an anatomically normal looking urethral orifice and providing a good urethra calibre without tense suture lines. With our modification the risk for development of urethral strictures following repair is decreased because this techniques ensures better blood supply and the advantage of the Mathieu-technique, that suture lines are not in one line above each other, remains, therefore the risk for development of fistula is lower. In our practice this modification has been applied successfully to a variety of distal hypospadias with significant improvement of functional and cosmetic results.

4. To close urethral fistulas developing after hypospadias repair we used free buccal mucosa graft. The use of buccal mucosa for this purpose has not been previously reported. Based on our results its use to close recurrent large urethral fistulas is a good and safe therapeutic choice.
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List of those original publications which were used in the PhD (abstracts of presentations at conferences are not listed here).

Publications in international peer reviewed journals:


**Kiss A., Nyirády P, Pirót L, Merksz M.** Combined use of perimeatal based flap urethroplastay (Mathieu) with midline incision or urethral plate in hypospadias repair. European Journal of Pediatric Surgery.(Közlésre elfogadva-in press) **Impakt faktor: 0,425**

Publications in national journals:


List of publications not used in the PhD:

Publications in international journals:

**Kiss A., Csontai Á., Berényi M.:** Urinary Bladder Stone Composed of Xanthine in an Infant Boy. Urologia Internationalis. 1999. 63. 4. **Impakt faktor: 0,478**


Horvath I, Donnelly LE, **Kiss A.** Paredi P. Kharitonov SA, Barnes, P.J.: Raised levels of exhaled carbon monoxide are associated with an increased expression of heme


**Publications in national journals:**


Nyirády P., Pirót L., Merksz M., Csontai Á., **Kiss A.:** Az enuresisról a gyermekürológus szemével. Gyermekgyógyászat 1998.6: 616-19.


**Cumulative Impakt Faktor: 13.963**

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**Number of citations without self-citation: 102**