HIGHLY POTENT AND MODERATELY POTENT TOPICAL STEROIDS ARE EFFECTIVE IN TREATING PHIMOSIS: A PROSPECTIVE RANDOMIZED STUDY

STEPHEN SHEI DEI YANG, YAO CHOU TSAI, CHIA CHANG WU, SHIH PING LIU AND CHUNG CHENG WANG*

From the Department of Urology, En Chu Kong Hospital, Taipei Medical University and Department of Urology, College of Medicine (SPL), National Taiwan University, Taipei, Taiwan

ABSTRACT

Purpose: We report a prospective randomized study comparing the effects of highly potent and moderately potent topical steroids in treating pediatric phimosis.

Materials and Methods: A total of 70 boys 1 to 12 years old with phimosis were randomly assigned to receive topical application of either betamethasone valerate 0.06% (a highly potent steroid) or clobetasone butyrate 0.05% (a moderately potent steroid). Parents of the boys were instructed to retract the foreskin gently without causing pain, and to apply the topical steroids over the stenotic opening of the prepuce twice daily for 4 weeks, then for another 4 weeks if no improvement was achieved. Retractability of the prepuce was graded from 0 to 5. Response to treatment was arbitrarily defined as improvement in the retractability score of more than 2 points.

Results: Mean treatment and followup periods were 4.3 and 19.1 weeks, respectively. The response rates in boys treated with betamethasone valerate and clobetasone butyrate were 81.3% and 77.4%, respectively (p = 0.63). Mean retractibility score decreased from 3.9 ± 1.0 to 1.7 ± 1.1, and 4.2 ± 1.0 to 1.9 ± 1.0 in the betamethasone and clobetasone groups, respectively. Both steroids were effective in all age groups. Pretreatment retractibility score did not affect treatment outcomes. No adverse effect was encountered.

Conclusions: Highly potent and moderately potent topical steroids are of comparable effectiveness in treating phimosis. A less potent steroid may be considered first to decrease the risk of the potential adverse effects.

KEY WORDS: steroids, phimosis, penis, circumcision

Because of medical, religious or social reasons, circumcision has long been advocated as an effective way to treat phimosis. Circumcision may result in complications such as meatal stenosis, meatitis, meatal ulceration, postoperative infection, anesthesia related adverse events and psychological trauma. To avoid the hazards of circumcision, topical corticosteroids have been used as an alternative for phimosis, and high success rates (67% to 95%) have been reported. The relative strengths of topical steroids are divided into ultrahigh, high, moderate and low potency categories according to the recommendations of the British National Formulary. Inhibition of the pituitary-adrenal axis by excessive application of stronger steroids has been well documented. Growth stunting in a child treated with long-term fluorinated steroids has been observed but the weaker steroids are considered safe in children. Thus, to decrease the possible adverse effects, it is sensible to prescribe the weakest effective topical steroid possible in pediatric practice. However, to date, all but 2 reports on topical steroids for pediatric phimosis used ultrahigh or high potency steroids. These 2 studies using less potent steroids were neither prospective nor randomized controlled trials. Therefore, we conducted a prospective randomized study to compare the effects of topical application of highly potent and moderately potent steroids in treating phimosis.

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* Correspondence: Department of Urology, En Chu Kong Hospital, 399 Fushing Rd., Taipei Hsien 237, Taiwan (telephone: 886-2-26729546, ext. 6351; FAX: 886-2-26719512; e-mail: ericwcc@ms27.hinet.net)

MATERIALS AND METHODS

A total of 70 boys 1 to 12 years old (mean age 4.7 ± 2.6 years) with phimosis were enrolled in this study between 2001 and 2003. The Appendix shows the grades of retractability of phimosis from 0 to 5 suggested by Kikiros et al. The associated presenting symptoms were penile pain and/or itching in 33 patients, preputial ballooning during voiding in 9, voiding pain in 6, slow urinary stream in 6, urinary frequency in 4 and concern over apparent phimosis in 12. Urinalysis and urine culture were performed in patients who complained of penile pain or voiding pain. Before application of topical steroids boys with balanitis and urinary tract infection were adequately treated with antibiotics. Boys with phimosis secondary to incomplete circumcision were excluded.

Patients were randomly assigned to receive topical application of either betamethasone valerate 0.06% (a highly potent steroid) or clobetasone butyrate 0.05% (a moderately potent steroid). Parents of the boys were instructed to retract the foreskin gently without causing pain, and to apply the topical steroids over the stenotic opening of the prepuce and glans twice daily for 4 weeks, then for another 4 weeks if no improvement was achieved. The principal investigator (SSDY), who was blinded to the treatment arm, evaluated the treatment outcomes and adverse effects at 2, 4 and 8 weeks after treatment. A clinical research nurse, also blinded to the treatment arm, telephoned the parents of patients with a structured questionnaire covering the grades of retractability, improve-
ment in associated presenting symptoms and possible side effects at 12 and 24 weeks after treatment.

Response to topical steroid application was arbitrarily defined as improvement in the retractability score of more than 2 points as suggested by Atilla et al.14 The results in boys older than 3 years were compared to those in boys 3 years or younger. The Wilcoxon signed rank, Student t and chi-square tests were used for statistical analysis.

RESULTS

Seven boys (3 in the betamethasone group and 4 in the clobetasone group) were lost to followup, leaving 63 eligible for investigation. Mean treatment duration was 4.3 weeks and mean followup was 19.1 weeks.

The table compares the demographic data and therapeutic results. There were no statistical differences in age (mean age 4.9 ± 2.5 and 4.5 ± 2.9 years, respectively, p = 0.31) or pretreatment retractability score (mean score 3.9 ± 1.0 and 4.2 ± 1.0, respectively, p = 0.32) between the 2 groups. The retractability score improved to 1.7 ± 1.1 and 1.9 ± 1.0 in the betamethasone and clobetasone groups, respectively (p < 0.01 in each group). The response rates were similar between the 2 groups (81.3% vs 77.4%, p = 0.63). Excellent results of grade 0 or 1 were achieved in 16 (50%) and 14 (45.2%) boys in the betamethasone and clobetasone groups, respectively. Patient age did not affect treatment outcomes significantly in each group. No significant differences were found in the pretreatment retractability score in the responders and nonresponders (4.0 ± 0.9 vs 3.8 ± 1.2 in the betamethasone group, p = 0.42, and 4.3 ± 0.9 vs 4.1 ± 1.0 in the clobetasone group, p = 0.80).

After treatment circumcision was recommended in boys with grade 4 or 5 phimosis. Two thirds of patients in the betamethasone group and half of those in the clobetasone group underwent circumcision because of remaining high grade phimosis.

No significant adverse effect was encountered during the study period. Therapeutic effects were maintained in all but 1 patient who responded to the application of topical steroids. The 1 reported recurrence of phimosis was successfully treated with topical clobetasone butyrate. During followup no recurrent infection or associated presenting symptoms were detected in boys with a history of balanitis and urinary tract infection.

DISCUSSION

We report the first known prospective randomized controlled study to compare different potency steroids in treating phimosis. The study reveals that highly potent and moderately potent topical steroids are equally effective. The achieved response rates (81.3% for highly potent and 77.4% for moderately potent steroids) are comparable to the success rates (67% to 95%) reported in previous studies. Almost all studies used ultrahigh or high potency steroids, and the 2 studies using less potent steroids were retrospective.2-9 Although this study was not placebo controlled, Golubovic7 and Chu4 et al have independently reported prospective studies demonstrating that the efficacy of steroid application was superior to that of gentle retraction or application of neutral cream only. The main purposes of this study were to investigate whether weaker potency steroids are similarly effective in boys with phimosis, and to determine the influence of age on treatment results.

Using steroid cream to treat phimosis was sensible and practical. Three possible mechanisms of action of topical steroids have been proposed in the treatment of phimosis. Steroids can cause thinning of skin and improve the elasticity of the foreskin by decreasing synthesis of hyaluronic acid, which has an anti-proliferative effect on the epidermis.15 In addition, topical steroids can inhibit the production of the mediators of skin inflammation, prostaglandins and leukotrienes.16 Finally, the lubricant effect of the cream allows boys to retract the foreskin easily.6

Elmore et al9 and we have proved the therapeutic effects of topical steroids for phimosis in children younger than 3 years. Adherence of the prepuce to the glans in infants and young boys is considered physiological, and expectant treatment has been suggested because of spontaneous resolution with age. But boys with physiological phimosis are often referred to urologists for surgery. Topical steroid therapy can offer a potential alternative to avoid unnecessary circumcision. In addition, although treatment is usually recommended after age 3 years, early treatment will be beneficial to boys younger than 3 years with signs of ballooning with voiding, urinary tract infection and balanitis,5,9 as circumcision has been proved to be effective in preventing recurrent urinary tract infection in patients younger than 6 months, who have a high incidence of periurethral bacterial colonization when left uncircumcised.17,18

There are no universally accepted criteria defining “successful therapy” for phimosis. To compare the effects of steroids, we adopted the “2-point difference” after treatment as suggested by Atilla et al.14 In daily practice adequate care and cleaning of the foreskin and glans are the concerns of genital hygiene. Even in cases of complete phimosis a 2-point difference will result in a grade of 3 or less. Thus, the prepuce can be pulled back easily to expose the glans and urethral meatus. As shown in this study, circumcision can be avoidable in most cases because of decreasing infection rate and subjective symptoms.

Compliance with medication, rather than age or pretreatment grades of phimosis, may be the key factor predicting successful treatment outcome. In the current study mean pretreatment score of phimosis was comparable in the responders and nonresponders in the 2 groups. Orsola et al reported that a highly potent topical steroid for phimosis was effective in boys older than and younger than 5 years.6 However, Monsour et al found that older boys applied the cream rather than their parents, so patients in whom treatment failed were older than those with a successful outcome (mean age 10.6 versus 6.3 years).5 We agree with the conclusion of Wright that parent and patient compliance was the key fac-

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**Demographic data and therapeutic results in boys with phimosis treated with highly potent and moderately potent topical steroids**

<table>
<thead>
<tr>
<th>No. Pts</th>
<th>Mean Age ± SD (yrs)</th>
<th>Retractability Score</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before Treatment</td>
<td>After Treatment</td>
<td></td>
</tr>
<tr>
<td>Betamethasone valerate group:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Yrs or younger</td>
<td>9</td>
<td>1.7 ± 0.6</td>
<td>3.8 ± 0.9</td>
</tr>
<tr>
<td>Older than 3 yrs</td>
<td>23</td>
<td>6.3 ± 1.8</td>
<td>3.9 ± 1.1</td>
</tr>
<tr>
<td>All pts</td>
<td>32</td>
<td>4.9 ± 2.5</td>
<td>3.9 ± 1.0</td>
</tr>
<tr>
<td>Clobetasone butyrate group:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Yrs or younger</td>
<td>11</td>
<td>1.4 ± 1.1</td>
<td>4.4 ± 0.9</td>
</tr>
<tr>
<td>Older than 3 yrs</td>
<td>20</td>
<td>6.2 ± 2.0</td>
<td>4.0 ± 0.9</td>
</tr>
<tr>
<td>All pts</td>
<td>31</td>
<td>4.5 ± 2.9</td>
<td>4.2 ± 1.0</td>
</tr>
</tbody>
</table>
tor in predicting successful treatment. In our series mean patient age was only 4.7 years. Good compliance (90%) was noted, because most topical steroid was applied by the parents. As a result, our study revealed that patient age did not affect treatment outcome.

No significant adverse effects were encountered from the use of the 2 topical steroids in this and previous studies of phimosis. Morning cortisol levels of boys treated with betamethasone did not differ from controls. However, when therapeutic trends change from surgical circumcision to local medical application more and more steroids will be used by physicians. Infants and young children have delicate, easily damaged skin and a high surface area-to-body volume, making them susceptible to systemic absorption of topical steroids. Using stronger topical steroids may carry a higher risk of adverse effects, including iatrogenic Cushing syndrome, adrenal suppression, delayed growth and skin atrophy, which have been observed in children treated with topical or intranasal steroids. Thus, it is practical to use moderately potent steroids first, since they are suggested by our study to be as effective as highly potent steroids. Further investigation is still needed to determine whether mildly potent (the weakest potency) topical steroids are also effective in treating phimosis.

CONCLUSIONS

Highly potent and moderately potent topical steroids are effective and of comparable therapeutic efficacy in treating phimosis. Patient age and pretreatment retractility score are not prognostic factors regarding the outcome of topical steroid treatment. When topical steroid application is attempted to treat phimosis moderately potent steroids should be considered first to avoid potential adverse effects, even the risk is low.

APPENDIX: GRADING OF PHIMOSIS

Grade 0—full retraction
Grade 1—full retraction of prepucce and tight ring behind glans
Grade 2—partial exposure of glans
Grade 3—partial retraction with urethral meatus just visible
Grade 4—slight retraction but urethral meatus and glans not exposed
Grade 5—absolutely no retraction

REFERENCES


