

Pediatric/Reconstructive Urology

Effect of Topical Steroid (0.05% Clobetasol Propionate) Treatment in Children With Severe Phimosis

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Purpose: We report our experience with the use of a topical steroid, 0.05% clobetasol propionate, for the treatment of phimosis with clinical complications.

Materials and Methods: This was a retrospective analysis of the clinical outcomes of all patients presenting with phimosis to a single institution during the time period from October 2008 to May 2012. A total of 88 patients who had a Kikiros retractability grade of 4 or 5 and phimosis-associated clinical complications, such as ballooning of the prepuce, balanoposthitis, or a history of urinary tract infection (UTI), were instructed to apply 0.05% clobetasol propionate cream to the slightly retracted foreskin and to massage gently while retracting the foreskin. The efficacy of treatment was evaluated at 4 weeks from the initiation of therapy.

Results: A total of 60 of the 88 patients (68.2%) showed a complete response (i.e., full retraction of the foreskin) to the therapy. The phimotic ring disappeared in 25 of the 88 patients (28.4%) after treatment. Patients who had a history of balanoposthitis, smegma, ballooning of the prepuce, or UTI showed significantly poorer improvement in preputial retraction ($p < 0.001$, $p < 0.001$, $p < 0.001$, and $p = 0.02$, respectively) and phimotic ring disappearance ($p < 0.001$, $p = 0.001$, $p < 0.001$, and $p = 0.001$, respectively) after treatment. No significant local or systemic side effects were associated with the administration of topical steroids.

Conclusions: Topical application of 0.05% clobetasol propionate cream and skin stretching is a safe, simple, and effective procedure with no significant side effects for severe phimosis in prepubertal boys.

Keywords: Circumcision; Phimosis; Steroids

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INTRODUCTION

Phimosis is a condition in which the foreskin of the prepuce cannot be retracted over the glans penis owing to a tight preputial ring distal to the glans [1]. In neonates, physiologic phimosis is observed owing to natural adhesion between the inner foreskin and the glans penis [2]. The incidence of physiologic phimosis in newborns is reported to be about 96% [3]. The foreskin naturally detaches from the glans penis within the first 2 to 3 years of age following the formation of keratinized pearls [4]. The incidence of physiologic phimosis falls to 10% and 1% at the ages of 4 and 14

years, respectively, without special treatment [5]. In contrast, pathologic phimosis occurs when the inability to expose the glans is secondary to scarring of the distal foreskin [5].

Because a nonretractile prepuce is one of the risk factors for recurrent urinary tract infection (UTI), newborn circumcision became an effective treatment method for preventing UTI [6,7]. However, because of the surgical complications and the need for general anesthesia for circumcision, some controversy exists over performing surgical therapy in young children [8,9]. Topical steroids were introduced in the treatment of phimosis by Kikiros et al. [10]

in 1993. Several articles have supported this conservative therapy as an effective and safe alternative to surgical treatment [5,11,12].

Despite the effectiveness of topical steroids in the treatment of phimosis, only a few studies have attempted to analyze the relationship between the success rate of the treatment and phimosis-associated clinical complications, such as ballooning of the prepuce, balanoposthitis, and history of UTI. Here we report our experience with the use of a topical steroid, 0.05% clobetasol propionate, for the treatment of phimosis with clinical complications.

MATERIALS AND METHODS

A retrospective analysis of the clinical outcomes of all patients presenting with phimosis to a single institution during the time period from October 2008 to May 2012 was carried out.

1. Patients

From October 2008 to May 2012, a total of 122 children were referred for the treatment of phimosis at the urology department and pediatric urology division of the Pusan National University Children's Hospital. We retrospectively collected and analyzed all data on phimosis and topical steroid use from the patients' electronic medical records.

At the first clinic visit, a clinical examination was performed and the category of phimosis was evaluated according to the classification of Kikiros and Woodward (Table 1). Before treatment initiation, we proposed treatment options including circumcision or application of a topical steroid. Among 122 patients, 21 boys with a concealed penis were excluded in the analysis and underwent surgical correction of the concealed penis. Thirteen patients who had partial exposure of the glans or partial retraction of the prepuce were also excluded from the analysis. The remaining 88 patients with a Kikiros retractability grade of 4 or 5 and phimosis-associated clinical complications, such as ballooning of the prepuce, balanoposthitis, or a history of UTI, were included in this analysis. Ethical approval was granted by the ethical committee at our institution.

TABLE 1. Grades of retractability of the foreskin according to Kikiros et al. [10]

Grade
0. Full retraction, not tight behind glans, or easy retraction limited only by congenital adhesions to the glans
1. Full retraction of foreskin, tight behind the glans
2. Partial exposure of glans, prepuce (not congenital adhesions) limiting factor
3. Partial retraction, meatus just visible
4. Slight retraction, but some distance between tip and glans, i.e., neither meatus nor glans can be exposed
5. Absolutely no retraction

2. Technique for application of the topical steroid ointment

The use of the topical steroid ointment was explained and demonstrated to parents before the initiation of the treatment at home. Although the most suitable application period of topical steroid ointment is still debatable, most studies regarding the use of topical steroids in phimosis suggest that application of a topical steroid for 4 weeks is safe and reliable [1,2,10-15]. For this reason, the parents of the boy were instructed to apply 0.05% clobetasol propionate cream to the slightly retracted foreskin and to massage gently while retracting the foreskin 20 times twice a day, after washing or bathing, for 4 consecutive weeks. No occlusive dressings were used and no attempt was made forcibly to retract the prepuce, which would cause splitting and bleeding of the foreskin. Prior to the treatment, we informed the parents about possible local side effects of the steroid ointment, such as striae, pigmentation changes, telangiectasia, and hypertrichosis. Verbal consent was also obtained for the application of the topical steroid.

3. Evaluation of the retractability of the foreskin and disappearance of the phimotic ring

The patients were reevaluated 4 weeks after treatment initiation by using the classification of Kikiros and Woodward by a single pediatric urologist. We retrospectively collected the data on phimosis and topical steroid use from the patients' electronic medical records. The response to topical steroid treatment was arbitrarily defined as full retraction of the foreskin, i.e., Kikiros retractability grade 0 or 1 (Table 1). The presence of any possible local side effects of the steroid ointment was checked, including striae, pigmentation changes, telangiectasia, and hypertrichosis. The effects of treatment were also evaluated with respect to age and phimosis-associated symptoms, such as ballooning of the prepuce, balanoposthitis, and history of UTI.

4. Statistical analysis

Statistical analysis was performed with IBM SPSS ver. 20.0 (IBM Co., Armonk, NY, USA) and statistical significance was defined as a p-value of < 0.05. The results were analyzed by using the chi-square test.

RESULTS

A total of 88 male children with an average age of 2.82 ± 1.78 years (range, 4 months to 9 years) were allocated to treatment with 0.05% clobetasol propionate ointment. Of the 88 patients, 49 (55.7%) had coexisting balanoposthitis and 35 (39.8%) had a history of UTI. A total of 55 (62.5%) had smegma and 63 (71.6%) had ballooning of the prepuce (Table 2). The history of UTI before treatment was assessed by dividing the patients into 2 groups based on coexisting conditions, such as balanoposthitis, smegma, and ballooning of the prepuce. The patients who had a history of balanoposthitis, smegma, or ballooning of the prepuce had a significantly increased history of UTI before treatment ($p < 0.001$, $p < 0.001$, and $p = 0.001$, respectively) (Table 3).

TABLE 2. Patient characteristics and treatment outcomes

Characteristic	Pretreatment, n (%)				Post-treatment, n (%)			
	Balanoposthitis	Smegma	Ballooning of the prepuce	History of UTI	Full retraction of the foreskin ^a	Disappearance of the phimotic ring	Voiding difficulty	Inflammation ^b
Age < 3 (n=45)	27 (60.0)	29 (64.4)	32 (71.1)	15 (33.3)	34 (76.5)	16 (35.6)	2 (4.4)	5 (11.1)
Age ≥ 3 (n=43)	22 (51.2)	26 (60.5)	31 (72.1)	20 (46.5)	26 (60.5)	9 (28.4)	2 (4.7)	13 (30.2)
Total (n=88)	49 (55.7)	55 (62.5)	63 (71.6)	35 (39.8)	60 (68.2)	25 (28.4)	4 (4.5)	18 (20.5)
p-value	0.40	0.70	0.91	0.20	0.13	0.13	0.96	0.03
Odds ratio	-	-	-	-	-	-	-	3.467 (1.14-10.78)

UTI, urinary tract infection.

^a:Kikiros retractability grade 0 or 1. ^b:Balanoposthitis, UTI.

TABLE 3. The relationship between phimosis-associated clinical complications and history of UTI before treatment

Variable	UTI, n (%)		Total	p-value	OR (95% CI)
	Yes	Never			
Smegma				< 0.001	13.91 (3.78-51.16)
Yes	32 (58.2)	23 (41.8)	55		
Never	3 (9.1)	30 (90.9)	33		
Total	35 (39.8)	53 (60.2)	88		
Balanoposthitis				< 0.001	22.58 (6.05-84.3)
Yes	32 (65.3)	17 (34.7)	49		
Never	3 (7.7)	36 (92.3)	39		
Total	35 (39.8)	53 (60.2)	88		
Ballooning of the prepuce				0.001	7.57 (2.05-27.87)
Yes	32 (50.8)	31 (49.2)	63		
Never	3 (12.0)	22 (88.0)	25		
Total	35 (39.8)	53 (60.2)	88		

UTI, urinary tract infection; OR, odds ratio; CI, confidence interval.

At the 4-week follow-up visit, 60 patients (68.2%) treated with the topical steroid cream showed a complete response (i.e., full retraction of the foreskin) to the therapy. The remaining 17 patients (19.3%) showed little improvement and 11 patients (12.5%) showed no response. The 28 patients who showed little improvement or no response were instructed to apply the topical steroid for another 4 weeks. Surgical intervention was also considered in the patients who showed no response. The phimotic ring disappeared in 25 of the 88 patients (28.4%) after treatment. Patients over 3 years of age and those under the age of 3 years demonstrated a similar success rate in terms of full retraction of the foreskin and disappearance of the phimotic ring ($p=0.12$ and $p=0.13$) (Table 2).

Full retraction of the foreskin and disappearance of the phimotic ring after treatment were also assessed by dividing the patients into 2 groups based on coexisting conditions, such as balanoposthitis, smegma, ballooning of the prepuce, and UTI. The patients who had a history of balanoposthitis, smegma, ballooning of the prepuce, or UTI showed significantly poorer improvement in preputial retraction after treatment ($p < 0.001$, $p < 0.001$, $p < 0.001$,

and $p=0.02$, respectively) (Table 4). The results were similar for phimotic ring disappearance after treatment ($p < 0.001$, $p=0.001$, $p < 0.001$, and $p=0.001$, respectively) (Table 5).

No significant local or systemic side effects, such as striae, pigmentation changes, telangiectasia, and hypertrichosis, were associated with the administration of the topical steroid.

DISCUSSION

In this study, we report that local application of 0.05% clobetasol propionate is an effective and safe conservative treatment in patients with severe phimosis and phimosis-associated clinical complications. During recent years, several articles on the use of topical steroids for the treatment of phimosis have reported similar success rates ranging from 70% to 90% [1,2,10-15]. The success rate in our study was 68.2%, which is relatively low compared with other studies. There are two reasons for this low success rate. First, unlike in other studies, only boys with severe phimosis, i.e., Kikiros retractability grade 4 or 5, were en-

TABLE 4. The relationship between phimosis-associated clinical complications and full retraction of the foreskin after treatment

Variable	Full retraction of the foreskin, n (%)		Total	p-value	OR (95% CI)
	Possible	Impossible			
Smegma				< 0.001	13.90 (3.03–63.84)
Never	31 (93.9)	2 (6.1)	33		
Yes	29 (52.7)	26 (47.3)	55		
Total	60 (68.2)	28 (31.8)	88		
Balanoposthitis				< 0.001	8.40 (2.59–27.23)
Never	35 (68.2)	4 (39.0)	39		
Yes	25 (51.0)	24 (28.0)	49		
Total	60 (68.2)	28 (31.8)	88		
Ballooning of the prepuce				< 0.001	3.23 (0.99–10.56)
Never	21 (84.0)	4 (16.0)	25		
Yes	39 (61.9)	24 (38.1)	63		
Total	60 (68.2)	28 (31.8)	88		
UTI				0.02	2.88 (1.14–7.26)
Never	41 (77.4)	12 (22.6)	53		
Yes	19 (54.3)	16 (45.7)	35		
Total	60 (68.2)	28 (31.8)	88		

OR, odds ratio; CI, confidence interval; UTI, urinary tract infection.

TABLE 5. The relationship between phimosis-associated clinical complications and the disappearance of the phimotic ring after treatment

Variable	Disappearance of the phimotic ring, n (%)		Total	p-value	OR (95% CI)
	Disappear	Exist			
Smegma				0.001	4.81 (1.79–12.92)
Never	16 (48.5)	17 (51.5)	33		
Yes	9 (16.4)	46 (83.6)	55		
Total	25 (28.4)	63 (71.6)	88		
Balanoposthitis				< 0.001	9.26 (3.03–28.33)
Never	20 (51.3)	19 (48.7)	39		
Yes	5 (10.2)	44 (89.8)	49		
Total	25 (28.4)	63 (71.6)	88		
Ballooning of the prepuce				< 0.001	10.67 (3.63–31.39)
Never	16 (64.0)	9 (36.0)	25		
Yes	9 (14.3)	54 (85.7)	63		
Total	25 (28.4)	63 (71.6)	88		
UTI				0.001	7.57 (2.056–27.87)
Never	22 (41.5)	31 (58.5)	53		
Yes	3 (8.6)	32 (91.4)	35		
Total	25 (28.4)	63 (71.6)	88		

OR, odds ratio; CI, confidence interval; UTI, urinary tract infection.

rolled in the present study. Moreover, because the definition of treatment success in our study was full retraction of the foreskin, patients who achieved partial retraction after treatment were excluded. Second, because our study was designed to determine the early effects of topical steroid treatment in phimosis, relatively early evaluation of treatment success was performed. In addition, although previous studies used topical steroids for various periods ranging from 4 to 12 weeks, we applied the topical steroid for only 4 weeks.

Interestingly, Ashfield et al. [1] reported that there were no statistical differences in success rates among patients

with phimosis alone, coexisting balanitis, or a history of UTI. In our study, however, the retractability of the foreskin was significantly lower in the patients who had a history of balanoposthitis, smegma, ballooning of the prepuce, or UTI before treatment ($p < 0.001$, $p < 0.001$, $p < 0.001$, and $p = 0.02$, respectively). This was mainly due to the ongoing process of pathologic phimosis. Because patients with complications are prone to developing a pathologic process, their foreskin tissue would have more collagen fiber and inflammatory cells, which is the main microscopic finding in late inflammatory tissue [16]. The same result was shown in a study analyzing the foreskin collected from

TABLE 6. Literature reporting topical steroid agents, regimens, and success rates of treatment

Study	Topical steroid	Classification of potency ^a	Application period	Evaluation of treatment from initiation of therapy	No. of patients	No. of cured patients (%)
Kikiros et al. (1993) [10]	Betamethasone valerate 0.05% (ointment)	Class II high potency	Average 4 wk (2-12 wk)	Immediately at the completion of treatment	42	37 (88)
	Hydrocortisone 1-2% (ointment)	Class VII least potency			21	18 (86)
Wright (1994) [12]	Betamethasone valerate 0.05% (cream)	Class II high potency	4-8 wk	4-8 wk	111	89 (80)
Jorgensen and Svensson (1993) [13]	Clobetasol propionate 0.05% (cream)	Class I super high potency	4-12 wk	4-12 wk	54	38 (70)
Orsola et al. (2000) [11]	Betamethasone valerate 0.05% (cream)	Class II high potency	4 wk	5 wk	137	112 (82)
Ashfield et al. (2003) [1]	Betamethasone valerate 0.1% (ointment)	Class III upper mid potency	6 wk	3 mo	194	168 (87)
de Oliveira Pileggi and Vicente (2007) [14]	Mometasone furoate 0.1% (cream)	Class IV mid potency	8 wk	8 wk	56	49 (88)
Zavras et al. (2008) [15]	Fluticasone propionate 0.05% (cream)	Class V lower mid potency	4-8 wk	4-8 wk	1,185	1,079 (91)
Kuehhas et al. (2012) [2]	Betamethasone valerate 0.1% (cream)	Class VI low potency	8 wk+2 wk (tapering reduction)	3 mo	36	25 (69)
This study	Clobetasol propionate 0.05% (cream)	Class I super high potency	4 wk	4 wk	88	60 (68)

^a: There are seven classes of potency of topical steroids, which are classified by their ability to constrict capillaries. Class I is the strongest, or super high potent. Class VII is the weakest and mildest [23].

40 patients who underwent circumcision [17]. In that study, the percentage of collagen fibers was significantly higher in the groups of patients with clinical complications diagnosed before surgery.

Exactly how topical steroids contribute to resolving phimosis remains speculative and multifactorial. Several studies have suggested possible mechanisms involved in the action of topical steroids [11,16]. The first mechanism is related to an anti-inflammatory and immunosuppressive effect. The inflammatory process is regulated by glucocorticoid activity, which stimulates the transcription of anti-inflammatory genes and decreases the transcription of inflammatory genes [18]. Kragballe [19] suggested that glucocorticoids enhance the production of lipocortin 1 (also known as annexin A1), which has been reported to inhibit the activity of phospholipase A2 [20]. Phospholipase A2 plays a key role in the inflammatory process through the synthesis of arachidonate-derived eicosanoids (prostaglandins, prostacyclins, leukotrienes, and thromboxanes) [21]. The immunosuppressive effect of glucocorticoids is achieved by inhibiting the humoral factors involved in the inflammatory response and leukocyte migration to sites of inflammation. Furthermore, glucocorticoids interfere with the function of endothelial cells, granulocytes, and fibroblasts [22]. The second mechanism is related to a skin thinning effect. Glucocorticoids play an active role in the inhibition of collagen synthesis and have antiproliferative effects on the epidermis. Because glucocorticoids inhibit the synthesis of hyaluronic acid, the main glycosaminoglycan produced by fibroblasts, the dermal extracellular matrix is reduced and collagen and elastin fibers become tightly packed and rearranged [16].

Although the efficacy of topical steroids for the treatment of phimosis has been shown in several studies, the best topical steroid agent and regimen has yet to be identified (Table 6). The reported topical steroid agents, regimens, and the success rate of treatment have varied [1,2,10-15]. Moreover, the potency of the topical steroids used ranges from class I to class VII. Even though clobetasol propionate 0.05%, a highly potent corticosteroid, was selected in the present study, there were no visible local or systemic side effects of the steroid. This may have been mainly due to the short-term use of the steroid. Further studies are needed to determine the best topical steroid agent and regimen.

In this study, we observed that short-term application of a topical steroid and retraction of the foreskin is beneficial for the treatment severe phimosis. We also observed that phimosis-associated symptoms, such as ballooning of the prepuce, balanoposthitis, and a history of UTI, affected the success rate of treatment.

CONCLUSIONS

The present study showed that topical application of 0.05% clobetasol propionate cream and skin stretching is a safe, simple, and effective procedure with no significant side effects for treating phimosis in prepubertal boys. Therefore,

this could be the first choice of treatment for boys with severe phimosis instead of circumcision.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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