

ORIGINAL ARTICLE

Efficacy of Preoperative Topical Testosterone Therapy for Micro Phallic Hypospadias: Experience in Dhaka Shishu (Children) Hospital

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Abstract

Introduction: Surgical correction of genital defect was formally proposed when the size of the penis is sufficient to permit easy surgical repair. Delaying surgical repair until the phallus is of suitable size or pretreatment with hormones is recommended. In micro phallic hypospadias, temporary stimulation with testosterone either topical or parenteral to enlarge the penile size has been reported.

Objective: Aim of this study was to evaluate the efficacy of preoperative topical testosterone therapy in micro phallic hypospadias patients.

Methods: This retrospective study was carried out in the division of pediatric surgery, Dhaka Shishu (Children) Hospital. Hospital records of patients with micro phallic hypospadias from July 2015 to December 2017 were analyzed. All patients received testosterone cream 3 times daily for three weeks. Alteration of penile length, glans width and the adverse effects of testosterone therapy were recorded. Data were analyzed by using SPSS version 22.

Results: Total 35 patients received topical testosterone therapy during the study period. The mean penile length of penis was changed from 2.71 ± 0.49 cm to 3.46 ± 0.26 cm, which was statistically significant ($p < 0.05$). The mean glans width was changed from 1.13 ± 0.18 cm to 1.29 ± 0.13 cm, which was statistically significant ($p < 0.05$). Minor adverse effects were noted like pubic hair, genital pigmentation, and dermatitis.

Conclusion: Significant penile growth was observed with minor adverse effects after using topical testosterone therapy.

Key Words: Hypospadias, testosterone, micro phallus.

Introduction

The word hypospadias is derived from the Greek words 'hypo', which means below, and 'spadon', which means rent or hole. This condition is characterized by urethral meatus located ectopically proximal to the normal location and on the ventral aspect of the penis. In the severe cases, the urethral meatus opens onto the scrotum and perineum.¹

Boys with hypospadias are termed micro phallic based on penile length < 2 standard deviations (SD) from normal.²

Hypospadias is a relatively common malformation. The growth in the penile length takes place for up to 5 years followed by little change until the onset of puberty. According to available data, a small penis in hypospadias is a result of fetal testosterone insufficiency or lack of scrotal fold receptivity during fetal life.³

A subgroup of boys with hypospadias, especially proximal cases, has been described as having a "significantly smaller than usual" penis in the context of selecting patients for preoperative androgen therapy. Others characterized boys with hypospadias

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as micro phallic based on penile length <2 standard deviations (SD) from normal (3.5cm), although accurately determining stretched penile length can be difficult in those proximal cases with ventral curvature and abnormal skin attachments from penoscrotal transposition. Glans size potentially is more readily measured, with several studies reporting circumferences in children with hypospadias selected for androgen stimulation.²

Micro phallic hypospadias is more common in severe hypospadias, which includes those with urethral opening on the shaft of penis or on the scrotum or perineum. Between 1968-1990, the incidence of severe hypospadias has increased from 1.1 to 2.7 per 10,000 live births and by 1993, 5.5 severe cases per 10,000 live births per year.⁴

The lack of hard scientific data, results in the use of empirical judgment when the surgeon confronts with a hypospadiac micro phallic case. Delaying surgical repair until the phallus is of suitable size or pretreatment with hormones and proceeding with early repair is the matter of concern. Surgeons who delay surgery usually do so based on the lack of compelling evidence that endocrine therapy is truly beneficial. It is a matter of concern that prepubertal androgens may be detrimental. In contrast, surgeons who proceed with hormonal treatment and early surgery argue that delaying the operative procedure results in undue and avoidable psychological stress to the infant and parents.⁵

It has been proposed that better surgical conditions are obtained when hormones are used prior to hypospadias surgery, temporarily increasing penile length and glans circumference, favoring better local skin conditions and reducing surgical complications. Different hormones have been proposed: human chorionic gonadotropin (HCG), dihydrotestosterone (DHT) or testosterone. However, there are divergences about the hormone therapy of choice, time of use, appropriate dose, and means of application (topical or parenteral).⁶

If the physician chooses to use testosterone, he/she will face two alternative treatment methods. One can use testosterone propionate cream 2% applied to the penile

shaft 3 times daily for 3 weeks or parenteral 2 mg/kg testosterone ethanate intramuscularly.⁵

So, considering the above mentioned facts, present study was undertaken to see the efficacy of topical testosterone therapy in micro phallic hypospadias patients.

Materials and Methods

This retrospective study was carried out in the division of pediatric surgery, Dhaka Shishu (Children) Hospital. Hospital records of patients with micro phallic hypospadias from July 2015 to December 2017 were analyzed. All patients received testosterone cream 3 times daily for three weeks. Alteration of penile length, glans width and the adverse effects of testosterone therapy were recorded. Data were analyzed by using SPSS version 22.

Results

The mean age of participants was 33.51±19.09 months (6 months to 60 months). Middle hypospadias was more common (65.8%) (Table I).

Table I
Types of hypospadias (n=35)

Types of hypospadias	No. (%)
Anterior	6(17.1)
Middle	23(65.8)
Posterior	6(17.1)

Before treatment, the mean length of penis of 35 patients was 2.71±0.49 cm. After 1st follow up, the penile length was increased and the mean was 2.97±0.45 cm. Then, after last follow up, the mean became 3.46±0.26 cm (Table II and Figure 1).

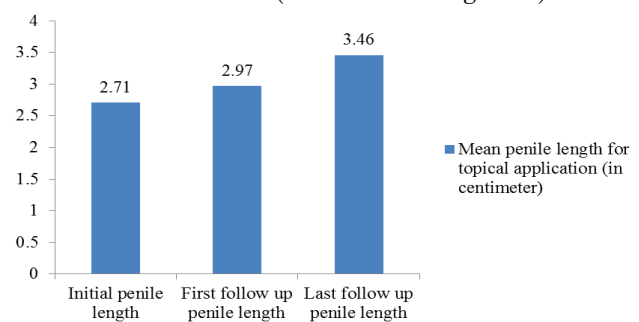


Fig 1 *Alteration of penile length*

Table II
Comparison of penile length before and after topical testosterone therapy

Penile length (In centimeters)	Before topical testosterone therapy (n=35)	After topical testosterone therapy (n=35)	P value*
Mean±SD	2.71±0.50	3.46±0.26	0.0001

*Paired 't' test

The penile length increases significantly in patients after topical testosterone therapy.

Table III
Comparison of glans width before and after topical testosterone therapy

Glans width (cm)	Before topical testosterone therapy (n=35)	After topical testosterone therapy (n=35)	P* value
Mean±SD	1.13±0.18	1.52±0.09	0.0001

* paired 't' test

Before treatment, the mean glans width of 35 patients was 1.13±0.18 cm. After 1st follow up, the glans width was increased and the mean was 1.29±0.13 cm. Then, after last follow up, the mean became 1.52±0.09 cm (Figure 2 & Table III).

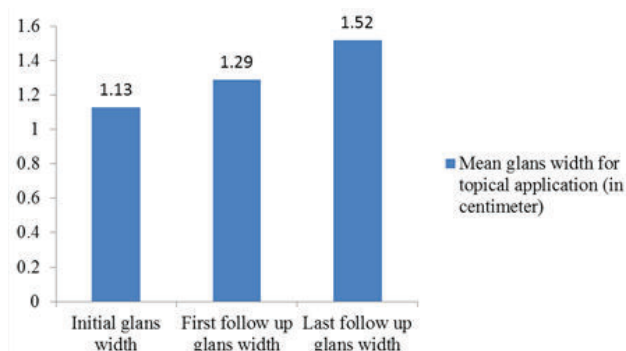


Fig 2 Mean glans width

The glans width also increased significantly ($p < 0.05$) after topical testosterone therapy.

Minor adverse effects were noted in table IV.

Table IV
Adverse effects

Adverse effects	n (%)
Pubic hair	13(37.1%)
Genital pigmentation	35(100%)
Dermatitis	10(28.6%)

Discussion

Local or systemic application of testosterone is reported to stimulate penile growth.² It is preferable to increase the penile size before surgery for appropriate preoperative surgical condition and to minimize post operative complications. In general consideration, penile size is measured in terms of penile length and glans circumference. Normal penile length is considered >3.5 cm (3.1-4.7cm), which is the measurement in newborn.⁷

Netto et al. had done a systematic review on hormone therapy in hypospadias surgery in 2013 and they found that adverse effect varies from study to study. Out of fourteen studies, ten articles reported adverse effects with quite varied results. Of the seven studies that evaluated topical administration, three described genital pigmentation as an adverse effect. Two articles also reported skin irritation at the site of topical application, but in a limited number of patients. The appearance of pubic hair was reported in half the studies, independently of the route of application, but in a limited number of patients. All of these side effects regressed after the end of hormone therapy.⁶

In this study preoperative topical testosterone was used in patients with penile length <3.5 cm and glans width <1.4 cm. Desired penile length was obtained after second follow up. So, their topical testosterone therapy was stopped after second follow up.

Before treatment, the mean length of penis of 35 patients was 2.71±0.50 cm. Then, after 4 weeks, the mean became 3.46±0.26 cm. The penile length increased significantly in patients after topical testosterone therapy as $p < 0.05$ (obtained by paired sample t test). So, significant penile growth was noticed after topical testosterone was used. In the study by Chalapathi et al.³ also, significant penile growth was noticed in topical testosterone therapy.

In boys with micro phallic hypospadias, it is difficult to measure stretched penile length especially in proximal cases with ventral curvature and abnormal skin attachment.³ Glans size is easy to measure in these cases. So, in this study, the maximum glans width was measured before, during and after the therapy. Before treatment, the mean glans width of 35 patients was 1.13±0.18 cm. Then, after 4 weeks, the mean became 1.52±0.09 cm. The glans width increased significantly after 4 weeks of topical testosterone therapy as $p < 0.05$ (obtained from paired sample t test). These observations are comparable to

the results of study by Gearhart and Jeffs, who reported that 2mg/kg testosterone enanthate, increased glans width from an average of 1.2 to 1.7 cm in 36 boys.⁸

Testosterone has various adverse effects which may limit its application. Adverse effects such as, development of pubic hair, facial hair, acne, bone growth, genital pigmentation and skin reactions occur topical testosterone therapy. In this study, three adverse effects, appearance of pubic hair, genital pigmentation and dermatitis has been reported. The bone growth was not evaluated due to time constrain.

When considering adverse effects of testosterone therapy, every patient developed genital pigmentation in topical testosterone therapy. This showed strong association of genital pigmentation with topical testosterone. The study by Chalapathi et al also reported that all patients, who were treated with topical testosterone, had pigmentation of genitalia². Topical testosterone is associated with application site skin reactions. It includes mild to moderate erythema, pruritus, blisters or dermatitis.¹⁶ this study revealed that ten patients in topical testosterone therapy developed dermatitis. The study by Chalapathi et al. reported that one patient in topical testosterone group suffered with dermatitis.³

Appearance of pubic hair is one of the secondary effects of testosterone. Systemic effect of topical testosterone causes fine pubic hair to appear. In this study, thirteen patients in topical testosterone therapy developed pubic hair. Nerli et al found that fine pubic hair was noted in two children receiving testosterone cream.⁹

A systemic review done by Netto et al. showed greater occurrence of adverse effects associated with topical use of testosterone, such as pigmentation of genitals (69% topical), appearance of pubic hair (35.2% topical) and skin irritation at the site of application (3.8%).⁶ The incidence of adverse effects such as genital pigmentation and dermatitis in topical testosterone therapy may relate to unpredictable absorption and uncontrolled application of testosterone by parents.³ Appearance of pubic hair is common adverse effect in topical testosterone therapy, as it is due to systemic

effect of testosterone, which is one of the secondary sexual characteristics in male. These side effects regress after the cessation of testosterone therapy.

Conclusion

Significant penile growth was observed with little or acceptable adverse effects after using topical testosterone therapy.

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