# Evaluation of Preoperative Application of Topical Testosterone Effect on The Result of Tabularized Incised Plate Repair Operation for Penile Hypospadias in Suez Canal University Hospitals

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# ABSTRACT

**Background:** For numerous years, the utilize of activating of hormones prior to surgical repair of a small sized phallus was deemed as a relatively common method. The beneficial influence of preoperative hormonal therapy remains contentious.

**Objective:** We aimed to evaluate the effect of topical testosterone application on result of tubularized incised plate (TIP) repair in distal hypospadias in Suez Canal University Hospitals.

**Methods:** A total of 96 male cases had distal hypospadias were recruited into the research and have been randomized to study or control group. Both groups were treated using the TIP repair. The study group patients received preoperative topical testosterone while the control group didn't, to evaluate the influence of topical testosterone application on result of TIP repair in distal hypospadias in Suez Canal University Hospitals.

**Results:** Mean glanular width was 14.83 mm prior to topical application of testosterone and increased to 16.9 mm with statistically significant variance (P below 0.05). There was statistically significant increase of glanular height with the use of topical testosterone. Mean glanular height increased from 9.2 mm to 13.1 mm with statistically significant variance (P below 0.05). there was a statistically insignificant variance among both groups according to late postoperative complications.

**Conclusion:** Our findings concluded that topical testosterone before TIP surgery for distal penile hypospadias had no significant impact on success rates or late complications but led to a higher rate of mild early postoperative complications.

Keywords: Hypospadias, Congenital Anomalies, TIP repair, Topical Testosterone.

# **INTRODUCTION**

Hypospadias is the greatest frequent congenital anomaly affecting between 0.3 and 0.7 percent of live male births. It is characterized by abnormally displaced male urethra ventrally, exiting the dorsal aspect of the penis anywhere within the, scrotum shaft, glans or even the perineum  $^{(1,2)}$ .

The main therapeutic option for uncomplicated hypospadias is operative repair <sup>(2)</sup>. A midline relaxing incision is essential for tubularized incised plate (TIP) hypospadias correction as it helps to enlarge the urethral plate for urethroplasty without the need to use of extra skin flaps. This incision widens the meatus and ensures the creation of a vertically oriented neomeatus with a slit-like entrance by extending from inside the meatus to the end of the plate. The approach has become more and more popular since it was first used in 1994 as a consequence of its versatility minimal risk of complications, and aesthetic outcomes <sup>(3)</sup>.

Due to the nature of the surgical site, pediatric urologists frequently have a very small site to operate on. Hence come the need to enlarge the penis size and girth prior to surgery to enlarge the surgical site and reduce the intraoperative and postoperative difficulties improving the postoperative outcome <sup>(3)</sup>.

Numerous investigations have evaluated hormonal stimulation to enhance functional and cosmetic results following hypospadias repair. Androgen stimulation may rise the growth rate of phallic, improving reconstruction and diminishing complications <sup>(4)</sup>.

Some reports have concluded that preoperative androgen therapy improves the cosmetic and surgical outcome <sup>(5,6)</sup>. In contrast, others involved that preoperative testosterone has been associated with a higher risk of complications <sup>(7)</sup>. So, it is still controversial to use preoperative hormonal therapy <sup>(8)</sup>. In this study, we prospectively conducted a clinical trial comparing two groups of patients regarding the effect of preoperative topical testosterone application on the result of tubularized incised plate repair surgery for cases that had distal penile hypospadias.

# PATIENTS AND METHODS

Following approval of Ethics Committee of Faculty of medicine, Suez Canal University, the current study was conducted as controlled randomized clinical trial among a total of 96 male cases who had distal penile hypospadias presented to the pediatric surgery outpatient clinic Suez Canal University hospitals. Patients older than 6 months of age with distal penile hypospadias according to Hadidi classification <sup>(9)</sup> eligible for tabularized incision plate surgical correction of distal penile hypospadias were included into the study. Any patient with disordered sex development, or allergy to topical testosterone were excluded from the study. The recruited study participants were randomly allocated to one of two groups using simple randomization. The study group included total of 48 male patients had distal penile hypospadias who were treated with topical testosterone gel 2% for 30 days, which was stopped 2 weeks before the time of surgery. Distal penile hypospadias was corrected using tubularized incised plate technique. The control group included total of 48 male patients with distal penile hypospadias. They didn't receive topical testosterone. Distal penile hypospadias was corrected using tubularized incised plate technique.

#### Methods of the study:

All of patients were subjected to full clinical assessment through history taking, general and local examination for the penile size and meatal position and caliber. The urethral plate was examined for its width, length or associated urethral dysplasia. Examination of the scrotal wall was done to check if it was either well developed or underdeveloped. The study was conducted from 2023 to 2024.

Routine preoperative laboratory investigations including CBC and coagulation profile was done. Pelviabdominal ultrasound and inguinoscrotal ultrasound were done to rule out associated urinary tract and genital anomalies like inguinal hernia or cryptorchidism.

## Preoperative intervention and assessment

Patients of the study group were treated with topical gel application containing testosterone 2%. They were treated for 30 days and treatment was stopped 2 weeks prior to the time of the surgery.

Glanular width, glanular height, and urethral plate width were reported before and after the application of topical testosterone.

# Surgical management:

Both group patients were treated using TIP procedure by the same surgeon. The penis was degloved following a circumferential subcoronal incision made approximately two millimeters proximal to the urethral native meatus. A U-shaped incision was made along the lateral margins of the urethral plate. The glans wings were subsequently established. A relaxing incision was performed along the midline of the urethral plate to permit tension-free tubularization of the urethra. Tubularization itself was then carried out with a 6/0 running suture.

A buttonholed dartos flap could be moved from the dorsal part of the penis to the ventral part allowing covering of the tubularized neo-urethra. Glans wings approximation initiates the glanuloplasty on the corona. The suturing of the skin margins and the meatus concluded the procedure. Levels of satisfaction in tubularized incised plate were excellent, with visual results deemed equal to those of typical penis <sup>(10)</sup>.

#### **Postoperative assessment:**

Patients were assessed for early postoperative complications as hematoma, bleeding, and edema. They were followed up and re-evaluated for 3 months for occurrence of wound dehiscence, fistula, or meatal stenosis. The incidence of re-do surgery was reported. Parent's overall satisfaction with the postoperative shape and function was evaluated using a scale from 0 to 10 as 0 indicating no satisfaction while 10 denotes fully satisfied with the outcomes.

#### **Ethical Considerations:**

The research ethics committee of the Faculty of Medicine at Suez Canal University accepted the research protocol. An informed consent has been attained from all parents of the recruited male infants. The Helsinki Declaration was followed throughout the study's conduct.

## Statistical Analysis

Statistical analysis has been carried out utilizing SPSS 25 program. Data were presented as tables. Quantitative information was explained as mean and standard deviation whereas qualitative data were described as percentages and numbers. Comparisons have been performed using chi square or Fisher's exact test (for qualitative information) and T test (for quantitative information). Statistical significance has been considered at p-value of < 0.05.

# RESULTS

# Table 1: Spreading of age among the examined cases.

The mean age of the study group cases was 23.2 months versus 22.9 months among the control group. Two groups of the investigation have been matched according to the patients' age without statistically significant difference (**Table 1**).

Age (months)	Study group (number=48)	Control group (number=48)	p- value
Mean ± SD	$23.2 \pm 4.6$	$22.9 \pm 5.2$	0.8
Range	7 – 72	8-60	(NS)

Table 1: Spreading of age among the examined case
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NS: No statistically significant difference

There was statistically significant increase of both glanular width and height with the use of topical testosterone. Urethral plate size also increased significantly with the application of topical testosterone.

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Measurements		Before topical testosterone (n=48)	After topical testosterone (n=48)	p-value
Glanular width (mm)	Mean $\pm$ SD	$14.83 \pm 0.7$	$16.9\pm0.9$	0.001*
Glanular height (mm)	$Mean \pm SD$	$9.2\pm1.8$	$13.1 \pm 1.5$	0.001*
Urethral plate size (mm)	Mean $\pm$ SD	$8.9\pm0.8$	$11.8 \pm 1.05$	0.001*

## Table 2: Pre- and post-topical testosterone application penile measurements at the study group.

\*: Statistically significant difference.

As presented in **table 3**, early postoperative complications were significantly more reported among the study group than control group. The most common early postoperative complication was hematoma. Hematoma was reported among 54.2% among the study group patients versus 25% of the control group patients. Minimal bleeding and postoperative edema were also significantly more common in the study group than the control group patients. There was a statistically insignificant variance among both groups according to late postoperative complications, e.g., fistula and wound dehiscence. Satisfaction rate was 85.4% among the study group patients versus 77.1% of the control group without statistically significant difference.

Table 3: ]	Early	and late	nostone	rative (	outcome	among t	he e	examined a	natients.
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		Study group (number=48)	Control group (number=48)	p-value	
Fauly postononative	Hematoma	26 (54.2%)	12 (25%)	0.003*	
complications	Bleeding	13 (27.1%)	2 (6.25%)	0.004*	
	Edema	22 (45.8%)	9 (18.75%)	0.005*	
Late postoperative complications	Fistula	2 (4.2%)	5 (10.4%)	0.4 (NS)	
	Meatal stenosis	0 (0%)	1 (2.1%)	1.0 (NS)	
	Dehiscence	1 (2.1%)	3 (6.25%)	0.6 (NS)	
Satisfa ation	Satisfied	41 (85.4%)	37 (77.1%)	0.2 (NS)	
Saustaction	Not satisfied	7 (14.6%)	11 (22.9%)	0.5(NS)	
Re-do rate		2 (4.2%)	3 (6.25%)	1.0 (NS)	

\*: Statistically significant difference.

#### DISCUSSION

The current randomized controlled clinical trial has been designed to assess the effectiveness of preoperative topical application of testosterone on the outcome of surgical correction of hypospadias using TIP procedure. A total of 96 male patients presented with hypospadias who were eligible for TIP procedure and aged more than 6 months were included into the study. They were randomly allocated to one of two groups: the study group and the control group. The study group patients were treated with topical gel containing 2% testosterone for 1 month and stopped 2 weeks before the surgery.

Topical administration of testosterone can be criticized for the less predictable drug dosage and spreading on the penis <sup>(11)</sup>. Nevertheless, this guideline has been selected due to easy applicability and also to avoid the potential unclear complications of parenteral testosterone which were unclear whereas reviewing the literature.Researches that in comparison with the parenteral and topical administration of testosterone didn't illustrate significant variances in penile length among the routes of application <sup>(12,13)</sup>. To date, there is no consensus on the guideline for preoperative activations of hormones operation according to method of administration, the proper dosage, concentration and frequency <sup>(11)</sup>.

According to the rate of postoperative complications, we found that early postoperative

complications were significantly more reported among the study group than control group. The most common early postoperative complication was hematoma. Minimal bleeding and edema were also higher among the study group with statistically significant difference.

In a study by **Wali and colleagues** <sup>(8)</sup> there was an insignificant variance among both cases who received topical application of testosterone versus who didn't in terms of the rate of postoperative complications. Unlike our results, **Asgari** *et al.* <sup>(6)</sup> have found significant lower rate of complications with the topical application of testosterone prior to hypospadias correction via TIP procedure.

The rate of re-operation observed by **Wali** *et al.* <sup>(8)</sup> was insignificantly different whether topical testosterone was applied or not prior to surgical correction of hypospadias using TIP procedure as well as parent satisfaction about function and shape. This is in accordance with the current study results.

We have found that topical application of testosterone has resulted in significant increase of both glanular width and height with the use of topical testosterone. Mean glanular width was 14.83 mm prior to topical application of testosterone and increased to 16.2 mm while glanular height increased from 9.2 mm to 13.1 mm with statistically significant variance (P below 0.05). Urethral plate size also increased significantly with the application of topical testosterone from 8.9 mm to 11.8 mm (p-value < 0.05). Comparable

to our outcomes, **Wali** *et al.* <sup>(8)</sup> have also reported a significant enhance in all penile valuables following activating of hormones by topical testosterone application. It has been previously reported that testosterone therapy prior to hypospadias operation is beneficial in increasing the penile length <sup>(12,14)</sup>. Testosterone is recognized for its ability to enhance the size of penile in prepubertal boys because of its androgenic effects. This was demonstrated to be beneficial in the surgical repair of hypospadias, as a larger phallus size makes correction less and easier risky.

Several studies have shown significant increase in the microvessel density with topical application of testosterone <sup>(15,16)</sup>.

We didn't evaluate this parameter but this could explain the increase in the rate of edema, bleeding and hematoma that was observed with topical application of testosterone in the current study.

The restrictions of the current investigation include the small sample size and we didn't assess the change of serum testosterone level. However, it has some strengthens as its design as randomized controlled trial and the homogeneity of the studied patients with one type of hypospadias.

## CONCLUSION

The current study has concluded that topical testosterone application prior to surgical correction of penile distal hypospadias has low rate of late postoperative complications that is not significantly different from untreated group. Although the rate of early postoperative complications was significantly greater for each of hematoma, bleeding and edema with topical application of testosterone but all of them were tolerable and resolved with treatment. Preoperative topical testosterone is also correlated with significant raise in glanular width and height but without significant effect on the surgery outcome.

#### DECLARATIONS

- **Consent for publication:** I certify that each author has granted permission for the work to be submitted.
- **Funding:** No fund
- Availability of data and material: Available
- Conflicts of interest: None
- Competing interests: None

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