Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Pediatric Surgery

Topical Testosterone Therapy Prior to Hypospadias Repair (Our experience at Queen Rania Al-Abdullah Hospital for Children)

Bahaa Abdallah[1*], Salim Masadeh[1], Amer Alibrahim[1], Salameh Samawi[1], Omar Alyabrodi[1], Ahmd Alremony[1]

[1]MD, Department of Pediatric Surgery, Jordanians Royal Medical Services, Queen Rania Hospital for Children, Amman, Jordan

DOI: 10.36347/sjams.2021.v09i10.009 | **Received:** 29.09.2021 | **Accepted:** 04.10.2021 | **Published:** 11.10.2021

***Corresponding author:** Dr. Bahaa Abdallah

Abstract **Original Research Article**

Objective: As hypospadias is one of the most common congenital male anomalies, furthermore, multiple approaches and methods of treatment were mentioned over the references, we tried to put our thumbs on one of the most preoperative steps which can be missed or has multiple debates during a discussion about it. Here in our study, we focused on the rule of topical testosterone treatment on multiple patients as an advantageous step to get a higher rate of success postoperatively side by side to achieve a good penile size intraoperatively. Deep detailed analysis of side effects of topical testosterone balanced with the duration of surgery, short and long-term outcome. ***Methodology:*** The study was carried out from January 2014 to January 2019 at Queen Rania Hospital for children, Amman, Jordan. The overall number was 182 patients. We divided them into two groups: (group A) 98 boys who did not receive the hormonal treatment and (group B) were referred to the patients who underwent the topical treatment and their number was 84. The age group was between 6 months and 6 years. Testosterone gel 1% was applied as a thin layer over the ventral aspect of the penis once daily for 3 weeks before surgery. The patient's degree of hypospadias as glandular, coronal, distal shaft, and midshaft to illustrate the benefits on each group. The local and systemic side effects of the gel were documented. Concomitantly we measure the difference in penile length, glans width along with serum testosterone level before and after applying it. After that, the mean duration of surgery was measured. The common complications of surgery were listed as fistula, glans dehiscence, meatal stenosis and the number of each complication for each group was documented and analyzed. ***Results:*** There were good results related to the mean penile length and glans width no significant change related to the serum testosterone level. No valuable change upon the duration of surgery. Local skin pigmentation with suprapubic hair growth 46% and 21% respectively which are transient and resolve post therapy. Complications were much higher in the first group 26.5% in compare with 16.6% to the second group the complications were listed as urethral fistula, glans dehiscence, and meatal stenosis. ***Conclusion:*** Topical testosterone has a good outcome which was reflected in group B of patients. However, a local side effects have been reported as transient genital pigmentation and suprapubic hair growth which resolve after therapy.

Keywords: Hypospadias, topical testosterone, tube urethroplasty.

INTRODUCTION

As hypospadias is one of the most common congenital male anomalies, furthermore, multiple approaches and methods of treatment were mentioned over the references, we tried to put our thumbs on one of the most preoperative steps which can be missed or has multiple debates during the discussion about it. Her on our study we focused on the rule of topical testosterone treatment on multiple patients as an advantageous step to get a higher rate of success postoperatively side by side to achieve a good penile size intraoperatively. Deep detailed analysis of side effects of topical testosterone balanced with the duration of surgery, short and long-term outcome.

METHODOLOGY

We report our experience with topical testosterone as an adjunct to reconstructive hypospadias surgery repair. The retrospective study was conducted at Queen Rania Hospital for children, Amman, Jordan from January 2014 to January 2019. The research received ethical approval from the hospital's scientific committee. Parents were told about the study's risks and benefits, and written consent was obtained. The overall number of patients included in the study was 182 patients. We divided them into two groups: the first one (group A) was 98 boys who did not receive the hormonal treatment and the second group (group B) was referred to the patients who underwent the topical

treatment and their number was 84. The candidate age group was between 6 months and 6 years. Testosterone gel 1% was applied once daily as a thin layer over the ventral aspect of the penis for 3 weeks before surgery. The patients on each group were classified according to their degree of hypospadias as glandular, coronal, distal shaft, and mid-shaft to illustrate the benefits of each group. Age less than 6 months or greater than 6 years, redo surgery, incomplete follow-up and staged repair for proximal hypospadias were all considered exclusion criteria. We started our reports by detecting the local and systemic side effects of the gel. The complications are anaphylaxis, genital pigmentation, growth of suprapubic hair, and dermatitis. Concomitantly we measure the difference in penile length, glans width along with elevation in serum testosterone level after applying it. After that, the mean duration of surgery was measured as it was defined as the actual duration of surgery without the anesthesia and recovery time. The common complications of surgery were listed as fistula, glans dehiscence, meatal stenosis and the number of each complication for each group was documented and analyzed .lastly, follow-up data of the patients who need revision surgery side by side with long term satisfaction for both parents and surgeons were collected. Statistical analysis including mean, stander deviation, and p-value were collected and analyzed using SPSS (IBM, version 20, 2018).

RESULT

Out of 182 patients, we have 84 patients who received topical testosterone (group B) preoperatively and 98 patients who did not receive it (group A), age range from 6 months to 6 years old. The most common type in group A was coronal hypospadias (n=39) while the highest percentage in group B was distal shaft hypospadias (n= 34).

Table-1: Illustrates the different verities of hypospadias we include in our study involving group A and group B.

	group A (N 98)		group B (N 84)	
	NUMBER	%	NUMBER	%
Glandular	26	26.5%	6	7.1%
Coronal	39	39.7%	33	39.2%
distal shaft	20	20.4%	34	40.4%
mid shaft	13	13.2%	11	13.0%

The post topical testosterone side effects upon group B. we reported 39 patients (46 %) with the growth of suprapubic hair along 18 patients (almost 21%) had genital pigmentation.

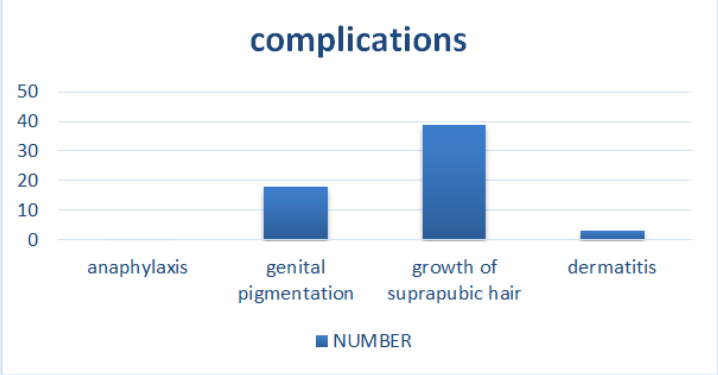

Chart-1: shows the post topical testosterone side effect upon group B

The mean difference in penile length before and after topical testosterone therapy was 1.1 cm, side by side with an increase in mean glans width by 0.51 cm for Testosterone level the mean difference was 3.9 ng/ml (Table-1).

Table-1: Shows that the mean difference in penile length, glans width and testosterone level before and after topical testosterone therapy

	Mean penile length (cm)	Mean testosterone level (ng/ml)	Mean glans width (cm)
Prior to topical testosterone treatment	3.1	0.33	1.21
Following the administration of topical testosterone	4.22	4.29	1.72
Mean difference	1.12	3.96	0.51
SD	0.4	0.72	0.18

Regarding postoperative complications, 26 out of 98 for group A (did not receive testosterone gel) have complications while 14 out of 86 for group B have complications (p-value = 0.15). In group A the most frequent complication was glans dehiscence in 14 % of the patients while dehiscence was accounted for 3.5% in group B (p-value = 0.02). On the other hand, the fistula was found in 7% of patients in group A and 4% of group B (Table-2).

Table-2: Postoperative complications

	GROUP A (N 98)		GROUP B (N 84)		P-value
	NUMBER	%	NUMBER	%	
Fistula	7	7.1%	4	4.7%	0.75
Dehiscence	14	14.2%	3	3.5%	0.02
Meatal stenosis	6	6.1%	7	8.3%	0.57
TOTAL COMPLICATIONS	26	26.50%	14	16.60%	0.15

For long-term outcomes, we found that 22out of 98 patients (22%) in group A require a revision procedure while 10 patients out of 86 patients (12%) in group B require a revision procedure for surgery outcome parents satisfaction, 73% in group A was satisfied with the outcome of surgery in comparison with 84 % for group B (Table-3).

Table-3: Compares between groups (A) and (B) in the terms of parents satisfaction and the need for a revision procedure

	GROUP A N(98)	GROUPB N(84)
Total number of patients who had revision procedure	22 (22.4%)	10 (11.9%)
Satisfaction with the surgery results	72 (73.4%)	71 (84.5%)

DISCUSSION

Hypospadias is defined as abnormal opening of the urethra along the ventral aspect, started from the glans penis up to the perineum. The most common congenital urogenital abnormality among the pediatric is undescended testis followed by hypospadias [1].

Embryology of urethral formation starts from the eighth to twelve-week on both sexes as an independent hormonal stage. the urethral plate starts on the midline of the genital tubercle. Later Androgen effect stimulates the elongation of the plate toward the glans penis followed by fusion of the urethral fold distally to form the penile urethra. Finally, fusion between glans and the foreskin in the midline [2].

Concerning the etiology of hypospadias, multifactorial causes have been documented including inadequate hormonal stimulation prenatally, genetic predisposition, maternal placental factors, and environmental factors [3, 4].

Hypospadias usually presents with three anatomic abnormalities started by hooded skin with deficient ventral foreskin, abnormal curvature of the skin toward the ventral area called Chordee, and ventrally opened urethral orifice below the normal position [5].

The only way to correct the hypospadias is surgery to create a new urethral orifice as close to the ventral tip of the penis as possible combined with correction of the chordee in a cosmetic way to simulate the normal site of opening and shape. Most pediatric urologist and references prefer to do surgery as an elective one before one and half year and even earlier to avoid psychiatric distress and to minimize the stranger anxiety [6, 7]. Accordingly, young age of patient combined with a very small area of surgery make the repair challenging as the complications are related to the size and length of the penis. As a result, many pediatric urologists focus more on the rule of testosterone either parenteral or topical on the circumference and length of the penis and its relation with the overall outcome. The target of this study is to illustrate the rule of topical testosterone in decreasing the duration of surgery and to document the pre and postoperative complications in comparison with the other people who underwent the same surgery without hormonal treatment.

Multiple randomized trials were performed to illustrate the rule of testosterone gel with optimizing the size balanced with least systemic and local side effects. In 1982, Monfort et al., Reported an increase in size and circumference by 50% after applying four weeks of 5% local dihydrotestosterone cream [8]. Another study from Kaya et al., illustrate the lower rate of complication including urethral stenosis, fistula, and glandular dehiscence among the group of patient who used topical testosterone along with minimal systemic side effect and local suprapubic hair [9]. In another study done in 2010 by Ahmad et al., in this study they give testosterone parenterally 2mg/kg and the outcome was statistically significant on penile enlargement. Moreover, there was a profound improvement in the texture, vascularity, and flexibility of the foreskin [10].

Another study was conducted by Chalapathi, et al.for the patient who has hypospadias with microphalus. In this study, topical and intramuscular injections of testosterone were used. both groups were given a combination of testosterone propionate and testosterone enanthate in a 2mg/kg/wk for three weeks. It was concluding that both groups achieve satisfactory phallus growth with no significant difference in size. However, a greater side effect was noted among the group of patients who applies the topical treatment [11].

Another study compares the various route of administration of testosterone with the benefits and side

effects. It concludes the same results of Chalapathi. However, there was no statistical difference in the side effect [12].

Asgari et al., did a prospective, randomized, controlled study including a two group of 182 patient, divided into testosterone group and controlled group .he reported the same surgeons and operation, TIP procedure, for all of them .and the complication is listed as meatal stenosis, urethrocutaneous fistula, urethral diverticulum, and glandular dehiscence the overall complication was statistically significantly higher in the control group, with a rate of 13.18% versus 5.45% (P=0.03). Importantly, most of the patients in the testosterone group developed genital pigmentation and suprapubic hair [13].

Here, we compared our results with the most popular same research on the topic we made. Concluding that we agreed with chapatti, Ahmad, Asgari with most of the point of discussion as penile size and length along with post-operative complication as urethral fistula, dehiscence, and meatal stenosis were noticeably improved after applying topical testosterone Importantly, there was no significant elevation upon the serum testosterone level. Also, the most benefit was obtained for the group of patients who have coronal, distal shaft, and midshaft hypospadias more than the glandular type as noticed .as mentioned in the previous studies there was significant suprapubic hair and genital skin hyperpigmentation with no documented anaphylaxis and only 3 cases of dermatitis with overall 4% of the whole study group.

CONCLUSION

Hypospadias repair is a challenging surgery as the outcome can be affected by multiple factors related to the patient and surgeon. We believe that topical testosterone therapy can be used safely to improve the outcomes of hypospadias repair. Postoperative complications were noticeably improved after applying topical testosterone with negligible side effects. Concerning the time of surgery, there was no significant difference.

REFERENCE

1. Blaschko SD, Cunha GR, Baskin LS. Molecular mechanisms of external genitalia development. Differentiation. 2012;84:261–268.
2. Baskin LS. Hypospadias and urethral development. J Urol. 2000;163:951–956.
3. Silver RI. Endocrine abnormalities in boys with hypospadias. Adv Exp Med Biol. 2004;545:45–72.
4. Bouty A, Ayers KL, Pask A, Heloury Y, Sinclair AH. The genetic and environmental factors underlying hypospadias. Sex Dev. 2015;9:239–259.
5. Kojima Y, Kohri K, Hayashi Y. Genetic pathway of external genitalia formation and molecular etiology of hypospadias. J Pediatr Urol. 2010;6:346–354.
6. Hypospadias. Shukla AR, Patel RP, Canning DA. Urol Clin North Am. 2004;31:445–460.
7. Timing of elective surgery on the genitalia of male children with particular reference to the risks, benefits, and psychological effects of surgery and anesthesia. American Academy of Pediatrics Section on Urology. http://peds.arizona.edu/sites/default/files/curriculum-files/aap-timingofelectivesurgeryongenitalia_002.pdf. Pediatrics. 1996;97:590–594. [PubMed] [Google Scholar]
8. Monfort G, Lucas C. Dehydrotestosterone penile stimulation in hypospadias surgery. European urology. 1982;8:201-3.
9. Kulkarni SS, Kulkarni SS, Vastrad PP, Kulkarni BB, Markande AR, Kadakol GS, Hiremath SV, Kaliwal S, Patil BR, Gai PB. Prevalence and distribution of high risk human papillomavirus (HPV) types 16 and 18 in carcinoma of cervix, saliva of patients with oral squamous cell carcinoma and in the general population in Karnataka, India. Asian Pac J Cancer Prev. 2011 Jan 1;12(3):645-8.
10. Ahmad R, Chana RS, Ali SM, Khan S. Role of parenteral testosterone in hypospadias: A study from a teaching hospital in India. Urology annals. 2011 Sep;3(3):138-140.
11. Chalapathi G, Rao KL, Chowdhary SK, Narasimhan KL, Samujh R, Mahajan JK. Testosterone therapy in microphallic hypospadias: topical or parenteral?. Journal of pediatric surgery. 2003 Feb 1;38(2):221-3.
12. Nerli RB, Koura A, Prabha V, Reddy M. Comparison of topical versus parenteral testosterone in children with microphallic hypospadias. Pediatric surgery international. 2009 Jan 1;25(1):57-9.
13. Asgari SA, Safarinejad MR, Poorreza F, Asl AS, Ghanaie MM, Shahab E. The effect of parenteral testosterone administration prior to hypospadias surgery: A prospective, randomized and controlled study. Journal of pediatric urology. 2015 Jun 1;11(3):143-e1.