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Research Article

Effect of Preoperative Hormonal Therapy on Hypospadias Repair

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Keywords

- Preoperative hormones; Hypospadias repair; Hypospadias complications

Abstract

Background: Hypospadias repair is frequently associated with numerous complications including bleeding and hematoma, edema, wound infection, wound dehiscence, skin and flap necrosis, meatal stenosis, urethral strictures, urethral diverticula, urethrocutaneous fistulization and scar formation.

Hormone therapy preceding surgical correction is indicated to obtain better intra-operative conditions. The logic behind the use of preoperative androgen is that it will lead to an increased vascularization of the prepuce, which will allow for a decrease fibrous tissue formation and inflammation. In addition to this, the increase blood flow postoperatively can potentially decrease complications and improve cicatrization through improved cutaneous nutrition and oxygenation.

Aim of the work: To find out the effect of Human Chorionic Gonadotrophin and androgen if given pre-operatively on the outcome of hypospadias surgery.

Patient and methods: Thirty male patients with different types of hypospadias were enrolled in this study, as **Group A** receiving preoperative hormonal therapy and other 30 patients with the same inclusion criteria included as control group B to be operated upon without receiving preoperative hormones. Patients in group A have received local dihydrotestosterone cream for 3 months.

Results: There were statistical significance differences between the two groups regarding the length, **Group A** (4.5 ± 0.33), **Group B** (3.17 ± 0.33) and in glandular width before and after hormonal therapy in **Group A** (1.7 ± 0.37), and **Group B** (1.5 ± 0.4). The mean duration of operation in **Group A** was 93.27 minutes. While in **Group B** it was 86.27 minutes. Postoperative complications were more in **Group B** with significant difference in meatal stenosis which was more in **Group B**.

Conclusion: Hormonal therapy before hypospadias operation is used by many pediatric surgeons and proved to achieve many beneficial results before the repair of hypospadias. These results include larger phallic size, more vascularity, better healing and less complications. Nevertheless, larger studies need to be done with more patients to develop more accurate treatment guidelines.

INTRODUCTION

Hypospadias repair is frequently associated with many complications including bleeding, edema, wound infection, wound dehiscence, flap necrosis, meatal stenosis, urethral strictures, urethral diverticula and urethra-cutaneous fistulae [1].

To improve the surgical outcome, preoperative hormone therapy with human chorionic gonadotropin (HCG), dihydrotestosterone (DHT) or testosterone (T) were used [2].

Hormonal therapy before surgical correction is used to obtain best operative circumstances. The aim of using preoperative androgen is that it would increase vascularization of the prepuce, hence decreasing fibrous tissue formation. In addition, the increased blood flow postoperatively could decrease complications and decrease fibrosis through improving cutaneous nutrition and oxygenation. Testosterone was successfully used to increase the width of the glans by a mean of 4.5 mm in proximal hypospadias patients with small glans, thus improving operative field and decreasing the incidence of complications associated with small glans size [3].

Koff, Jayanthi in 1999 stated that HCG (human chorionic gonadotrophins) and local androgens preoperatively increase penile size, which advances the meatus distally to decrease the severity of hypospadias and chordee [1].

The idea of using preoperative hormonal therapy has been based on using the following hormones in treatment of micropenis

- Testosterone Treatment (intramuscular injection or topical application)
- Topical 5-Dihydrotestosterone (DHT) Gel
- H.C.G injections
- LH-FSH Applications [4]

HCG stimulates Endogenous testosterone secretion which causes penile enlargement as well as increased testicular volume.

HCG also has a stimulatory effect on testicular steroidogenesis [5].

PATIENTS AND METHOD

This study was conducted at both pediatric surgery department at zagazig university hospitals and pediatric surgery unit at Al-Ahrar Educational hospital. During the period from January 2015 to January 2016.

The study include 60 male patients with different types of hypospadias ; they were randomized into two equal groups. Group 1 (30 patients) received local dihydrotestosterone cream for 3 months, and group 2 (30 patients) did not receive any intervention before surgery

Ages of patients ranged from 6 months to 2 years with a mean age of (12.5) months for all patients.

Inclusion criteria

All patients included in this study have mid to distal penile hypospadias with no or minimal chordee needs no division of the urethral plate.

Exclusion criteria

- Patients with severe proximal and penoscrotal hypospadias.
- Previously circumcised patients.
- Patients with chordee whose repair requires interruption of the urethral plate.
- Patients undergoing redo hypospedias repair
- The study with its benefits and complications were explained to the parents and consents were taken.

All patients were subjected to the following

History taking, physical examination and full clinical examination including measuring penile size, site of external meatus and presence of chordee. Then, certain data is collected in weekly follow up e.g.

- The penile length, glans width was measured in millimeters in all patients using calipers
- The site of external urethral meatus and the distance between it and the base and the tip of the organ.
- Appearance of any complication of hormonal therapy like supra pubic hair and mood changes like aggressive behavior.
- Tubularized incised plate urethroplasty (T.I.P) was done for all patients.
- Amount of bleeding during the operation and whether it impedes the dissection.
- Whether the enlargement of the penile size has provided plenty of tissues for flaps, making the operation easier or not.
- Hemostasis: easy or difficult.
- Presence of complications and their severity.

TIP repair was performed under general anesthesia and caudal analgesia using 2.5_ magnification by the same surgeon. The surgical technique was uniform in all cases. After full degloving and correction of any minor chordee, a midline urethral plate incision was made and urethroplasty was performed over a 6F silastic catheter, tabularization of the urethral plate with 6-0 subcuticular continuous vicrele sutures. A second layer from the Inner prepuce was used as a waterproofing layer. Glans wings were adequately mobilized and glansplasty was done with 6/0 vicrele sutures. The Excess dorsal foreskin was excised after leaving adequate skin to cover the ventral skin deficiency. Compression dressing with antibiotic impregnated gauze was applied in all cases. Intravenous antibiotics were given for three doses, followed by prophylactic oral antibiotics. Intra-operative bleeding was calculated by weighing the gauzes before and just after soaking, using a sensitive scale, and subtracting the two weights.

Patients were discharged after 48 h with dressings and a catheter; Parents were given full instructions on catheter care to prevent blockage or dislodgement of catheter. Dressings and the catheter were removed on the 5th day. Follow-up was performed after one week and monthly for 6 months, and yearly.

Complications such as urethrocutaneous fistula, glans dehiscence, meatal stenosis, and requirement for reoperations were recorded in both groups. Urethrocutaneous fistula was defined as the presence of an additional ventral opening through which the patient voided in a stream or drops. Glans dehiscence was defined as separation of the glans, with or without a glans bridge or glans fistula. Meatal stenosis was diagnosed when the patient presented with straining or a thin stream and the meatus could not be calibrated beyond 6F with urethral dilators. Uroflowmetry was not performed postoperatively as all patients were infants or toddlers in diapers.

Statistical analysis was performed with the Student t test, Fisher exact test, and one-way ANOVA using SPSS version 21. All tests were two-sided and $p < 0.05$ was considered statistically significant.

RESULTS

In Table (1) shows that there was no statistical significance differences between the two groups in Type. Table (2) shows that there were statistical significance differences between the two groups in length and glandular width before and after hormonal therapy.

Operative difficulty was assessed by

- The need for blood transfusion due to massive bleeding during the procedure.
- the duration of the operation in all patients and also,

Blood transfusion was not needed for any patients in this study. Duration of operation in **group A** which received preoperative hormonal therapy ranged from 65 minutes to 122 minutes with mean 93.27 minutes. While in **group B** it ranged from 64 minutes to 116 minutes with mean 86.27 minutes Table (3) shows that there were no statistical significance differences between the two groups in duration of operation. Duration of operation among the two studied groups (Figure 1).

Table 1: Analysis of Types of hypospadias in the two groups.

Variable	Group A (n=30)		Group B (n=30)		χ^2	P
	No	%	No	%		
Type:						
Coronal	12	40	12	40		
Distal penile	6	20	12	40	2.8	0.42
Glandular	8	26.7	2	6.7		NS
Mid penile	4	13.3	4	13.3		

Table 2: analysis of penile length and glanular width before & after using hormones:

Variable	Group A (n=30)	Group B (n=30)	P
Length			
Mean ± SD	4.5 ± 0.33	3.17 ± 0.33	0.04
Range	3.2 – 4.5	3.4 – 5.5	<0.001
Glans width			
Mean ± SD	1.7 ± 0.37	1.5±0.4	<0.001
Range	1.5±0.3	1.2 – 2.6	

Table 3: Analysis of operation length.

Variable	Group A (n=30)	Group B (n=30)	T	P
Duration: (min.)				
Mean ± SD	93.27 ± 17.47	86.27 ± 14.93	0.05	0.96
Range	65 - 122	64 - 116		NS
This table shows that there were no statistical significance differences between the two groups in duration of operation.				

Preoperative complications: Three complications were measured after the completion of the hormonal course in "**group B"** only. Which was anaphylaxis, appearance of suprapubic hair and skin pigmentation.

Postoperative complications

Measured after the operation in **"both groups**" and included infection, stenosis, fistula and dehiscence (Table 4,5).

Postoperative complications

Among the two studied groups (Figure 2). An example photo for difference in size of the penis before and after hormonal therapy and the method of measurement and a postoperative photo (Figure 3).

DISCUSSION

Hormonal therapy before surgical correction of hypospadias is indicated to improve surgical conditions. HCG and topical androgens as a preoperative hormonal therapy produces penile enlargement which facilitates surgical procedure and appears to improve surgical results due to increased vascularity. The definite indication for preoperative hormonal therapy is a small-appearing penis or glans. Some advice its use before repeat surgery to increase availability and vascularity of penile tissues.

The 1st pre-repeat hypospadias hormonal therapy was in Mayo clinic, with topical testosterone 5% application on small penis, with successful results [6].

The dose used in this study was local dihydrotestosterone cream daily for 3 months. These doses were given regardless the

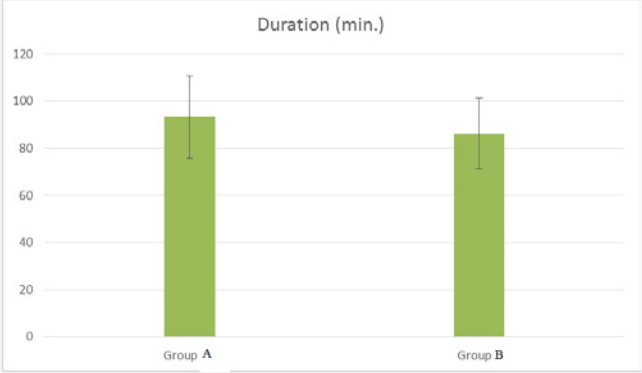

Figure 1 Duration of operation among the two studied groups.

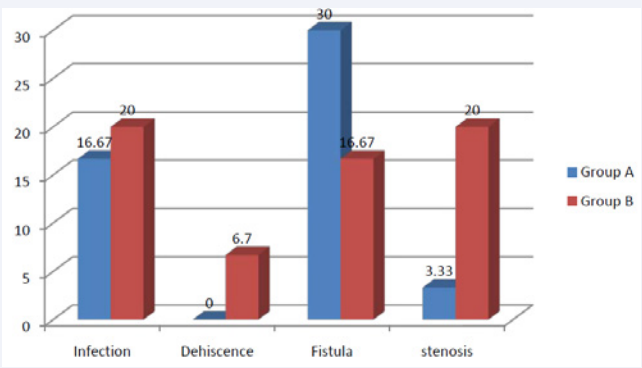

Figure 2 Postoperative Complications among the two studied groups.

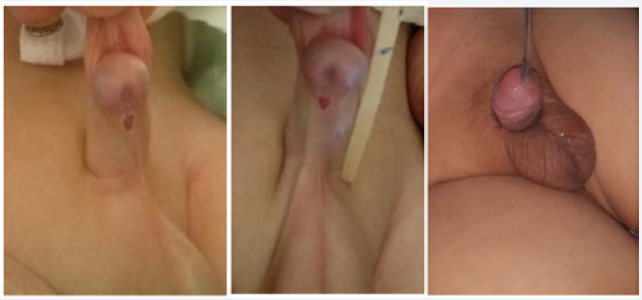

Figure 3 An example photo for difference in size of the penis before and after hormonal therapy and the method of measurement and a postoperative photo.

Table 4: Complications after hormonal therapy in group A.

Type	Number	%
Anaphylaxis	0	0
Supra-pubic hair	15	50%
Skin pigmentation:	7	23.3%

mean increase in penile circumference and length by 50% of pretreatment measurements, without any permanent side effects.

Wong and Braga [10] studied the influence of pre-operative hormonal stimulation on hypospadias repair and made a meta-analysis and a systemic review in which they concluded that androgen stimulation prior to hypospadias repair has demonstrated a substantial increase in penile length, glans circumference, and tissue vascularity. However, it might be related to higher complication rates, and treatment regimens are not standardized.

This increased rate of complication after surgery wasn't noted in our studied group of patients. On the contrary, improvement in healing was noticed with lower rate of complications.

A complication rate of 7.1% was reported in the study done by *Vikram Satav, Vilas P. Sabale et al.* [11], which is significantly lesser when compared to available reported literature which confirms our results of lesser complication rate when the hormones are used prior to surgery than the complication rate in group B.

Table 5: Results of postoperative Complications in both groups.

P value	χ^2	Group B (N=30)		Group A (N=30)		Variable
		%	No	%	No	
0.73 NS	0.111	80.0 20.0	24 6	83.33 16.67	25 5	**Infection** No yes
0.55 NS	0.35	93.33 6.7	28 2	100.0 0.0	30 0	**Dehiscence** No yes
0.44 NS	0.57	83.33 16.67	25 5	90.0 30.0	27 3	**Fistula** No yes
0.04* S	4.04	80.0 20.0	24 6	96.67 3.33	29 1	**Meatal stenosis** No yes

size of phallus or the glans.

Chalapathi et al., 2003 used topical testosterone twice daily for 3 weeks versus intramuscular testosterone 2mg/Kg once weekly for three weeks [7].

An impressive increase in penile length and glans circumference was noticed in almost all patients subjected to the hormonal therapy in both groups of our study. *R.B Nerli and Ashish Koura* [8], also noticed this impressive increase in length in their study performed on 21 patients with hypospadias. In their study two of the 21 patients did not respond adequately to the therapy which did not occur in our study and all patients responded well.

Both studies also concluded the same results about fine pubic hair that appeared when using hormonal therapy and this effect proved to be reversible and this hair disappears after the stopping hormones.

Monfort and Lucas **[9]** employed a 4-week period of local penile stimulation with daily application of dihydrotestosterone (DHT) cream before hypospadias repair. They reported a

Cevdet Kaya et al. [12], suggested that pretreatment with DHT transdermal gel is beneficial in decreasing complication and reoperation rates after hypospadias repair. In their study the rates of meatal stenosis and fistula were higher in the first year of follow up in children not receiving DHT. The number of patients with glandular dehiscence and, consequently, the reoperation rates were also significantly higher without the use of the hormone.

Scar formation after hypospadias repair which is an important parameter for cosmetic assessment, was found to be significantly lower in children receiving DHT treatment.

CONCLUSION

Hormonal therapy proved to be beneficial before operating on the phallus as it increases penile length size which facilitates the steps of the operation. It also increases the blood supply of the penis which promotes healing and decreases complications.

A well-established treatment guidelines for hormonal stimulation before hypospadias repair must be developed, and

continuous investigations and studies including the standardized dosing protocols of the hormones tested on a large number of patients with a control group should be used.

Intra-operative bleeding was calculated by weighing the gauzes before and just after soaking, using a sensitive scale, and subtracting the two weights. Every 10 min, the used gauze was discarded and weighed to minimize the effect of water vaporization on the gauze weight.

Intraoperative blood loss was determined by weighing all surgical gauzes used during the procedure with a digital scale.

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