

Our Experience of Using Preoperative Testosterone Therapy in Hypospadias Patients

Ashlesha Shimpi¹, Pranav Jadhav², Sanjay Raut³, Adarsh Hegde⁴,
Dhananjay Vaze⁵, Aniruddha Bhagwat⁶

Author's Affiliation: ¹Senior Resident, ²Professor and HOD, ^{3,6}Associate Professor, ^{4,5}Assistant Professor Department of Paediatric Surgery, Dr. D Y Patil Medical College, Hospital and Research Centre, Pimpri, Pune 411018, India.

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Abstract

Context: Surgical correction of uncomplicated hypospadias involves bringing the meatus closer to ventral tip and correction of any presence of chordee. These genital repairs are performed when patients are young. Increasing the length of penis may have an additional advantage in these repairs.

Aims: Study objectives were to explore the functional and cosmetic outcomes of use of parenteral testosterone and its effect on reducing postoperative complications.

Settings and Design: A randomized prospective study was conducted amongst patients who were diagnosed with hypospadias between January 2019 and January 2020 in department of Pediatric Surgery at a large institution in India.

Methods and Material: Random groups included surgery with and without intramuscular injection of testosterone, respectively. Patients were evaluated pre testosterone therapy for: 1) stretched penile length (SPL), 2) glans circumference at the base. And postoperatively for: 1) reoperation rate, 2) complications. The surgical outcome was compared among the two groups on the basis of cosmesis and postoperative complication rate.

Results: A total of 42 patients (21 in each group) matched the eligibility criteria and were recruited in the study. Overall 85% of Group 2 patients showed an increased SPL of approximately 1.15cm. As compared to Group 1, Group 2 performed well in

terms of reduced complications, increased SPL and glans circumference at base.

Conclusions: Overall, study findings showed better functional outcomes with use of preoperative testosterone treatment and reduced complications. A follow-up study is planned to explore the long-term surgical outcomes of these surgical repairs of preoperative testosterone therapy.

Keywords: Hypospadias; Testosterone; Treatment; Genital Organs; Male.

Key Messages: The manuscript presents with cases of hypospadias and the effectiveness of use of preoperative testosterone in terms of functional and cosmetic benefits.

Introduction

Treating Hypospadias is a surgical challenge. Although it is one of the most common genital abnormality, yet the etiology remains largely unknown.¹ However studies have shown that there is a likelihood of developing defects at any point along the pathway of androgen production, leading to occurrence of hypospadias.² In current practice, the genetic repair involves surgical management to achieve a straight penis, a conical reconfigured glans and an acceptable cosmetic outcome.³ Surgeries are performed in patients between the age of 6–12 years to avoid any risks associated with psychological stress.³ Numerous procedures have been carried out to correct both distal and proximal hypospadias.^{4–6} Evidence based practice shows that tubularised incised plate (TIP) urethroplasty, the onlay procedure, and the meatal advancement and

Corresponding Author: Ashlesha Shimpi, senior resident Department of Paediatric Surgery, Dr. DY Patil Medical College, Hospital and Research Centre, Pimpri, Pune 411018, India..

E-mail: : ashlesha12@gmail.com

glanuloplasty procedure (MAGPI) procedures are commonly performed for surgical management of hypospadias.⁵⁻⁸

A 2019 report estimates the global prevalence of Hypospadias for years between 1980–2010 as 20.9 (95% CI: 19.22–22.6) per 10,000 births.⁹ The majority of children with hypospadias present with small phallus.¹⁰ Studies have been conducted since 1971 to address this deficiency using testosterone in patients with hypospadias and have remained as a treatment of choice since then due to its action of peripherally acting androgen and pronounced effect on the genitalia. This is the basis of using androgen stimulation preoperatively in cases of hypospadias.

In the present study, our objective was to analyse the effect of parenteral testosterone in paediatric patients presenting with hypospadias in the paediatric surgery department at Dr. D. Y. Patil Hospital, Pune, India. It has been postulated that the use of testosterone preoperatively may increase the size and girth of the penis thus allowing for a larger area for surgical interventions and less postoperative complications.

Material and Methods

A randomized prospective study was conducted amongst patients who were diagnosed with hypospadias between January 2019 and January 2020 in department of Paediatric Surgery at D. Y. Patil Medical College, Hospital and Research Centre, Pune, India. Inclusion criteria included patients with distal and mid penile hypospadias without chordee. Severe degree of hypospadias i.e. penoscrotal, scrotal and perineal hypospadias and patients undergoing redo hypospadias repair were excluded. A written consent including information on risks and benefits were taken from the Parents/guardians. The patients were randomly assigned into two groups. Group 1 also the observational arm underwent surgery with no intramuscular (IM) injection of testosterone, while Group 2 also the interventional arm underwent surgery and were administered three doses of IM testosterone 2 mg/kg at an interval of 4 weeks. The surgical repairs were performed by the same surgeon. The patients were followed up for 3 months to check for their surgical and cosmetic outcomes and if there were any complications associated with the surgical repair. For example: urethrocuteaneous fistula, glans dehiscence, and meatal stenosis. Stretched Penile length (SPL) was measured from penile length from pubic bone to the tip of the glans

in centimetres and glans circumference at the base of the glans were measured using Vernier's calliper before and after the therapy.

The surgical outcome was compared among the two groups on the basis of cosmesis and post operative complication rate. All the patients were evaluated pre therapy and post testosterone therapy for: 1) SPL, 2) glans circumference at the base. And postoperatively were evaluated for 1) reoperation rate, 2) complications. The study was approved by the Institutional ethical committee.

Results

A total of 42 patients with hypospadias were recruited with 21 patients in each group. The mean age of presentation was 5.3 years (range, 6 months to 10 years). Of the 42 patients, familial incidence of hypospadias was seen in two patients. Out of these, one patient's father and second patient's brother suffered from hypospadias. Unilateral undescended testis was found in one patient and two patients had inguinal hernia.

The study participants in interventional arm (Group 2) showed the following characteristics: 14 cases of proximal and 7 mid penile hypospadias received injection Testoviron deep intramuscularly at the dose of 2mg/kg body weight at an interval of 4 weeks.

1. *Penile length:* The mean penile length of 3.4 cm increased to 4.55 cm for the patients receiving preoperative injections of testosterone. The mean increase in penile length was 1.15 cm ($P < 0.001$). In group 2, 14.2% patients did not respond to testosterone, whereas 85.8% showed significant increase in penile length.
2. *Glans circumference:* In group 2, 19.04% did not respond to testosterone where as 80.96% showed significant increase in glanular circumference at the base of glans. The mean increase in glanular circumference was 0.21cm in group 2.
3. *Complications:* Total complications were significantly less in group 2 (19%) than in group 1 (28.5%).
4. *Reoperation rate:* The reoperation rate was less in group 2 patients (14.3%) compared to group 1 patients (19%).

There was no significant change in the penile length and the glanular circumference in group 1. There was no untoward bleeding noted during surgery in any of the children. Out of 21 patients,

Table 1: Outcomes in Group 1 (control group).

Sr.No	Age (mths)	Type	SPL	SPL	Glans circumference	Glans circumference	Complications
			At presentation	At 12 wks	At presentation	At 12 wks	
1	30	Distal	3.42	3.52	3.32	3.32	None
2	37	Mid	3.62	3.78	3.35	3.37	None
3	14	Distal	2.92	3.01	2.74	2.75	None
4	17	Mid	2.98	3.12	2.76	2.79	Fistula
5	51	Distal	4.02	4.3	3.71	3.71	None
6	32	Distal	2.78	3.01	2.62	2.63	None
7	42	Mid	3.54	3.78	3.42	3.45	Meatal stenosis
8	16	Distal	2.82	2.94	2.74	2.79	None
9	22	Distal	3.36	3.56	2.93	2.94	None
10	84	Mid	4.22	4.42	4.01	4.08	Sub coronal fistula
11	13	Distal	3.11	3.39	2.83	2.85	None
12	78	Mid	3.98	4.19	3.76	3.79	None
13	34	Distal	3.45	3.78	3.22	3.28	Fistula
14	57	Mid	4.12	4.35	3.98	4.01	None
15	9	Mid	3.26	3.52	2.89	2.92	Fistula
16	109	Distal	4.66	4.99	4.41	4.41	None
17	14	Mid	2.91	3.12	2.71	2.71	None
18	33	Distal	3.77	3.99	3.55	3.58	None
19	8	Distal	2.61	2.98	2.44	2.49	None
20	11	Mid	2.99	3.26	2.71	2.76	None
21	28	Distal	3.26	3.49	2.91	2.98	Glans dehiscence
Mean			3.42	3.64	3.19	3.21	

Table 2: Outcomes in Group 2 (treated with Inj testosterone).

Sr.No	Age (mths)	Type	SPL	SPL	Glans circumference	Glans circumference	Complications
			Pre therapy (at first visit)	Post therapy (at 12 wks)	Pre therapy	Post therapy	
1	24	Distal	3.22	4.32	3.02	3.30	None
2	48	Mid	3.82	5.12	3.42	3.62	None
3	12	Distal	2.92	4.04	2.74	2.96	None
4	11	Distal	2.84	4.24	2.66	2.75	Meatal stenosis
5	41	Distal	3.73	4.13	3.51	3.80	None
6	50	Distal	3.68	4.88	3.22	3.45	None
7	40	Mid	3.54	4.66	3.42	3.69	None
8	24	Distal	2.92	4.24	2.82	3.04	None
9	15	Distal	3.16	4.16	2.93	3.19	None
10	74	Mid	4.18	4.8	3.82	4.00	Sub coronal fistula
11	9	Distal	3.02	4.32	2.72	3.00	None
12	72	Mid	3.91	5.31	3.63	3.74	None
13	24	Distal	3.25	4.67	3.14	3.35	None
14	48	Distal	3.94	5.16	3.88	4.02	None
15	7	Mid	3.26	4.42	2.89	3.04	Fistula
16	120	Distal	4.87	5.37	4.61	4.85	None
17	17	Mid	2.98	4.32	2.64	2.89	None
18	26	Distal	3.55	4.88	3.10	3.36	None
19	8	Distal	2.61	3.91	2.44	2.69	None
20	6	Mid	2.86	4.18	2.60	2.85	None
21	25	Distal	3.26	4.36	2.91	3.02	Glans dehiscence
Mean			3.40	4.55	3.15	3.36	

17 patient's parents indicated that they were satisfied with cosmetic outcomes of glans/meatus. Table 1 shows the observations for Group 1 study participants and Table 2 for Group 2.

Discussion

Overall, the study results showed that patients who received parenteral testosterone therapy had a mean increase in SPL of 1.15cm and an increase of 0.21 cm in glanular circumference. An increase in local vascularity was also seen in Group 2 patients with no adverse effects. The control group without receiving pre-operative treatment showed that there was no significant increase in penile length or glanular circumference. These patients also presented with higher complication rate and re-operation rate. Cosmetic results post-operatively were almost similar to the patients in group 2.

We identified that the first dose of testosterone was the most effective one. Androgen side-effects were not uncommon however were mainly mild. Although the study was done on small number of children, study findings show that the testosterone therapy had acceptable surgical and cosmetic outcomes. Functional outcomes are considered favourable if pre-operative parenteral testosterone is administered before surgeries as it provides temporary penile stimulation allowing a larger area to operate.

A similar study done by Ahmad et al showed similar results of increase in penile length by 1.35+/- 0.40cm.¹⁰ The study showed a decrease in the total number of complications in the patients treated with testosterone, consistent with our present study. The authors observed that there was unpredictable absorption of local testosterone hence intramuscular is preferred treatment, although the study population was on a smaller number.

The study would like to acknowledge some limitations. The study did not evaluate the patients for endocrinopathies. The study did not involve any chromosomal analysis for the patients who were recruited in the study.

Conclusion

Study findings show that better surgical outcomes are obtained in the case of hormonal treatment prior to hypospadias surgery, favouring better local skin conditions, increasing penile length and glans circumference resulting in reduced surgical complications. We conclude that parenteral

testosterone can be safely used to improve the results of reconstructive surgery on hypospadias.

A well established treatment guideline for hormonal stimulation before hypospadias repair must be developed and studies including the standardised dosing protocol of the hormones tested on a large number of patients with a control group should be used.

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