

Effect of Preoperative Hormonal Therapy in Hypospadias Surgery: Evaluation of the current practice at the Pediatric surgery Clinic, Clinical Center University of Sarajevo

Asmir Jonuzi^{1*}, Zlatan Zvizdic¹, Nusret Popovic¹, Emir Milisic¹, Edin Begic², Benjamin Kulovac³

¹Clinic of Pediatric Surgery, Clinical Centre University of Sarajevo, 71000 Sarajevo, Bosnia and Herzegovina

²Department of Pharmacology, School of Medicine, Sarajevo School of Science and Technology; 71000 Sarajevo, Bosnia and Herzegovina

³ Clinic of Urology, Clinical Centre University of Sarajevo, 71000 Sarajevo, Bosnia and Herzegovina

*Address for Corresponder: Dr. Asmir Jonuzi, Clinic of Pediatric Surgery, Clinical Centre University of Sarajevo, Patriotskelige 81, 71000 Sarajevo, Bosnia and Herzegovina (e-mail: jonuziasmir@hotmail.com)

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Abstract

Introduction: The most common congenital abnormality of the penis is hypospadias. Although the main treatment is surgical; hormone therapy with dihydrotestosterone is also used.

Materials and Methods: This randomized clinical trial was carried out between January 2012 and December 2017 on 79 children with hypospadias (in the Clinic of Pediatric Surgery, Clinical Centre University of Sarajevo). Their mean age was 38.2 ± 2.8 months. Group I included 36 children whom were treated with 2.5% dihydrotestosterone gel which was applied twice a day to the penile shaft and glans for one month prior to surgery. Group II included 43 children whom did not receive any treatment preoperatively.

Results: Mean age of patients in group I was 37.3 ± 6.3 months and in group II it was 39.1 ± 5.9 months which were comparable. Complications occurring postoperatively were: urethrocutaneous fistula in 6 patients (13.9%) in group II, versus 1 patient (2.7%) in group I. There were 2 patients with meatal stenosis in group II (4.7%), and 3 (8.3%) in group I. Finally, there was a significant difference ($p < 0.05$) between the overall reoperation rates between groups ($p < 0.05$).

Conclusion: Pretreatment with 2.5% dihydrotestosterone transdermal gel before hypospadias repair is beneficial in decreasing complication rates.

Keywords

- Hypospadias
- Dihydrotestosterone
- child

Introduction

Hypospadias the most common congenital abnormality of the penis has an incidence of 1 in 250 male newborns.¹ Hypospadias surgery is carried out in order to position the opening of urethra at the correct anatomic position on the tip of the glans. Surgical procedures are challenging and have well known complications such as: glans dehiscence, urethrocutaneous fistula, meatal stenosis and unacceptable cosmetic results. Some believe that hormonal stimulation prior to surgery may result in better functional and cosmetic outcomes.¹ This approach which was first described in 1971 is a matter of debate. Hormonal stimulation (using: testosterone, Dihydrotestosterone (DHT) or human chorionic gonadotropin)² before surgery is used in cases with proximal hypospadias or small penile or glanular size.³ It can enhance vascularization of the prepuce and also increases penile size and glanular diameter.^{4,5,6} It is useful to the surgical technique since scarcity of glanular and penile tissue may compromise ventral closure of the neourethra. Testosterone is useful whether it is applied locally or systemic.⁷ It seems that externally administered DHT is more effective than testosterone (because it does not require 5 alpha-reductase).⁸

Materials and Methods

During 6 years (January 2012 to December 2017) 79 cases of primary hypospadias with a mean age of 38.2 ± 2.8 months that underwent the TIP (tubularized incised plate urethroplasty) procedure at the Clinic for Pediatric Surgery of the Clinical Center University of Sarajevo were studied. Informed consents were obtained from parents and the children were randomized into 2 groups. Group 1 which consisted of 36 cases received topical DHT 2.5% transdermal gel twice a day directly onto the penile shaft and glans for a month preoperatively (it was discontinued 2 weeks before the operation) and group 2 which consisted of 43 cases did not receive any kind of hormonal therapy. Exclusion criteria were: any endocrinological or clinical evidence of hypopituitarism and having a history of hypospadias surgery.

All cases underwent the TIP urethroplasty procedure with or without chordee correction.

Results

Mean age of patients in the 2 groups were similar (group 1: 37.3 ± 6.3 months and group 2: 39.1 ± 5.9). Patient characteristics for the 2 groups are shown in **Table 1**.

Table 1: Patients characteristics

	Group 1	Group 2
Coronal	11 (30.5%)	20 (46.5%)
Penile	25 (69.5%)	23 (53.5%)
Chordae corrections	28 (77.7%)	30 (69.7%)
Orchidopexy	1(2.7%)	1(2.7%)
Herniectomy	1(2.7%)	2(5.4%)
Total	36 (100%)	43 (100%)

At 1-year follow-up urethrocutaneous fistula was found in 1 patient (2.7%) in group 1 and 6 patients (13.9%) in group 2 had. **Figure 1** Also glanular dehiscence was only found in 2 patients (4.7%) in group. ² In group 1 three patients (8.3%) had meatal stenosis, compared to 2 patients (4.7%) in group. ² In group 1 and 2 one patient had a urethral stricture and scar formation. Analysis of the overall complications revealed that fistula, glanular dehiscence and meatal stenosis were found in 8.9%, 2.5% and 6.3% of the patients, respectively. A significant difference was found between the

reoperation rates in the 2 groups ($p < 0.05$). Eight patients in group 2 needed reoperation due to fistula and/or dehiscence, compared to only 1 patient in group. ¹ We had no serious hormone therapy related complications in our patients. Only 2 parents (5.5%) reported penile skin symptoms such as itching and redness at the first couple of weeks of treatment which disappeared after 2 weeks of ongoing therapy. Parents also reported penile skin hyperpigmentation during treatment which was back to normal after topical treatment finished.

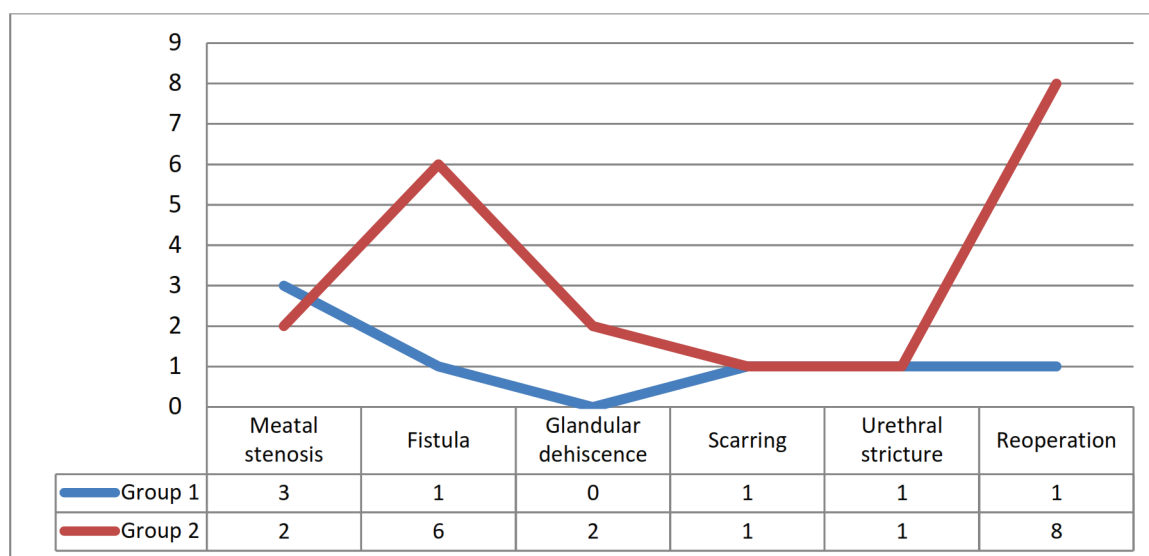


Figure 1: Comparison of complications between groups 1 and 2

Discussion

Surgical treatment of hypospadias is done in order to enhance the aesthetic and functional aspects of the penis. Hormone therapy before surgery aims to achieve superior surgical results. Testosterone has the ability to increase penile size in pre-pubertal boys. This fact helps the surgical repair of hypospadias, since having more tissue to work

with and a more robust vascular structure improves healing and makes correction easier and lowers the risk of failure.⁴ In a prospective RCT by Bastos, et al. they showed an absolute increase in the number of blood vessels and vascular volume density after using a 1% testosterone ointment.⁶ Another study by Monfort, et al. in 1982 using 5% dihydrotestosterone (DHT) cream also proved its

capability in stimulating growth of penile length and circumference.² A study by Kaya, et al. showed that using DHT topical cream preoperatively reduced complication rates of TIP surgery in hypospadias patients.⁴ There are not many prospective clinical trials that have assessed complication rates related to preoperative hormonal therapy in hypospadias patients. Recently an RCT by Asgari, et al. showed that preoperative testosterone administration is beneficial in reducing complications.⁹ Post operative complications of hypospadias repair such as urethrocutaneous fistula, stricture and scar formation are not rare, even in cases when an expert surgeon carries out careful preoperative evaluation and performs precise surgical techniques and post operative care.¹⁰ Thus, any method by which the natural tissue of this anatomic region is increased can be useful in reducing the complications of repair especially in severe cases of hypospadias; for example in cases of micropenis, IV testosterone can facilitate glanuloplasty by enlarging the glans.¹¹ In our study we found that patients with glanular dehiscence which needed reoperation were significantly higher in group 2 compared to group 1. The number of fistula formation was higher in the first year of follow-up in children not receiving DHT; although this difference was not statistically meaningful. In all, our results are consistent with other studies in the literature. There is no consensus regarding the exact indication of preoperative hormonal therapy but in a study by Snodgrass et al. they reported that 63% of patients received testosterone stimulation preoperatively without undergoing any endocrine testing, when patients had glans width <14 mm, which is less than the average normal newborn glans diameter.¹²

Indications have been considered for administering hormones such as ventral curvature, a small-appearing penis and/or glans and also before reoperation in order to increase the availability and vascularity of penile skin. Side effects of treatment with androgens include: aggressive behavior, pubic hair growth and adult full height compromise which will all regress after treatment has stopped.^{13,14} but we did not receive any compliments regarding these side effects in our study. Histological studies have shown that androgens increased the number and density of blood vessels, supporting a theory of formation of new blood vessels.¹⁵ Although many years of research have been dedicated to surgical treatment of proximal hypospadias it is still one of the most challenging conditions in pediatric urology and result in many unwanted postoperative complications. We recorded complication rates such as fistulas, urethral strictures, diverticula, meatal stenosis, glanular dehiscence and scar formation up to one year after surgery and found that pre-treatment with DHT can be considered to be effective in reducing complications and improving the cosmetic outcomes of hypospadias repair. In a randomized, controlled study of DHT gel administration before hypospadias surgery, complication rates were lower in the DHT treatment group (2.7%) compared to the control group (18.6%), thus the need for reoperation was lower in the DHT treatment group and better cosmetic outcomes were obtained due to lower rates of scar formation. Considering the results of studies evaluating the use of preoperative testosterone therapy in male patients with hypospadias we can assume that preoperative testosterone therapy is effective in increasing penile length

and circumference which helps in reducing post operative complications and is consistent with the findings of our study.

Conclusion

Penile augmentation with DHT transdermal gel is beneficial in terms of increasing the size of the phallus and penile skin in hypospadias. We conclude that DHT transdermal gel can be safely used to improve the results of reconstructive surgery on hypospadias.

Ethics Approval:

Ethics committee approval was received for this study from the Ethics Committee of the Clinical

Center University of Sarajevo.

Informed Consent: Written informed parental consent was obtained from parents of the patients who participated in this study.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORCID ID:

Asmir Jonuzi  <https://orcid.org/0000-0002-5637-9510>

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