

Does Testosterone Advance the Meatus in Children with Proximal Hypospadias?

Chukwubuike Kevin Emeka*, Eze Balantine Ugochukwu and Anijunsi Livinus Patrick

Department of Surgery, Enugu State University Teaching Hospital, Enugu, Nigeria

ABSTRACT

Background: Pre-operative preparation of the children with hypospadias may involve the administration of testosterone to argument penile dimensions. However, the effect of testosterone on the urethral meatus is not established. The aim of this study was to prospectively evaluate the effect of testosterone on the location of the hypospadiac meatus.

Materials and Methods: This was a prospective observational study of children, aged 15 years and younger, who are being prepared for hypospadias repair at the pediatric surgery unit of a teaching hospital in Enugu, Nigeria. This study covered a 5-year period. The following data were analyzed: age of the patients at presentation, type of hypospadias, proximal and distal penile measurements at onset and at 4 weeks after testosterone injection.

Results: A total of 24 cases of proximal hypospadias were recruited into the study. The ages of the patients at presentation ranged from 1 month to 18 months with a median age of 3 months. Majority of the patients had mid-penile hypospadias. Regarding response to testosterone, proximal part of the penile shaft responded more than the distal part. However, statistical analysis showed no advancement in the location of the meatus.

Conclusion: This study has shown that a single dose of testosterone has no effect on the location of meatus in children with hypospadias.

*Corresponding author

Chukwubuike Kevin Emeka, Department of Surgery, Enugu State University Teaching Hospital, Enugu, Nigeria.

Received: February 01, 2023; **Accepted:** March 07, 2023; **Published:** April 20, 2023

Keywords: Children, Hypospadias, Single Dose, Testosterone, Meatus

Introduction

Hypospadias is a common congenital anomaly of the penis in which the urethral meatus opens on the undersurface of the penis and this is the most consistent symptom of hypospadias [1]. Hypospadias is one of the most common abnormalities of the urogenital system with an incidence of 1: 300 live births [2, 3]. Other components of hypospadias which may or may not be present include: ventral curvature of the penis, deficiency of the prepuce ventrally leaving a dorsal hood [4]. Testosterone administration to children with hypospadias results in increase in the length and circumference of the penis by up to 50 percent, without any significant side effects [5]. One study from Belgaum, India reported the significant increase in penile growth irrespective of the method of testosterone application (topical or parenteral) [6]. Pre-operative testosterone primarily increases the penile length, glans width/circumference and inner preputial area [7]. Testosterone also increases the diameter at the base of the penis [8]. Overall, testosterone makes the penis more vascular, increases the penile size and thus maximizes the chance of a better surgical outcome [9]. Although it is established that testosterone has effects on penile dimensions, controversy still exists on the effect of testosterone on the degree (type) of hypospadias. Khokar et al reported that

some patients with proximal and mid-penile hypospadias can be converted to either mid- or distal penile hypospadias by the differential response of different parts of the penis [9]. Surgical repair of hypospadias is a challenging surgical proposition and the location of the urethral meatus is an important consideration. The aim of this study was to prospectively evaluate the effect of testosterone on the location of the hypospadiac meatus.

Materials and Methods

This was a prospective observational study of children aged 15 years and younger who are being prepared for hypospadias repair at the pediatric surgery unit of Enugu State University Teaching Hospital (ESUTH) Enugu, Nigeria. This study covered a 3-year period, from January 2019 to December 2021. All consecutive children who presented with hypospadias during the study period were recruited. Only children with proximal hypospadias were considered. Children who had undergone hypospadias surgery or previous testosterone injection and those with chordee were excluded. ESUTH is a tertiary hospital located in Enugu, South East Nigeria. The hospital serves the whole of Enugu State, which according to the 2016 estimates of the National Population Commission and Nigerian National Bureau of Statistics, has a population of about 4 million people and a population density of 616.0/km². The hospital also receives referrals from its neighboring states.

Preparatory Protocol

On presentation to the outpatient clinic, children with hypospadias were evaluated and penile measurements taken using Vernier calipers. Two measurements were taken, one measurement proximal and another measurement distal to the hypospadiac meatus. The proximal measurement extends from penoscrotal junction to the meatus. The distal measurement starts from the hypospadiac meatus to the tip of the glans penis. At least, two measurements of each aspect were made by the same person (the surgeon) and the average taken. This minimized observer and operator variability. The measurements were documented in millimeters (mm). The brand of testosterone given was Sustanol. Sustanol is an oily (arachis oil) solution, one milliliter (ml) contains 30 milligrams (mg) of testosterone propionate, 60 mg of testosterone phenylpropionate, 60 mg of testosterone isocaproate and 100 mg of testosterone decanoate. Sustanol, manufactured by Aspen pharmaceuticals Ireland, was given intramuscularly at the dose of 2 mg per kilogram (kg) body weight. Only a single dose of testosterone was given to each patient.

Post-injection Protocol

Four weeks post testosterone injection, repeat proximal and distal measurements of the penile shaft were performed and the results obtained were compared statistically. The decision to take the repeat measurements at 4 weeks (post injection) was based on the fact that the effects of testosterone begins at 3 weeks and plateaus at 6 weeks with maximum effect at about 4 weeks [10]. The reason for repeat measurement at 4 weeks was to assess the effect of testosterone at its point of maximum action and to encourage patients' compliance.

Data Collection

The following data were analyzed: age of the patients at presentation, type of hypospadias, proximal and distal penile measurements at onset and at 4 weeks after testosterone injection.

Data Analysis

IBM Statistical Package for Social Science (SPSS) for windows version 23 (IBM Corp., Armonk, NY) was used for data entry and analysis. Data were expressed as percentages, median, means and standard deviation. Chi square test or student's T test was used to test for significance. P value < 0.05 was considered statistically significant.

Results

Patients' Demographics

A total of 24 cases of proximal hypospadias were recruited into the study. The ages of the patients at presentation ranged from 1 month to 18 months with a median age of 3 months.

Types of hypospadias

The type of hypospadias is shown in Table 1.

Table 1: Types of hypospadias

Type of hypospadias	Number of patients (%)
Mid penile	18 (75)
Proximal penile	6 (25)

Penile measurements

The proximal and distal penile measurements before and after testosterone injection are illustrated in Table 2.

Table 2: Mean penile measurements in relation to testosterone injection

	Mean penile measurements	
	Proximal	Distal
Pre-testosterone	25 mm	32 mm
Post-testosterone	29 mm	33 mm
	p value = 0.23	

mm = millimeter

Discussion

The use of hormonal therapy prior to hypospadias repair was first described in 1971. However, this has consistently remained a matter of debate [11]. Administration of parenteral testosterone increases penile length, transverse preputial diameter and diameter at the base of the penis [5]. Following exogenous testosterone injection for penile argumentation, serum testosterone level has been found to be within normal range and minimal side effects, in the form of fine pubic hair, has been reported [5]. The exact etiology of hypospadias is not known. However, a combination of monogenic and multifactorial (gene and environmental) inheritance have been implicated [12]. At a molecular level, screening patients with hypospadias for single gene defects found mutations in certain genes. Howbeit, investigators are not convinced that single mutation can cause majority of the hypospadias [12].

In the present study, a total of 24 cases of proximal hypospadias were recruited. This small number of patients recruited could be due to the fact that distal (anterior) hypospadias were excluded from this study. Distal hypospadias has been reported to be more common than proximal (posterior) hypospadias [13]. It is worthy to note that some researchers have observed more proximal hypospadias in children of Asian descent [3].

At presentation, the median age of the patients was 3 months. This is a relatively prompt presentation and could be related to obvious unpleasant appearance of the hypospadiac penis and the urine that comes from the ventrum of the penis. Parental anxiety may have also informed this early presentation. Ordinarily, patients from developing countries do not present early to the hospital due to poverty and ignorance. However, there was no delayed presentation of the patients with hypospadias in the current study. Regarding the appropriate time for hypospadias repair, the recommended age lies between 6 months and 18 months. These age ranges were arrived at based on risk of anesthesia, penile dimension, treatment outcome, caregivers' choice and psychological impact. At 6 months to 18 months, the child has no genital awareness and does not ambulate. Moreover, hospitalization and anxiety of separation are easier to handle in this age group [14, 15].

In the current study, three-quarters of the patients had mid penile hypospadias. This could be explained by the fact that only proximal hypospadias were considered in this study. Overall, coronal hypospadias has been documented as the most common type of hypospadias [16]. However, other series on hypospadias reported other classes of hypospadias as the most common types in some parts of the world [3, 17, 18]. The geographical location and cohort of patients recruited into a particular study may determine the most prevalent type of hypospadias.

Regarding the effect of testosterone on the penile shaft, the impact of testosterone was more on the proximal part (25 vs 29 mm) when compared to the distal part (32 vs 33 mm), relative to the

site of the hypospadiac meatus. In other words, proximal tissues of the penis respond more to exogenous testosterone. The reason for the discrepancies in the proximal and distal responses remains unknown. This differential response of different parts of the penis is consistent with the report of a study from Maharashtra, India [9]. However, the differences in the proximal and distal dimensions of the penile shaft were found not to be statistically significant. The lack of statistically significant response in the present study could be due to the fact that only a single dose of testosterone was administered in the current study. It is worthy to note that Khokar et al documented the significant advancement of the location of the hypospadiac meatus following multiple testosterone intramuscular injection [9].

The surgical significance of achieving a distal hypospadiac meatus is that the choice of surgical technique for repair may be influenced.

Conclusion

This study has shown that a single dose of testosterone has no effect on the location of meatus in children with hypospadias. A randomized controlled study, involving a large number of patients, may be required in the future to determine the reason for differential response of the proximal and distal penile tissue.

References

1. Keays MA, Dave S (2017) Current hypospadias management: Diagnosis, surgical management, and long-term patient-centered outcomes. *Can Urol Assoc* 11: S48-S53.
2. Anand S, Lotfollahzadeh S (2022) Hypospadias Urological Reconstruction. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing Available from: <https://www.ncbi.nlm.nih.gov/books/NBK564407/>
3. Baskin LS (2000) Hypospadias, anatomy, embryology and reconstructive techniques. *Brazilian Journal of urology* 28: 621-629.
4. Chukwubuike KE, Obianyo NEN, Ekenze SO, Ezomike UO (2019) Assessment of the effect of urethral plate width on outcome of hypospadias repair. *J Pediatr Urol* 15: 627. e1-627.e6.
5. Ahmad R, Chana RS, Ali SM, Khan S (2011) Role of parenteral testosterone in hypospadias. A study from a teaching hospital in India. *Urol Ann* 3: 138-140.
6. Nerli RB, Koura A, Prabha V, Reddy M (2009) Comparison of topical versus parenteral testosterone in children with microphallic hypospadias. *Pediatr Surg Int*. 25: 57-59.
7. Taghavi K, O'Hagen LA, Hewitt JK, Mouriquand PD (2022) Defining the role of pre-operative hormonal therapy in hypospadias. *J Paediatr Child Health* 58: 1508-1519
8. Godse S, Kumar A, Singh H, Choudhary G, Chhabra MK (2022) Parenteral testosterone therapy's effect on penile size before hypospadias surgery. *Indian J Med Surg* 128: 1-3.
9. Khokar DS, Patel RV (2021) Can testosterone alter the degree of hypospadias? A comprehensive study. *J Indian Assoc Pediatr Surg* 26: 38-43
10. Saad F, Aversa A, Isidori AM, Zafalon L, Zitzmann M, et al. (2011) Onset of effects of testosterone treatment and time span until maximum effects are achieved. *Eur J Endocrinol* 165: 675-685.
11. Rynja SP, De Jong TPVM, Bosch JLHR, De Kort LMO (2018) Testosterone prior to hypospadias repair: Postoperative complication rates and long-term cosmetic results, penile length and body height. *J Pediatr Urol* 14: 31 e1-31e8.
12. Van der Zanden LF, Van Rooij IA, Feitz WF, Franke B, Knoers NV, et al. (2012) Aetiology of hypospadias: a systemic review

- of genes and environment. *Hum Reprod Update* 18: 260-283.
13. Kraft KH, Shukla AR, Canning DA (2010) Hypospadias. *Urol Clin North Am* 37: 167-181.
 14. Schneuer FJ, Holland AJ, Pereira G, Bower C, Nassar N (2015) Prevalence, repair and complications of hypospadias: an Australian population-based study. *Arch Dis Child* 100: 1038-1043
 15. Weber DM, Schonbucher VB, Gobet R, Gerber A, Landolt MA (2009) Is there an ideal age for hypospadias repair? A pilot study. *J Pediatr Urol* 5: 345-350.
 16. Pramod S, Prakash GS (2018) Outcome of anterior hypospadias repair: A single center experience. *Arch Int Surg* 8: 1015.
 17. Afzal M, Ansari GA, Tabash A, Alghnam RH, Ahmed AM, et al. (2022) Is the Snodgrass technique suitable for different types of hypospadias? Single center experience. *J Pediatr Adolesc Surg* 2: 3-7.
 18. Subramanian R, Spinoit AF, Hoebeke P (2011) Hypospadias repair: an overview of the actual techniques. *Semin Plast Surg* 25: 206-212.

Copyright: ©2023 Chukwubuike Kevin Emeka, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.