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Single dose of testosterone in children with hypospadias: any effect on the diameter of the glans penis?

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Abstract

Background: The purpose of this study was to assess the effect of a single dose of testosterone on the diameter of the glans penis.

Methods: This was a prospective evaluation of the effect of a single dose of testosterone on the diameter of the glans penis of children with hypospadias. The diameter of the glans penis was measured transversely at the level of the coronal sulcus using Vernier calipers. The patients were categorized into two groups: Group A and Group B. Group A received intramuscular testosterone at the dose of 2 mg per kilogram body weight. Group B did not receive any testosterone and served as control. The diameter of the glans penis was evaluated at the beginning of the study and at 4 weeks after the testosterone injection.

Results: Overall, 64 patients were evaluated. There were 32 patients in group A (50%) and 32 patients in group B (50%). The mean diameter in group A before and after testosterone injection was 17.6 mm \pm 2.5 SD and 17.8 \pm 2.3 SD, respectively. The mean diameter in group B at onset and after 4 weeks was 17.6 mm \pm 2.4 SD and 17.7 \pm 2.4 SD, respectively. $p=0.12$ which is statistically insignificant.

Conclusion: Single dose of testosterone in children with hypospadias does not produce significant increase in the diameter of the glans penis.

Keywords: Children, Diameter, Glans penis, Hypospadias, Testosterone

1 Background

Hypospadias is a male-specific congenital birth defect and is a combination of three anatomic anomalies of the penis, which are an abnormal ventral opening of the urethral orifice, ventral curvature of the penis and abnormal distribution of the foreskin around the glans with a dorsally hooded foreskin [1, 2]. The aim of hypospadias repair is to achieve excellent functional and cosmetic results [3]. A conical glans penis contributes significantly to this excellent cosmetic outcome [4]. Anthropometry of the penis particularly the biometrics of the glans penis is

an important consideration prior to hypospadias repair [5]. Some studies have shown that small glans diameter measuring less than 14 mm (mm) is associated with glans dehiscence following hypospadias repairs [6, 7]. Increase in glans diameter is associated with improved cosmetic and functional outcome of hypospadias repair. This observation has made pediatric surgeons to administer testosterone to increase the glans diameter prior to hypospadias repair. The use of testosterone for penile enlargement before hypospadias repair is commonly practiced, but is rarely reported [3]. Most published series on pre-operative use of testosterone in hypospadias involved multiple doses; the effect of a single dose of testosterone on penile anthropometry is rarely assessed. The hypothesis for this study was that 2 or 3 doses of testosterone

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are usually administered to children before hypospadias repair, but there is no data regarding the extent of effect of a single dose of testosterone on glans diameter. The objective of this study was to assess the effect of a single dose of testosterone on the diameter of the glans penis.

2 Methods

This was a prospective study of pediatric patients with hypospadias, 15 years and below, who had testosterone injection for penile augmentation at the pediatric surgery unit of (Enugu State University Teaching Hospital) between April 2014 and March 2019. (Enugu State University Teaching Hospital) 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. The present study protocol was reviewed and approved by the ethics and research committee of (Enugu State University Teaching Hospital) and conforms to the provisions of the Declaration of Helsinki. Informed consent was obtained from the patients' caregivers when they were enrolled. Patients for hypospadias reoperation, genital anomaly, undescended testis and those above 15 years of age were excluded from the study. Patients whose caregivers refused to give consent for the study were also excluded.

2.1 Protocol

This study was carried out on outpatient basis. Consecutive children who presented with hypospadias during the study period were recruited into the study. The patients were categorized into two groups. Categorization of the patients into each group was by simple randomization, where the first patient was assigned to group A and the next patient to group B and so on. Group A patients had testosterone injection; group B patients did not receive testosterone injection and served as control (No placebo was given). On presentation, the patients were clinically evaluated and appropriate investigations done. The investigations included full blood count and genotype. After retracting the prepuce, the maximum transverse diameter of the glans penis at the coronal sulcus was measured using Vernier calipers. At least two measurements of the diameter 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). For the group A patients, Sustanol containing testosterone was used. Sustanol is an oily (arachis oil) solution; one milliliter (ml) of it contains 30 mg (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. One dose of Sustanol was given to each patient. For the group B patients (control), Sustanol was not given. Only measurement of the diameter of the glans penis was performed. The penile volume was not calculated in the present study. Similar studies on the effect of glans penis on hypospadias repair assessed the glans diameter [6, 8]. One surgeon was involved in the measurement and management.

Four weeks after, repeat measurement of the diameter of the glans penis at the level of the corona sulcus for both groups of patients was performed and the results obtained were statistically compared. The decision to measure the glans penis at 4 weeks (post-injection) was based on the fact that the effects of testosterone on sexual interests begin at 3 weeks and plateaus at 6 weeks with maximum effect at about 4 weeks [9]. The measurement of glans diameter was not done weekly. The reason for this was to assess the effect of testosterone at its point of maximum action and to encourage patients' compliance.

2.2 Data collection

The following data were collected: age of the patient, type of hypospadias, diameters of the glans penis at onset and 4 weeks after (of both the test and control groups). The author confirms the availability of, and access to, all original data reported in this study.

2.3 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.

3 Results

3.1 Patients' demographics

The ages of the patients ranged from 1 to 7 years with a median of 3.1 years. Seventy-two percent of the patients were below 4 years of age.

3.2 Type of hypospadias

The type of hypospadias was based on the location of the urethral meatus, as shown in Table 1.

3.3 Mean diameter of the glans penis

The diameters are shown in Table 2.

Table 1 Types of hypospadias

Type	Number (%)	Group A	Group B
Coronal	36 (56.3)	19	17
Distal penile	14 (21.9)	6	8
Mid penile	8 (12.5)	4	4
Proximal penile	6 (9.3)	3	3
Total	64 (100)	32	32

Table 2 Mean glans diameters of the two groups of patients

	Group A		Group B		p value
	Mean (mm ^a)	SD	Mean (mm)	SD	
At onset	17.6	2.5	17.6	2.4	0.16 ^b
At 4 weeks	17.8	2.3	17.7	2.4	

^a mm millimeter, SD standard deviation

^b Statistically insignificant p value

Table 3 Mean glans diameter in relation to the types of hypospadias

	Group A		Group B		p value
	Mean (mm ^a)	SD	Mean (mm)	SD	
<i>Coronal</i>					
At onset	17.5	2.5	17.5	2.5	0.15
At 4 weeks	17.7	2.2	17.6	2.5	
<i>Distal penile</i>					
At onset	17.7	2.5	17.7	2.3	0.17
At 4 weeks	17.9	2.3	17.8	2.3	
<i>Mid penile</i>					
At onset	17.5	2.5	17.5	2.4	0.15
At 4 weeks	17.7	2.2	17.6	2.5	
<i>Proximal penile</i>					
At onset	17.7	2.5	17.7	2.4	0.17
At 4 weeks	17.9	2.3	17.8	2.3	

^a mm = millimeter; SD = standard deviation

3.4 Mean glans diameter in relation to the type of hypospadias

These measurements are depicted in Table 3.

3.5 Adverse effect of testosterone

Two (3.2%) patients in group A developed scanty pubic hair. The effect of testosterone on bone age, behavior, clothing profile and erection were not assessed.

4 Discussion

Testosterone plays an important role in the treatment of genital abnormalities, and its use for penile augmentation is not a recent concept. Testosterone increases size of the penis in prepubertal male due to its androgenic effects: This effect is beneficial for surgical repair of hypospadias because a larger penile size makes correction easier and less risky [10]. One study that administered human chorionic gonadotrophin (hCG) to children over a 5-week period found that hCG produces disproportionate penile enlargement and decreases the severity of hypospadias [11]. However, certain problems have been identified with the use of hCG and its use is not widely accepted. Such problems include lack of treatment protocol and wide variations in response [11]. Topical application of testosterone has also been found effective in increasing penile length and glans circumference [12, 13]. The drawback of topical testosterone is that the results of its use are inconsistent due to variable absorption [14].

In the present study, the median age of our patients was 3.1 years. This finding is similar to the findings of Ahmad et al. [15]. However, majority of our patients was less than 4 years of age, while the peak age in Ahmad’s study was between 2 and 6 years of age. The age differences may be explained by the discrepancies in the time of presentation of the patients to the hospital.

Coronal hypospadias was the most common type of hypospadias noticed in the cohort of our patients. This is consistent with the report of other series on hypospadias [4, 16, 17]. However, there are reports of mid penile and penoscrotal hypospadias as the most common type, respectively [18, 19]. The exact reason for these differences is not known but may be explained by the cohort of patients that were studied. In the present study, the difference in glans diameter of the two groups (test and control) of patients was found not to be statistically significant. In a systemic review on hormone therapy in hypospadias surgery, the authors concluded that penile improvement following hormonal therapy has not been defined [20]. However, other researchers have reported the significant increase in diameter of the glans penis following testosterone administration [12, 15, 21]. The inability of the present study to detect significant differences in glans diameter may be due to the single dose of testosterone unlike in other studies where more than one dose of testosterone were given [15, 21]. Exogenous administration of testosterone in prepubertal males may be complicated by the appearance of pubic/axillary hair. Pubic hair was noticed in two of our patients. Other authors also reported the occurrence of pubic and axillary hairs as a result of testosterone administration [15, 22].

4.1 Limitation of the study

Although this was a prospective study, it was limited by the small number of cases. A larger number of cases would have availed better analysis.

The effects of testosterone on bone age, stretched penile length and vascularity were not assessed.

5 Conclusion

This study did not find any statistically significant difference in diameter of the glans penis, when compared with control, 4 weeks following administration of a single dose of testosterone. Single dose of testosterone is inadequate to achieve the desired increase in glans diameter before hypospadias repair. Therefore, more than one dose of testosterone is required to achieve optimal result.

Abbreviations

mm: Millimeter; SD: Standard deviation; hCG: Human chorionic gonadotrophin.

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Author contributions

The author contributed solely to the concept and all the works involved in the production of this manuscript.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethics approval was obtained from ethics and research of the Enugu State University Teaching Hospital (ESUTH/C-MAC/RA/034/VOL.11/176) and the patients' parents gave informed written consent.

Consent for publication

Not applicable.

Competing interests

The author declare there is no competing interest.

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