ANDROGEN SUPPLEMENT IN HYPOSPADIAS REPAIR

Study

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In Urosurgery

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Abbreviations

TDF	Testis determining factor
DHT	Dihydrotestosterone
IVF	in vitro fertilization
MIS	Mullerian inhibiting substance
CYP17	cytochrome P450c17 hydroxylase/lyase
TIP	Tubularized Incised Plate
OIF	Onlay Island flap
DPH	Distal penile hypospadias
MPH	Mid penile hypospadias
CBC	Complete blood picture
UP	Urethral plate
SD	Standard deviation
HCG	Human Chorionic Gonadotropin
IU	International unit
EGF	Epidermal growth factor
NADPH	Nuclear adenosine diphosphate H
LH	Luteinizing hormone

Introduction

Hypospadias, in boys, is defined as an association of three anomalies of the penis: (1) an abnormal ventral opening of the urethral meatus that may be located anywhere from the ventral aspect of the glans penis to the perineum, (2) an abnormal ventral curvature of the penis (chordee), and (3) an abnormal distribution of foreskin with a "hood" present dorsally and deficient foreskin ventrally ***(Mouriquand, 1995).***

Hypospadias is a relatively common congenital defect of the male external genitalia. It is present in approximately 1 in 250 male newborns. Hypospadias may be an isolated defect or a phenotypical component of a more complex condition such as an intersex state. There are a multitude of techniques at the disposal of the experienced surgeon faced with reconstruction of hypospadias. ***(Duckett, 1995)***

Responsible etiologic factors of hypospadias may include one or more of an environmental or other endocrine disruptor. ***(Duckett, 1995)***

Other possible causes include insufficient testosterone and/or dihydrotestosterone synthesis (presumably defective or deficient 5α-reductase enzyme activity) and/or defective androgen receptor quality and/or quantity. ***(Griffin, 1992)***

Innovative concepts and techniques continue to emerge in the field of hypospadiology, and with time may herald improvements to even the most basic of principles necessary for successful hypospadias repair. Hypospadiologists must be cognizant of the general principles of repair, be well versed in several appropriate techniques for all levels of hypospadias, and, most importantly, be dedicated to meticulous and uncompromising surgical technique and patient care as they strive for perfection in this ever-flourishing field ***(Duckett, 1995)***

There are many reports stated the usefulness of androgen supplementation to hypospadiac patients prior to surgery to help improve the blood supply of skin as wll as the dartos muscle in the help to improve outcome of hypospadias surgery. However there are reports stated that solve no help as proposed.

In order to avoid complications of hypospadias surgery, it had to find a way that presents a solution for these difficulties and minimizes complications by improvement vascularity of penile skin, penile length and abundance of genital skin for more pliability of the skin and easy handling, so good configuration and cosmoses. It is our aim by using testosterone that we hope to improve and solve these problems.

Embryology of male urethra

Formation of the external male genitalia is a complex process starting with genetic programming which means the presence of the Y chromosome and its associated sex-determining region Y [SRY] and its protein product, testis-determining factor [TDF], which are necessary for cell differentiation, hormonal signaling, enzyme activities, and tissue remodeling ***(Yamada, 2003).***

At 24th day of gestation, the wolffian system appears as 2 longitudinal ducts connected cranially to the mesonephros and caudally draining into the urogenital sinus meanwhile, the müllerian duct develops as an invagination in the coelomic epithelium just lateral to the wolffian duct at approximately the sixth week of gestation ***(Baskin, 2008).***

By the end of the fourth week of gestation, both the hindgut and future urogenital system have reached the cloacal membrane on the ventral surface of the developing embryo and from this indifferent stage until the end of the eighth week of gestation, the urorectal septum continues to develop and divides the cloacal membrane into anterior and posterior segments ***(Baskin, 2008).***

The anterior aspect destined to be the urogenital membrane and the posterior segment the future rectum,up to this point, the male and female genitalia are essentially indistinguishable with the surge in luteinizing hormone, coupled with the influence of testosterone and 5[alpha]-dihydrotestosterone (DHT), masculinization of the external genitalia occurs,one of the first signs of masculinization is an increase in the distance between the anus and the genital structures, followed by elongation of the phallus ***(Baskin, 2008).***

Formation of the penile urethra from the endodermal urethral groove, by 11–12 weeks and at 16–17 weeks of gestation, the urethral folds have completely fused in the midline on the ventrum of the penile shaft with medial fusion of the urethra and fusion of the ectodermal edges, meanwhile the glandular urethra, which consists of squamous epithelium, completes its formation during this period ***(Yamada, 2003).***

The mechanism of the glandular urethral formation remains controversial since two theories have been proposed

- endodermal cellular differentiation, wherein the glandular urethra formed by an extension of urogenital sinus epithelium undergoes transdifferentiation.
- primary intrusion of the ectodermal tissue from the skin of the glans penis.

Anatomical and immunohistochemical studies support the new hypothesis of endodermal differentiation, which shows that the epithelium of the entire urethra is of urogenital sinus origin and the entire male urethra, including the glandular urethra, is formed by dorsal growth of the urethral plate into the genital tubercle and ventral growth and fusion of the urethral folds which can be explained by that under proper mesenchymal induction, the urothelium has the ability to differentiate into a stratified squamous phenotype with characteristic keratin staining, thereby explaining the cell type of the glans penis**(figure 1).*(David, 2008)***

The future prepuce is formed at the same time as the urethra and is dependent on normal urethral development at about the eighth week of gestation, low preputial folds appear on both sides of the penile shaft, which join dorsally to form a flat ridge at the proximal edge of the corona, the ridge does not entirely encircle the glans because it is blocked on the ventrum by the incompletely developed glandular urethra, the process of preputial formation continues until it covers all of the glans, forming a midline seam and if the genital folds fail to fuse (i.e., if there is a defect in the formation of the urethra), the preputial tissues do not form ventrally ***(Baskin, 2008).***