The Effects of Hyaluronic Acid in Preventing Recurrence of Urethral Stricture after Visual Internal Urethrotomy

Thesis

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List of Abbreviations

Abb.	Full term
CISC	Clean Intermittent Self-Catheterization
CTU	Core-Through Urethrotomy
DVIU	Direct Visual Internal Urethrotomy
HA	Hyaluronic Acid
IPSS	International Prostate Symptom Score
NaH	Sodium Hyaluronate
KTP	Potassium Titanyl Phosphate
QoL	Quality of Life
TUR	Transurethral Resection
VAS	Visual Analogue Scale
VCUG	Voiding Cystourethrography
VIU	Visual Internal Urethrotomy

INTRODUCTION

Urethral stricture is the preferred term for abnormal narrowing of the anterior urethra, or the scarring process that involve the spongy erectile tissue of the corpus spongiosum (spongiofibrosis). The spongy erectile tissue of the corpus spongiosum underlies the urethral epithelium, and in some cases, the scarring process extends through the tissues of the corpus spongiosum and involves the adjacent tissues. Contraction of the scar reduces the urethral lumen. In contrast, posterior urethral strictures are referred to as contractures or stenosis that involve prostatic and membranous urethra caused by distraction in this area after trauma or radical prostatectomy ***(Bhargava & Chapple, 2004).***

Today, most urethral strictures are the result of trauma (usually straddle trauma), iatrogenic, idiopathic and infectious diseases ***(Park & McAninch, 2004).***

Patients who have urethral strictures often present with obstructive voiding symptoms or genitourinary infections such as prostatitis and epididymitis. Some patients may present with urinary retention ***(Morey & McAninch, 1996).***

For an appropriate management plan, it is important to determine the location, length, density and depth of the stricture. The length and location of the stricture can be determined with radiography, urethroscopy, and ultrasonography. The degree of

spongiofibrosis is difficult to be determined objectively ***(Morey & McAninch, 1996).***

Dilatation, visual internal urethrotomy, laser urethrotomy, permanent urethral stent applications and urethroplasty have been used for management of urethral strictures ***(Wessells et al., 2017).***

It is an easy, minimally invasive technique; however, one shortcoming of this technique is the frequent recurrence of stricture. The short-term success rate of VIU varies from 39% to 73% for strictures shorter than 1.5 cm .Although VIU is the most common treatment for urethral strictures but recurrence rate is 26.9% to 56% ***(Bullock & Brandes, 2007).***

To reduce recurrence, laser surgery, self-catheterization after VIU, application of angiotensin-converting enzyme inhibitor gels, and steroid injection have been used. Several materials have been developed to prevent postoperative adhesions including hyaluronic acid ***(Dogra et al., 1999; Shirazi et al., 2007; Korhonen et al., 1990).***

Lim et al., reported that the efficacy of a hyaluronic acid (HA) that reduced postoperative adhesions improved with the intraoperative coadministration of a neurokinin 1 receptor antagonist in a rat model ***(Lim et al., 2010).***

Da-Silva et al. reported that the tissues involved in urethral stricture have a low level of hyaluronic acid and a high level of dermatan sulfate, which suggests that administration of HA into stricture sites might decrease the possibility of recurrence ***(Da-Silva et al., 2002).***

AIM OF THE WORK

To evaluate the effect of hyaluronic acid (HA) instillation during visual internal urethrotomy (VIU) for decreasing the incidence of recurrent urethral stricture.

Chapter 1

EMBRYOLOGY OF THE URETHRA

Embryos of both male and female sexes are indistinguishable from one another early in life. Migrating mesenchymal cells spread themselves around the cloacal membrane and accumulate to form swellings. A pair of swellings called cloacal folds develops on either side of the cloacal membrane early in the fifth week. These folds meet just anterior to the cloacal membrane to form the genital tubercle which is a midline swelling ***(Hynes and Fraher, 2004a)*** (Fig. 1).

During the cloacal division into the posterior anorectal canal and the anterior urogenital sinus, the portion flanking the opening of the anorectal canal becomes the anal folds. The urogenital folds are formed from the portion of the cloacal folds that are flanking the opening of the urogenital sinus. Then a new pair of swellings, called the labioscrotal folds, appears on either side of the urogenital Folds ***(Hynes and Fraher, 2004b)*** (Fig. 2).

The most popular hypothesis of external genital and urethral development is based on study performed in the early part of the 20th century. Most embryology books today quote the mechanism of urethral development proposed by ***Glenister (1954).***

During the sixth week in males as the genital tubercle elongates, a groove appears on its ventral aspect (called the urethral groove). An ectodermal epithelial tag is present at the tip of the genital tubercle In both sexes ***(Glenister, 1954)*** (Fig.3).

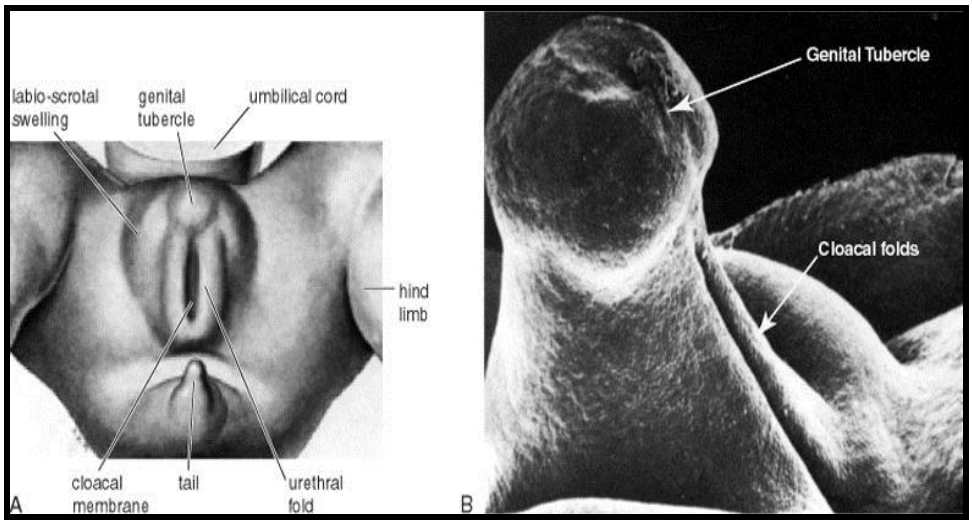

Fig. (1): The early stages of cloacal fold development. (A, From Hamilton WJ, Mossman HW: Human Embryology Prenatal Development of Form and Function. New York, McMillan, 1976; B, from Waterman RE: Human embryo and fetus. Atlas of Human Reproduction, Hafez ESE, Kenemans P [eds], ***(Hinghan, MA, Kluwer Boston, 1982.)***

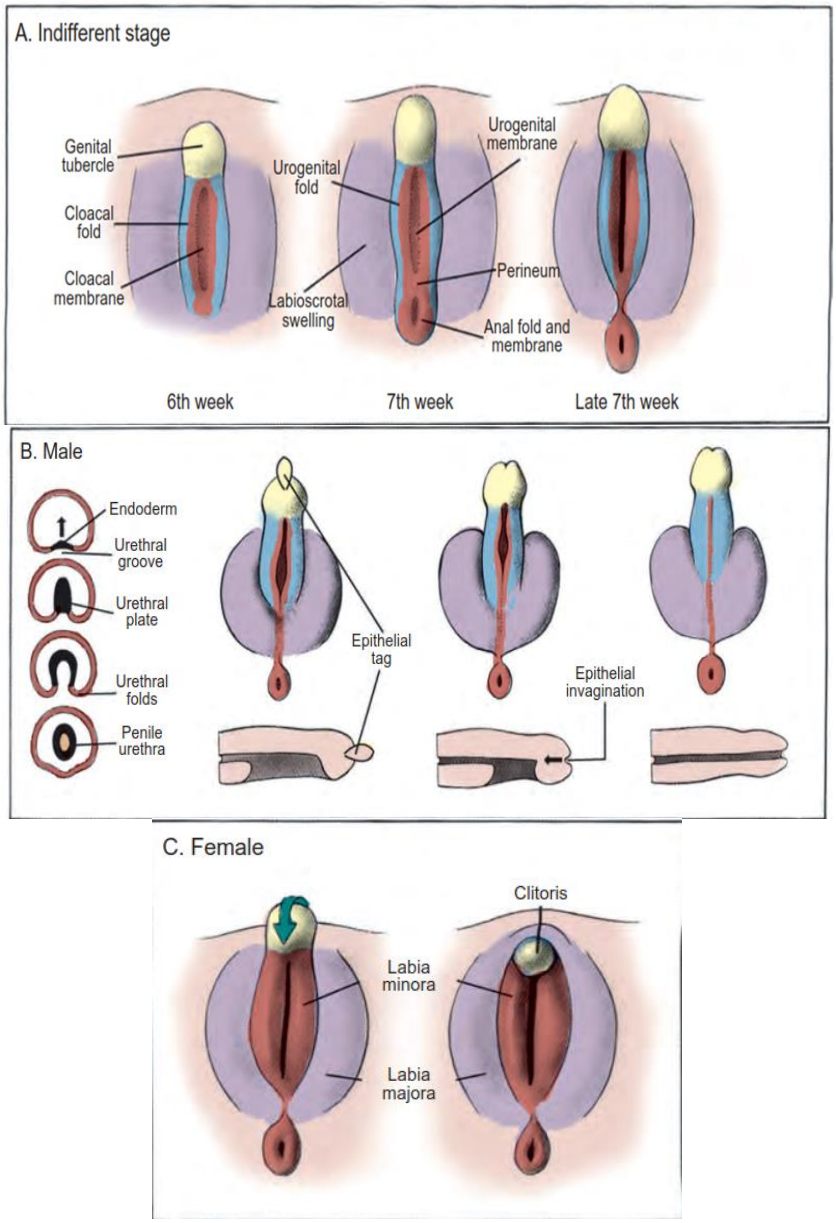

Fig. (2): Development of external genitalia in male and female fetuses. A, The external genitalia derive from a pair of labioscrotal swellings, a pair of urogenital folds, and an anterior genital tubercle. Male and female genitalia are morphologically indistinguishable until the 7th week. B, In males, the urogenital folds fuse and the genital tubercle elongates to form the penile shaft and glans ***(Modified from Larsen WJ. Human embryology. New York: Churchill Livingstone; 1997).***

Initially, the urethral groove extends-part of the way distally along the shaft of the elongating genital tubercle. The distal portion of the urethral groove terminates in the urethral plate. The solid urethral plate canalizes and thus extends the urethral groove toward the glans distally. The urethral groove is thought to be lined by endoderm. Likewise, the solid urethral plate, the distal precursor of the urethral groove, is also believed to derive from the endodermal source ***(Baskin et al., 2018).***

The formation of the distal glanular urethra may occur by a combination of two separate processes the fusion of urethral folds proximally and the ingrowth of ectodermal cells distally ***(Kurzrock et al., 1999).***

In the female, because of the absence of androgen receptor signaling via dihydrotestosterone the primitive perineum does not lengthen and the labioscrotal and urethral folds across the midline do not occure. The phallus bends inferiorly to form the clitoris, and the definitive urogenital sinus becomes the vestibule of the vagina. The urethral folds become the labia minora, and the labia majora is formed from the labiosacral folds ***(Baskin et al., 2018).***

The information regarding the molecular mechanism of genital development is few and incomplete. The transcription factor complex of HOX4 genes, is expressed in a tissue-specific manner in the mouse genital tubercle, This factor complex has been shown to be important in the directional growth of various structures in the developing embryo ***(Dolle et al., 1991).***