Abbrreviations

Ach: Acetylcholine

AUA: American urologic association

BMI: Body mass index

DUC: Distal ureteral calculi

EAU: European association of urology

ESWL -SWL:Extracorporeal shock wave lithotripsy - shock wave lithotripsy

GIT: gastrointestinal tract

IVP: Intravenous urography

KUB:Plain x-ray of kidneys,ureter and bladder

MET: Medical expulsion therapy

mRNA : Messanger ribonucleic acid

MRU: magnetic resonance urography

NCSCT: Non-contrast spiral Computed tomography

NSAIDs:Non-steroidal anti-inflammatory drugs

RMP: Resting membrane potential

SFR: stone-free rate

TENS: Transcutaneous electerical nerve stimulation

UPJ: ureteropelvic junction

URL: ureteroscopic lithotripsy

URS: ureteroscopy

US: Ultrasonography

UTI: urinary tract infections

UVJ: ureterovesical junction

VAS: Visual analogue scale

INTRODUCTION

Urinary system stone disease is observed in 12% of population. Of all types of urinary stones, 20% are ureteral stones, almost 70% of these are distal ureteral stones.

The spontaneous expulsion rate of ureteral stones less than 5mm is almost 85% during observation. Consequently, the priority of observation in this group as treatment is recommended ***(Dellabella et al., 2003).***

The factors affecting the stone passage are the location, size, number and structure of stones; and spasm of ureteral muscles; mucosal edema or inflammation and ureteral anatomy ***(Coll, 2002).***

The alpha-1 adrenergic receptors are localized intensely at the bladder neck, bladder trigone, posterior urethra and distal one-third of the ureter, and their stimulation leads to spasm of the distal ureteral end ***(Hancock, 2000).***

The use of alpha1-adrenoreceptor antagonists (alpha blockers) in treatment of lower ureteral stones that has been introduced recently shows an advance in the medical expulsion therapy of these stones accelerating their passage by inducing relaxation of distal ureteral smooth muscles ***(Cervenakov et al., 2002).***

The available studies on the use of alpha blockers in the treatment of lower ureteric stones have shown them to be effective than standard treatment with regard to expulsion time, colic episodes, use of analgesics and quality of life ***(Dellabella et al., 2003).***

A comparative evaluation of the use of alpha-blockers in one side and shock wave lithotripsy (SWL) and ureteroscopy on the other side shows that the latter has more possible morbidity, more significant cost and is in need for highly specialized equipments and special expertise ***(Resim et al., 2005).***

The use of alpha-blockers in conjunction with ESWL or other medications e.g. steroids, non-steroidal anti-inflammatory or calcium-channel blockers gives more best results than either types alone and the expulsion rate of stones may reach 100% in combination ***(Kupeli et al., 2004).***

As a conclusion, the latest researches clearly demonstrates that alpha-blockers can be used safely and effectively in treatment of lower ureteric stones.

AIM OF THE WORK

To review the role of alpha blockers in the medical expulsion therapy of distal ureteric stones in comparison to other methods of treatment.

ANATOMY OF HUMAN URETER

The ureters are bilateral tubular structures responsible for transporting urine from the renal pelvis to the bladder (Fig. 1).

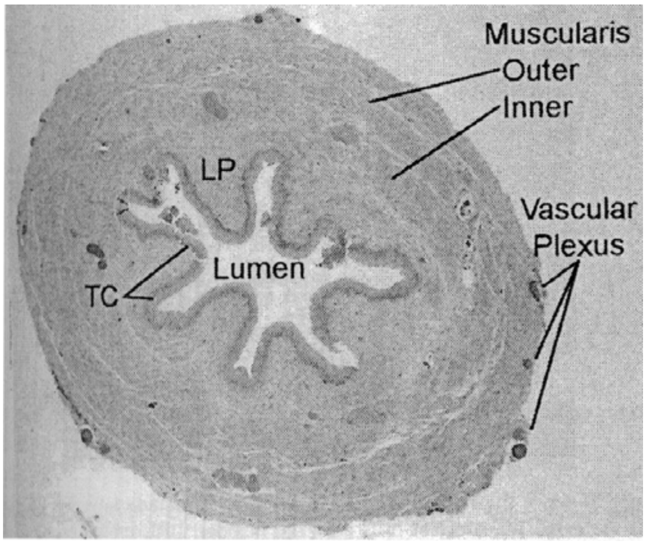

Fig. (1): Transverse microscopic section through the ureter. Inner longitudinal layer is distinguished from outer circular and oblique muscle fibers. The rich vascular supply of the ureter I also demonstrated. LP: lamina propria; TC: transitional epithelium ***(courtesy Dr Hussein saborian; WB Saunder`s, Campbell`s urology,9th edition, Philadelphia, 2007; 1: 35).***

They are generally 22 to 30 cm in length with a wall composed of multiple layers. The inner layer transitional epithelium. Next is the lamina propria, which is a connective tissue layer that along with the epithelium makes up the mucosal lining. Overlying the lamina propria is a layer of smooth muscle that is contiguous with muscle covering the renal calyces and pelvis, although in the ureter this layer is divided into an inner longitudinal and an outer circular layer. Together, these muscular layers provide the peristaltic wave that actively transports urine from the renal collecting system through the ureter to the bladder. The outermost layer is the adventitia. This layer surrounds the ureter and encompasses the blood vessels and lymphatics that travel along the ureter.

Ureteral segmentation and nomenclature:

The ureter is often arbitrarily divided into segments to facilitate ureteral description. The simplest system divides the ureter into the abdominal ureter extending from renal pelvis to the iliac vessels, and the pelvic ureter extending from the iliac vessels to the bladder. Alternatively, the ureter can be divided into upper, middle, and lower segments. The upper ureter extends from the renal pelvis to the upper border of the sacrum. The middle ureter comprises the segment from the upper to the lower border of the sacrum. The lower (distal or pelvic) ureter extends from the lower border of the sacrum to the bladder ***(Anderson et al 2007)***..

Normal variations in ureteral caliber:

The normal ureter is not of uniform caliber, with three distinct narrowings classically described (Fig. 2): the ureteropelvic junction, crossing of the iliac vessels, and the ureterovesical junction. The third site of narrowing observed in the normal ureter is ureterovesical junction where. There is a true physical restriction of the ureter as it makes the intramural passage through the bladder wall to the ureteral orifice.

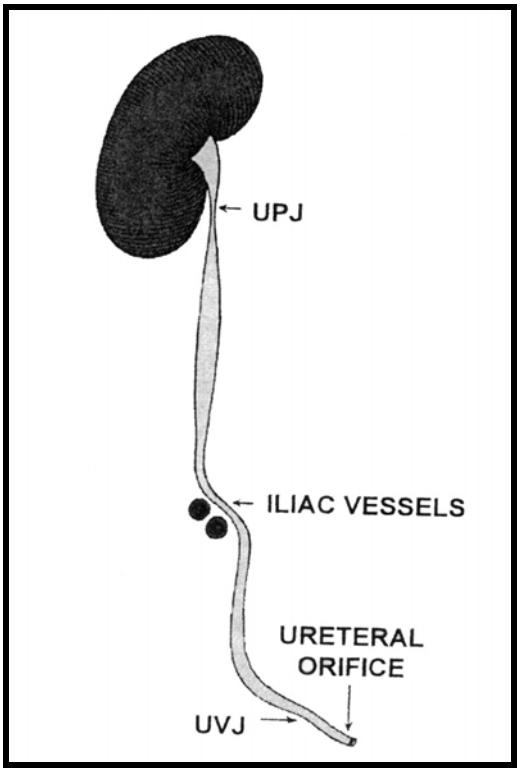

Fig. (2): The ureter demonstrating sites of normal functional or anatomic narrowing at the uretero pelvic junction (UPJ), the iliac vessels, and the ureterovesical junction (UVJ). Note also the anterior displacement and angulation of the ureter, which occurs over the iliac vessels, as shown here diagrammatically ***(Campbell`s urology, 9th edition, Philadelphia, 2007; 1: 36)***.

Ureteral innervation:

The exact role of the ureteral autonomic input is unclear. Normal ureteral peristalsis does not require an external autonomic input but, rather, originates and is propagated from intrinsic smooth muscle pacemaker sites located in the minor calyces of the renal collecting system. The autonomic nervous system may exert some modulating effect on this process, but the exact role is unclear. The ureter receives preganglionic sympathetic input from the 10th thoracic through 2nd lumbar spinal segments. Postganglionic fibers arise from several ganglia in the aorticorenal, superior, and inferior hypogastric autonomic plexuses. Parasympathetic input is received from the 2nd through 4th sacral spinal segments ***(Anderson et al., 2007).***

Pelvic ureter:

Intraoperatively, the ureter is identified by its peristaltic waves and is readily found anterior to the bifurcation of the common iliac artery. At ureteroscopy, pulsations of this artery can be seen in the posterior ureteral wall. The ureters come within 5 cm of each other as they cross the iliac vessels. On entering the pelvis, they diverge widely along the pelvic side walls toward the ischial spines. The ureter travels on the anterior surface of the internal iliac vessels and is related laterally to the branches of the anterior trunk. Near the ischial spine, the ureter turns anteriorly and medially to reach the bladder. In females, The ovarian vessels (infundibulopelvic ligament) cross the iliac vessels anterior and lateral to the ureter, and dissection of the ovarian vessels at the pelvic brim is a common cause of ureteral injury In males ***(Daly and Higgins, 1988)*** the anteromedial surface of the ureter is covered by peritoneum, and the ureter is embedded in the retroperitoneal connective tissue.

As the ureter coursed medially, it is crossed by arteries, veins, and nerves in the lateral vesical ligaments. In females, the ureter first runs posterior to the ovary and then turns medially to run deep to the base of the broad ligament before entering a loose connective tissue tunnel through the substance of the cranial ligament, the ureter can be found slightly lateral and deep to the rectouterine folds of peritoneum. It is crossed anteriorly by the uterine artery and is therefore subject to injury during hysterectomy. As it passes in front of the vagina, it crosses 1.5 cm anterior and lateral to the uterine cervix. The ureter courses 1 to 4 cm on the anterior vaginal wall to reach the bladder. Occasionally, a stone lodged in the distal ureter can be palpated through the anterior vaginal wall. The pelvic ureter receives abundant blood supply from the common iliac artery and most branches of the internal iliac artery. The inferior vesical and uterine arteries usually supply the ureter with its largest pelvic branches. Blood supply to the pelvic ureter enters laterally; thus, the pelvic peritoneum should be incised only medial to the ureter.

Intramural vessels of the ureter run within the adventitia and generally follow one of two patterns in approximately 85% of specimens, longitudinal vessels run the length of the ureter and are formed by anastomoses of segmental ureteral vessels. In the remaining ureters, the vessels form a fine interconnecting mesh (plexiform) with less collateral flow ***(Shafik, 1972)***. The pelvic ureter appears to have a high preponderance of plexiform vessels, which render it more susceptible to ischemia and less suitable for ureteroureterostomy ***(Hinamn, 1993).*** Lymphatic drainage of the pelvic ureter is to the external, internal, and common iliac nodes. Pathologic enlargement of the common and internal iliac nodes can encroach on and obstruct the ureter.

The pelvic ureter has rich adrenergic and cholinergic autonomic innervation derived from the pelvic plexus. The functional significance of this innervation is unclear, as the ureter continues to contract peristaltically after denervation. Afferent neural fibers travel through the pelvic plexus and account for the visceral quality of referred pain from ureteral irritation or acute obstruction.

Ureterovesical junction and the trigone:

As the ureter approaches the bladder, its spirally oriented mural smooth muscle fibers become longitudinal. Two to 3 cm from the bladder; a fibromuscular sheath (of Waldeyer) extends longitudinally over the ureter and follows it to the trigone ***(Tanagho, 1992).*** The ureter pierces the bladder wall obliquely, travels 1.5 to 2 cm, and terminates at the ureteral orifice. As it passes through a hiatus in the detrusor (intramural ureter), it is compressed and narrows considerably. This is a common site in which ureteral stones become impacted. The intravesical portion of the ureter lies immediately beneath the bladder urothelium and therefore is quite pliant; it is backed by a strong plate of detrusor muscle. With bladder filling, this arrangement is thought to result in passive occlusion of the ureter, like a flap valve (Fig. 3).

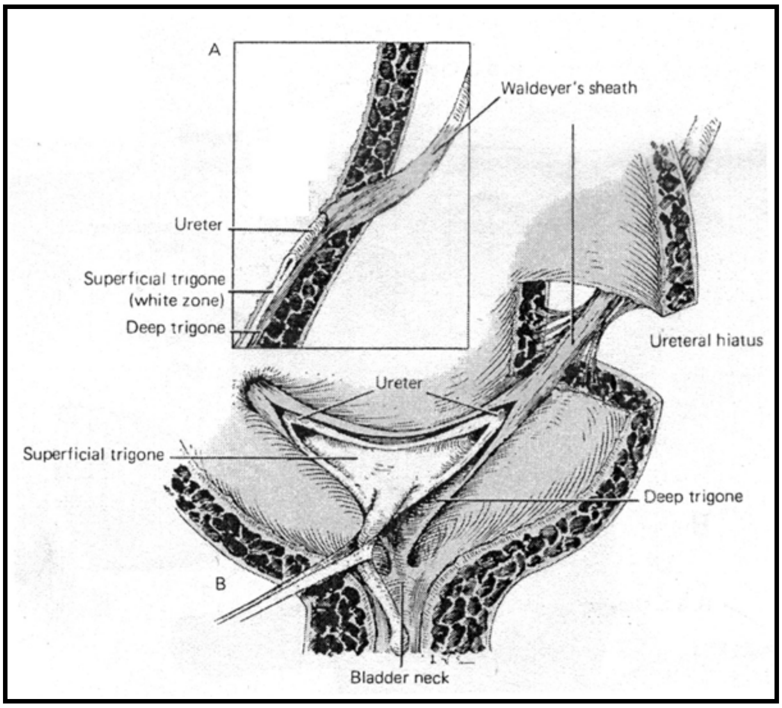

Fig. (3): Normal ureterovesical junction and trigone, A, section of the bladder wall perpendicular to eh ureteral hiatus shows the oblique passage of the ureter through the detrusor and also shows the submucosal ureter with its detrusor backing. Waldeyer's sheath surrounds the prevesical ureter and extends inward to become the deep trigone. B, Waldeyer's sheath continues in the bladder as the deep trigone, which is fixed at the bladder neck. Smooth muscle of the ureter forms the superficial trigone and is anchored at the verumontanum ***(from Tanagho EA,***

Pugh RC: the anatomy & function of the ureterovesical junction Br J. urol.1963; 35:151-165).

Ureteral pain:

Ureteral pain is usually acute and secondary to obstruction. The pain results from acute distention of the ureter and by hyperperistalsis and spasm of the smooth muscle of the ureter as it attempts to relieve the obstruction, usually produced by a stone or blood clot. The site of ureteral obstruction can often be determined by the location of the referred pain (Fig. 4).

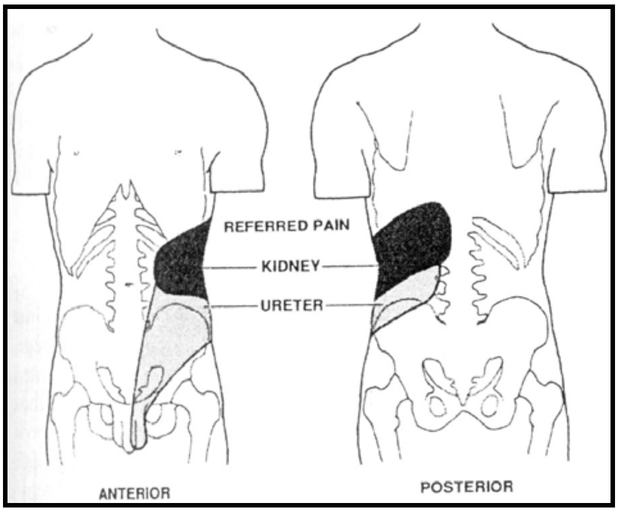

Fig. (4): Patterns of referred somatic pain from the upper urinary tract.

An obstruction of the upper ureter causes pain that radiate across the flank anteriorly toward the upper abdomen & umbilicus, confused with pain resulting from irritation of costal nerves T_{10}-T_{12} but the latter is not colicky in nature. With obstruction of the midureter, pain on the right side is referred to the right lower quadrant of the abdomen (McBurney's point) and thus may simulate appendicitis; pain on the left side is referred over the left lower quadrant and resembles diverticulitis. Also, the pain may be referred to the scrotum in the male or the labium in the female. Lower ureteral obstruction frequently produces symptoms of vesical irritability, including frequency, uregency, and suprapubic discomfort that may radiate along the urethra in men to the tip of the penis. Often, by taking a careful history, the clinician can predict the location of the obstruction. Ureteral pathology that arises slowly or produces only mild obstruction rarely causes pain. Therefore, ureteral tumours and stones that cause minimal obstruction are seldom painful.

PHYSIOLOGY OF CONTRACTION OF URETERAL SMOOTH MUSCLES

The electrical properities of all excitable tissues depend on the distribution of ions n both the inside and the outside of the cell membrane and on the relative permeability of the cell membrane to these ions ***(Hodgkin, 1958)***.

Resting potential:

When a ureteral muscle cell is in a non-excited or resting state, the electrical potential difference across the cell membrane, transmembrane potential, is referred to as the resting membrane potential (RMP). The RMP is determined primarily by the distribution of potassium ions (K^+) across the cell membrane and by the permeability of the membrane to K^+ ***(Hendrickx et al., 1975).***

Action potential:

The action potential, which is the primary event in the conduction of the peristaltic impulse, has the capability to act as the stimulus for excitation of adjacent quiescent cells and through a complicated chain of events gives rise to the ureteral contraction.

When a ureteral cell is stimulated, depolarization occurs, with the inside of the cell membrane becoming less