Effect of Silodosin versus Darifenacin versus Combination of Both Drugs for Ureteric Stent Related Symptoms

Thesis

Submitted for Partial Fulfillment
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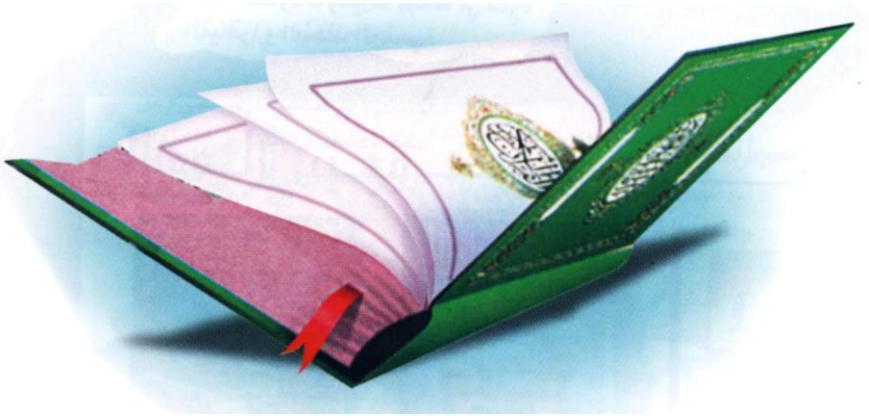
بسم الله الرحمن الرحيم

وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ
عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ



صدق الله العظيم

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Ahmed Elsayed Rashad Mohamed

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List of Abbreviations

Abb.	Full term
ANOVA	*Analysis of variance*
AUA	*American Urological Association*
AUC	*Area under the curve*
BCG	*Bacillus Calmette–Guérin*
BPH	*Benign prostatic hyperplasia*
CNS	*Central nervous system*
CVS	*Cardiovascular system*
DAG	*Diacylglycerol*
DJ	*Double-J*
EAU	*European Association of Urology*
GIT	*Gastrointestinal tract*
IP 3	*Inositol trisphosphate*
IPSS	*International Prostate Symptom Score*
KUB	*Kidneys, ureters and bladder*
LUTS	*Lower urinary tract symptoms*
PCN	*Percutaneous nephrostomy*
PCNL	*Percutaneous nephrolithotomy*
PLC	*Phospholipase C*
QOL	*Quality of life*
RCT	*Randomized controlled trial*
SPSS	*Statistical Package for the Social Sciences*
SRS	*Stent related symptom*
SWL	*Shock wave lithotripsy*
URSL	*Ureteroscopic lithotripsy*
USSQ	*Ureteral stent symptom questionnaire*
UTI	*Urinary tract infection*
VAPS	*Visual pain analogue score*

INTRODUCTION

Temporary drainage of the upper urinary tract by internal ureteral stents is a routine procedure in endourology ***(Joshi et al., 2002).***

Ureteric stents represent a simple and effective method for renal and ureteric drainage and perserve renal function due to ureteric obstruction without external or visible devices ***(Joshi et al., 2001).***

However, ureteric stents are associated with a clear side-effect profile.Stents are associated with significant morbidity and a negative impact on the patient's quality of life.Patients are suffering from lower urinary tract symptoms such as frequency (60%), incomplete emptying (76%) urgency (60%) and dysuria (40%),as well as pain (80%) and hematuria (54%) This is associated with a considerable economic burden ***(Richter et al., 2000).***

There have been studies evaluating the impact of a-blockers in stent-related lower urinary tract symptoms and have been shown to relax ureteric smooth muscle. Silodosin is highly uroselective for the alpha (1A) receptors located in the prostate, urethra and bladder trigone in the lower urinary tract. Blocking these receptors inhibits sympathetic stimulation and relaxes the smooth muscles tone in the lower urinary tract which relieves the related symptoms. Most common adverse reactions of

silodosin (incidence > 2%) are retrograde ejaculation, dizziness, diarrhea, orthostatic hypotension, headache, nasopharyngitis, and nasal congestion ***(Zhou et al., 2015).***

Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of the urinary bladder smooth muscle and other systems. Darifenacin selectively antagonizes the muscarinic M3 receptor. M3 receptors are involved in contraction of human bladder. It is well establish drug for the treatment of overactive bladder and urge urinary incontinence. Recent studies had stated that Darifenacin is effective and well-tolerated in improvement of double J related lower urinary tract symptoms. Common unwanted anti-cholenergic effects of darifinacin include dry mouth, constipation, nausea, stomach pain, blurred vision, dry eyes, dizziness, and weakness ***(Sakr et al., 2015).***

AIM OF THE WORK

To analyze and compare the safety and efficacy of Silodosin versus Darifenacin versus combination of both drugs in the relief of ureteric stent related symptoms.

Chapter 1

THE URETER (ANATOMY-HISTOLOGY-NERUROPHYSIOLOGY)

- **Gross anatomy:**

The ureters are a pair of thick walled, narrow, distensible, cylindrical muscular tubes that carry the urine from the kidneys to the urinary bladder. Each ureter measures from 25 to 30 cm in length. Its course follows a smoothly shaped "s". The ureter is entirely a retroperitoneal structure with approximately equal upper abdominal and lower pelvic segments. The abdominal segment is directly continuous superiorly with the funnel shaped renal pelvis; a slight constriction may mark the site of transition. It passes downwards and medially lateral to the transverse processes of the lumber vertebrae and anterior to the psoas muscle and genito-femoral nerve. The ureter enters the lesser pelvis by crossing anterior to either the end of the common, or the beginning of the external iliac vessels ***(Anderson et al., 2009)***.

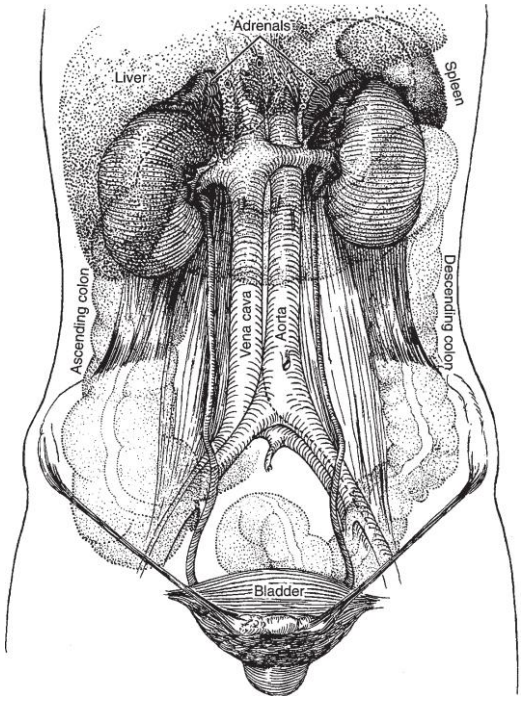

Figure (1): Relations of kidney, ureters, and bladder (anterior aspect). ***Emil A. anagho, MD, & Tom F. Lue, MD, FACS, ScD (Hon): Anatomy of the Genitourinary Tract. Smith & Tanagho's General Urology 18th EDITION 2012 p3).***

The pelvic part lies in the extra-peritoneal areolar tissue. At first it descends posterior-laterally on the lateral wall of the lesser pelvis, following the anterior border of the great sciatic notch, where it is anterior to the internal iliac artery and the commencement of its anterior trunk, dorsal to which are the lumbo-sacral nerve, internal iliac vein and sacroiliac joint. Laterally it lies on the fascia covering the obturator internus and it progressively crosses medial to the inferior vesical artery, the middle rectal artery and the obturator artery, vein and nerve. Opposite the ischial spine the ureter turns antero-medial to run in the fibrous adipose tissue above the levator ani to reach the

base of the bladder. It inserts obliquely in a tunnel in the posterior bladder wall at an angle of approximately 90 to 135 degree to open into the bladder at the lateral angle of the trigon ***(Brooks et al., 2007).***

In the male, as the ureter descends anteromedially, it is crossed in front, above and from lateral to medial, by the ductus deferens just before the ureter enters the bladder. Thereafter the ureter passes in front of and slightly above the upper end of the seminal vesicle. It finally enters the bladder wall.

In the female, the pelvic part of the ureter at first has the same general relations as in the male, though where it lies anterior to the internal iliac artery, it is situated immediately behind the ovary and here forms the posterior boundry of the ovarian fossa. In its later forward and medial course to the bladder it has important relations to the uterine artery, the fornices of the vagina and the cervix of the uterus. It lies in the extraperitoneal connective tissue in the lower and medial part of the broad ligament of the uterus, here it is immediately related to the uterine artery, which lies above and in front of the ureter for a distance of 2.5 cm and then crosses to gain the medial side of the ureter to ascend along side the uterus. The ureter runs forward slightly above the lateral fornix of the vagina and is here situated commonely about 2 cm lateral to the supravaginal portion of the cervix of the uterus, though this distance may vary from 1 to 4 cm ***(Moore et al., 2013).***

The ureter has 3 physiologic narrowings:

1) The ureteropelvic junction.

2) The crossing over the iliac vessels.

3) The ureterovesical junction.

This is crucial in the manifestations of calculus disease. These narrowings may result in ureteral stones becoming trapped and obstructing at these specific levels ***(Park, 2007).***

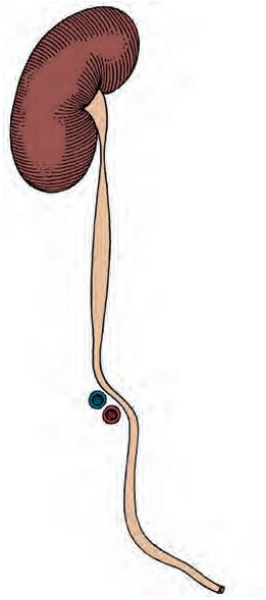

Figure (2): The ureter demonstrating sites of normal functional or anatomic narrowing at the ureteropelvic junction (UPJ), the iliac vessels, and the ureterovesical junction (UVJ) ***(Mohamed Aly Elkoushy, MD, MSc, PhD, and Sero Andonian, MD, MSc, FRCS(C), FACS: Surgical, Radiologic, and Endoscopic Anatomy of the Kidney and Ureter. Campbell- Walsh urology 11th edd.2016 p.974).***