INTRODUCTION

Benign prostatic hyperplasia (BPH), which is a common cause of lower urinary tract symptoms (LUTS), is a progressive disease of aging men ***(Chute et al., 1993).***

Data have suggested that the incidence of symptomatic BPH is 23 % in 2012. LUTS related to BPH influence the quality of life (QOL) with time and hence require treatment ***(Chen et al., 2012).***

Pharmacological therapy, minimally invasive treatment such as transurethral microwave therapy and surgery are the treatment option of BPH. Alpha blockers are the first step of the treatment in patients with BPH Tamsulosin is a highly selective α1a blocker and also affects α1d-adrenergic receptors which are in prostate, bladder neck and urethra. Thus, tamsulosin provides comfortable micturition which can be measured by uroflowmetry (UFM) parameters such as maximum urinary flow rate (Qmax) and average urinary flow rate (Qave) and which improves QoL. The maximum serum concentration of tamsulosin can be measured 6 hr after oral administration and the effectiveness of drug can continue 24 hr ***(Buzelin et al., 1997).***

However, there are some concerns about the time interval required to decide whether the α blocker treatment is successful or not ***(Chapple et al., 1998).***

This trial has been claimed to be 1 week up to 1 month depending on the type of the α blocker ***(Lepor et al., 2007)***.

First dose effect is also another concern alpha blockers. There have been some studies on the effect of the first dose of alpha blockers for patients particularly on acute urine retention ***(Kapoor et al., 2007).***

Tamsulosin is known to have the serum peak levels at the 6^{th} hour but tissue peak levels can be achieved in 7–10 days ***(Chapple et al., 2005).***

Therefore, single dose effect of tamsulosin is under debate. In this study, we aimed to investigate the first dose effects of tamsulosin on LUTS related to BPH and the predictive value of the change in UFM parameters at the first dose of tamsulosin on the improvement of LUTS symptoms in terms of UFM parameters and IPSS and QOL index.

AIM OF THE WORK

To investigate the effects of the first single and 1st week dose of tamsulosin 0.4 mg on clinical B.P.H patient as predictive factor for the response and thereafter (3 months).

ANATOMY OF THE PROSTATE

The normal prostate weighs 18-22 grams; measures 3 cm in length, 4 cm in width, and 2 cm in depth and is traversed by the prostatic urethra. Although ovoid, the prostate is referred to as having anterior, posterior, and lateral surfaces, with a narrowed apex inferiorly and a broad base superiorly that is continuous with the base of the bladder ***(James, 2007).***

Anatomic relationships:

Posterolaterally:

Microscopic bands of smooth muscle extend from the posterior surface of the capsule to fuse with Denonvillier's fascia. Loose areolar tissue defines a thin plane between Denonvillier's fascia and the rectum ***(James, 2007).***

Anteriorly and anterolaterally:

The capsule blends with the visceral continuation of endopelvic fascia. Towards the apex, the puboprostatic ligaments extend anteriorly to fix the prostate to the pubic bone. The superficial branch of the dorsal vein lies outside this fascia in the retropubic fat and pierces it to drain into the dorsal vein complex ***(James, 2007).***

The deep dorsal vein is an unpaired vein in the dorsal midline of the penis. It drains into the periprostatic plexus and then into the internal pudendal veins.

Laterally:

The prostate is cradled by the pubococcygeal portion of levator ani and is directly related to its overlying endopelvic fascia ***(Myers, 1994).***

Superiorly:

The prostate is continuous with the neck of the bladder. The urethra enters the upper aspect of the prostate near its anterior border ***(Harold, 2006).***

Inferiorly:

The apex of the prostate is continuous with the striated urethral sphincter. Histologically, normal prostatic glands can be found to extend into the striated muscle with no intervening fibromuscular stroma or capsule ***(Epstein, 1989).***

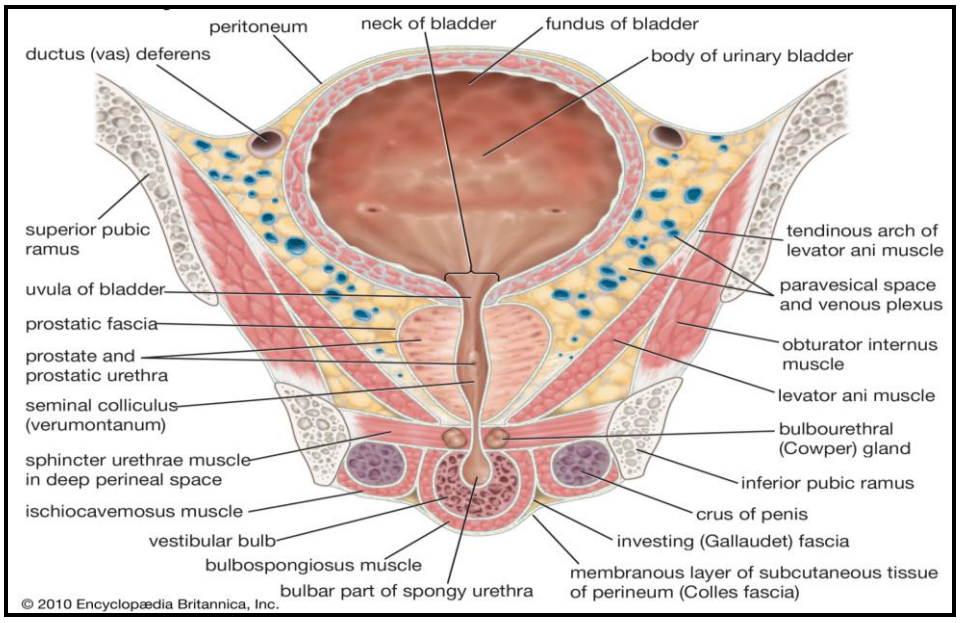

Figure (1): Anatomic relationships of the prostate ***(Encyclopaedia Britannica, inc. 2010).***

Structure:

The prostate is composed of approximately 70% glandular elements and 30% fibromuscular stroma. The stroma is continuous with the capsule and is composed of collagen and abundant smooth muscle. It encircles and invests the glands of the prostate and contracts during ejaculation to express prostatic secretions into the urethra ***(James, 2007).***

The urethra runs the length of the prostate and is usually closest to its anterior surface. It is lined by transitional epithelium, which extends into the prostatic ducts. The urothelium is surrounded by an inner longitudinal and an outer circular layer of smooth muscle. A urethral crest projects inward from the posterior midline, runs the length of the

prostatic urethra, and disappears at the striated sphincter. To either side of this crest, a groove is formed (prostatic sinuses) into which all glandular elements drain ***(McNeal, 1972).***

At its midpoint, the urethra turns approximately 35 degrees anteriorly, but this angulation can vary from 0 to 90 degrees. This angle divides the prostatic urethra into proximal (preprostatic) and distal (prostatic) segments that are functionally and anatomically discrete. In the proximal segment, the circular smooth muscle is thickened to form the involuntary internal urethral (preprosatatic) sphincter ***(McNeal, 1972).***

Beyond the urethral angle, all major glandular elements of the prostate open into the prostatic urethra. The urethral crest widens and protrudes from the posterior wall as the veromontanum. The small slit like orifice of the prostatic utricle is found at the apex of the veromontanum and may be visualized cystoscopically. The utricle is a 6-mm müllerian remnant in the form of a small sac that projects upward and backward into the substance of the prostate ***(James, 2007).***

To either side of the utricular orifice, the two small openings of the ejaculatory ducts may be found. The ejaculatory ducts form at the juncture of the vas deferens and seminal vesicles and enter the prostate base where it fuses with the bladder. They enter the prostate posteriorly taking an oblique course nearly 2 cm in length and are surrounded by circular smooth muscle ***(James, 2007).***

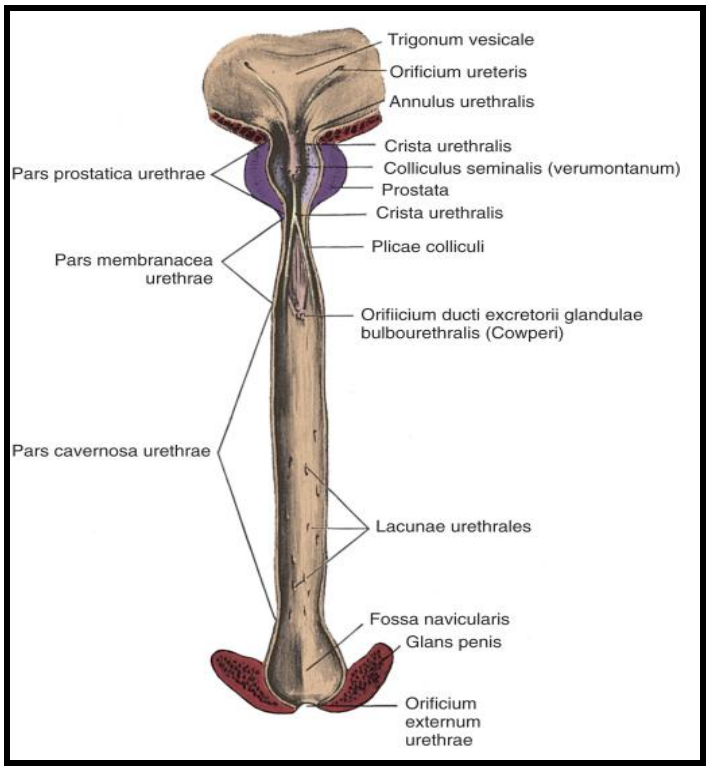

Figure (2): Posterior wall of the male urethra ***(Anson, 1984).***

Zonal anatomy of the prostate:

The glandular elements of the prostate have been divided into discrete zones, distinguished by the location of their ducts in the urethra, by their differing pathologic lesions, and, in some cases, by their embryologic origin.

1- The transition zone:

At the angle dividing the preprostatic and prostatic urethra, the ducts of the transition zone arise and pass beneath the preprostatic sphincter to travel on its lateral and posterior sides. Normally, the transition zone accounts for 5% to 10% of the glandular tissue of the prostate. A discrete fibromuscular

band of tissue separates the transition zone from the remaining glandular compartments and may be visualized at transrectal ultrasonography of the prostate. The transition zone commonly gives rise to benign prostatic hyperplasia, which expands to compress the fibromuscular band into a surgical capsule seen at enucleation of an adenoma. It is estimated that 20% of adenocarcinomas of the prostate originate in this zone ***(James, 2007).***

2- The central zone

The ducts of the central zone arise circumferentially around the openings of the ejaculatory ducts. This zone constitutes 25% of the glandular tissue of the prostate and expands in a cone shape around the ejaculatory ducts to the base of the bladder. In keeping with this suggestion, only 1% to 5% of adenocarcinomas arise in the central zone, although it may be infiltrated by cancers from adjacent zones ***(McNeal, 1988).***

3- The peripheral zone:

The peripheral zone makes up the bulk of the prostatic glandular tissue (70%) and covers the posterior and lateral aspects of the gland. Its ducts drain into the prostatic sinus along the entire length of the (postsphincteric) prostatic urethra. Seventy percent of prostatic cancers arise in this zone, and it is the zone most commonly affected by chronic prostatitis ***(McNeal, 1988).***

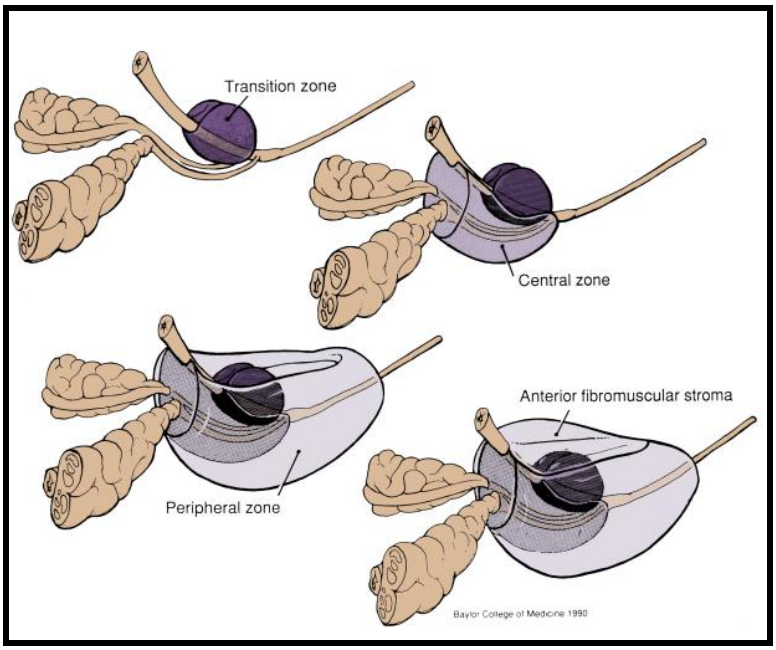

Figure (3): Zonal anatomy of the prostate ***(McNeal, 1988)***.

Lobes of the prostate:

Clinically, the prostate is often spoken of as having two lateral lobes, separated by a central sulcus that is palpable on rectal examination, and a middle lobe, which may project into the bladder in older men. These lobes do not correspond to histologically defined structures in the normal prostate but are usually related to pathologic enlargement of the transition zone laterally and the periurethral glands centrally ***(James, 2007).***

The prostatic capsules:

These are normally two, pathologically three, in number:

1- ***The true capsule:*** a thin fibrous sheath that surrounds the gland.

2- ***The false capsule:*** condensed extraperitoneal fascia which continues into the fascia surrounding the bladder and with the fascia of Denonvilliers posteriorly. Between layers 1 and 2 lies the prostatic venous plexus.

3- ***The pathological capsule:*** when benign adenomatous hyperplasia of the prostate takes place, the normal peripheral part of the gland becomes compressed into a capsule around this enlarging prostatic tissue.

(Harold, 2006)

Histology of the prostate:

In general, the glands of the prostate are tubuloalveolar with relatively simple branching and are lined with simple cuboidal or columnar epithelium. Scattered neuroendocrine cells, of unknown function, are found between the secretory cells. Beneath the epithelial cells, flattened basal cells line each acinus and are believed to be stem cells for the secretory epithelium. Each acinus is surrounded by a thin layer of stromal smooth muscle and connective tissue ***(James, 2007).***

Vascular supply:

Most commonly, the arterial supply to the prostate arises from the inferior vesical artery. As it approaches the gland, the artery (often several) divides into two main branches. The urethral arteries penetrate the prostatovesical junction posterolaterally and travel inward, perpendicular to the urethra.

They approach the bladder neck in the 1- to 5-o'clock and 7- to 11-o'clock positions, with the largest branches located posteriorly. They then turn caudally, parallel to the urethra, to supply it, the periurethral glands, and the transition zone. Thus, in benign prostatic hyperplasia, these arteries provide the principal blood supply of the adenoma. When these glands are resected or enucleated, the most significant bleeding is commonly encountered at the bladder neck, particularly at the 4- and 8-o'clock positions.

The capsular artery is the second main branch of the prostatic artery. This artery gives off a few small branches that pass anteriorly to ramify on the prostatic capsule. The bulk of this artery runs posterolateral to the prostate with the cavernous nerves (neurovascular bundles) and ends at the pelvic diaphragm. The capsular branches pierce the prostate at right angles and follow the reticular bands of stroma to supply the glandular tissue ***(Flocks, 1937).***

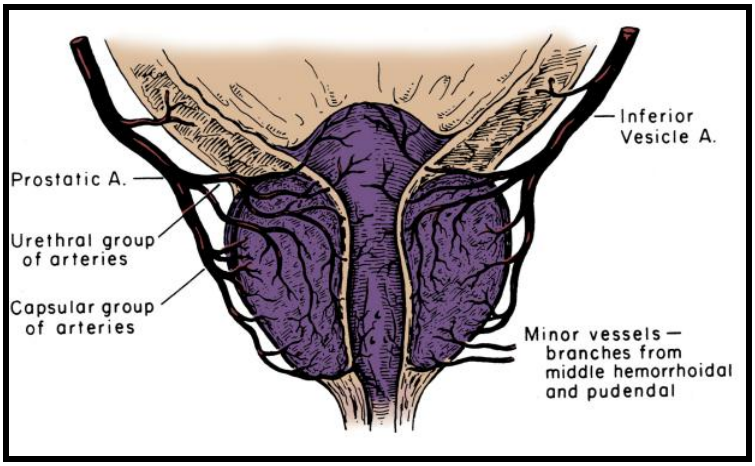

Figure (4): Arterial supply of the prostate ***(Flocks, 1937).***

Venous drainage:

Venous drainage of the prostate is abundant through the periprostatic plexus ***(Burnett, 1995).***

Lymphatic drainage:

Lymphatic drainage is primarily to the obturator and internal iliac nodes. A small portion of drainage may initially pass through the presacral group, or less commonly, the external iliac nodes ***(Burnett, 1995).***

Nerve supply:

Sympathetic and parasympathetic innervation from the pelvic plexus travels to the prostate through the cavernous nerves. Nerves follow branches of the capsular artery to ramify in the glandular and stromal elements. Parasympathetic nerves end at the acini and promote secretion; sympathetic fibers cause contraction of the smooth muscle of the capsule and stroma. α-Adrenergic blockade diminishes prostate stromal and preprostatic sphincter tone and improves urinary flow rates in men affected with benign prostatic hypertrophy; this emphasizes that this disease affects both the stroma and the epithelium. Peptidergic and nitric oxide synthase–containing neurons also have been found in the prostate and may affect smooth muscle relaxation ***(Burnett, 1995).***

PATHOPHYSIOLOGY OF BPH

Hyperplasia:-

In a given organ, the number of cells, and thus the volume of the organ, is dependent upon the equilibrium between cell proliferation and cell death. An organ can enlarge not only by an increase in cell proliferation but also by a decrease in cell death ***(Isaacs and Coffey, 1987).***

Although androgens and growth factors stimulate cell proliferation in experimental models, the relative role of cell proliferation in human BPH is questioned because there is no clear evidence of an active proliferative process. Although it is possible that the early phases of BPH are associated with a rapid proliferation of cells ***(Kyprianou et al., 1996).***

BPH may be viewed as a stem cell disease. Presumably, dormant stem cells in the normal prostate rarely divide, but when they do, they give rise to a second type of transiently proliferating cell capable of undergoing DNA synthesis and proliferation ***(Barrack and Berry, 1987).***

The Role of Androgens: -

Although androgens do not cause BPH, the development of BPH requires the presence of testicular androgens during prostate development, puberty, and aging. Patients castrated prior to puberty or who are affected by a variety of genetic diseases that impair androgen action or production do not

develop BPH. It is also known that prostatic levels of dihydrotestosterone (DHT) as well as the androgen receptor (AR) remain high with aging despite the fact that peripheral levels of testosterone are decreasing. Moreover, androgen withdrawal leads to partial involution of established BPH ***(McConnell et al., 1994).***

Assuming normal ranges, there is no clear relationship between the concentration of circulating androgens and prostate size in aging men ***(Roberts et al., 2004).***

Despite the importance of androgens in normal prostatic development and secretory physiology, there is no evidence that either testosterone or DHT serves as the direct mitogen for growth of the prostate in older men. However, many growth factors and their receptors are regulated by androgens. Thus, the action of testosterone and DHT in the prostate is mediated indirectly through autocrine and paracrine pathways ***(Wang et al., 1997).***