

## Effect of Doxazosin on Prostatic Resistive Index in Patients with Benign Prostate Hyperplasia

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### ABSTRACT

**Objective:** In recent years several studies revealed that prostatic resistive index (RI) was increased on power Doppler imaging (PDI) in patients with benign prostate hyperplasia (BPH). In the present study we aimed to evaluate the effect of Doxazosin on prostatic RI in BPH patients.

**Materials and Methods:** Forty BPH patients with lower urinary tract symptoms included in this study. All patients received 8mg Doxazosin daily for six months. International prostatic symptom scores (IPSS), maximal urine flow rates (Qmax), total prostate volumes and prostatic RI determination with PDI were compared before and after the treatment.

**Results:** The mean age, IPSS and Qmax of the patients was 60.2±2 years, 20.3±4.5 and 11.3±3.0 mL/s respectively. There was a positive correlation between prostatic RI, total prostate volume and IPSS before the treatment ( $r=0.37$   $p=0.02$  and  $r=0.40$   $p=0.017$ , respectively). On the other hand there was a negative correlation between prostatic RI and Qmax values ( $r=-0.38$   $p=0.021$ ). There was a significant improvement in IPSS scores and Qmax values after the treatment (7.9±5.3 and 16.8±5.8 mL/s respectively,  $p<0.05$ ). It was demonstrated that prostatic RI of the patients significantly decreased when compared to pretreatment levels (0.74±0.06 and 0.69±0.05 respectively,  $p<0.05$ ).

**Conclusion:** Our data demonstrated that Doxazosin treatment significantly decreased prostatic RI of the patients with BPH. We believe that prostatic RI could be a useful parameter for the follow-up of patients receiving medical treatment with BPH.

**Key words:** Benign prostate hyperplasia, doxazosin, power doppler imaging, resistive index, transrectal ultrasonography

### ÖZET

#### Benign Prostat Hiperplazili Hastalarda Doksazosinin Prostatik Rezistif İndeks Üzerine Etkisi

**Amaç:** Son yıllarda yapılan birkaç çalışmada benign prostat hiperplazili (BPH) hastaların power doppler ultrasonografi (USG) ile tespit edilen prostatik rezistif indekslerinde artış tespit edilmiştir. Bu çalışmada BPH'lı hastalarda doksazosin tedavisinin prostatik rezistif indeks üzerine etkisi değerlendirildi.

**Gereç ve Yöntemler:** Çalışmaya alt üriner sistem semptomları nedeniyle BPH düşünülen 40 hasta alındı. Tüm hastalara 6 ay boyunca günde 8 mg doksazosin tedavisi verildi. Tedavi öncesi ve sonrası hastaların uluslararası semptom skorları (IPSS), maksimal akım hızları (Qmax), total prostat volümleri (TPV) ve power doppler USG ile tespit edilen prostatik rezistif indeksleri karşılaştırıldı.

**Bulgular:** Hastaların ortalama yaşı 60.2±2 yıl, IPSS 20.3±4.5 ve Qmax 11.3 ±3.0 m/sn idi. Tedavi öncesi hastaların prostatik rezistive indeksi ile TPV ve IPSS arasında pozitif (sırasıyla,  $r=0.37$   $p=0.02$  ve  $r=0.40$   $p=0.017$ ), Qmax arasında negatif korelasyon tespit edildi ( $r=-0.38$   $p=0.021$ ). Tedavi sonrası hastaların IPSS ve Qmax değerlerinde anlamlı derecede iyileşme mevcuttu (sırasıyla, 7.9±5.3 ve 16.8±5.8,  $p<0.05$ ). Tedavi öncesine göre hastaların prostatik rezistif indekslerinin anlamlı derecede azaldığı tespit edildi (sırasıyla, 0.74±0.06 ve 0.69±0.05,  $p<0.05$ ).

**Sonuç:** Elde ettiğimiz veriler BPH'lı hastalarda doksazosin tedavisinin prostatik rezistif indeksi anlamlı derecede azalttığını göstermiştir. Bu nedenle medikal tedavi verilen BPH'lı hastaların takibinde prostatik rezistif indeks faydalı bir parametre olabilir.

**Anahtar Sözcükler:** Benign prostat hiperplazisi, doksazosin, prostatik rezistif indeks, power doppler görüntüleme, transrektal ultrasonografi

Benign prostatic hyperplasia (BPH) is the most common benign disease in older men. Autopsy studies have revealed histologic evidence of BPH in 42% of men aged 51-60 years, rising to 85% among men older than 80 years (1). Severe BPH leads to deterioration in the quality of life of afflicted men and its treatment has serious economic implications (2). Infravesical obstruction in symptomatic BPH is considered to be the combined effect of both mechanic obstructions (static component) by an enlarged adenoma and prostate smooth muscle tone (dynamic component) (3).

Current therapy for BPH includes watchful waiting,

pharmacological therapy and surgical intervention. In the past decade there has been a growing affinity for pharmacological therapy as the first-line management; it is preferred by physicians and patients because it is reversible and less invasive than surgery (4). Alpha-1 adrenoreceptor antagonists, e.g. Doxazosin, Alfuzosin, Terazosin and Tamsulosin, reduce prostatic smooth muscle tone (relax the bladder outlet to improve urinary flow) through the blockade of sympathetic adrenergic receptors (5, 6).

Uroflowmetry, pressure-flow studies and IPSS (International prostatic symptom scores) are frequently used for

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evaluation of patient with BPH (7). Although the pressure-flow studies provide the most valuable information in patients with lower urinary tract symptoms (LUTS), there are various morbidity reports published on the literature. Additionally researchers reported that urodynamic studies are expensive and hardly tolerated by the patients (8, 9).

In the recent years prostatic resistive index (RI) measured by power Doppler imaging (PDI) used for to evaluate patients BPH (10-12). Kojima et al. (13) are the first authors who proposed prostatic RI as a diagnostic tool to differentiate BPH patients from normal patients. Researchers reported that BPH development increased vascular resistance and prostatic RI measurements. Additionally RI of the prostatic capsular arteries positively correlated with IPSS and negatively correlated with maximal urine flow rate (Qmax) (14). However the effect of alpha-adrenoreceptor blocker treatment on prostatic RI is not clear yet. In the present study we evaluated the effect of alpha-adrenoreceptor blocker treatment with Doxazosin on prostatic RI.

## MATERIALS AND METHODS

Between January and July 2007, 40 consecutive BPH patients with LUTS, whose age  $\geq 50$ , seen in the urology outpatient clinic, included in this prospective study. Patients with a history of prostatic malignancy, surgery of the prostate, bladder neck or urethral stricture, who received previous treatments for LUTS and those with neurologic diseases affecting the lower urinary tract, excluded from the study. Before the treatment all patients were evaluated in details including past medical history, IPSS, physical examination, digital rectal examination, complete blood count, blood biochemistry, urine analysis, prostate specific antigen (PSA) and uroflowmetry. Serum PSA levels were measured by using monoclonal Tandem-R assay (Hybritech Inc., San Diego, CA, USA). All patients fully informed about the medical treatment and consent forms were provided.

Prostatic RI was measured using PDI by single radiologist (TD). Ultrasound examination consisted of transrectal ultrasonography (TRUS) and PDI using an SSA 380A unit (Toshiba Corp., Japan) with a convex, 7-MHz transrectal probe. Each patient was asked to empty his urinary bladder to

preclude compression of the intraprostatic vasculature. At the area of greatest transverse diameter in the axial plane, the antero-posterior and transverse dimensions of prostate were measured and recorded. Blood flow measurements were obtained from capsular arteries on the largest transverse section of prostate, followed by spectral waveform analysis. When pulsatile waveforms of a given Doppler spectrum became stable, RI (maximum velocity-minimum velocity/maximum velocity) was measured from each blood flow sample using on-board software and the mean value was recorded. During the whole ultrasonographic study, care was taken to avoid excess probe pressure on the rectal wall.

After the PDI measurements, 8mg/day Doxazosin were administered starting from 2mg/day and titrating the dose every 2 weeks to 4mg and finally 8mg/day, and was continued for 6 months. After the treatment all patients were re-evaluated with PDI, IPSS and uroflowmetry.

All statistical analyses were performed by using Statistical Packet for Social Science (SPSS) software, version 11.5 (SPSS Inc., Chicago, USA). Descriptive statistics were presented as mean $\pm$ standard deviation (SD). Statistical analyses were performed by using the Spearman's Correlation Coefficient and Wilcoxon Sign Rank test. When p values  $<0.05$  considered as statistically significant.

## RESULTS

Mean age of the patients was 60.2 $\pm$ 2 years, IPSS 20.3 $\pm$ 4.5 and Qmax was 11.3 $\pm$ 3.0 mL/s. The mean prostatic RI of the patients before Doxazosin treatment was 0.74 $\pm$ 0.06 and 65% of the patients had prostatic RI  $\geq 0.70$ . Prostatic RI correlated positively with total prostate volume and IPSS ( $r=0.37$   $p=0.02$  and  $r=0.40$   $p=0.017$  respectively) and negatively correlated with Qmax ( $r=-0.38$   $p=0.021$ ) prior to treatment.

After six months of alpha-adrenoreceptor blocker treatment with Doxazosin, mean IPSS and prostatic RI significantly decreased (7.9 $\pm$ 5.3 and 0.69 $\pm$ 0.05 respectively,  $p<0.05$ ), whereas mean Qmax was increased (16.8 $\pm$ 5.8 mL/s, Table 1). Furthermore 70% of the patients had prostatic RI of  $<0.70$  after the treatment.

**Table 1.** Changes in parameters from before to after treatment.

	Pretreatment	Posttreatment	*p value
** IPSS (0-35)	20.3 $\pm$ 4.5	7.9 $\pm$ 5.3	0.0001
Maximal urine flow rate (mL/s)	11.3 $\pm$ 3.0	16.8 $\pm$ 5.8	0.0001
Post voiding residual urine (mL)	66.6 $\pm$ 79.6	55.8 $\pm$ 68.4	0.17
Total Prostate volume (mL)	34.8 $\pm$ 10.9	35.0 $\pm$ 10.8	0.55
Prostate specific antigen (ng/mL)	1.8 $\pm$ 2.2	1.7 $\pm$ 1.8	0.37
Prostatic resistive index	0.74 $\pm$ 0.06	0.69 $\pm$ 0.05	0.0001

\* Wilcoxon sign rank test

\*\* International prostatic symptom scores

## DISCUSSION

The recent advancement of PDI has greatly improved the ability to detect and analyze Doppler signals from blood

flows in organs. Additionally power and color Dopplers are now available on transrectal probes and this improvement has

provided a new potential for improved diagnosis of BPH through the detection of intraprostatic vascularity (12,13). PDI is 3-5 fold sensitive when compared to conventional color Doppler imaging, because it does not have angle dependence, lack of aliasing and does not have background noise. Additionally PDI provided a significant improvement in recognizing and analyzing prostatic blood flow signals (15-17).

In the recent years researchers demonstrated that the measurement of prostatic RI could be useful for differentiate BPH patients from patients which do not have lower urinary tract symptoms (12,14). Kojima et al. (13) showed that prostatic RI was  $\geq 0.7$  in 70% of the patients with BPH. Similarly in our study prostatic RI was  $\geq 0.7$  in 65% of the patients with BPH.

Increase in the intraprostatic pressure due to the massive effect of the prostate could compress the prostatic vessels like the urethra. The increase in the intraprostatic pressure in the prostatic vessels due to BPH could lead to a change in the Doppler signals. Furthermore it is proposed that RI is increased in BPH development because of increasing intraprostatic pressure (12,13). Significant decrease in the prostatic RI following surgery in BPH patients supports this assumption (10). In previous studies it was demonstrated that prostatic RI significantly related to IPSS and Qmax (11,14). Similarly in our study prostatic RI positively correlated with total prostate volume and IPSS, and negatively correlated with Qmax.

Previous studies also reported that Doxazosin treatment significantly improved IPSS and Qmax in patients with BPH (18,19). Additionally MacDiarmid et al. (20) stated that 8mg

Doxazosin was more effective for relieving lower urinary tract symptom compared to 4mg Doxazosin in patients with BPH. Similarly in our study 8mg Doxazosin treatment provided significant improvements in IPSS and Qmax levels. Clinical response to alpha-adrenoreceptor blocker treatment in BPH patients is related to smooth muscle density in the prostate (21,22). Prostatic RI is reported to be a good ecographic index for to determine epithelium/smooth muscle rate in the glandular portion of the prostate (11). These types of investigations are efficacious for determining the therapeutic effect of alpha-adrenoreceptor blocker drugs.

Previous studies demonstrated that alpha-adrenoreceptor blocker treatment in patients with BPH significantly decreased IPSS whereas Qmax significantly increased in the follow-up (18,19). On the other hand the effect of alpha-adrenoreceptor blocker treatment on prostatic RI is not clear yet. In the present study alpha-adrenoreceptor blocker treatment significantly improved maximal urine flow rate and IPSS whereas significantly decreased prostatic RI. Additionally 70% of the patients had prostatic RI of  $< 0.70$  after alpha-adrenoreceptor blocker treatment.

## CONCLUSIONS

Our data demonstrated that Doxazosin treatment significantly increased Qmax whereas decreased IPSS and prostatic RI in BPH patients. On this purpose prostatic RI measured with PDI in addition to IPSS and Qmax in BPH patients could be a useful parameter for the follow-up after alpha-adrenoreceptor blocker treatment. These results should be confirmed with larger placebo controlled studies.

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