Influence of Tamsulosin on the Anterior Segment Parameters and Central Corneal Thickness

Tamsulosinin Ön Segment Parametreleri ve Santral Kornea Kalınlığına Etkisi

Melis PALAMAR,[a]
Sinan EMRE,[b]
Burak TURNA,[c]
Ayşe YAĞCI[a]

Departments of
[a]Ophthalmology,
[c]Urology,
Ege University Faculty of Medicine,
İzmir,
[b]Department of Ophthalmology,
Celal Bayar University
Faculty of Medicine, Manisa

Yazışma Adresi/Correspondence:
Melis PALAMAR
Ege University Faculty of Medicine,
Department of Ophthalmology, İzmir,
TÜRKİYE/TURKEY
melispalamar@hotmail.com

ABSTRACT Objective: To investigate the effects of tamsulosin (α-1 adrenergic receptor antagonist) on the main numerical parameters of anterior segment using Pentacam rotating Scheimmpflug camera, and on biomechanical parameters using Reichert Ocular Response Analyser (ORA) in patients with benign prostate hyperplasia. **Material and Methods:** In addition to full eye examination [best corrected visual acuity, keratometry, intraocular pressure (IOP) measured with Goldmann applanation tonometry], Pentacam [central corneal thickness (CCT), anterior chamber depth, anterior chamber volume, anterior chamber angle, pupil diameter] and ORA (corneal hysteresis, corneal resistance factor, corneal compensated IOP, Goldmann correlated IOP) measurements of 30 eyes of 15 male patients were performed before and one month after tamsulosin therapy. Paired t-test and non-parametric Wilcoxon test were used for comparisons. **Results:** Mean age in the study group was 61.50±6.10 (range 47-69) years. After tamsulosin treatment, CCT increased and this increment was statistically significant (p=0.002). None of the other parameters that were evaluated showed statistically significant difference after tamsulosin use. **Conclusion:** Tamsulosin leads to significant increment in CCT. The effects of tamsulosin on CCT should be taken into consideration for proper clinical interpretation in patients using tamsulosin.

Key Words: Anterior eye segment; corneal topography; tamsulosin

ÖZET Amaç: Tamsulosinin (α1 adrenerjik reseptör antagonisti) benign prostat hiperplazili olgularda Pentacam Scheimmpflug kamera sistemi ile çekilen ön segment nümerik parametrelerine ve Reichert Ocular Response Analyser (ORA) cihazı ile korneanın biomekanik parametreleri üzerine olan etkilerinin değerlendirilmesi. **Gereç ve Yöntemler:** Toplam 15 erkek olgunun 30 gözüne tamsulosin tedavisi öncesi ve sonrası tam oftalmolojik muayene (en iyi düzeltilmiş görme keskinliği, keratometri, Goldmann aplanasyon tonometrisi ile ölçülmüş göziçi basıncı (GİB), Pentacam [santral kornea kalınlığı (SKK), ön kamara derinliği, ön kamara hacmi, ön kamara açısı, pupil çapı] ve ORA (korneal histerezis, korneal direnç faktörü, korneal düzeltilmiş GİB, Goldmann düzeltilmiş GİB) ölçümleri yapıldı. Karşılaştırmalar için eşleştirilmiş t-testi ve non-parametrik Wilcoxon testleri kullanıldı. **Bulgular:** Çalışma grubunun ortalama yaşı 61,50±6,10 (47 ve 69 arasında) idi. SKK tamsulosin tedavisi sonrasında öncesine göre artış gösterdi ve bu artış istatistiksel olarak anlamlı idi (p=0,002). Değerlendirilen diğer parametrelerden hiçbiri tamsulosin kullanımı sonrasında istatistiksel olarak anlamlı farklılık göstermemekteydi. **Sonuç:** Tamsulosin SKK'da belirgin artışa neden olmaktadır. Tamsulosinin SKK üzerine etkisi tamsulosin kullanan hastalarda doğru klinik yorumlama için göz önünde tutulmalıdır.

Anahtar Kelimeler: Anterior göz segmenti; kornea topografisi; tamsulosin

Benign prostatic hyperplasia (BPH) is a common urological condition treated widely with α-1 adrenergic receptor antagonists because of their good clinical efficacy. Intraoperative Floppy Iris Syndrome

(IFIS) is a problem complicating cataract surgery, usually observed in patients receiving systemic α-1 adrenergic receptor antagonists-most commonly with tamsulosin (Flomax®), a specific α-1-a adrenergic receptor antagonist.[1,2] The overall prevalence of IFIS in patients undergoing cataract surgery is reported to be around 2%, whereas as many as 63% IFIS positive patients were found to be receiving tamsulosin.[1] In a typical IFIS case, a flaccid, poorly dilated iris undulates and billows in response to ordinary fluid currents, and the stroma of the iris tends to prolapse through the main and side-port incisions.[1] These effects on the iris and pupil have been evaluated previously with various instruments and techniques since 2005.[2-5] Although, tamsulosin is a broadly prescribed medication in patients with lower urinary tract symptoms associated with BPH, little is known regarding its effects on the other compartments of the eye. We therefore have decided to evaluate the effects of tamsulosin on the cornea and anterior chamber in a prospective study based on the reported changes on the iris.

The Pentacam, rotating Scheimmpflug camera (Oculus Optikgeräte GmbH, Wetzlar, Germany) promises quantitative information and qualitative imaging of the anterior and posterior surfaces of the cornea, anterior chamber depth, anterior chamber angle, iris and lens.[6]

Hysteresis is a measurement of viscous properties, whereas the corneal resistance factor (CRF) is dominated by elastic properties of cornea and is an overall indicator of the corneal resistance. It has been shown that corneal hysteresis (CH) and CRF measured by Ocular Response Analyzer (ORA) are correlated with central corneal thickness (CCT).[7] These results suggest CH and CRF are closely related, but they do not represent the same physical/biomechanical properties. A new device, ORA (Reichert, Inc, Depew, NY), has been developed to measure the intraocular pressure (IOP) and CH and CRF. In addition to being a non-contact tonometer, this new device has an electro-optical detector system, which monitors the corneal curvature in the central 3.0-mm diameter throughout the 20-millisecond measurement.

To our knowledge, no study to date has evaluated the effects of tamsulosin on the other structures of anterior segment, except for iris, and central corneal thickness. For this purpose, the anterior chamber parameters, central corneal thickness and corneal biomechanics were evaluated with Scheimmpflug camera system and ORA in this prospective study in patients with clinical symptoms of BPH treated with tamsulosin.

MATERIAL AND METHODS

A total of 15 male patients with clinical symptoms of BPH of whom tamsulosin was prescribed were enrolled in this study. Patients with corneal pathology, glaucoma, uveitis, previous eye surgery or eye trauma, posterior segment pathology, and those using topical/systemic medications that might influence anterior segment parameters were excluded. No patients with any systemic diseases, even systemic hypertension, were included in the study. All patients signed informed consents.

Between November 2010 and March 2011, 30 eyes of these 15 patients underwent full ocular examination prior to tamsulosin therapy initiation, and one month following tamsulosin use. Besides full ocular examination [best corrected visual acuity (BCVA), IOP with Goldmann applanation tonometry, etc.] measurements with Pentacam and ORA were performed. IOP was measured with Goldmann applanation tonometry, and as corneal compensated (IOPcc) and as Goldmann correlated (IOPg) on the computer screen attached to the ORA.

All Pentacam measurements were obtained under standard dim light conditions, as described previously.[8] The Pentacam CES system is based on a 180° rotating Scheimpflug camera which can take 12-50 single images to reconstruct the anterior chamber. In this study, anterior segment reconstructions were produced with 25 single captures. After completing a scan, Pentacam software constructs the 3-dimensional image of the anterior segment and calculates the anterior chamber parameters. This imaging provides measurements

of anterior chamber depth (ACD), anterior chamber volume (ACV), anterior chamber angle (ACA) width, CCT, pupil size, and keratometry.

Non-contact IOP and hysteresis were measured by ORA. The patients were asked to fixate at the target in the instrument (red-blinking light), and ORA was activated by pressing a button attached to the computer as described previously.[9] A non-contact probe scanned the central area of the eye and released an air puff and then sent a signal to the ORA. ORA calculated and then displayed the hysteresis, CRF, and IOP both as corneal compensated (IOPcc) and as Goldmann correlated (IOPg) on the computer screen attached to the ORA. Subjects underwent testing with the ORA by an experienced ophthalmologist. Four to five measurements were obtained for each eye, and the average of these measurements per eye was considered for analysis.

Repeatability analysis of study parameters measured with Pentacam was previously evaluated with coefficient of variation (CV).[8] CV is defined as the ratio of the standard deviation to the mean:

$$cv = \frac{\sigma}{\mu}$$

For CV calculation of study parameters measured by Pentacam, 10 consequential measurements were performed by same operator to the same adult volunteer's same eye with a period of 2 min.

Statistical analysis was performed with SPSS for Windows Version 16.0 (SPPS Inc., Chicago, IL, USA). Except BCVA, all data were reported as mean±standard deviations (SD). BCVA values were reported as median. A paired t-test was used to compare variables between the pre- and post-tamsulosin conditions except for BCVA comparison in which Wilcoxon test was used for pre-post comparison. A value of p<0.05 was considered statistically significant.

RESULTS

The mean age of the patients was 61.50±6.10 (range 47-69) years. Median pre-tamsulosin BCVA was 0.00000 (min-max: 0-0.3) logMAR. Median post-tamsulosin BCVA was 0.00000 (min-max: 0-0.3) logMAR (p=0.180, Wilcoxon test).

Mean horizontal keratometric value was 45.03±1.38 D before tamsulosin initiation, and 44.89±1.48 D one month after tamsulosin use (p= 0.254, paired t-test) (Table 1). Mean vertical keratometric value was 45.20±1.70 D and 45.29±1.83 D, before and after tamsulosin use, respectively. This difference was statistically insignificant (p= 0.265; paired t-test).

Mean ACD was 2.79±0.50 mm and 2.80±0.50 mm in pre- and post-tamsulosin periods, respectively (p =0.0671; paired t-test). Mean ACV was 128.05±23.67 mm³ before the treatment, and

TABLE 1: The pre- and post-tamsulosin measured values of keratometry, CCT, ACD, ACV, ACA, pupil diameter, CH, and CRF.					
	Study Group (n=30)				
	Pre-tamsulosin	Post- tamsulosin	Mean Difference	SD of the difference	p value
Mean horizontal keratometry	45.03 (±1.7)	44.89 (±1.4)	-0.14	0.56	0.254
Mean vertical keratometry	45.20 (±1.8)	45.29 (±1.8)	0.08	0.35	0.265
CCT	549.18 (±25)	556.77 (±24)	7.5	9.9	0.002*
ACD	2.79 (±0.4)	2.80 (±0.5)	0.01	0.16	0.0671
ACV	128.05 (±23)	126.32 (±24)	-1.72	6.0	0.196
ACA	33.20 (±5)	33.90(±5)	-0.65	2.5	0.247
Pupil diameter	2.60 (±0.5)	2.55 (±0.4)	-0.05	0.22	0.279
CH	9.23 (±1.6)	8.79 (±2.2)	-0.44	1.76	0.404
CRF	10.73 (±1.6)	9.45 (±1.4)	-1.28	1.37	0.071

SD: Standard deviation; CCT: Central corneal thickness; ACD: Anterior chamber depth; ACV: Anterior chamber volume; ACA: Anterior chamber angle; CH: Corneal hysteresis; CRF: Corneal resistance factor.

126.32±24.67 mm³ after the treatment (p=0.196; paired t-test). Mean ACA was 33.2±5.0 degrees pre-treatment, and 33.9±5.0 degrees post-treatment (p=0.247; paired t-test).

Mean CCT was 549.18±28.84 micrometers and 556.77±24.86 micrometers pre- and post-tamsulosin use, respectively. There was a mean of 7.50±9.98 micrometers increment in CCT after tamsulosin use, and this difference was statistically significant (p=0.002; paired t-test). Mean pupil size diameters were 2.60±0.38 micrometers and 2.55±0.48 micrometers pre- and, post-tamsulosin, respectively. However, this difference was statistically insignificant (p=0.279; paired t-test).

Mean CH was 9.23±1.78 mmHg in pre-treatment period, and 8.79±2.26 mmHg in the post-treatment period (p=0.404; paired t-test). Although there was a trend towards mean CRF differences between the pre- and post-treatment periods, this did not reach statistical significance (pre-: 10.73±1.05 mmHg, post-: 9.45±1.51 mmHg; p=0.071; paired t-test).

Mean IOP measured by Goldmann applanation tonometry was 15.43±2.84 mmHg (range 12-21) before the treatment, and 15.63±3.50 mmHg (range 12-21) after the treatment (p=0.604; paired t-test) (Table 2).

Mean IOPcc was 18.09±3.68 mmHg and 18.08±4.39 mmHg pre- and post-tamsulosin, respectively (p=0.987; paired t-test). Mean IOPg was 16.56±3.13 mmHg and 16.19±3.65 mmHg, pre- and post-tamsulosin, respectively (p=0.512; paired t-test).

DISCUSSION

Tamsulosin, an α-1-a/α-1-d subtype selective α-1-adrenoreceptor antagonist, is the most frequently prescribed medication for the treatment of lower urinary tract symptoms suggestive of BPH.[2,10,11] Tamsulosin was reported to lead IFIS, by causing diffuse atrophy and flaccidity of the iris by selectively blocking α-1-a-adrenergic receptors of the dilator iris muscle.[1] Several studies reported that patients taking tamsulosin did not only have a sluggish iris, but also a small pupil diameter, both making cataract surgery more challenging.[1,2] Some studies suggest that discontinuing tamsulosin preoperatively does not return the IFIS condition, which supports the hypothesis that the effects of tamsulosin are not temporary.[12,13] The effects of other α-1-adrenoreceptor antagonists regarding their effects on the iris are still under investigation.[14,15] Although there are various reports on the effect of tamsulosin on pupil diameter and iris morphology, there are no reports on the rest of anterior segment, central corneal thickness and corneal biomechanical changes.

Anterior segment evaluation is possible with various devices which provide quantitative and qualitative data.[8] Pentacam is a relatively new, non-contact optical system, specifically designed to image the anterior segment of the eye. It is an easy-to-use anterior segment analyzer with high reliability and repeatability.[16] However, the least trustable parameters of Pentacam were found to be ACA and pupil size as calculated by repeatability analysis.[8]

ORA is a new non-contact tonometer developed by Reichert, that measures IOP and new met-

TABLE 2: The pre- and post-tamsulosin measured IOP-G, IOPcc and IOPg values.					
	Study Group (n=30)				
	Pre-tamsulosin	Post- tamsulosin	Mean Difference	SD of the difference	p value
Mean IOP-G	15.43	15.63	0.2	2.09	0.604
Mean IOPcc	18.09	18.08	-0.01	3.82	0.987
Mean IOPg	16.56	16.19	-0.37	2.72	0.512

IOP-G: Intraocular pressure with Goldmann applanation tonometry; IOPg: Goldmann correlated intraocular pressure; IOPcc corneal compensated intraocular pressure.

rics, CH and CRF. It uses a metered collimated air pulse to applanate the cornea and an infrared electro-optical system to record inward and outward applanation events. The air pulse deforms the cornea through an initial applanation event, then beyond into concavity, and gradually subsides, allowing the cornea to rebound through a second applanation. This dynamic assessment of corneal biomechanical properties yields metrics of both the cornea's viscous and elastic qualities as CH and CRF, respectively.[17]

In the present study, there were no changes regarding BCVA, horizontal and vertical keratometric values after tamsulosin use. Similarly, no changes were detected as regards to ACD, ACV, and ACA measured with Pentacam. However, the increase in CCT was statistically significant one month after initiation of tamsulosin treatment. The presence of α-1 receptors in freshly fixed human corneal epithelium and endothelium was demonstrated by Grueb et al.[18] Moreover, direct radioligand binding studies indicate that intact corneal epithelial and endothelial cells exhibit α-1 adrenergic receptors.[19] Alpha-1 adrenergic receptors seem to be associated with regulation of inositol-1,4,5-tris-phospate formation.[20] The physiological role of α-1 adrenergic receptors and their second messengers phosphatidyl inositol and cyclic AMP in corneal epithelium and endothelium is not clear. However, they may be involved in the regulation of corneal homeostasis and fluid transportation. This possibility might explain the CCT increment after tamsulosin use due to α-1 receptor blockage.

Parsinen et al. measured the pupillary diameter of 16 patients on tamsulosin underwenting cataract surgery.[2] Pupil diameter of these patients were measured by a pupillometer 20 minutes after dilation with phenylephrine and tropicamide.[2] However, no statistical difference was noted between the pupil size of patients under tamsulosin treatment and the healthy controls. The authors concluded that the size of the pupil in patients under tamsulosin treatment was only significantly smaller than control healthy individuals under mesopic low and high levels of illumination prior to dilation.[2] There are other studies reporting no

changes in the mesopic and dilated pupil diameters after tamsulosin and other α-antagonists' use.[12] In the present study, we did not observe any significant changes in the pupil diameter size under dim light conditions as measured by Pentacam. Although pupil diameter is the least repeatable and reliable parameter of Pentacam, our findings are similar to Issa et al., in which they used gauge for measurement.[8,12]

The Goldmann-IOP, IOPcc and IOPg values did not display any differences one month after the tamsulosin treatment. Despite the increment in CCT measurements, we did not observe any changes in none of the IOP values.

Although there was no statistically significant changes in CH and CRF following one month of tamsulosin therapy, the increment in CRF was close to statistical significance (p=0.071). One may concern that if the follow-up period was longer, this increase would have been more distinct.

The limitation of our study is the short follow-up time after the initiation of tamsulosin therapy. However, the steady-state plasma concentration is reported to be reached at the fifth day of tamsulosin therapy, and maximum effect is reported to take place in the second week.[21-23] Moreover, tamsulosin related IFIS was observed after 2 weeks of use as reported by Chang et al.[24] Therefore, we believe one month period is sufficient to observe any possible changes of tamsulosin use in the anterior segment.

In conclusion, there were no differences in terms of BCVA, IOP, keratometry, pupil diameter, ACD, ACV, ACA, CH, and CRF compared with pre- and post-tamsulosin use. However, one month use of tamsulosin affects the CCT parameter in the anterior segment of the eye. This might influence not only the outcome of corneal surgical procedures such as laser in situ keratomileusis, but also the decision of cataract surgery in the long term, and should be regarded for proper interpretation of these patients. Therefore, long term effects of tamsulosin on the anterior segment parameters as well as corneal biomechanics require further investigation.

REFERENCES

1. Chang DF, Campbell JR. Intraoperative floppy iris syndrome associated with tamsulosin. J Cataract Refract Surg 2005;31(4):664-73.

2. Pärssinen O, Leppänen E, Keski-Rahkonen P, Mauriala T, Dugué B, Lehtonen M. Influence of tamsulosin on the iris and its implications for cataract surgery. Invest Ophthalmol Vis Sci 2006;47(9):3766-71.

3. Prata TS, Palmiero PM, Angelilli A, Sbeity Z, De Moraes CG, Liebmann JM, et al. Iris morphologic changes related to alpha(1)-adrenergic receptor antagonists implications for intraoperative floppy iris syndrome. Ophthalmology 2009;116(5):877-81.

4. Arikan G, Demir O, Yaman A, Bozkurt O, Saatci AO, Durak I, et al. The effect of various alpha1-adrenergic receptor antagonists on pupillary dilation. Ann Ophthalmol (Skokie) 2008;40(1):19-21.

5. Santaella RM, Destafeno JJ, Stinnett SS, Proia AD, Chang DF, Kim T. The effect of alpha1-adrenergic receptor antagonist tamsulosin (Flomax) on iris dilator smooth muscle anatomy. Ophthalmology 2010;117(9):1743-9.

6. Kim JH, Lim T, Kim MJ, Tchah H. Changes of higher-order aberrations with the use of various mydriatics. Ophthalmic Physiol Opt 2009;29(6):602-5.

7. Shah S, Laiquzzaman M, Cunliffe I, Mantry S. The use of the Reichert ocular response analyser to establish the relationship between ocular hysteresis, corneal resistance factor and central corneal thickness in normal eyes. Cont Lens Anterior Eye 2006;29(5):257-62.

8. Palamar M, Egrilmez S, Uretmen O, Yagci A, Kose S. Influences of cyclopentolate hydrochloride on anterior segment parameters with Pentacam in children. Acta Ophthalmol 2011;89(5):e461-5.

9. Emre S, Kayikçioğlu O, Ateş H, Cinar E, Inceoğlu N, Yargucu F, et al. Corneal hysteresis, corneal resistance factor, and intraocular pressure measurement in patients with scleroderma using the reichert ocular response analyzer. Cornea 2010;29(6):628-31.

10. Dunn CJ, Matheson A, Faulds DM. Tamsulosin: a review of its pharmacology and therapeutic efficacy in the management of lower urinary tract symptoms. Drugs Aging 2002;19(2):135-61.

11. Chapple C, Andersson KE. Tamsulosin: an overview. World J Urol 2002;19(6):397-404.

12. Issa SA, Hadid OH, Baylis O, Dayan M. Alpha antagonists and intraoperative floppy iris syndrome: A spectrum. Clin Ophthalmol 2008;2(4):735-41.

13. Nguyen DQ, Sebastian RT, Kyle G. Surgeon's experiences of the intraoperative floppy iris syndrome in the United Kingdom. Eye (Lond) 2007;21(3):443-4.

14. Altan-Yaycioglu R, Yaycioglu O, Gul U, Pelit A, Adibelli FM, Akova YA. The effects of two systemic alpha1-adrenergic blockers on pupil diameter: a prospective randomized single-blind study. Naunyn Schmiedebergs Arch Pharmacol 2007;375(3):199-203.

15. Carifi G, Theoulakis P. The effect of alpha antagonists on pupil dynamics: implications for the diagnosis of intraoperative floppy iris syndrome. Am J Ophthalmol 2012;154(3):611-2; author reply 612-3.

16. Barkana Y, Gerber Y, Elbaz U, Schwartz S, Ken-Dror G, Avni I, et al. Central corneal thickness measurement with the Pentacam Scheimpflug system, optical low-coherence reflectometry pachymeter, and ultrasound pachymetry. J Cataract Refract Surg 2005;31(9):1729-35.

17. Pepose JS, Feigenbaum SK, Qazi MA, Sanderson JP, Roberts CJ. Changes in corneal biomechanics and intraocular pressure following LASIK using static, dynamic, and noncontact tonometry. Am J Ophthalmol 2007;143(1):39-47.

18. Grueb M, Wallenfels-Thilo B, Denk O, Mielke J, Reinthal E, Rohrbach JM, et al. Monoamine receptors in human corneal epithelium and endothelium. Acta Ophthalmol Scand 2006;84(1):110-5.

19. Walkenbach RJ, Bylund DB, Chao WT, Gibbs SR. Adrenergic and cholinergic receptors in the cornea. Invest Ophthalmol Vis Sci 1983;24(Suppl):198.

20. Walkenbach RJ, Ye GS, Reinach PS, Boney F. Alpha 1-adrenoceptors in human corneal epithelium. Invest Ophthalmol Vis Sci 1991;32(12):3067-72.

21. Franco-Salinas G, de la Rosette JJ, Michel MC. Pharmacokinetics and pharmacodynamics of tamsulosin in its modified-release and oral controlled absorption system formulations. Clin Pharmacokinet 2010;49(3):177-88.

22. Wilde MI, McTavish D. Tamsulosin. A review of its pharmacological properties and therapeutic potential in the management of symptomatic benign prostatic hyperplasia. Drugs 1996;52(6):883-98.

23. Buzelin JM, Fonteyne E, Kontturi M, Witjes WP, Khan A. Comparison of tamsulosin with alfuzosin in the treatment of patients with lower urinary tract symptoms suggestive of bladder outlet obstruction (symptomatic benign prostatic hyperplasia). The European Tamsulosin Study Group. Br J Urol 1997;80(4):597-605.

24. Chang DF, Osher RH, Wang L, Koch DD. Prospective multicenter evaluation of cataract surgery in patients taking tamsulosin (Flomax). Ophthalmology 2007;114(5):957-64.