



Research

Retrospective Evaluation of P-wave Dispersion on ECG in Terms of Atrial Fibrillation Dispersion in Patients Using Alpha-blockers for Lower Urinary Tract Symptoms

Alt Üriner Sistem Semptomları Nedeni ile Alfa-bloker Kullanan Hastalarda EKG’de P-dalga Dispersiyonunun Atriyal Fibrilasyon Dispersiyonu Açısından Retrospektif Olarak Değerlendirilmesi

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ABSTRACT

Objective: The incidence of benign prostatic hyperplasia (BPH) directly increases with age, and side effects related to drugs in the alpha-blocker group used in these patients are more important. In this study, we evaluated the safety of tamsulosin in cardiac arrhythmias, which are common in this age group.

Methods: Between May and June 2017, 835 patients with BPH were evaluated retrospectively. Patients with cardiovascular and endocrine system diseases were excluded from the study. In 55 patients who met the study criteria, tamsulosin was started as BPH treatment. Moreover, a control group was formed with patients who had not on tamsulosin treatment yet. Electrocardiographies (ECGs) of 37 patients who completed 3 weeks of tamsulosin use were obtained. Control and reference P-wave distribution (PWD) were calculated for each patient. The difference between the largest and narrowest p-waves on the ECG was calculated to determine the PWD. PWD values before and after treatment were compared.

Results: The mean age was 53.6±8 years. PWD values in reference and control ECG were calculated and compared. While the mean PWD was 55 ms (30-75) before tamsulosin use, it was 60 ms (45-70) 3 weeks after tamsulosin use.

Conclusion: PWD change in ECG was found to be significant in patients with BPH patients treated with tamsulosin. According to the results, an increase in PWD is a finding that indicates an increased risk of supraventricular tachycardia. Therefore, the clinician should be more careful when using tamsulosin in these patients.

Keywords: Alpha-blocker, arrhythmogenic, benign prostate hyperplasia

ÖZ

Amaç: Benign prostat hiperplazisinin (BPH) insidansı yaşla birlikte doğrudan artmaktadır ve bu hastalarda kullanılan alfa-bloker grubundaki ilaçlara bağlı yan etkilerin sonuçları daha kritik olabilmektedir. Bu nedenle, bu çalışmamızda, BPH tedavisi alan yaş grubunda sık görülen kardiyak aritmiler açısından, alfa-bloker olarak tamsulosin kullanarak tedavinin güvenilirliğini değerlendirmeyi amaçladık.

Gereç ve Yöntem: Mayıs-Haziran 2017 tarihleri arasında BPH şikayeti olan 835 hasta retrospektif olarak değerlendirildi. Kardiyovasküler ve endokrin sistem hastalığı olanlar çalışmaya alınmadı. Çalışma kriterlerine uyan 55 hastaya tamsulosin başlandı. Üç haftalık tamsulosin kullanımını tamamlayan 37 hastanın elektrokardiyografileri (EKG) çekildi. Her bir hasta için kontrol ve referans P-dalga dağılımı (PWD) hesaplandı. PWD, EKG’deki en büyük ve en dar P-dalgaları arasındaki fark bulunarak hesaplandı. Kontrol grubu henüz ilaç tedavisine başlanmamış hastalardan oluşturuldu. Tedavi öncesi ve sonrası ortalama PWD değerleri karşılaştırıldı.

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ÖZ

Bulgular: Ortalama yaş $53,6 \pm 8$ bulundu. Referans ve kontrol EKG'sinde PWD değerleri hesaplandı ve karşılaştırıldı. Tamsulosin kullanımından önce ortalama PWD 55 ms (30-75) iken tamsulosin kullanımından 3 hafta sonra ortalama PWD 60 ms (45-70) olarak ölçüldü.

Sonuç: Tamsulosin kullanan hastalarda EKG'de PWD artışı istatistiksel olarak anlamlı bulundu. PWD artışı supraventriküler taşikardi riskinin arttığını gösteren bir bulgu olduğundan, bu grup hastalarda tamsulosin kullanırken klinisyenin daha dikkatli olması gerektiğini düşünmekteyiz.

Anahtar Kelimeler: Benign prostat hiperplasia, aritmi, alfa-bloker

INTRODUCTION

The use of alpha-adrenergic receptor blockers has opened a new era since the 1980s, particularly in the symptomatic treatment of patients who do not require surgery due to benign prostate hypertrophy (BPH). Initially developed to treat hypertension, the antihypertensive efficacy of these molecules is not very potent, the effects are short-acting, and the development of tolerance to the effect over time have made these drugs more or less adjuvant medication for treating hypertension (1). Lately noticed that they showed their primary effects on the urinary system. Over the years, molecules with more selective affinity for alpha-receptor subgroups and longer half-lives have been developed (2,3).

Alpha-adrenergic receptors are found in the heart, at the adrenergic nerve endings, and on the cell surface of myocytes. Roughly, clinical observations have shown that alpha receptor blockers neither cause cardiac arrhythmias, or significant changes inotropic. Studies on QT dispersion in electrocardiography (ECG) are available in the literature (4).

P-wave distribution (PWD) is a noninvasive indicator of atrial remodeling and an early predictor of atrial fibrillation (AF). PWD represents prolonged interatrial transmission and an insufficiently coordinated transmission system. In the ECG, the PWD is the value obtained by subtracting the duration of the shortest P-wave from the longest P-wave duration measured by evaluating the entire ECG in ms. The P-wave indicates the depolarization of the atria. The fact that the duration of P-waves is heterogeneous means that PWD increases. This is a sign that the current sinus rhythm is replaced by AF and less frequently atrial flutter (4,5).

We have not found any study in the literature whether PWD was altered by the use of alpha-adrenergic receptor blocking drugs. Therefore, we investigated the existence of this relationship in appropriate patients who will use alpha-blockers for symptoms of prostate hypertrophy and the lower urinary tract system.

METHODS

Between May 2017 and June 2017, 835 patients who applied to our clinic due to lower urinary tract symptoms (LUTS) were evaluated.

Patients have cardiovascular, endocrine system disease, and drug addiction were excluded from the study. The current study protocol was reviewed and approved by the University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital Institutional Review Board (decision no: 823, date: 22.08.2017). Informed consent was obtained from all the subjects upon enrollment.

Alpha-adrenergic blocker (tamsulosin) was started in 55 patients who met the study criteria. Each patient's pre-treatment electrolyte (which may cause ECG changes such as K, Ca, Mg, P) checked. Five patients who use their drugs intermittently due to the alpha blockers side effects were removed from the study even though they came to the control. Three patients were excluded because of gastrointestinal symptoms. Ten patients who did not come to the control were also excluded from the study. After 3 weeks of alpha-adrenergic blocker use, ECGs of 37 patients were recorded. PWD was compared in reference and control ECGs of all patients in the study. A control group was formed from patients who did not use the medication.

PWD was calculated manually by finding the difference between the largest and narrowest P-waves on the ECG. PWD measurements were compared before and after treatment. ECGs performed with ECG-9020K NIHON KOHDEN brand machine.

Statistical Analysis

Sample size calculated with G*Power Version 3.1.6. SPSS 15.0 for Windows program was used for statistical analysis. Descriptive statistics are determined as number and percentage for categorical variables, mean, standard deviation, minimum, maximum, and median for numerical variables. If differences in the variables provided the normal distribution condition, the two dependent group comparisons were analyzed by the Paired t-test. When the normal distribution condition not provided, then the Wilcoxon signed-rank test was used. The statistical significance level of alpha was accepted as $p < 0.05$.

RESULTS

Mean PWD before the administration of tamsulosin was 55 ms (30-75), while PWD was 60 ms (45-70) when tamsulosin

was used after 3 weeks (Figure 1, 2). The p-value was calculated as <0.001 (Table 1). Therefore, the p-value was considered statistically significant. The mean age is 53.6 ± 8 . The distribution of P-wave dispersions are shown in Figure 1. Moreover, we measured the P-wave dispersions and shown in Figure 2.

DISCUSSION

The use of alpha-blockers for LUTS and BPH is a treatment model that has been in used for many years in urology practice. In the choice of medication, the severity of symptoms, age, sexual activity of the patients should be questioned, as well as the patient's comorbidities, medications, and performance status (6,7).

The need to stop treatment due to orthostatic hypotension due to the use of alpha-blockers and to switch to more selective alpha-blockers has always led to the development of more selective drugs. Meanwhile, retrograde ejaculation, more frequently questioned in the first years, has become less questionable due to the increase in selectivity and the decrease in hypotensive side effects and increased efficacy (3,8,9).

It is hard to find patients who do not use any medication at this age. For this reason, investigating pure drug-related side effects is challenging. In particular, the side effects of urological drugs have begun to be questioned more and more recently, as in the FORTA study, due to changes in our patients' age, additional morbidities, and drug diversity (10).

Cardiac and especially pro arrhythmogenic side effects of alpha blockers have been studied in several studies based on the QT interval in the ECG. In a study by Herbert Lepor (11), it was determined that alfuzosin prolonged the QT interval statistically significant.

Recently, patients with no comorbidities and normal coronary angiography, who subsequently underwent embolism, acute coronary syndrome, and AF, were studied retrospectively (10). There are lots of studies that suggest P-wave variability exists in these patients and that PWD detected in these patients are pro important arrhythmogenic

markers. Dilaveris et al. (5) found that PWD significantly prolonged idiopathic paroxysmal AF.

In our study, the effect-side effect profile of alpha-blockers are planned to investigate. Especially the proarrhythmic effects of these drugs. For this purpose, P-wave morphology and P-wave dispersion, which are accepted as decisive criteria, especially in detecting the tendency of AF, have been used in the literature today.

PWD is a simple ECG finding used to evaluate the spread of non-homogeneous sinus impulses in the atrium and inter-atrium communication (12). Prolonged PWD periods may be associated with stabilized angina pectoris and acute coronary syndrome, as well as in patients undergoing coronary artery bypass surgery. Studies conducted by Cheema et al. (4) and Tükek et al. (13) have reported that P-wave and PWD durations can be affected by autonomic control and increased sympathetic activity.

The primary outcome of our study is that the duration of PWD and the duration of the maximum P-wave measured

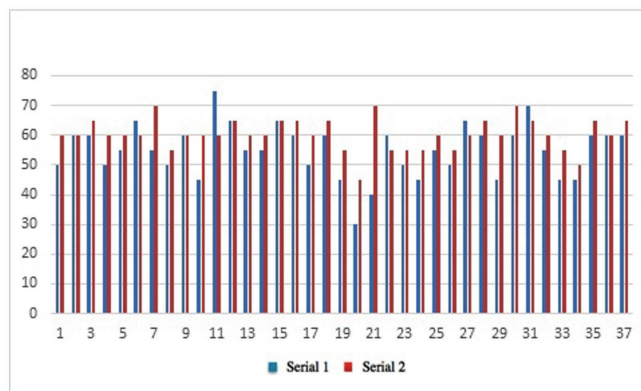


Figure 1. Distribution of P-wave dispersions
Serie 1: Without using tamsulosin
Serie 2: Using tamsulosin

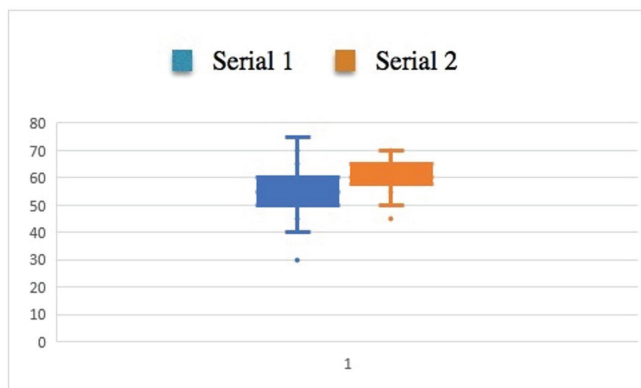


Figure 2. Measured P-wave dispersions
Serie 1: P-wave dispersion measured before tamsulosin
Serie 2: P-wave dispersion measured after tamsulosin

Table 1. Median P-wave dispersions

	Before the treatment	After the treatment	p-value
Median P dispersion (min-max)	55 (30-75)	60 (45-70)	<0.001
Serie 1: P-wave dispersion measured before tamsulosin usage Serie 2: P-wave dispersion measured after tamsulosin usage min-max: Minimum-maximum			

in the ECG of the patients who use of alpha-blockers due to BPH and LUTS are statistically significantly longer than in patients without drug use.

Additionally, patients with BPH without comorbidities were included in the study. Tamsulosin, a selective alpha blocker, was preferred. In polyclinics, 80% of patients were admitted with additional disease and multiple drug use. Considering the high use of non-selective alpha blockers in our country, the results of our study become more valuable.

CONCLUSION

In our study, we found that P-wave dispersion was prolonged in patients using tamsulosin due to benign prostate hyperplasia and lower urinary system symptoms. An increase in PWD is a finding that indicates an increased risk of supraventricular tachycardia. We should be more careful when using tamsulosin in these patients:

ETHICS

Ethics Committee Approval: The current study protocol was reviewed and approved by the University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital Institutional Review Board (decision no: 823, date: 22.08.2017).

Informed Consent: Informed consent was obtained from all the subjects upon enrollment.

Authorship Contributions

Surgical and Medical Practices: C.K., C.Y., Concept: C.K., S.L.K., Design: S.L.K., E.A., Data Collection or Processing: P.J., A.T.A., Analysis or Interpretation: C.Y., A.T.A., Literature Search: P.J., E.A., Writing: C.K., A.T.A., E.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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