The effect of basal heart rate on the antihypertensive efficiency of beta-blocker treatment

Bazal kalp hızının beta-bloker tedavisinin antihipertansif etkinliği üzerine etkisi

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Objectives: Beta-blockers are widely used in the treatment of hypertension. Although decrease in heart rate has a major role in beta-blocker treatment, data are limited on the association between heart rate and the effectiveness of beta-blockers. This study was designed to evaluate the effect of basal heart rate on the efficiency of beta-blocker treatment in patients with essential arterial hypertension.

Study design: This prospective study included 20 patients (13 males, 7 females, mean age 53±10 years) with grade I/II essential hypertension, who did not receive any antihypertensive drugs and did not have any disease affecting the heart rate. Following 24-hour ambulatory blood pressure monitoring for daytime and nighttime systolic, diastolic, and arterial blood pressures, and mean heart rates, oral metoprolol succinate treatment (50 mg/day) was started. At the end of 20 days, 24-hour ambulatory blood pressure monitoring was repeated.

Results: There were significant decreases in mean daytime systolic, diastolic, and arterial ($p<0.001$) blood pressures ($p<0.001$) with corresponding decreases in nighttime blood pressures ($p=0.021$, $p=0.039$, and $p<0.001$, respectively). Changes in daytime and nighttime mean heart rates were also significant ($p<0.001$). There was a significant correlation between the daytime basal heart rate and the decline in daytime arterial blood pressure ($r=0.666$, $p=0.001$). ROC (receiver operating characteristics) curve analysis showed that patients with a daytime basal heart rate of 72/min or higher had a significantly greater reduction in arterial blood pressure ($p=0.04$).

Conclusion: Our results suggest that patients with higher basal heart rates benefit more from beta-blocker treatment for arterial hypertension.

Key words: Adrenergic beta-antagonists; heart rate; hypertension/drug therapy; metoprolol/therapeutic use.

Amaç: Beta-blokerler hipertansiyon tedavisinde yaygın olarak kullanılmaktadır. Beta-bloker tedavisinde kalp hızında azalmanın önemli bir rolü olmasına karşın, kalp hızı ile beta-blokerlerin etkinlikleri arasındaki ilişki hakkında çok az veri vardır. Bu çalışmada, esansiyel arteryel hipertansiyonlu hastalarda bazal kalp hızının beta-bloker tedavisinin antihipertansif etkinliği üzerindeki etkileri araştırıldı.

Çalışma planı: Bu ileriye dönük çalışmaya, antihipertansif tedavi görmeyen ve kalp hızını etkileyebilecek herhangi bir hastalığı olmayan, I/II derece esansiyel arteryel hipertansiyonlu 20 hasta (13 erkek, 7 kadın; ort. yaş 53±10) alındı. Tüm hastaların gündüz ve geceki sistolik, diyastolik ve arteryel kan basınçları ve kalp hızlarının belirlenmesi için 24 saatlik ambulatuvar kan basıncı izlemesine başvuruldu. Daha sonra, 50 mg/gün dozla oral metoprolol süksinat tedavisine başlandı. Yirmi gün sonunda 24 saatlik ambulatuvar kan basıncı izlemesi tekrarlandı.

Bulgular: Tedavi sonunda güniçi ortalama sistolik, diyastolik ve arteryel kan basınçları anlamlı düşüş gösterdi ($p<0.001$); gece ölçülen basınçlarda da anlamlı düşüş görüldü (sırasıyla $p=0.021$, $p=0.039$, ve $p<0.001$). Gündüz ve geceki ortalama kalp hızlarındaki düşüşler de anlamlıydı ($p<0.001$). Güniçi bazal kalp hızı ile arteryel kan basıncındaki gündüz düşüşü arasında anlamlı ilişki izlendi ($r=0.666$, $p=0.001$). ROC (receiver operating characteristics) eğrisi analizinde, güniçi bazal kalp hızının 72/dk veya üzerinde olduğu hastalarda, arteryel kan basıncında elde edilen düşüşün anlamlı derecede daha fazla olduğu görüldü ($p=0.04$).

Sonuç: Bulgularımız, bazal kalp hızı yüksek olan hastaların arteryel hipertansiyon için beta-bloker tedavisinden daha fazla yarar gördüklerini göstermektedir.

Anahtar sözcükler: Adrenerjik beta-antagonisti; kalp hızı; hipertansiyon/ilaç tedavisi; metoprolol/terapötik kullanım.

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Beta-blockers are widely used in the treatment of cardiovascular disease and essential hypertension. Although there is a controversy about the effectiveness of beta-blocker treatment in hypertensive patients, beta-blockers are still a choice of treatment in arterial hypertension as reported in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VII).[1] Their antihypertensive effect is primarily based on decreasing cardiac output and renin release from the kidney by beta-adrenergic blockage.[2-4] Decrease in heart rate has a major role in beta-blocker treatment.[5-7] However, there are reports that addition of beta-blockers to the treatment of hypertensive patients who are already receiving angiotensin converting enzyme inhibitor treatment provides no or little additional antihypertensive benefit if basal heart rate is 84/min or lower.[8]

This study was designed to examine the effect of basal heart rate on the efficiency of beta-blocker treatment and to determine the target heart rate below which beta-blocker treatment might be less favorable.

PATIENTS AND METHODS

This prospective study included 20 patients (13 males, 7 females; mean age 53±10 years) with grade I/II essential hypertension, who did not receive any antihypertensive drugs. Exclusion criteria were diabetes mellitus, coronary artery disease, impaired left ventricular systolic function (ejection fraction <60%), abnormal thyroid hormone level, anemia (hemoglobin <10 g/dl), and drug usage affecting the heart rate. Written informed consent was obtained from each patient.

After taking a careful clinical history, physical examination was performed in all the patients. Body weight and height were measured. An average of three consecutive arterial blood pressure measurements was obtained by a standard mercury sphygmomanometer after the patient had been supine for five minutes. In addition, a 12-lead electrocardiogram was obtained and transthoracic echocardiography was performed. After an overnight fasting of 12 hours, blood samples were drawn for routine blood chemistry and hematologic studies. All the patients underwent 24-hour ambulatory blood pressure monitoring (Tracker NIBP 2, Reynolds Medical Ltd., Hertford, UK) to obtain mean systolic, diastolic, and arterial blood pressures, and mean heart rates for daytime and nighttime. After obtaining baseline data, oral metoprolol succinate treatment (50 mg/day) was started. At the end of 20 days of treatment, arterial blood pressure measurements and 24-hour ambulatory blood pressure monitoring were repeated.

For statistical analysis, t-test was used for evaluation of demographic data and Spearman's correlation analysis was used for correlations between variables. A *P* value of less than 0.05 was accepted as statistically significant.

RESULTS

Compared to the basal values, mean daytime systolic and diastolic blood pressures decreased from 145.2 mmHg to 133.5 mmHg (p<0.001) and from 85.3 mmHg to 78.2 mmHg (p<0.001); mean nighttime systolic and diastolic blood pressures decreased from 131.2 mmHg to 125.0 mmHg (p=0.021) and from 77.1 mmHg to 73.0 mmHg (p=0.039), respectively. Mean daytime arterial blood pressure decreased from 100.8 mmHg to 92.3 (p<0.001), and mean nighttime arterial blood pressure decreased from 89.7 mmHg to 83.0 mmHg (p<0.001). After beta-blocker treatment, changes in daytime and nighttime mean heart rates were also significant. Daytime mean heart rate decreased from 80.4/min to 69.7/min (p<0.001) and nighttime mean heart rate decreased from 67.3/min to 60.1/min (p<0.001).

There was a significant positive correlation between the basal daytime heart rate and the decline in mean daytime arterial blood pressure (r=0.666, p=0.001; Fig. 1). However, the mean basal nighttime heart rate was not correlated with the decline in nighttime mean arterial blood pressure (r=0.283, p=0.226; Table 1).

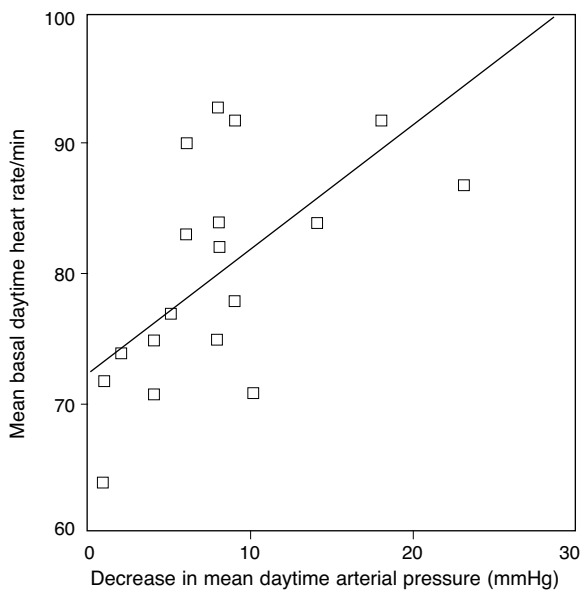

Figure 1. Correlaton between basal daytime mean heart rate and decrease in daytime mean arterial pressure (r=0.666, p=0.001).

Table 1. Correlations between daytime and nighttime basal heart rates and decreases in mean arterial pressure

	Arterial pressure			
	Daytime		Nighttime	
	r	*p*	r	*p*
Daytime heart rate	0.666	0.001	0.142	0.549
Nighttime heart rate	0.339	0.144	0.283	0.226

There was no significant correlation between age and reduction in mean arterial blood pressure (p>0.05). Partial correlation analysis performed by excluding the effect of age also showed a significant correlation between the mean basal daytime heart rate and the percentage of decline in the mean daytime arterial blood pressure (r=0.676, p=0.001).

In ROC (receiver operating characteristics) curve, it was observed that patients whose mean basal daytime heart rate was 72/min or higher had a significantly greater reduction in mean arterial blood pressure (p=0.04; Fig. 2).

DISCUSSION

Our study documented a strong correlation between basal heart rates and antihypertensive efficiency of beta-blockers. It was determined that antihypertensive effect of beta-blockers was much more evident in patients with higher basal heart rates than in those with lower heart rates. A statistically significant decrease in mean daytime arterial blood pressure was observed with beta-blocker treatment in patients with a mean basal daytime heart rate equal or higher than 72/min. Conversely, decreases in mean daytime arterial blood pressure were less in patients whose basal mean heart rate was lower than 72/min. Our data support the hypothesis that antihypertensive efficiency of beta-blockers will be less at lower basal heart rates. On the other hand, declines in mean nighttime arterial blood pressures were not correlated with mean basal nighttime heart rates. This may be related to taking the drug in the morning.

A consensus document reported that, in hypertensive patients already receiving angiotensin converting enzyme inhibitors, addition of a beta-blocker to the treatment would not result in further decreases in arterial blood pressure at heart rates lower than 84/min.[8] However, data on the efficiency of beta-blockers when they are used alone at different heart rates are limited.[1,8-10] Our study showed that, in patients receiving only beta-blocker treatment for arterial hypertension, the efficiency of the drug was much more evident when the basal heart rate was high. This suggests that patients with a low basal heart rate are not good candidates for beta-blocker treatment for the treatment of arterial hypertension. In addition, our study showed that antihypertensive efficiency of beta-blockers was prominent when the cutoff value for basal heart rate was 72/min.

Despite several reports indicating that beta-blockers are less effective in older people due to a physiological beta-adrenergic blockage,[11-15] we did not find age-related differences in the efficiency of beta-blocker treatment for hypertension. However, this may be due to the limited number of older patients (only two patients were ≥70 years old) in the study group.

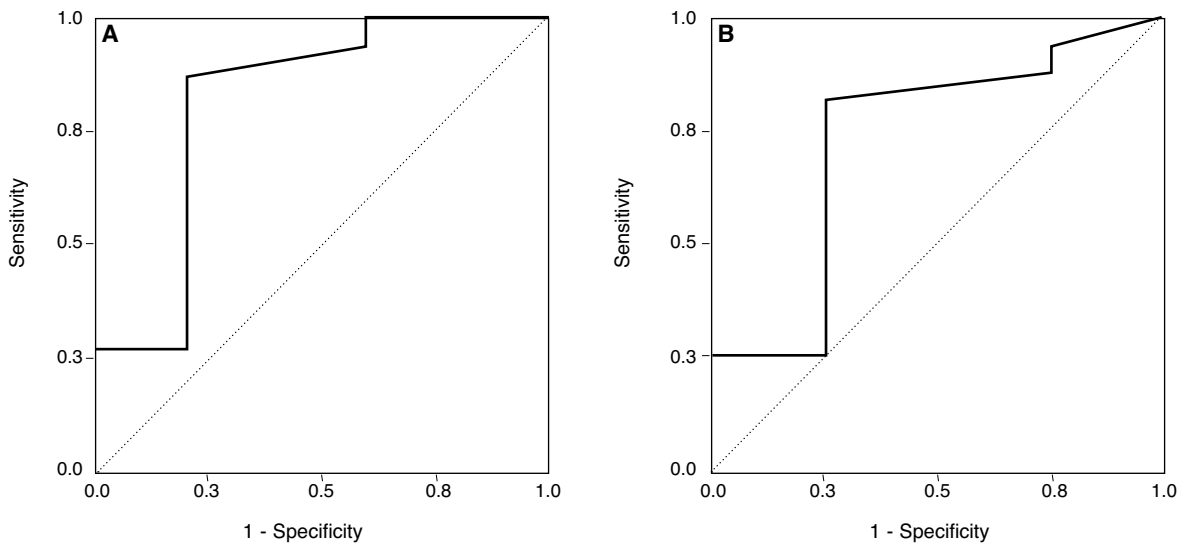

Figure 2. ROC analysis performed for basal daytime mean heart rates, **(A)** ≥72/min, **(B)** <72/min.

In conclusion, our results suggest that patients with higher basal heart rates benefit more from beta-blocker treatment for arterial hypertension; thus, it may be useful to take basal heart rate into consideration in the selection of antihypertensive agents.

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