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Beta-Blocker Therapy on Blood Pressure in Subclinical Hyperthyroidism: A Retrospective Observational Study

Subklinik Hipertiroidizmde Beta-Bloker Tedavisinin Kan Basıncına Etkisi: Retrospektif Bir Gözlemsel Çalışma

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ABSTRACT

This study aimed to investigate the effect of beta-blocker therapy on blood pressure in patients with subclinical hyperthyroidism and to elucidate the potential benefits of this treatment approach. This retrospective observational cohort study included 56 hypertensive patients with subclinical hyperthyroidism who received beta-blocker therapy. Patient data, including demographic characteristics, thyroid function tests, and blood pressure measurements, were collected from medical records and evaluated using statistical analysis with SPSS Statistics software. The cohort of hypertensive patients included 35 patients with uncontrolled blood pressure and 21 newly diagnosed patients, with a total average age of 55 and 73.2% of them being female. In newly diagnosed and uncontrolled hypertensive patients, TSH levels were below the average, and T3 levels were high ($p<0.001$). Significant reductions in systolic and diastolic blood pressure were observed in both groups after beta-blocker therapy ($p<0.001$). The most significant decrease in blood pressure in beta-blocker therapy occurred in newly diagnosed hypertensive patients, with an average decrease of 37.85 mmHg. Additionally, a significant reduction in the number of antihypertensive medications was observed in patients receiving beta-blocker therapy ($p<0.001$).

In conclusion, our study demonstrates the positive effects of beta-blocker therapy on blood pressure control in patients with subclinical hyperthyroidism. Particularly, the significant decrease in blood pressure in newly diagnosed hypertensive patients indicates the potential of beta-blockers as a preferred treatment option. This study highlights the necessity of a causal approach in treating hypertension with thyroid disorders. However, considering the limitations of the study design, further comprehensive research is needed to confirm these findings.

Keywords: Beta-blockers, Blood pressure, Hypertension, Subclinical hyperthyroidism, Thyroid function tests.

ÖZ

Bu çalışma, subklinik hipertiroidizmi olan hastalarda beta-bloker tedavisinin kan basıncı üzerindeki etkisini araştırmayı ve bu tedavi yaklaşımının potansiyel faydalarını ortaya koymayı amaçlamıştır. Bu retrospektif gözlemsel kohort çalışmaya subklinik hipertiroidizmi olan ve beta-bloker tedavisi alan 56 hipertansif hasta dahil edildi. Hastaların demografik özellikleri, tiroid fonksiyon testleri ve kan basıncı ölçümlerini içeren hasta verileri, tıbbi hasta kayıtlarından toplanarak SPSS Statistics yazılımı kullanılarak istatistiksel analizle değerlendirildi. Çalışmaya dahil edilen kan basıncı kontrol altında olmayan 35 ve yeni teşhis konmuş 21, toplam 56 hipertansif hastanın kohortunda ortalama yaş 55 ve %73,2 si kadınlar hastalardan oluşmaktaydı. Yeni teşhis edilen ve kan basıncı kontrol altında olmayan hipertansif hastalarda, TSH düzeylerinin ortalamanın altında olduğu ve T3 düzeylerinin ise yüksek olduğu görüldü ($p<0,001$). Her iki grupta da beta-bloker tedavisi sonrasında sistolik ve diyastolik kan basıncında anlamlı düşüşler gözlenmiştir ($p<0,001$). Beta-bloker tedavisinde en büyük kan basıncı düşüşü, yeni teşhis edilen hipertansiyonlu hastalarda ortalama 37,85 mmHg azalma olarak ortaya çıkmıştır. Ek olarak, beta bloker tedavisi alan hastalarda antihipertansif ilaç kullanımı sayısında anlamlı azalma görülmüştür ($p<0,001$).

Sonuç olarak çalışmamızda, beta-bloker tedavisinin subklinik hipertiroidizmli hastalarda kan basıncı kontrolüne olumlu etkileri olduğunu gösterilmektedir. Özellikle yeni tanılı hipertansiyonlu hastalarda belirgin kan basıncı azalması, beta-blokerlerin tercih edilen bir tedavi seçeneği olarak potansiyelini göstermektedir. Bu çalışma, tiroid bozuklukları ile ilişkili hipertansiyon tedavisinde nedene yönelik bir yaklaşımın gerekliliğini vurgulamaktadır. Bununla birlikte, çalışmanın tasarım kısıtlamaları göz önüne alındığında, bu bulguların doğrulanması için daha kapsamlı araştırmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Beta-bloker, Hipertansiyon, Kan basıncı, Subklinik hipertroidi, Tiroid fonksiyon testleri

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INTRODUCTION

According to the World Health Organization, hypertension is a global public health challenge affecting an estimated 1.28 billion adults aged 30-79 worldwide, putting a strain on healthcare services and raising the risk of cardiovascular disease.[1, 2] Currently, the prevalence of hypertension in the adult population is estimated to be 31% worldwide, emphasizing the urgent need for effective prevention and management strategies.[3]

Many risk factors contribute to hypertension, including age, sex, race, obesity, excessive salt intake, high-fat diet, genetic composition, family history, inactivity or lack of exercise, and lifestyle choices.[4] Among these risk factors, thyroid dysfunctions have been identified as an important consideration.[5] Hyperthyroidism has been associated with hypertension due to increased cardiac output and elevated levels of renin, angiotensin, and aldosterone.[6,7] The treatment approach for hypertension associated with thyroid dysfunctions varies based on the specific thyroid disease. Beta-blocker therapy has been suggested as an effective approach in cases of hypertension accompanied by hyperthyroidism.[8] However, regional differences should be considered, particularly in areas with a high prevalence of clinical or subclinical hyperthyroidism.[9]

Subclinical hyperthyroidism (SCHyper) is diagnosed biochemically based on decreased serum thyroid-stimulating hormone (TSH) levels, with normal thyroxine (T4) and triiodothyronine (T3) concentrations.[10] Subclinical hyperthyroidism has been found to have various cardiovascular effects, such as increased heart rate, ventricular mass, arterial stiffness, and left atrial size, which can lead to diastolic dysfunction and impaired left ventricular performance.[11] Additionally, SCHyper has been associated with increased risks of cardiovascular-related adverse outcomes. However, the clinical significance and optimal cutoff values for subclinical thyroid dysfunction remain debated.[12, 13] In most cases, elevated or depressed TSH levels are associated with nonspecific and benign symptoms.[14] Nevertheless, some studies suggest that abnormal TSH levels may increase the risk of cardiovascular disease.[15,16]

Current guidelines emphasize the importance of blood pressure control to prevent cardiovascular morbidity and mortality.[17,18] Since hyperthyroidism is an important risk factor in blood pressure control, and it is essential to determine the blood pressure target values for this patient group taking beta-blockers, which also brings identifying the optimal blood pressure targets in subclinical hyperthyroidism as well for their management. In this study, we aimed to evaluate the effectiveness of beta-blocker treatment in patients predisposed to subclinical hyperthyroidism, which has been recommended for their high blood pressure.

MATERIALS AND METHOD

Study Design

This study employed an observational cohort design, which focused on retrospective case series.

Population Selection

This study involved a cohort of fifty-six hypertensive patients with subclinical hyperthyroidism who were receiving beta-blocker treatment. Patient information was obtained from the hospital records of individuals who visited the Family Medicine outpatient clinic between June 2016 and May 2019 due to irregular blood pressure. Various data, including physical examination findings, demographic characteristics, office blood pressure measurements, and biochemistry panels (such as serum glucose, thyroid function tests, and lipid parameters), were recorded on a data form. Patients who were started on beta-blockers due to palpitation complaints or suppressed TSH levels or for treatment compliance who switched to beta-blocker therapy for

treatment compliance were included in this study; in contrast, patients with any chronic disease other than hypertension were excluded from the study.

Statistical Analyses

The statistical analysis was performed using IBM SPSS Statistics software (version 25). Descriptive statistics were used to summarize the data. Categorical data were presented as frequencies and percentages, while numerical data were reported as mean ± standard deviation (SD). The average TSH and T3 values were calculated based on the laboratory reference lower and upper values, resulting in a population mean TSH of 2.65 and a population mean T3 of 2.71. Skewness and kurtosis analyses were conducted to assess the normal distribution of the data. The distribution of demographic data was analyzed using frequency tests, and the chi-square test was employed to compare categorical data. Independent sample t-tests and paired sample t-tests were used to compare numerical data between groups. A p-value of less than 0.05 was considered statistically significant.

Ethical Approval

Approval for the study was obtained from the University of Health Sciences Training and Research Hospital Clinical Research Ethics Committee, with the decision date of February 24, 2023, and reference number 49.

RESULTS AND DISCUSSION

A total of 56 patients were included in the study, with 21 being newly diagnosed and 35 having uncontrolled blood pressure. Among the patients, 41 (73.2%) were female, and 15 (26.8%) were male, with a mean age of 55 years (Table 1).

Table 1. Demographic Distribution of the Study Participants

Variables	N	%
Hypertension		
New Diagnose	35	62.5
Non-regulated Hypertension	21	37.5
Sex		
Female	41	73.2
Male	15	26.8
Age, year (Mean±SD)	55.00±12.57	
Laboratory results		
TSH, micro-IU/ml (Mean±SD)	0.84±0.95	
T3, pg/ml (Mean±SD)	2.95±0.38	
T4, ng/dl (Mean±SD)	1.03±0.15	

*SD: Standard Deviation; TSH: thyroid-stimulating hormone; T3: triiodothyronine; T4: thyroxine

In both newly diagnosed and non-regulated hypertension patients, TSH values were found to be below the population mean. In contrast, T3 values were higher than the population mean values ($p<0.001$, $p<0.002$, respectively) (Table 2).

Table 2. Comparison of Thyroid Function Tests with The Population Means Values

	Hypertension	N	Population Mean	Mean±SD	p-value*
TSH	Total	56	2.65	0.84±0.95	< 0.001
	New diagnoses	35		0.78±0.89	< 0.001
	Non-regulated	21		0.93±1.06	< 0.001
T3	Total	56	2.71	2.95±0.38	< 0.001
	New diagnoses	35		2.91±0.36	0.002
	Non-regulated	21		3.01±0.40	0.002

SD: Standard Deviation; TSH: thyroid-stimulating hormone; T3: triiodothyronine; *Independent sample t-test is significant at the P < 0.05 level (2-tailed).

Beta-blocker administration resulted in a statistically significant reduction in both systolic and diastolic blood pressure in patients with newly diagnosed and non-regulated hypertension. Among the study participants, the most significant decrease in blood pressure was observed in newly diagnosed hypertensive patients, with a mean reduction of 37.85 mmHg ($p<0.001$ for both groups) (Table 3).

Table 3. Comparison of Mean Systolic and Diastolic Blood Pressures Before and After Treatment with Selective Beta-1 Blockers in Paired Groups

	Hypertension	N	Before	After	p-value*
			Mean±SD	Mean±SD	
Mean SBP (mm/Hg)	Total	56	152.32±12.46	116.79±10.11	< 0.001
	New diagnoses	35	154.43±9.29	116.57±10.55	< 0.001
	Non-regulated	21	148.81±16.11	117.14±9.56	< 0.001
Mean DBP (mm/Hg)	Total	56	93.04±7.30	76.25±6.69	< 0.001
	New diagnoses	35	94.00±5.91	77.00±5.96	< 0.001
	Non-regulated	21	91.43±9.10	75.00±7.74	< 0.001
Antihypertensive Medication Requirement: Mean tablets/day	Non-regulated	21	1.71±0.64	1.05±0.21	< 0.001

SD: Standard Deviation; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure, *Paired samples test is significant at the P < 0.05 level (2-tailed).

Additionally, treatment with beta-blockers was associated with a decrease in the number of antihypertensive medications required, as indicated by a mean 31.67 mmHg reduction in systolic blood pressure among patients with non-regulated hypertension ($p<0.001$).

All groups observed statistically significant reductions after treatment for both systolic and diastolic blood pressures. The newly diagnosed hypertension group observed the most significant decrease in both systolic and diastolic blood pressure. Additionally, the table shows the mean number of antihypertensive tablets per day before and after treatment for the non-regulated hypertension group, with a significant decrease in medication requirement after treatment. A significant difference was observed between the patient groups and the population mean for TSH levels. The TSH values in the patient groups were significantly below the population mean ($p<0.001$). The most significant difference from the population mean was observed in the new diagnoses group. Regarding T3 levels, a significant difference was also found between the patient groups and the population mean. The T3 values in the patient groups were significantly higher than the population mean ($p<0.001$). Similar to TSH, the new diagnoses group showed the most significant deviation from the population mean.

The findings of the study revealed that both newly diagnosed and uncontrolled hypertension patients exhibited lower-than-average TSH levels and higher T3 mean values, indicating a potential predisposition to subclinical hyperthyroidism in the study population while also experiencing significant decreases in blood pressure with beta-blocker treatment.[19, 20] Previous literature suggests that subclinical hyperthyroidism may increase the risk of hypertension and contribute to higher morbidity and mortality rates, mainly through its association with cardiovascular events such as arrhythmia, hypercoagulability, stroke, and pulmonary embolism.[21-23] Both hyperthyroidism and hypothyroidism have been linked to hypertension, with hypothyroidism primarily associated with diastolic hypertension.[24, 25]

Hypothyroidism is also known to increase cardiovascular risk by causing hypertension, hyperlipidemia, and endothelial dysfunction.[5, 26] The choice of treatment for hypertension associated with

thyroid disorders depends on the clinical effects of the thyroid disease.[8] In the case of hyperthyroidism, beta-blockers are recommended to control blood pressure, although alternative medications like angiotensin-converting enzyme inhibitors or calcium channel blockers can be used when contraindicated or not tolerated.[8]

In the present study, treatment with beta-blockers was found to significantly reduce both systolic and diastolic blood pressure among newly diagnosed and uncontrolled hypertension patients with subclinical hyperthyroidism. Additionally, in hypertensive patients with a predisposition to hypothyroidism, salt restriction, calcium channel blockers, alpha-blockers, and diuretic drugs have also been shown to be effective.[8, 27]

The study observed the most significant improvement in systolic blood pressure among newly diagnosed hypertensive patients, with a notable reduction of 37.85 mmHg. This finding suggests that beta-blockers may be the treatment of choice for newly diagnosed hypertension patients with a predisposition to subclinical hyperthyroidism. Treating isolated systolic hypertension in patients with a predisposition to hyperthyroidism is crucial due to its impact on coronary heart disease, stroke, heart failure, end-stage renal disease, and overall mortality.[5] Moreover, antihypertensive therapy with beta-adrenergic receptor blockers not only reduces blood pressure but also improves other symptoms of hyperthyroidism, including palpitations, tachycardia, tremor, and anxiety.[28, 29] A recent systematic review and meta-analysis of randomized clinical trials have demonstrated that monotherapy with an antihypertensive agent typically leads to a 10-15 mmHg reduction in systolic blood pressure.[28]

In the current study, beta-blocker therapy resulted in a significant mean decrease of 31.67 mmHg in systolic blood pressure among patients with non-regulated hypertension and subclinical hyperthyroidism. This reduction likely contributed to the observed decrease in the mean number of antihypertensive medications required. These findings suggest that a cause-oriented approach, such as beta-blocker therapy for hyperthyroidism-induced hypertension, can result in a more substantial reduction in blood pressure and a decreased need for multiple antihypertensive medications.

In light of these findings, it is important to consider the implications of beta-blocker therapy for the management of hypertension in patients with subclinical hyperthyroidism. The significant decreases in blood pressure observed in this study highlight the potential benefits of beta-blockers in this patient population. Beta-blockers not only effectively control blood pressure but also have the potential to address the underlying thyroid dysfunction. Beta-blocker therapy offers a comprehensive approach to managing cardiovascular risk in these patients by targeting both hypertension and subclinical hyperthyroidism.

Study limitations

The limitations of this study, including the challenge of establishing control groups due to the predominance of female participants and the retrospective design, should be taken into consideration when interpreting the findings.

CONCLUSION AND RECOMMENDATIONS

In this study, treatment with beta-blockers demonstrated a significant decrease in both systolic and diastolic blood pressure among patients with subclinical hyperthyroidism. Furthermore, beta-blocker treatment was associated with a reduction in the number of required antihypertensive medications.

Based on these findings, the study suggests developing a cause-oriented approach to managing hypertension associated with thyroid disorders, especially

in patients with subclinical hyperthyroidism. However, it is important to note that further studies are necessary to validate these results and provide more comprehensive insights into the topic.

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