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Relationship between N-Terminal Pro B-Type Natriuretic Peptide and Body Mass Index

N-Terminal Pro B-Tip Natriüretik Peptit ve Vücut Kitle İndeksi Arasındaki İlişki

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Abstract

Objective: N-terminal pro B-type natriuretic peptide (NT-pro BNP) is secreted from the cardiac ventricles in response to volume expansion. The effect of obesity on natriuretic peptide has yet to be fully elucidated. We aimed to compare the NT-pro BNP levels in obese and in healthy individuals with normal body mass index.

Method: Forty-two obese patients (37 women, 5 men; body mass index ≥ 30) and thirty-five normal body mass index individuals (27 women, 8 men; body mass index ≤ 25) were analyzed regarding NT-pro BNP.

Results: The serum levels of NT-pro BNP was significantly higher in obese patients than normal body mass index individuals (p=0,027). No correlation was found between body mass index and NT-pro BNP. Statistically significant difference was found between systolic and diastolic blood pressures in both groups (p<0.001 and p<0.001; respectively)

Conclusion: We found that NT-pro BNP was higher in obese than control groups. Elevated NT-pro BNP in obese patients may be explained by changes in the heart structure that hypertension leads.

Keywords: obesity, N-terminal proB-type natriuretic peptide, hypertension

Özet

Amaç: N-terminal pro B-tip natriüretik peptid (NT-pro BNP) hacim genişlemesinde yanıt olarak kardiyak ventriküllerden salgılanır. Natriüretik peptid üzerine obezitenin etkisi henüz tam olarak aydınlatılmış değildir. Bu çalışmada normal kilolu ve obez bireylerde NT-pro BNP düzeylerinin karşılaştırılması amaçlandı.

Yöntem: Çalışmaya kırkiki obez hasta (37 kadın, 5 erkek; vücut kitle indeksi ≥ 30) ve normal kilolu otuzbeş kişi (27 kadın, 8 erkek; vücut kitle indeksi ≤ 25) kontrol grubu olarak alındı. Hasta ve kontrol grubunun NT-pro BNP düzeyleri karşılaştırıldı.

Bulgular: NT-pro BNP düzeyleri obez hastalarda kontrol grubuna göre anlamlı olarak yüksek bulundu (p=0.027). Vücut kitle indeksi ile NT-pro BNP arasında korelasyon yoktu. Obez hastalarda sistolik ve diyastolik kan basınçları istatistiksel olarak yüksekti (sırasıyla; p <0.001 ve p <0.001).

Sonuç: Obezlerde kontrol grubuna göre NT-pro BNP düzeyleri daha yüksek olduğu bulundu. Obez hastalardaki yüksek NT-pro BNP hipertansiyonun yol açtığı kalp yapısındaki değişiklikler ile açıklanabilir.

Anahtar Kelimeler: obezite, N-terminal pro B-tip natriüretik peptid, hipertansiyon

Introduction

Obesity is a well-known risk factor for cardiovascular disease and for the development of chronic heart failure (1). In obesity, changes in the heart structure can be partially explained by the increase of total blood volume leading to volume overload, hypertension, left ventricular hypertrophy (LVH), and/or left ventricular dysfunction (LVD)(2). The mechanisms linking obesity to the development of hypertension have not been established. Several mechanisms have been suggested to play a role in the pathogenesis of obesity-related hypertension, such as increased plasma volume and cardiac output (3), enhanced sympathetic nervous activity (4), hyperinsulinemia, insulin resistance (5) and nutritional factors such as high sodium intake and/or sodium retention (6).

Plasma brain natriuretic peptide (BNP) and the N-terminal of the prohormone (NT-pro BNP) are well-established powerful risk markers in chronic heart failure. These natriuretic peptides are secreted in response to increased wall tension the atria and ventricles (7) and plasma levels of these are increased in subjects with left ventricular hypertrophy (8), asymptomatic ventricular dysfunction (9, 10), and overt heart failure (11).

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Because obesity is associated with salt retention and increased cardiac output (12), which would be expected to produce elevated natriuretic peptide levels. However, NT-pro BNP levels have recently shown to be inversely proportional to body mass index (BMI) in individuals without heart failure (13, 14). Reduced secretion of natriuretic peptides from diminished myocardial hormone release (15), impaired synthesis or increased peptide clearance (16, 17) may also be an important explanation for low plasma natriuretic peptide levels in obese patients. The aim of the present study was to evaluate the association between obesity and natriuretic peptides.

Method

Forty-two obese subjects with BMI ≥ 30 and without heart failure were included in the study. Seventeen of obese subjects (48 %) were hypertensive. The hypertensive subjects consisted of previously untreated patients affected by mild to moderate uncomplicated essential hypertension. Thirty-five non-obese healthy individuals with BMI ≤25 served as the control groups.

All subjects underwent a complete physical examination, with detailed medical history, laboratory assessment of cardiovascular disease risk factors, electrocardiography. BMI (kg/m²) was calculated as weight in kilograms divided by height in meters square. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg (18). No participant had clinical signs of acute or chronic heartdisease or left ventricular hypertrophy (LVH) in the electrocardiogram.

Blood samples were drawn from subjects in a fasting state, typically between 8:00 and 9:00 A.M.Blood samples were collected via the antecubital vein of the subjects. Samples were drawn in tubes containing EDTA, placed on ice, and centrifuged within 30 minutes. The plasma was frozen at -80ºC until assay. Plasma levels of NT-pro BNP were measured by a double-antibody sandwich technique with electrochemiluminescence as signal (Modular Analytics E 170, Roche Diagnostics, Tokyo, Japan). Plasma pro-BNP concentration was measured using commercially available immunoassays (ElecsysproBNP, Roche Diagnostics GmbH, Mannheim, Germany). The lower limits of the working range were 5 pg/ml for pro-BNP. The average interassay coefficient of variation was 20% for NT-pro BNP.

Data are presented as means ± SD. Statistical comparison between groups was performed with Mann-Whitney U test. The r_s values of correlation between clinical and laboratory variables were calculated with the non-parametric Spearman rank test $p < 0.05$ was considered as statistically significant.

Results

At total of 42 obese patients (37 female and 5 male) were enrolled in the study. The mean ±SD age was 40.38 ± 8.84 years (range 18 to 55). Mean BMI was 37.90 ± 5.70 kg/m² (range 31 to 54) and mean NT-pro BNP levels were 57.45 ± 68.4 pg/ml (range 5 to 306) Control group were 35 non-obese healthy individuals (27 female, 8 male). Mean age was 36.03 ± 11.63 years (range 18 to 74 years) and mean BMI was 23.20 ± 1.66 (range 20 to 25) and mean NT-pro BNP levels were 38.23 ± 32.95 pg/ml (range 5 to 148).

NT-pro BNP levels of obese patients (mean 57.45 ± 68.4 pg/ml; range 5 to 306) were significantly higher than control groups (mean 38.23 ± 32.95 pg/ml; range 5 to 148) (p=0.027). No correlation was found between BMI and NT-pro BNP in both obese and control groups (p=0.181, r=0.211; p=0.988, r=-0.003, respectively).

Mean systolic blood pressure and mean diastolic blood pressure in obese patients was 131.95 ± 21.12 mmHg (range 90 to 200) and 82.44 ± 11.35 mmHg (range 70 to 110), respectively. Mean systolic blood pressure and mean diastolic blood pressure in normal body mass index individuals was 115.31 ± 11.84 mmHg (range 100 to 135) and 71.72 ± 8.29 mmHg (range 60 to 85) respectively. Both systolic and diastolic blood pressures were higher in obese

subjects than control groups (p<0.001 and p<0.001; respectively).

Tablo 1. Characteristics of study and control group

	Obese, n=42	Controls, n=35	*p
Age (years)	40.38 ± 8.84	36.03 ± 11.63	0.190
Male/female	5/37	8/27	0.064
BMI (kg/m^2)	37.90 ± 5.70	23.20 ± 1.66	0.001
NT-proBNP (pg/ml)	57.45 ± 68.4	38.23 ± 32.95	0.027
Systolic blood pressure (mmHg)	131.95 ± 21.12	115.31 ± 11.84	0.001
Diastolic blood pressure (mmHg)	82.44 ± 11.35	71.72 ± 8.29	0.001

Discussion

Recently, pro-BNP have received major attention as cardiovascular marker because this peptide is secreted in case of volume overload and increased ventricular wall tension (19-21). In addition, pro-BNP was identified as a discerning marker of LVH and/or early LVD. Obesity and hypertension are accompanied by LVH and LVD. This novel parameter could serve as a screening method to enable earlier diagnosis (22).

This study demonstrated that serum levels of NT-pro BNP in obese patients are higher than non-obese individuals. Minami et al. (23) proved significant decrease of plasma BNP and ANP levels in obese subjects on a 3-week hypocaloric diet. These researchers demonstrated that the reduction in BNP concentration's largely reflected by the decrease in total blood volume after weight loss. Messaoudi et al. (24) reported that no significant variation BNP was noted during the 8-day-period of semistarvation. However, Wang et al. (14) demonstrated an inverse relation between body mass index and natriuretic peptide levels. Reduced secretion of natriuretic peptides from diminished myocardial hormone release (15), impaired synthesis or increased peptide clearance (16, 17) may also be an important explanation for low plasma natriuretic peptide levels in obese patients.

Our data indicate that the influence of obesity on natriuretic peptide levels may be dependent on hypertension. Because, 40.4% of our patients have hypertension. In most reports that in general population of hypertensives in which mean plasma of natriuretic peptide are usually slightly higher than in normotensives (25, 26) In hypertensive patients, left ventricular mass has been reported to correlate with plasma natriuretic peptide levels (26, 27). Ursula et al. (28) have been shown that the surgically induced weight loss resulted in a significant decrease of systolic (9.2%) and diastolic (10.1%) blood pressure and a reduction to almost normal range. The extent of weight loss might contribute to the reduction of NT-pro BNP.

A limitation of this study is that the numbers of patients and controls were relatively small. In summary, we found that NT-pro BNP was higher in obese than normal individuals. It is rational to consider the changes in heart structure caused by increments of total blood volume, and left ventricular dysfunctional the causative mechanism for elevation of NT-pro BNP in obese patients. Therefore, further studies are needed to establish the changes in serum natriuretic peptide levels in obese subjects.

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