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Investigation Of NT-proBNP Level In Hyponatremia Due To Endocrine Causes

Endokrin Nedenlere Bağlı Gelişen Hiponatremide NT-proBNP Düzeyinin İncelenmesi

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ABSTRACT

Introtuction: Inappropriate ADH secretion syndrome and pituitary insufficiency are endocrine causes of hyponatremia. The main reason in both groups is the direct or indirect increase in ADH secretion.Fluid retention occurs with the increase in ADH secretion. Fluid retention leads to cardiac strain, and it is thought that it may cause increased secretion of BNP and NT-proBNP .
Aim: Studies on the effects of natriuretic peptides on hyponatremia are scarce due to endocrine causes. The relationship between thyroid hormone disorders and Brain natriuretic peptide (BNP) has been examined in existing studies. Within the scope of this research.we aimed to elucidate the relationship between NT-proBNP and hyponatremia in inappropriate ADH secretion syndrome and pituitary insufficiency.
Method: This prospective study included 14 patients with hyponatremia, inappropriate ADH secretion syndrome, nine patients with pituitary insufficiency who applied to our institution, and 21 healthy volunteers with no systemic disease and serum sodium levels within the normal range. Laboratory tests of the patient group (fasting blood sugar, serum sodium level, spot urine sodium, creatinine, urine osmolarity, and anterior pituitary hormones of patients with suspected pituitary insufficiency) were recorded from the patient files .
Results: Basal sodium levels were statistically significant among the three groups. The median basal sodium level was 127 (meq/l) in the pituitary insufficiency group, 124 (meq/l) in the inappropriate ADH secretion syndrome group, and 138 (meq/l) in the control group ($p<0.0001$). The median NT-proBNP level was found to be 671 (pg/ml) in the pituitary insufficiency group, 499 (pg/ml) in the inappropriate ADH secretion syndrome group, and 119 (pg/ml) in the control group ($p<0.0001$). As a result of ROC analysis, serum NT-proBNP values were found to have diagnostic value in predicting hyponatremia due to endocrinological reasons (inappropriate ADH secretion syndrome and pituitary insufficiency) (AUC:0.87 95% confidence interval 0.763 – 0.977, $p<0.0001$). This value's recommended limit value is 141 (sensitivity: 91.3% and specificity: 66.7%).
Conclusion: This research elaborated that while plasma sodium levels were low in the inappropriate ADH secretion syndrome and pituitary insufficiency groups, the NT-proBNP levels were higher, showing a statistically significant difference between the three groups.

Keywords: NT-proBNP, Syndrome of inappropriate secretion of ADH, Hyponatremia, Hypophyseal insufficiency.

ÖZET

Giriş: Uygunsuz ADH salgı sendromu ve hipofiz yetmezliği hiponatreminin endokrin nedenleridir. Her iki grupta da temel neden ADH salgısının doğrudan veya dolaylı olarak artmasıdır. ADH salgısının artmasıyla sıvı tutulumu meydana gelir. Sıvı tutulumu kalpte zorlanmaya neden olur ve BNP ve NT-proBNP salgısının artmasına neden olabileceği düşünülmektedir.
Amaç: Natriüretik peptidlerin endokrin nedenlere bağlı gelişen hiponatremide etkileri üzerine yeterli sayıda çalışma bulunmamaktadır. Var olan çalışmalarda ise tiroid hormon bozukluklarıyla Brain natrüretik peptid (BNP) arasındaki ilişki incelenmiştir. Bu araştırma kapsamında uygunsuz ADH salgı sendromu ve hipofiz yetmezliğinde NT-proBNP ile hiponatremi arasındaki ilişkiyi aydınlatmayı amaçladık.
Yöntem: Bu prospektif çalışmaya hiponatremili, uygunsuz ADH salgı sendromu olan 14 hasta, kurumumuza başvuran hipofiz yetmezliği olan 9 hasta ve herhangi bir sistemik hastalığı olmayan, serum sodyum düzeyi normal sınırlarda olan 21 sağlıklı gönüllü dahil edildi. Hasta dosyalarından hasta grubunun laboratuvar testleri (açlık kan şekeri, serum sodyum düzeyi, spot idrar sodyumu, kreatinin, idrar osmolaritesi ve hipofiz yetmezliği şüphesi olan hastaların ön hipofiz hormonları) kaydedildi. Hasta grubuna kalp yetersizliğini dışlamak amacıyla ekokardiyografi yapıldı.
Bulgular: Bazal sodyum seviyeleri üç grup arasında istatistiksel olarak anlamlıydı. Bazal sodyum düzeyi ortanca hipofiz yetmezliği grubunda 127 (meq/l), uygunsuz ADH sekresyonu sendromu grubunda 124 (meq/l) ve kontrol grubunda 138 (meq/l) ($p <0.0001$).
Ortanca NT-proBNP düzeyi; hipofiz yetmezliği grubunda 671 birim, uygunsuz ADH salgı sendromu grubunda 499 (pg/ml), kontrol grubunda 119 (pg/ml) ($p <0.0001$). ROC analizi sonucunda serum NT-proBNP değerlerinin; endokrinolojik nedenlere bağlı hiponatremiyi öngörmede tanı değeri vardır (uygunsuz ADH salgı sendromu ve hipofiz yetmezliği) (AUC:0,87 %95 GA 0.763 – 0.977, $p <0.0001$). Bu değerin önerilen sınır değeri 141'dir (duyarlılık: %91.3 ve özgüllük: %66.7).

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Sonuç: Bu araştırma, uygunsuz ADH salgı sendromu ve hipofiz yetmezliği gruplarında plazma sodyum düzeylerinin düşük olmasına rağmen, NT-proBNP düzeylerinin daha yüksek olduğunu ve üç grup arasında istatistiksel olarak anlamlı bir fark olduğunu ortaya koydu.

Anahtar Kelimeler: NT-proBNP, Uygunsuz ADH Salınımı Sendromu, Hiponatremi, Hipofizer Yetmezlik.

INTRODUCTION

Hyponatremia is the plasma sodium concentration below 135 mmol/l and is the most common electrolyte disorder in clinical practice. It is seen in 30% of hospitalized patients and causes a wide spectrum of clinical findings, ranging from mild to life-threatening (1). Inappropriate ADH secretion syndrome and pituitary insufficiency are endocrine causes of hyponatremia. The main reason in both groups is the direct or indirect increase in ADH secretion. Inappropriate ADH secretion is the most common cause of normovolemic hyponatremia in clinical practice. It causes inappropriate ADH release, regardless of effective serum osmolality and volume. This increased release may be from the pituitary gland or an ectopic focus (2).

As a result of an inappropriate increase in ADH, water reabsorption increases with the stimulation of specific receptors in the collecting ducts of the kidney and the ascending branch of the hen. However, the intravascular volume and the amount of Na^+ reaching the distal nephron increase, proximal tubular Na^+ reabsorption decreases, and ultimately, hypoosmolar hyponatremia develops. Hypervolemia does not develop because volume receptors are activated, and a proportional increase in urinary Na^+ and water excretion is achieved. The net result is water retention and Na^+ loss (3). Increased plasma ADH levels occur due to impaired water excretion in the anterior pituitary, especially ACTH (adrenocorticotropic hormone) deficiency. It has been shown that in pure glucocorticoid deficiency, ADH levels inappropriately increase without a decrease in extracellular volume. This ADH increase can be corrected with physiological doses of glucocorticoids (4).

Natriuretic peptides are a class of hormones that regulate blood pressure, electrolyte balance, and fluid volume. Members of the natriuretic peptide family are brain natriuretic peptide (BNP), atrial natriuretic peptide (ANP), C type natriuretic peptide (CNP), and dendroapsis natriuretic peptide (DNP) (5). BNP is produced in the heart in bursts-sudden oscillations in precursor BNP "pro-BNP," which contains 108 amino acids.

Since increased wall tension is the common denominator of many cardiac diseases, circulating BNP levels may serve as a “clinical marker” of these diseases. When there is a sustained ventricular expansion and pressure increase, proBNP is released into the blood and is broken down into the physiologically active hormone BNP and its inactive metabolite, N-terminal BNP. Plasma concentrations of NT-proBNP and BNP

are similar in normal individuals. Both are continuously released from the heart and detected in healthy people's venous blood at picomolar concentrations. With a half-life of approximately 22 minutes, BNP accurately reflects pulmonary capillary wedge pressure changes every two hours. The plasma half-life of the inactive form, NT proBNP, is longer than BNP; therefore, its amount in the blood is easier to determine (6).

The main source of BNP is the ventricles. This makes BNP more sensitive and specific as a determinant of ventricular disorders than other natriuretic peptides. It has been shown in various studies that the amount of BNP released from the ventricle is directly proportional to volume expansion and pressure load (7). Although the main control is by myocyte stretching, natriuretic peptide synthesis is affected by tachycardia, glucocorticoids, thyroid hormones, vasoactive peptides (endothelin-1), and angiotensin II, independent of their hemodynamic effects (2). Fluid retention occurs with the increase in ADH secretion. Fluid retention leads to cardiac strain, and it is thought that it may cause increased secretion of BNP and NT-proBNP (5). Within the scope of this research, we aimed to elucidate the relationship between NT-proBNP and hyponatremia in inappropriate ADH secretion syndrome and pituitary insufficiency.

METHOD

This prospective study included 14 patients with hyponatremia, inappropriate ADH secretion syndrome, and nine patients with pituitary insufficiency (gonadotropin deficiency, corticotropin deficiency, and central hypothyroidism) who applied to the Internal Medicine Clinic of Ankara Keçiören Training and Research Hospital, and 21 healthy volunteers with no systemic disease and serum sodium levels within the normal range. Of the nine patients in the pituitary insufficiency group, 3 had corticotropin deficiency, 2 had central hypothyroidism and accompanying gonadotropin deficiency, and 4 had gonadotropin deficiency alone.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution with protocol number 2012-KAEK-15/1806, and informed consent has been obtained from all participants.

Laboratory tests of the patient group (fasting blood sugar, serum sodium level, spot urine sodium, creatinine, urine osmolarity, and anterior pituitary hormones of patients with suspected pituitary insufficiency) were recorded from the patient files. Echocardiography was performed on the patient group to rule out heart failure. The records of healthy volunteers forming the control group were also from the hospital system. Blood samples were taken into EDTA tubes and centrifuged to measure NT-ProBNP levels from blood samples taken from the patient and control groups. The plasma was separated and stored at -20 C. Samples were studied with the NT-proBNP kit and the sandwich immunoassay method on the Dade Behring brand Dimension Plus device.

Inclusion Criteria

Individuals ≥18 years old, with serum sodium <130 (mild hyponatremia levels of 130 – 135 were not included to detect a significant difference in NT-pro BNP levels) were enrolled.

Exclusion Criteria

Individuals <18 years old with acute and chronic cardiac disease, chronic kidney failure, chronic liver disease, and diastolic heart failure who had hyponatremia secondary to hypovolemia, EF below 50%, using diuretics were excluded.

Statistical Analysis

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 26.0 (IBM Corp., Armonk, NY) package program. Frequency and percentage for categorical data and mean and standard deviation for continuous data were given as descriptive values. For comparisons between groups, the “Independent Sample T–test” was used for two groups, and the “Pearson Chi-Square Test” was used to compare categorical variables. The results were considered statistically significant when the p-value was less than 0.05.

RESULTS

This study included 14 patients with hyponatremia, inappropriate ADH secretion syndrome, and nine patients with pituitary insufficiency (gonadotropin deficiency, corticotropin deficiency, and central hypothyroidism) who applied to the Internal Medicine Clinic of Ankara Keçiören Training and Research Hospital, and 21 healthy volunteers with no systemic disease and serum sodium levels within the normal range. Of the nine patients in the pituitary insufficiency group, 3 had corticotropin deficiency, 2 had central hypothyroidism and accompanying gonadotropin deficiency, and 4 had gonadotropin deficiency alone. The median age of patients with pituitary insufficiency was 74, the median age of patients with inappropriate ADH secretion syndrome was 72.5, and the median age of the control group was 74. No statistically significant difference was found between the groups in terms of age and gender (Table 1).

Table 1. Comparison Of Demographic And Biochemical Data Between Groups

	Pituitary Insufficiency	Inappropriate ADH Secretion Syndrome	Control Group	*p-value*
Age	74(11)	72.5(12.75)	74(10.5)	NS
Gender	Female:5 (%55.6) Male:4 (%44.4)	Female:10 (%71.4) Male:4 (%28.6)	Female:11 (%52.4) Male:10 (%47.6)	NS
FPG (mg/dl)	107(55)	139(89)	99(3.5)	**0.007**
Sodyum$_1$ (meq/l)	127(9,5)	124(9.75)	138(3)	**<0.0001**
Sodyum$_2$ (meq/l)	136(3)	136.5(3)		AD
NT-proBNP$_1$ (pg/ml)	671(1061.5)	499(763.75)	119(188.05)	**<0.0001**
NT-proBNP$_2$ (pg/ml)	1076(1066)	185.5(276.08)		**0.004**
TSH (mIU/l)	1.01(2.62)	1.175(0.88)		AD
Free T3 (pg/ml)	1.88(0.54)	2.2(0.53)		**0.002**
Free T4 (pg/ml)	0.9(0.33)	1.475(0.37)		**0.001**
FSH (mIU/ml)	1.47(11.39)	32.5(56.32)		AD
LH (mIU/ml)	0.38(3.09)	12.5(20.35)		**0.021**
GH (ng/ml)	0.1(0.71)	0.4(0.35)		AD
PRL (ng/ml)	4.05(8.5)	9.5(13.25)		AD
ACTH (pg/ml)	16.4(26.75)	14.5(8.28)		AD
Cortisol (mg/dl)	12.4(14.04)	15(7.25)		AD
IGF-1 (mmol/l)	40(93.4)	81(20.7)		AD
EF (%)	55(5)	55(10)		AD

Median(IQR), NS: Not Significant, FPG: Fasting Plasma Glucose, NT-proBNP: N-Terminal Brain Natriuretic Peptide, TSH: Thyroid Stimulating Hormone, St3: Free Triiodothyronine, St4: Thyroxine, SH: Follicle *S*timulating Hormone, LH: Luteinizing Hormone, GH: Growth Hormone, PRL: Prolactin, IGF-1: Insulin-Like Growth Factor, EF: Ejection Fraction.

The difference between fasting plasma glucose was statistically significant between the three groups. Median fasting plasma glucose was 107 (mg/dl) in the pituitary insufficiency group, 139 (mg/dl) in the inappropriate ADH secretion syndrome group, and 99 (mg/dl) in the control group (p=0.007), (Table 1).

No statistically significant difference was detected between the pituitary insufficiency and inappropriate ADH secretion syndrome groups in terms of TSH, FSH, LH, GH, prolactin, ACTH, cortisol, IGF-1, and EF levels. The median TSH value was 1.01 (mIU/l) in the pituitary insufficiency group, 1.175 (mIU/l) in the inappropriate ADH secretion syndrome group, the median FSH value was 1.47 (mIU/ml) in the pituitary insufficiency group, and 32.5 (mIU/ml) in the inappropriate ADH secretion syndrome group. The median LH level was 0.38 (mIU/ml) in the pituitary insufficiency group, 12.5 (mIU/ml) in the inappropriate ADH secretion syndrome group, the median GH level was 0.1 (ng/ml) in the pituitary insufficiency group, median prolactin level was 0.4 (ng/ml) in the inappropriate ADH secretion syndrome group, median prolactin value was 4.05 (ng/ml) in the pituitary insufficiency group, median ACTH level was 9.5 (pg/ml) in the pituitary insufficiency group. The median IGF-1 level was 40 (pg/ml) in the pituitary insufficiency group and 81 (pg/ml) in the inappropriate ADH secretion syndrome group. The median EF level was 55% in the pituitary insufficiency group and 55% in the inappropriate ADH secretion syndrome group (Table 1).

St3 value in the pituitary insufficiency group was statistically significantly lower than in the inappropriate ADH secretion syndrome group. The median free T_3 value was 1.88 (pg/ml) in the pituitary insufficiency group and 2.2 (pg/ml) in the inappropriate ADH secretion syndrome group (p=0.002) (Table 1). The free T_4 value in the pituitary insufficiency group was statistically significantly lower than in the inappropriate ADH secretion syndrome group. The median free T4 value was 0.9 (pg/ml) in the pituitary insufficiency group and 1.475 (pg/ml) in the inappropriate ADH secretion syndrome group (p=0.001) (Table 1).Basal sodium levels were statistically significant among the three groups. The median basal sodium level was 127 (meq/l) in the pituitary insufficiency group, 124 (meq/l) in the inappropriate ADH secretion syndrome group, and 138 (meq/l) in the control group (p<0.0001) (Figure 1).

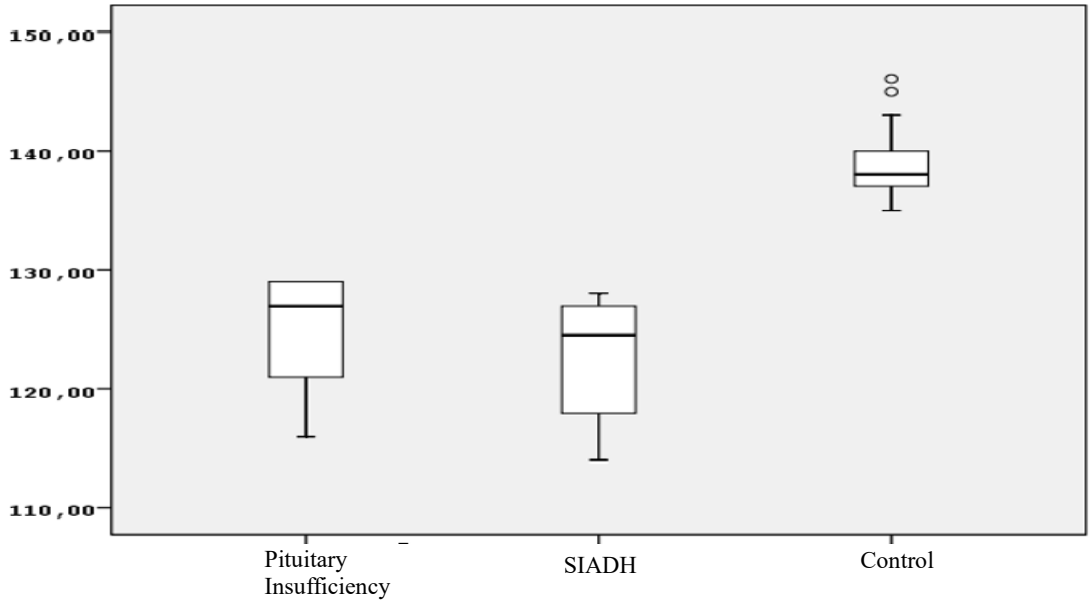

Figure 1. Basal Sodium Levels Between Groups (p <0.0001).

Basal NT-proBNP levels were statistically significant among the three groups. The median NT-proBNP level was found to be 671 (pg/ml) in the pituitary insufficiency group, 499 (pg/ml) in the inappropriate ADH secretion syndrome group, and 119 (pg/ml) in the control group (p<0.0001) (Figure 2).

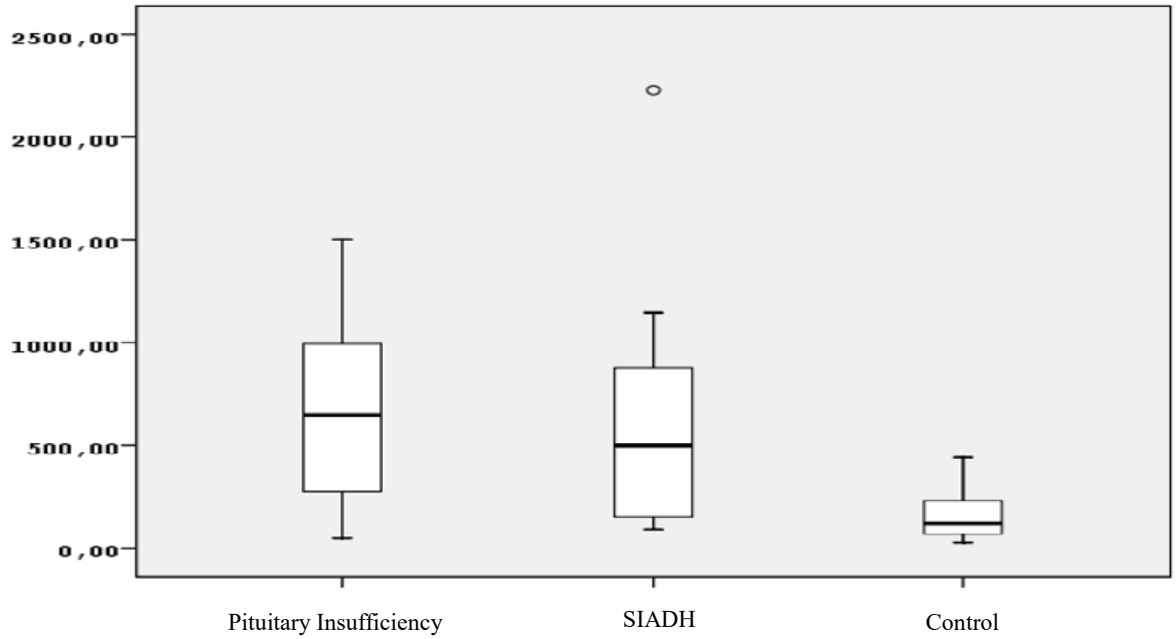

Figure 2. Comparison Of Baseline BNP Measurements Between Groups (Prepared By Removing One Patient With An Outlier Value, p<0.0001).

While the plasma sodium value was within the normal range between the pituitary insufficiency group and the inappropriate ADH secretion syndrome group, the NT-proBNP value was statistically significantly lower in the inappropriate ADH secretion syndrome group than in the pituitary insufficiency group. The median NT-proBNP level was found to be 1076 (pg/ml) in the pituitary insufficiency group and 185.5 (pg/ml) in the inappropriate ADH secretion syndrome group (p=0.004) (Figure 3).

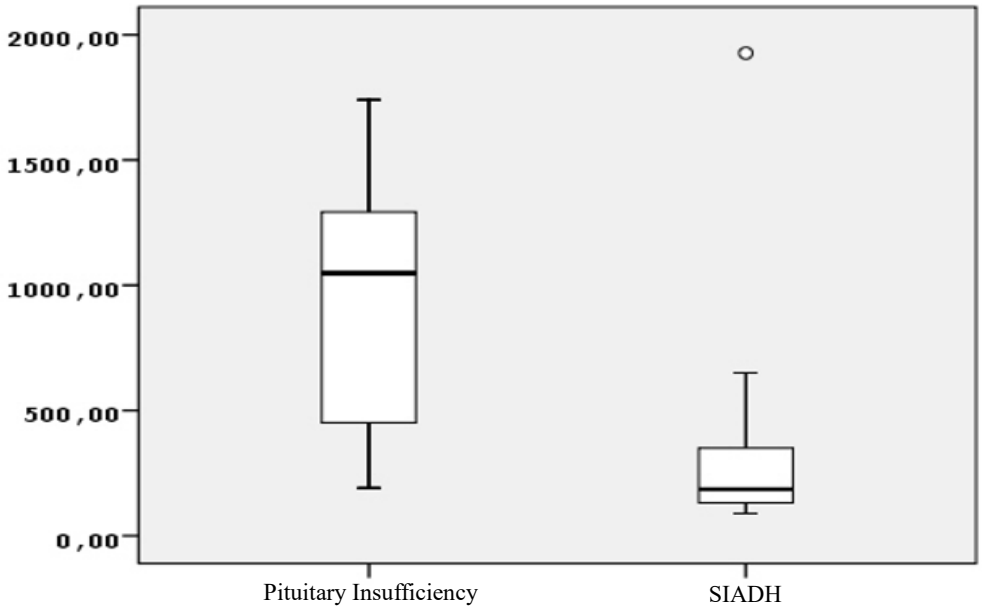

Figure 3. Comparison Of NT-proBNP Levels Measured When The Plasma Sodium Level Was Within The Normal Range In The Pituitary İnsufficiency Group And The Syndrome of İnappropriate ADH Secretion Group (p =0.004).

In the pituitary insufficiency group, the basal NT-proBNP level measured when the plasma sodium level was low was statistically significantly lower than the NT-proBNP level measured when the plasma sodium level was within the normal range. The median basal NT-proBNP level was 671 (pg/ml), and the median NT-proBNP level when sodium was within the normal range was 1076 (pg/ml) (p=0.008) (Figure 4).

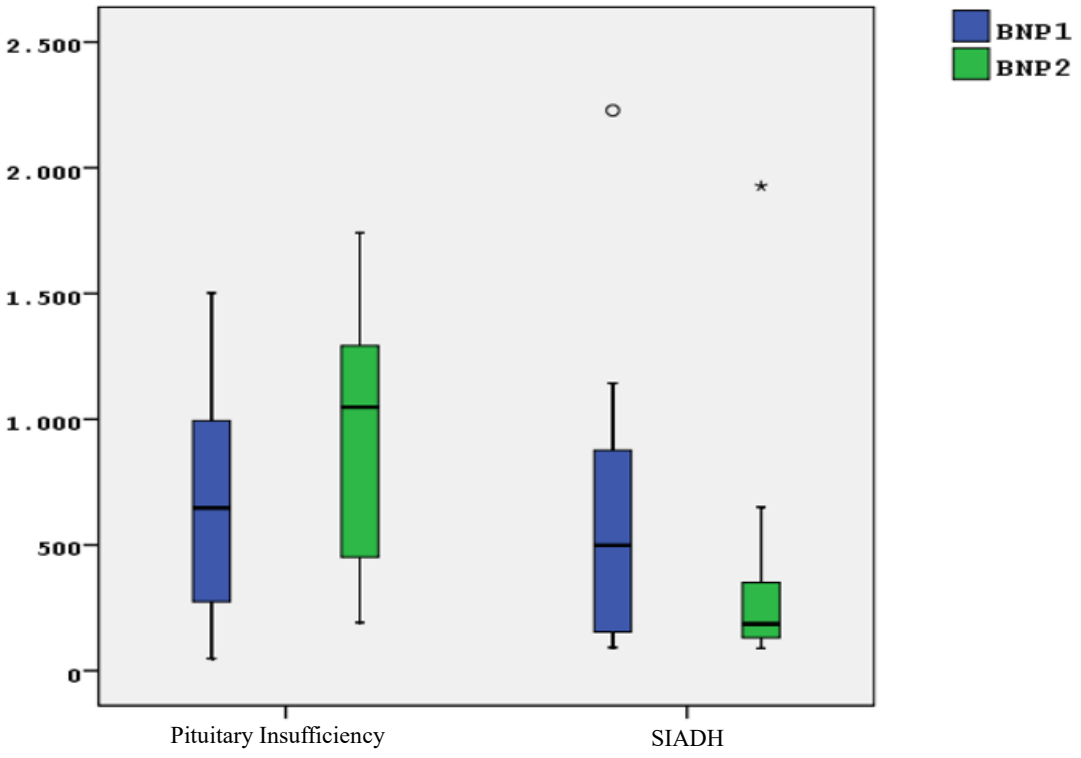

Figure 4. Comparison Of Basal NT-proBNP And Secondary NT-proBNP Levels. As A Result of The Evaluation Made By ROC Analysis, Serum NT-proBNP Values Were Found To Have Diagnostic Value İn Predicting Hyponatremia Due To Endocrinological Reasons (Inappropriate ADH Secretion Syndrome And Pituitary Insufficiency). (AUC:0.87 95% Confidence Interval 0.763-0.977, p<0.0001). This Value's Recommended Limit Value Is 141 (Sensitivity: 91.3% And Specificity: 66.7%).

In the inappropriate ADH secretion syndrome group, the basal NT-proBNP level measured when the sodium level was low was statistically significantly higher than the NT-proBNP level measured when the plasma sodium level was within the normal range. The median basal NT-proBNP level was 499 (pg/ml), and the median NT-proBNP level when sodium was within the normal range was 185.5 (pg/ml) (p=0.004) (Figure 4).

As a result of the evaluation made by ROC analysis, serum NT-proBNP values were found to have diagnostic value in predicting hyponatremia due to endocrinological reasons (inappropriate ADH secretion syndrome and pituitary insufficiency) (AUC:0.87 95% confidence interval 0.763 – 0.977, p<0.0001). This value's recommended limit value is 141 (sensitivity: 91.3% and specificity: 66.7%).

DISCUSSION

In this study, it was aimed to examine NT-proBNP levels in hyponatremia due to endocrine reasons. NT-proBNP measured during low plasma sodium levels were statistically significantly higher in the pituitary insufficiency and inappropriate ADH secretion syndrome group compared to the control group. In the inappropriate ADH secretion syndrome group, the NT-proBNP level measured after the plasma sodium level returned to normal was lower, with a statistically significant difference, compared to the NT-proBNP level measured when the plasma sodium level was low. In the pituitary insufficiency group, the NT-proBNP level measured after the plasma sodium level returned to normal was higher, with a statistically significant difference, compared to the NT-proBNP level measured when the plasma sodium level was low.

NT-proBNP has been very useful in diagnosing heart failure in clinical practice. Diagnosis of heart failure is difficult because its symptoms and signs are not sensitive and specific. Diagnosis becomes even more difficult if the patient is elderly and the symptoms are mild or if he/she has comorbid diseases such as pulmonary diseases that mimic heart failure or obesity (8). Hyponatremia can be observed in many patients diagnosed with heart failure, and most often the cause is hypervolemic hyponatremia. However, endocrine causes and accompanying hyponatremia may also be observed in these patients. The fact that the NT-proBNP test used in the diagnosis of heart failure is affected by various hormonal disorders may cause errors in the diagnosis of heart failure and incorrect treatments (9).

In previous literature, only a few articles investigated the relationship between BNP and endocrine disorders. In the study of Schultz et al., NT-pro-BNP levels of 17 overt hypothyroid, 21 subclinical hypothyroid, 13 overt hyperthyroid, and six subclinical hyperthyroid patients without heart disease and dyspnea were measured. Then, NT-proBNP measurements were repeated after euthyroidism was achieved. However, in this study, echocardiography could not detect that the ejection fractions were normal, which was stated as a deficiency. In this study, it was determined that NT-proBNP levels were affected by thyroid hormones. Serum-free T3, T4, and TSH levels were associated with NT-proBNP. NT-proBNP levels were not found to be related to the age of the patients. There was a significant decrease in NT-proBNP levels with treatment in the overt and subclinical hyperthyroid groups. There was a significant increase in NTproBNP levels in the overt and subclinical hypothyroid groups. In multiple linear regression analysis, fT4 and fT3 were associated with high NT-proBNP levels. This study showed a change in NT-proBNP levels with treatment in subclinical thyroid diseases, and it was stated that this was a finding that subclinical thyroid disorders affected the heart at the tissue level. In the study conducted by Schultz M. et al., NT-proBNP levels were high in overt and subclinical hyperthyroidism, which may cause false-positive results in the diagnosis of heart failure. For this reason, it has been recommended that thyroid hormones be studied simultaneously when using the NT-proBNP test to diagnose heart failure (10).

In a similar study conducted by Ertuğrul et al., NT-proBNP levels measured in 48 overt hyperthyroid patients during overt hyperthyroidism and after they became euthyroid after treatment were compared. NT-proBNP levels measured during hyperthyroidism were statistically significantly higher than NT-proBNP levels measured during euthyroidism (p <0.001) (11). Individuals with thyroid dysfunction, among endocrine causes, were examined, and the serum sodium levels of those participating in the study

were within the normal range. In our study, the pituitary insufficiency group consists of hyponatremia patients with central hypothyroidism, gonadotropin deficiency, and ACTH deficiency. There is no other study in the literature examining these patient groups.

In the study by Oelkers et al., the relationship between hyponatremia and pituitary insufficiency was investigated in five patients. It was thought that ACTH deficiency caused the syndrome of inappropriate ADH secretion, and it was concluded that the main factor causing this condition was cortisol deficiency (12). Unlike Oelkers et al., our study examined NT-proBNP in patients with pituitary insufficiency. We examined the relationship between pituitary insufficiency, hyponatremia, and NT-proBNP. The occurrence of hyponatremia in the pituitary insufficiency group was similar and statistically significant. It was thought that the impairment of ADH secretion and the increase in volume caused the increase in ventricular tension, and NT-proBNP was released into the circulation from the stretched ventricle (13).

There are studies examining the relationship between inappropriate ADH secretion syndrome and NT-proBNP, but they include insufficient numbers and limited patient groups. In a study by Tobin et al., 31 postoperative neurosurgical patients with hyponatremia were investigated. The patients participating in the study were divided into hypovolemic and normovolemic, according to central venous pressure measurement. The hypovolemic group was evaluated as cerebral salt loss, and the normovolemic group was evaluated as inappropriate ADH secretion syndrome. NT-proBNP values between these two groups were compared at the end of the study. NT-proBNP values were lower in the group with inappropriate ADH secretion syndrome than in the group with cerebral salt loss. It has been concluded that NT-proBNP is an important marker in distinguishing between inappropriate ADH release and cerebral salt loss (14). In our study, the inappropriate ADH secretion syndrome group does not consist of postoperative patients. The patients included in our study had lung and urinary system infections. Patients with cerebral salt loss were not included in our study. Therefore, a comparison between cerebral salt depletion and inappropriate ADH secretion syndrome regarding NT-proBNP could not be made. There are no definitive criteria for the differential diagnosis of cerebral salt depletion and inappropriate ADH secretion syndrome. Patients were evaluated according to volume status. Volume evaluation was conducted based on physical examination. In our study, NT-proBNP, measured in the inappropriate ADH secretion syndrome group after the serum sodium level returned to normal, was within the normal range as expected.

Tobin et al.'s study concluded that NT-proBNP could be used as a marker in the differential diagnosis of inappropriate ADH secretion syndrome and cerebral salt wasting (14). Our study observed that it could be used as a marker in the differential diagnosis of inappropriate ADH secretion syndrome and pituitary insufficiency. In our study, there were patients with central hypothyroidism, gonadotropin deficiency, and corticotropin deficiency in the pituitary insufficiency group. It is a known fact that NT-proBNP levels are high in corticotropin deficiency (15). However, there is no similar study on high NT-proBNP levels in patients with central hypothyroidism and gonadotropin deficiency. On the other hand, it is a known fact that BNP is secreted in the brain, especially in the hypothalamus (16). In the study conducted by Sayan et al. on 70 patients, it was aimed to examine the levels of BNP as a marker for the diagnosis and prognosis of acute ischemic stroke. BNP levels were examined among 40 patients and 30 healthy volunteers. As a result of the research, it was concluded that plasma BNP levels increased in the acute phase of stroke. Therefore, BNP could be used as a marker of morbidity and mortality even in patients without heart failure (17). This study by Sayan et al. supports the secretion of BNP from the brain triggered by an acute ischemic cerebrovascular event. In our study, the basal NT-proBNP values in the pituitary insufficiency group were statistically significantly higher than the control group, indicating that the release of BNP from the hypothalamus was triggered. In addition, NT-proBNP values measured when plasma sodium values were within the normal range were statistically significantly higher, suggesting that the high NT-proBNP values in the pituitary insufficiency group were high independently of hyponatremia (17).

As a result, the underlying cause in patients with hyponatremia may be pituitary insufficiency and inappropriate ADH release syndrome. NT-proBNP levels are affected in these patients. Patients whose dyspnea etiology is being investigated should be evaluated for pituitary insufficiency and inappropriate

ADH secretion syndrome. In cases of hyponatremia, which we encounter in heart failure cases, we recommend that normovolemic patients be investigated for pituitary insufficiency and inappropriate ADH secretion syndrome. In addition, NT-proBNP can be used as a marker in the differential diagnosis of patients with inappropriate ADH secretion syndrome and pituitary insufficiency.

Our study aimed to examine NT-proBNP levels in hyponatremia due to endocrine reasons. In the inappropriate ADH secretion syndrome group, we found that the NT-proBNP level measured after the plasma sodium level returned to normal was lower than the NT-proBNP level measured when the plasma sodium level was low, showing a statistically significant difference. In the pituitary insufficiency group, we found that the NT-proBNP level measured after the plasma sodium level returned to normal was higher, with a statistically significant difference, compared to the NT-proBNP level measured when the plasma sodium level was low.

CONCLUSION

This research elaborated that while plasma sodium levels were low in the inappropriate ADH secretion syndrome and pituitary insufficiency groups, the NT-proBNP levels were higher, showing a statistically significant difference between the three groups. In patients with hyponatremia, the underlying cause may be pituitary insufficiency and inappropriate ADH secretion syndrome. NT-proBNP levels are affected in these patients. Patients whose dyspnea etiology is being investigated should be evaluated for pituitary insufficiency and inappropriate ADH secretion syndrome. NT-proBNP can be used as a marker in the differential diagnosis of patients with inappropriate ADH secretion syndrome and pituitary insufficiency.

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