



Study the Effect of Hyperthyroidism on Heart Function by Using BNP as Indicator

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Abstract

The aim was made to specify the effect of hyperthyroidism on B-type natriuretic peptide (BNP) level. Twenty patients with hyperthyroidism, 20 patients with hyperthyroidism treated with (35) mg Carbimazole, 12 patients with hyperthyroidism associated with heart failure and 20 healthy participants were included in this study. Serum Triiodothyronine (T₃), Thyroxin (T₄) and Thyroid stimulating hormone (TSH) have been used for hyperthyroidism diagnosis test, also serum BNP level was measured. The results showed that the mean \pm SE of serum BNP was significantly ($P < 0.05$) increased in hyperthyroid group (420.76 ± 83.43) pg/mL and hyperthyroid with heart failure group (728.58 ± 149.06) pg/mL when compared with the control group (23.18 ± 10.10) pg/mL. While, no significant ($P > 0.05$) differences between hyperthyroid treated with (35) mg carbimazole group (65.00 ± 16.21) pg/mL and control group (23.18 ± 10.10) pg/mL. But, there was a significant ($p < 0.05$) decrease in serum BNP level in hyperthyroid treated with (35) mg carbimazole group when compared with the hyperthyroid group and hyperthyroid with heart failure group. The present study demonstrated that the hyperthyroidism may lead to impaired heart function, and thus the high level of the BNP hormone

Keywords: Hyperthyroidism, B-type natriuretic peptide (BNP), Heart failure.

دراسة تأثير فرط نشاط الغدة الدرقية في وظيفة القلب بقياس مستوى هرمون الببتيد الدماغي كمؤشر

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الخلاصة:

أجريت الدراسة لمعرفة مدى تأثير نشاط الغدة الدرقية في وظائف القلب باستخدام هرمون B- نوع الببتيد الناتريوتريك (BNP) كمؤشر. شملت الدراسة 20 مريضاً يعانون من فرط نشاط الغدة الدرقية و 20 مريضاً يعانون من مرض زيادة نشاط الغدة الدرقية المعاملين بـ (35) ملغ كاربامازول و 12 مريضاً يعانون من زيادة نشاط الغدة الدرقية المرتبطة بقصور في القلب بالإضافة إلى 20 شخصاً من الأصحاء (كمجموعة سيطرة). تم قياس مستوى ثلاثي يودوثيرونين المصل (T₃) و الثايروكسين (T₄) وهرمون تنشيط الغدة الدرقية (TSH) كاختبارات رئيسية لتشخيص فرط نشاط الغدة الدرقية. بالإضافة إلى قياس مستوى BNP في المصل. أوضحت النتائج وجود زيادة معنوية ($P < 0.05$) في تركيز هرمون BNP في مصل مجموعة فرط نشاط الغدة الدرقية (420.76 ± 83.43) pg/mL والمجموعة المصابة بفرط نشاط الغدة مع فشل القلب

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النتائج بوجود فروق معنوية ($P > 0.05$) بين مجموعة فرط نشاط الغدة المعاملة بـ (35) mg كارباميزول (10.10 ± 23.18) pg/mL وبينما لم تظهر النتائج انخفاضاً معنوياً ($p < 0.05$) في مستوى هرمون BNP في مجموعة فرط نشاط الدرقية المعاملة بـ (35) mg كارباميزول (16.21 ± 65.00) pg/mL بالمقارنة مع مجموعة السيطرة (10.10 ± 23.18) pg/mL. ولكن أظهرت النتائج انخفاضاً معنوياً ($p < 0.05$) في مستوى هرمون BNP في مجموعة فرط نشاط الدرقية المعاملة بـ (35) mg كارباميزول (16.21 ± 65.00) pg/mL بالمقارنة مع مجموعة فرط نشاط الغدة (83.43 ± 420.76) pg/mL والمجموعة المصابة بفرط نشاط الغدة الدرقية مع فشل القلب (149.06 ± 728.58) pg/mL. أظهرت هذه الدراسة أن الإصابة بفرط نشاط الغدة الدرقية قد يؤدي إلى ضعف نشاط القلب وبالتالي إرتفاع في مستوى هرمون BNP.

Introduction

Heart failure (HF) is a progressive disorder that encompasses overlapping hemodynamic and neurohormonal facets [1]. It is a major public health issue, with a prevalence of over 5.8 million in the USA and over 23 million worldwide [2]. Heart is the one of target for thyroid hormones (T_3 , T_4) action [3, 4]. Untreated hyperthyroidism is a cause of heart failure and associated with increase morbidity and mortality [3, 5].

The concept of the heart as an endocrine organ emerged in the middle of 20th century [6]. In 1988, a structurally related peptide was purified from the porcine brain; accordingly it was named "Brain Natriuretic Peptide" (BNP) [7]. It was later ascertained that BNP was synthesized primarily in the myocardium [8, 9]. Therefore, to avoid confusion "Brain Natriuretic Peptide" is often called B-type natriuretic peptide [6]. B-type natriuretic peptide: A cardiac peptide hormone belonging to the natriuretic peptide family predominantly synthesized and secreted by the cardiac ventricles myocytes in response to stretching forces [10]. The messenger RNA for proBNP is unstable, so there is active regulation of BNP levels according to ventricular wall tension. Hence, it acts as a reliable biomarker of heart function [11]. Several pathophysiological mechanisms such as ventricular hypertrophy and fibrosis stimulate BNP production and release from ventricular cardiomyocytes [12].

The principal function of BNP is to protect the cardiovascular system from volume overload, it is a key regulator in the homeostasis of salt and water balance and in maintaining peripheral vessel tone, BNP antagonize the renin-angiotensin system, inhibit endothelin secretion, and reduce systemic and renal sympathetic activity thereby increasing natriuretic (excretion of sodium), diuretic (excretion of water) and vasorelaxant activity (by relaxing vascular smooth muscle). Thus, it is act as a compensatory mechanism to promote cardiac function [13]. The utility of BNP has been demonstrated in several studies and is perhaps the most widely used biomarker in the assessment of HF [2,13]. Measurement of BNP level may help to detect heart failure in patients with clinical hyperthyroidism [14]. Therefore, this study aimed to investigate the effect of an overactive thyroid (hyperthyroidism) on the heart by measuring the level of BNP.

Materials and methods

Four groups have been investigated, informed consent was obtained from all patients. Twenty patients with Hyperthyroidism group, Twenty patients with hyperthyroidism treated with (35) mg Carbimazole. Twelve patients with hyperthyroidism associated with heart failure and twenty healthy participants included in this study were taken as a control group. Five milliliter (5mL) of venous blood was collected from each subject. The sera separated from the samples were analyzed to determine (T_3 , T_4 and TSH), by a full automated immunoassay analyzer (AIA-360), Tosoh, Japan and BNP concentration by ELISA method, RayBiotech, USA. All results were expressed as mean \pm SE. The statistical Analysis System-SAS (2010) was applied to assess the effect of different factors in the study parameters.

Results and Discussion

The results in table 1 showed a significant ($P < 0.05$) increase in serum T_3 level for hyperthyroid group (2.45 ± 0.26) ng/mL and hyperthyroid with heart failure group (2.11 ± 0.12) ng/mL when compared with the control group (1.15 ± 0.03) ng/mL. Also, the results revealed a significant ($p < 0.05$) decrease in serum T_3 level in hyperthyroid treated with (35) carbimazole group (1.19 ± 0.08) ng/mL in comparison with the hyperthyroid group and hyperthyroid with heart failure group. Whereas, table 1

showed a non significant differences ($P>0.05$) in T_3 level in hyperthyroidism treated with (35) mg carbimazole when compared with the control group.

Table 1 revealed a significant ($P<0.05$) increase in the mean serum T_4 concentration for hyperthyroid group (12.49 ± 0.59) ug/mL and hyperthyroid with heart failure group (11.11 ± 0.71) ug/mL when compared with the control group (7.69 ± 0.22) ug/mL. Also the result revealed a significant ($p<0.05$) decrease in T_4 concentration in hyperthyroid treated with (35) carbimazole group (7.89 ± 0.38) ug/mL in comparison with those of hyperthyroid group and hyperthyroid with heart failure group. While the result showed a non significant differences ($P>0.05$) in serum T_4 between hyperthyroid treated with (35) mg carbimazole group and the control group table 1.

The statistical analysis for the results in table (1) revealed a significant ($P<0.05$) decrease in serum TSH level in hyperthyroid group (0.422 ± 0.11) uIU/mL and hyperthyroid with heart failure group (0.362 ± 0.07) uIU/mL when compared with the control group (1.92 ± 0.21) uIU/mL. While a significant ($p<0.05$) increase was observed in serum TSH level in hyperthyroid treated with (35) mg carbimazole (2.15 ± 0.72) uIU/mL when compared with hyperthyroid group and hyperthyroid with heart failure group. But a non significant ($P>0.05$) differences in serum TSH level between hyperthyroid treated with (35) mg carbimazole group and the control.

Table 2 and figure 1 showed a significant ($P<0.05$) increase in serum BNP level in hyperthyroid group (420.76 ± 83.43) pg/mL and hyperthyroid with heart failure group (728.58 ± 149.06) pg/mL when compared with the control group (23.18 ± 10.10) pg/mL. Also a significant ($p<0.05$) decrease was observed in serum BNP level in hyperthyroid treated with (35) mg carbimazole (65.00 ± 16.21) pg/mL when compared with hyperthyroid group and hyperthyroid with heart failure group. While the result showed a non significant ($P>0.05$) differences in serum BNP level between hyperthyroid treated with (35) mg carbimazole group and control group.

Table 1- Levels of serum thyroid hormones in hyperthyroidism, hyperthyroid treated with (35) mg carbimazole and hyperthyroidism with heart failure groups (means \pm SE).

Groups	Thyroid hormones		
	T_3 (ng/mL)	T_4 (ug/mL)	TSH (uIU/mL)
Control	1.15 ± 0.03 b	7.69 ± 0.22 b	1.92 ± 0.21 a
Hyperthyroid	2.45 ± 0.26 a	12.49 ± 0.59 a	0.422 ± 0.11 b
Hyperthyroid treated with (35)mg carbimazole	1.19 ± 0.08 b	7.89 ± 0.38 b	2.15 ± 0.72 a
Hyperthyroid with heart failure	2.11 ± 0.12 a	11.11 ± 0.71 a	0.362 ± 0.07 b

Table 2- Serum BNP level in hyperthyroidism, hyperthyroid treated with (35) mg carbimazole and hyperthyroidism with heart failure groups (means \pm SE).

Groups	BNP concentration (pg/mL)
Control	23.18 ± 10.10 c
Hyperthyroid	420.76 ± 83.43 b
Hyperthyroid treated with (35) mg carbimazole.	65.00 ± 16.21 c
Hyperthyroid with Heart failure	728.58 ± 149.06 a

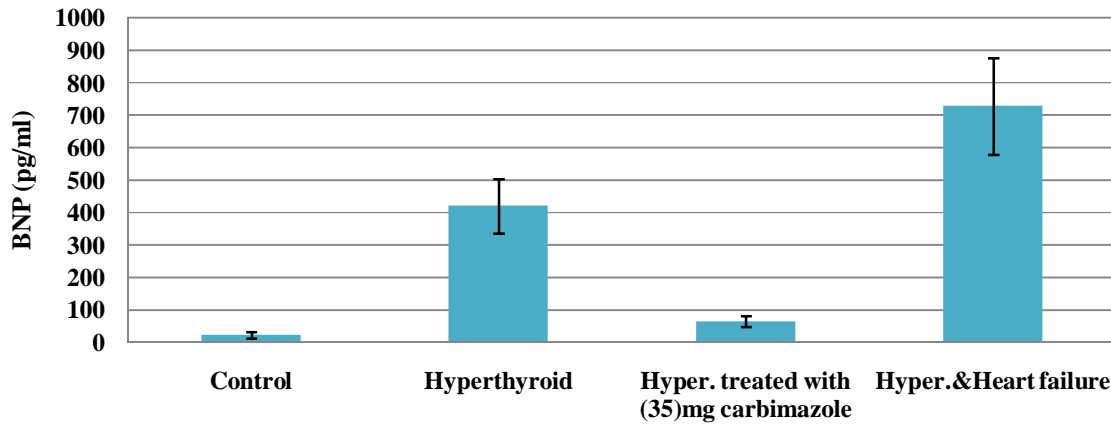


Figure 1- Serum BNP level in control, hyperthyroidism, hyperthyroid treated with (35) mg carbimazole and hyperthyroid with heart failure groups.

The results showed that there were a significant ($P < 0.05$) increase in serum BNP level in hyperthyroid group when compared with the control group. This result is in agreement with [14] who reported that patients with hyperthyroidism have six times higher BNP levels than controls, elevated BNP levels were mainly found in hyperthyroid patients who had clinical and echocardiographic evidence of left ventricular (LV) dysfunction. Also, Ertugrul *et al.* [15] reported that BNP levels were more than five times higher in hyperthyroid than euthyroid control subjects. The findings of a current study agree with above observation and with other previous reports submitted by [16, 17]. On the other hand the results of the present study revealed a non significant difference in serum BNP level in hyperthyroid treated with (35) mg of carbimazole when compared with the control. This observation is in agreement with [16] who found that the treatment of thyroid dysfunctions could result in normalization of BNP and NT-proBNP levels in hyperthyroid groups. This may be due to the effect of carbimazole therapy that gave rise to normalize hyperthyroid state thereby minimize the action of thyroid hormone on the heart, resulting in decrease the BNP level.

Likewise, the results of current study showed that serum of BNP level was significantly higher in hyperthyroid with heart failure group in comparison with control, this in agreement with other authors [18,19] they found that the BNP levels in heart failure with hyperthyroid group were significantly high than the control group.

The most recognizable features of hyperthyroidism are those that resulted from the effects of (T_3) on the heart and cardiovascular system which includes hemodynamic changes such as: decreased systemic vascular resistance increased resting heart rate, ventricular contractility, total blood volume, blood pressure and cardiac output [14, 20]. The impairment of left ventricular function is well-known in patients with hyperthyroidism [21]. The increase in pulse rate and cardiac output seen in hyperthyroidism represents a situation of increased cardiac stretch [22]. Mehta and Dubrey [23] found that elevation of heart rate, stroke and minute volumes, acceleration of blood flow, decrease of systemic vascular resistance result in increase in ventricular stretch and pressure overload which might cause concomitant rise in BNP concentrations. This increase is may be due to hyperthyroidism cause heart failure.

Also, Goetze *et al.*, [24] explained that the BNP concentration in heart failure was increased approximately four-fold in peripheral plasma when it compared with the control subjects. Hyperthyroidism may lead to cardiac dysfunction by the genomic and non-genomic effects resulting from high levels of thyroid hormone, these imbalances in cardiac physiological and functional may lead to elevation of BNP hormone levels, probably reflecting more severe form of impaired cardiac function and heart failure.

The findings of our study revealed a significant ($p < 0.05$) increase in serum BNP level in hyperthyroid with heart failure group and hyperthyroid group in comparison with hyperthyroid treated with (35) mg carbimazole group, this in agreement with [25] who documented that BNP levels were significantly higher in hyperthyroid and a significant decreased in BNP level were observed after euthyroidism was achieved. This may be attributed to the effect of the carbimazole treatment.

Subsequently result in reduction in BNP levels. Restoration of euthyroidism state improves cardiovascular parameters (reduction in heart rate and the number of atrial and ventricular premature beats and cardiac output) [26].

The significant increase in serum level of BNP in hyperthyroid with heart failure group when it compared with hyperthyroid group, are quite compatible with Li-ling, [27] who reported that the levels of BNP were significantly higher in the patients with hyperthyroid heart disease than those of hyperthyroidism group .Serum BNP concentrations in heart failure patients are found to increase proportionally to the severity and duration of the clinical condition [28].

Conclusion: The BNP hormone increases in hyperthyroidism associated with heart failure and there were a negative correlation between the level of BNP and carbimazole therapy, that normalize hyperthyroid state thereby minimize the action of thyroid hormone on the heart, resulting in decrease the BNP level.

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