SUBCLINICAL HYPERTHYROIDISM AND OVERT HYPERTHYROIDISM AS A RISK FACTORS FOR ATRIAL FIBRILLATION IN AL- NASIRIYAH CITY

Dr. Wajdy J. Majid*

ABSTRACT

Background: Atrial fibrillation is a well known manifestation of hyperthyroidism, we studied whether subclinical hyperthyroidism in clinically euthyroid persons is a risk factor for atrial fibrillation.

Method: We studied 267 persons, the subject was classified into 3 groups according to the serum TSH.

Group I: (174) persons compromised those with normal values of serum TSH (0.25 – 5 μU/ml) and T3, T4 within normal limit, this group considered as control group.

Group II: (61) persons those with low serum TSH ( < 0.25 μU/ml) and with elevated serum T3 and T4, i.e., overt hyperthyroidism.

Group III: (32) persons those with low serum TSH ( < 0.25 μU/ml) and T3 and T4 within normal limit, i.e., subclinical hyperthyroidism.

Result: Atrial fibrillation (AF) was presented in 4 only from 174 with a percent of (2.3%) in group I, but 9 only from 61 persons with a percent of (13.8%) were presented in group II, while 4 only from 32 persons with a percent of (12.7%) in group III. There is significant difference (P < 0.01) between group I when it compared with other groups.

Conclusion: Low serum thyrotropin concentration is associated with more than 5 fold higher likelihood for the presence of AF with no significance difference between subclinical and overt hyperthyroidism.

INTRODUCTION

Atrial fibrillation (AF) is a common dysrhythmia representing an independent risk factor for cardiovascular events [1]. The rapid and irregular heartbeat produced by AF increases the risk of blood clot formation inside the heart. These clots may eventually become dislodged, causing embolism, stroke, and other disorders [1,2]. AF may occur in patients with a variety of cardiovascular or chronic diseases as well as in normal subjects. It is the most common cardiac complication of hyperthyroidism. AF in thyrotoxicosis is associated with significant mortality and morbidity resulting from embolic events [3]. Generally, AF is associated with advancing age and cardiovascular conditions such as hypertension, coronary artery disease, valvular disease, cardiomyopathy (heart enlargement and weakening), and congestive heart failure [4]. Thyroxine (T4) and triiodothyronine (T3) are tyrosine-based hormones produced by the thyroid gland. The major form of thyroid hormone in the blood is thyroxine (T4). The ratio of T4 to T3 in the blood is roughly 20 to 1. Thyroxine is converted to the active T3 form (3 to 4 times more potent than T4) by

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deiodinases. TSH stimulates the thyroid gland to secrete the thyroid hormones. TSH production is controlled by thyrotropin releasing hormone (TRH), which is synthesised in the hypothalamus and transported to the anterior pituitary gland via the superior hypophyseal artery(5). Hyperthyroidism is a well established cause of atrial fibrillation (AF) and Atrial fibrillation in thyrotoxicosis is associated with significant mortality and morbidity resulting from embolic events. Somatostatin is also produced by the hypothalamus, and has an opposite effect on the pituitary production of TSH, decreasing or inhibiting its release. [6.)

Thyroid hormones exert their cardiovascular effects either directly through nuclear thyroid receptors or indirectly by influencing sympathoadrenergic system and altering peripheral vascular resistance (figure 1). Binding of thyroid hormones to nuclear receptors result in increased gene transcription of cardiac myocyte proteins [7]. Thyroid hormones up regulate sarcoplasmic Calcium ATPase, myosin heavy chain alfa, voltage gated K+ channels, Na+ channels and beta1 adrenergic receptors [8]. These effects result in increased heart rate, systolic hypertension, increased ventricular contractility and cardiac hypertrophy. Changes in electrophysiological characteristics of atria result in dysrhythmias, especially atrial fibrillation, in patients with hyperthyroidism [9]. Thyroid hormones reduce peripheral vascular resistance [10] and increase oxygen demand of tissues, thus increasing cardiac workload. The availability of sensitive assays for thyrotropin (TSH) has resulted in the identification of patients who have low serum TSH concentrations (<0.5 μU/mL) but normal serum thyroxine (T4) and triiodothyronine (T3) concentrations, a constellation of findings defined as subclinical hyperthyroidism. These patients have few or no symptoms or signs of hyperthyroidism. [10]

PATEINTS AND METHOD

A- patients selection : we studied 267 persons ( age 39 ± 2.9 ) , those persons classified into 3 groups :

**group I**: ( 174 ) persons include those with normal values of serum TSH (0.25 – 5 µU/ml) and T3 , T4 within normal limit , this group considered as a control group .

**group II**: ( 61 ) persons those with low serum TSH ( < 0.25 μU/ml) and T3 , T4 were elevated i.e overt hyperthyroidism .

**group III**: ( 32 ) persons those with low serum TSH ( < 0.25 μU/ml ) and T3, T4 within normal limit i.e subclinical hyperthyroidism .

All those persons were collected from Al-Hussein teaching hospital ( Cardiac centre , outpatient and inpatient ) for ten months from April 2009 to February 2010 , most of patients in group II are a known cases of overt hyperthyroidism , while group III either treated on previously or accidental finding.

B- Laboratory Data : 3 CC of serum sample were collected from persons onby using an automated quantitative test for use on the VIDAS instruments by the assay principle combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA) by the assay principle for measurement of thyroid hormone test 11 . These subjects were matched on the basis of thyroid function test TSH ( 0.25 – 5.00 μU/L) , Free T3 ( 0.92 – 2.33 nmol/L) and Free T4 ( 60 -120 nmol/L) (12).

Electrocardiography were done for all patients and control groups (13) .

C- Statistical analysis : All the values were expressed as means ± standard deviation . Data were analyzed by one way analysis of variance ( ANOVA) for equal sample size and independent sample T- test to differentiate between two groups . Using computerized SPSS program . P .value < 0.05 considered to be lowest limit of significance

RESULTS

The characteristic of this study ( control and case ) were shown in table I
Atrial fibrillation was presented in 4 only from the (174) persons with a percent of (2.3%) in group I, while in group II, AF was found in 9 only from 61 persons with a percent of (14.7%).

In group III (subclinical hyperthyroidism) AF it had been found in 4 only from 32 patients with a percent of (12.5%).

There were a significance difference in patients with AF in group II or group III in compared with control group (group I) i.e (P < 0.01) …Table 2

The biochemical parameters of all groups with their values were shown in Table 3

**DISCUSSION**

Atrial fibrillation is reported in 10 - 15% of patients with hyperthyroidism [13]. and sinus tachycardia is the most common arrhythmia in hyperthyroidism [14]. AF in thyrotoxicosis is associated with significant mortality and morbidity resulting from embolic events [12]. The risk factors for AF in patients with hyperthyroidism (age, male sex, ischemic heart disease, congestive heart failure and valvular heart disease) are similar to those in the general population [15]. AF occurs in up to 15% of patients with hyperthyroidism [14] compared with 4% incidence in the general population [16] and is more common in men and in patients with triiodothyronine (T$_3$) toxicosis [3]. Overt hyperthyroidism induces a hyperdynamic cardiovascular state (high cardiac output with low systemic vascular resistance), which is associated with a faster heart rate, enhanced left ventricular systolic and diastolic function, and increased prevalence of supraventricular tachyarrhythmias [17].

Thyroid hormones may exert both genomic and nongenomic effects on cardiac myocytes [17]. The genomic effects of thyroid hormones are mediated by transcriptional activation or repression of specific target genes that encode both structural and functional proteins [18]. In this study we have showed that the prevalence of atrial fibrillation increased in subclinical and overt hyperthyroidism, when they compared with normal person. In a large study by Krahn et al, overt hyperthyroidism accounted for <1% of cases of new onset atrial fibrillation. According to these investigators, although serum thyroid hormone should be measured in all patients with new onset atrial fibrillation to rule out hyperthyroidism, [19]. Therefore, although serum thyrotropin should be measured in all patients with new-onset atrial fibrillation in order to rule out thyroid disease, [19]. However, as many as 13 percent of patients with unexplained atrial fibrillation have biochemical evidence of hyperthyroidism [20-21].

**CONCLUSION**

Atrial fibrillation is well known manifestation of overt hyperthyroidism, in this study we found that subclinical hyperthyroidism i.e. low serum T.S.H and with normal both T3 and T4 in clinically euothyroid person a risk factor of atrial fibrillation and no significant difference of overt hyperthyroidism.

**RECOMMENDATION**

We suggest that thyroid function test should be done for any patient with atrial fibrillation specially first attach.

**TABLES AND FIGURES**

<table>
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<th>Parameters</th>
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<th>Patients %</th>
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<td>37.6 ± 2.7</td>
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<tr>
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<td>35.3</td>
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Table 2

<table>
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<th>patients</th>
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<tbody>
<tr>
<td>control</td>
<td>4 (2.3%)</td>
<td>170 (97.7%)</td>
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</tr>
<tr>
<td>Hyperthyroidism</td>
<td>9 * (14.7%)</td>
<td>52 (85.3%)</td>
<td>61 (100%)</td>
</tr>
<tr>
<td>Subclinical hyperthyroidism</td>
<td>4 * (12.5%)</td>
<td>28 (87.5%)</td>
<td>32 (100%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>17 (6.4%)</td>
<td>250 (93.6%)</td>
<td>267</td>
</tr>
</tbody>
</table>

* Significantly different as compared with control group (P< 0.01)
While there was no significance between group II in compared with group III.

Table 3

<table>
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<th>Subclinical hyperthyroidism</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>No. 174</td>
<td>No. 61</td>
<td>No. 32</td>
</tr>
<tr>
<td>TSH</td>
<td>2.7 ± 1.3</td>
<td>0.084 ± 0.062*</td>
<td>0.075 ± 0.05*</td>
</tr>
<tr>
<td>T3</td>
<td>0.701± 0.16</td>
<td>7.855 ± 2.33*</td>
<td>0.92 ± 0.79</td>
</tr>
<tr>
<td>T4</td>
<td>60.488± 29.7</td>
<td>141.52± 14.54*</td>
<td>60.8 ± 25.3</td>
</tr>
</tbody>
</table>

Figure 1. Sites of Action of Triiodothyronine on Cardiac Myocytes.
REFERENCES


Subclinical Hyperthyroidism And Overt Hyperthyroidism As A Risk Factors For Atrial Fibrillation In Al- Nasiriyah City

زيادة افراز الغدد الدرقية الغير سريري و زيادة افراز الغدد الدرقية السريري كعوامل خطوره للارتجاف الاندسي في مدينة الناصريه

الخلاصة

خلفية الدراسة: ارتفاع الاندسي هو علامة سريرية مميزة لأمراض الغدد الدرقية ولا سيما هولاء الذين يعانون من زيادة افراز الغدة الدرقية السريري، هنا ندرس فيما إذا كانت حالة زيادة افراز الغدد الدرقية الغير سريري كعامل مساعد لهذا الارتجاف أم لا.

الممرض وطريقة العمل: شملت الدراسة 376 شخص باعمار (39 ± 09) وقد قسم إلى ثلاث مجموعات.

المجموعة الأولى: هولاء الاشخاص الذين نسبة TSH معنويه 0.20-0.55 وكذلك نسبة T3 وطبيعيه و عدد هولاء المرضى 174 مريض.

المجموعة الثانية: هولاء الاشخاص الذين نسبة TSH عدت واطئه (أقل من 0.25) و نسبة T3 و T4 هي عاليه أي زيادة افراز الغدة الدرقية السريري و عددهم 31 مريض.

المجموعة الثالثة: هولاء الاشخاص الذين نسبة TSH عندم واطئه (أقل من 0.25) و نسبة T3 و T4 ضمن الحدود الطبيعيه.. أي زيادة الافراز غير السريري و عددهم 33 مريض.

كل هولاء المرضى جمعوا من مستشفى الحسين التعليمي في الناصريه و مركز القلب والراقدين في المستشفى تمت هذه الدراسة لفترة عشرة أشهر وتعادل من شهر نيسان 2009 ولغاية شهر شباط 2010.

النتائج: الارتجاف الاندسي قد وجد في أربع مرضى بنسبة (2.3%) عند المجموعة الأولى من أصل 174 شخص، أما المجموعه الثانية فان الارتجاف الاندسي قد وجد في 9 مريض من أصل 31 مريض مصاب بزيادة افراز الغدة الدرقية السريري و بنسبة (28.8%) ، أما المجموعه الثالثه فان الارتجاف الاندسي قد وجد في 4 مريض من اصل 33 شخص و بنسبة (12.3%) ، حيث كانت هناك علاقة وثيقة بين المجموعه الأولى عندما قورنت مع بقية المجموعات (نسبة الخطأ أقل من 0.01) ولا توجد علاقة وثيقة عندما قورنت المجموعه الثانية مع المجموعه الثالثه.

الاستنتاج والتصويتات: ظننا أن الارتجاف الاندسي علامة سريرية مميزة في مرضى زيادة افراز الغدد الدرقية وهذا أيضا فرض بأنه علامة سريرية مميزة لمرضي زيادة الافراز غير السريري لذا فأنا نقترح عمل تحليل افراز الغدد الدرقية لكل مرضى الارتجاف الاندسي وخاصه للمره الأولى.

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