A More Appropriate Algorithm of Thyroid Function Test in Diagnosis of Hyperthyroidism for Thai Patients

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Background : *Thyroid function test is an essential tool in the diagnosis of thyroid dysfunction. To date, it is still controversial which diagnostic algorithm is best applicable to clinically hyperthyroidism patients.*
Objective : *To compare various algorithms of thyroid function tests in the diagnosis of hyperthyroidism.*
Method : *Patients from the endocrine clinic, King Chulalongkorn Memorial Hospital were investigated for thyroid function tests (T_3, T_4, FT_3, FT_4 and TSH). Hyperthyroidism was defined as an elevated either FT_3 or FT_4 with suppressed TSH. The authors compared the effectiveness in hyperthyroidism diagnosis among algorithms by using sensitivity, specificity, positive predictive value and negative predictive value.*
Results : *Of all 452 patients in the present study, 94.24 percent were women. There were 206 hyperthyroidism, 30 subclinical hyperthyroidism, 1 subclinical hypothyroidism, 8 primary hypothyroidism and 207 normal subjects. The incidence of T_3 toxicosis was 16.02% while that of T_4 toxicosis was 2.16%. After the effectiveness analysis of these algorithms, FT_3 and TSH is the most optimal test with 97.57% sensitivity and 100% specificity. Compared to FT_4 and TSH, it gave 83.98% sensitivity and 100% specificity.*
Conclusion : *According to the high incidence of T_3 toxicosis in the present study, FT_3 and TSH should be the initial test for diagnosis of hyperthyroid patients in an outpatient setting and FT_4 should be measured subsequently in case of suspected T_4 toxicosis.*

Keywords *: Hyperthyroid, Thyroid function test, T_3 toxicosis, T_4 toxicosis*

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Thyroid dysfunction is one of the most common clinical problems encountered by primary care physicians. Due to its diverse clinical manifestations, confirmation by thyroid function test is crucial. Free thyroid hormone and higher sensitivity thyroid stimulating hormone (TSH) measurement have improved the accuracy and precision of tests in recent years. Despite these technical improvements, the appropriate use of these tests remains non-uniformly recommended. The purpose of the present study was to search for an optimal algorithm in diagnosis of hyperthyroidism for Thai patients.

Material and Method

A total of 452 cases, including 207 normal controls and 26 men, at the Endocrine Clinic of King Chulalongkorn Memorial hospital were recruited consecutively from May 2000 to April 2002. The patients with pregnancy, hospitalization or taking medications which affected thyroid function were excluded from the study. The thyroid function tests, (T_3, T_4, FT_3 FT_4 and TSH) were measured by electrochemiluminescent assay while TSH by 4th generation assay (Elecsys 2010, RoChe Diagnostics GmBH, USA). The internal quality control was included in each batch of tests performed. Detailed clinical profile was recorded in performa to evaluate the thyroid function of each patient and to exclude the possible confounding effect of systemic illness or drugs on the thyroid function tests. Hyperthyroidism is defined as elevated FT_3, FT_4 or both and decreased TSH levels and primary hypothyroid as the state of high circulating TSH accompanied with low FT_4 level. Occasionally, however, FT_3 or FT_4 alone is increased in hyper-thyroidism, and this condition is coined T_3 or T_4 toxicosis, respectively. Subclinical hypothyroidism is defined as the state of elevated TSH and normal FT_4 levels in asymptomatic subjects, whereas subclinical hyperthyroid is defined as the state of low circulating TSH with normal free thyroid

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hormones. After comparing the sensitivity, specificity, positive predictive value and negative predictive value of each algorithm, the authors propose the optimal algorithm in diagnosis of hyperthyroidism.

Results

Based on thyroid function test results; 206 patients with hyperthyroidism were identified. Thirty patients had subclinical hyperthyroidism, 1 subclinical hypothyroidism, 8 primary hypothyroidism and 207 normal thyroid function. Table 1 showed the characteristic of patients. The majority of the study population was in an active age (21-40 years). Table 2 showed the efficacy of each pair of thyroid function test in diagnosis of hyperthyroidism. Among hyperthyroid patients, the incidence of T_3 toxicosis was 16.02% (33/206 cases) and the incidence of T_4 toxicosis was 2.91% (5/206 cases). Mean age of the patients with T_3 toxicosis was 39.5 years and T_4 toxicosis was 58.6 years. All of them were women. Of note was a high incidence of T_3 toxicosis in the present study.

Discussion

Thyroid function tests are among the most common endocrine laboratory procedures. Since thyroid hormones and TSH balance each other through a regulatory feedback loop mechanism, patterns of each hormone are usually considered together for diagnosis. As a diagnostic test, its cost-effectiveness should be a priority ,whereas in case of the screening test, its sensitivity and readiness should be considered [1]. Various clinical practice guidelines for diagnosis of thyroid dysfunction have been published [2-4], mostly from Western countries. While in other parts of the world, the diagnosis scheme may be different due to local epidemiological factors, costs, healthcare systems along with availability of medical insurance and reimbursement practices. American Thyroid Association (ATA) suggested that both FT_4 and TSH are necessary for diagnosis [5-8]. FT_3 measurement is mainly advocated as a third-level due to its high sensitivity to technical factor and sick euthyroid state and indicated when T_3 toxicosis is suspected [9,10].

The present study showed the higher incidence of T_3 toxicosis compared with the previous studies. The incidence of T_3 toxicosis was reported by Bellabarba[11] who found 7 cases in 62 consecutive cases. Hollander et al [12] found 10 cases of T_3 toxicosis in 200 cases of hyperthyroidism. The large epidemiologic studies in US populations from Becker et al[8] and Figge et al[9] showed the incidence of T_3 toxicosis was only 2-5%. Hollander et al [13] reported that the incidence of T_3 toxicosis is much higher in iodine deficiency areas. The studies about urine iodine in a Thai populations showed lower levels compared with Japanese and American population[14,15], which may explain the higher incidence of T_3 toxicosis. The clinical significance of T_3 toxicosis is still elusive; some authors suggest that T_3 toxicosis may be the early state of hyperthyroidism and the patients with T_3 toxicosis are more likely to have long-term remission after withdrawal of antithyroid drug therapy.

The present study demonstrates that FT_3 and TSH is the most optimal test in the diagnosis of hyperthyroidism in an ambulatory setting. FT_4 should be measured subsequently in cases of suspected T_4 toxicosis. However, thyroid function tests can be misleading in hospitalized patients or abnormal thyroid binding proteins and the use of multiple tests is, therefore, appropriate[16].

Table 1. Demonstrate the characteristic of patients

	Male	Female
Age (range, y)	18-72	15-75
Hyperthyroidism (n)	13	193
Subclinical hyperthyroidism (n)	1	29
Subclinical Hypothyroidism (n)	-	1
Primary hypothyroidism (n)	-	8
Normal (n)	12	195

Table 2. Demonstrate the efficacy of each algorithm to diagnose hyperthyroidism

Test	Sensitivity	Specificity	PPV	NPV	Efficacy of test
TSH	100	87.80	87.29	100	93.36
T_3 TSH	81.07	97.97	97.09	86.07	90.26
T_4 TSH	74.27	99.19	98.71	82.15	87.83
FT_3 TSH	97.57	100	100	98	98.89
FT_4 TSH	83.98	100	100	88.17	92.70
T_3 T_4 TSH	87.38	99.18	98.90	90.44	94.25
T_3 FT_4 TSH	91.26	91.26	100	93.18	96.02

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ขั้นตอนการตรวจธัยรอยด์ฮอร์โมนที่เหมาะสมในการวินิจฉัยภาวะต่อมธัยรอยด์เป็นพิษในผู้ป่วยชาวไทย

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บทนำ *: การตรวจธัยรอยด์ฮอร์โมนเป็นขั้นตอนสำคัญในการวินิจฉัยความผิดปกติการทำงานของต่อมธัยรอยด์ ปัจจุบันยังไม่มีการศึกษาถึงประสิทธิภาพหรือขั้นตอนที่เหมาะสมของการตรวจฮอร์โมนของผู้ป่วยชาวไทยสำหรับการวินิจฉัยภาวะต่อมธัยรอยด์เป็นพิษ*

วัตถุประสงค์ *: เพื่อเปรียบเทียบประสิทธิภาพของการตรวจระดับธัยรอยด์ฮอร์โมนชนิดต่าง ๆ เพื่อกำหนดแนวทางที่เหมาะสมในการวินิจฉัยภาวะต่อมธัยรอยด์เป็นพิษ*

วิธีการ *: ศึกษากลุ่มผู้ป่วยที่มารับการรักษาที่คลินิกต่อมไร้ท่อ โรงพยาบาลจุฬาลงกรณ์ โดยทำการตรวจระดับธัยรอยด์ฮอร์โมนชนิดต่าง ๆ ได้แก่ T_3, T_4, FT_3, FT_4 และ TSH และ นำมาเปรียบเทียบประสิทธิภาพในการวินิจฉัยโดยพิจารณาจากค่าความไว ความจำเพาะ สัดส่วนของการเป็นโรคเมื่อตรวจได้ผลบวก และ สัดส่วนการไม่เป็นโรคเมื่อตรวจได้ผลลบ*

ผลการวิจัย *: ผู้เข้าร่วมการวิจัยทั้งหมด 452 ราย แยกกลุ่มตามผลการตรวจระดับธัยรอยด์ฮอร์โมนได้ดังนี้ ภาวะต่อมธัยรอยด์เป็นพิษ 206 ราย ภาวะต่อมธัยรอยด์เป็นพิษชนิดแฝง 30 ราย ภาวะต่อมธัยรอยด์ทำงานต่ำชนิดแฝง 1 ราย ภาวะต่อมธัยรอยด์ทำงานต่ำ 8 รายและปกติ 207 ราย พบอุบัติการณ์ภาวะ T_3 toxicosis 16.02% และ T_4 toxicosis 2.91% พิจารณาในด้านประสิทธิภาพ การวัดระดับ FT_3 และ TSH มีค่าความไว 97.57% และ ค่าความจำเพาะ 100% เมื่อเปรียบเทียบกับการวัดระดับ FT_4 และ TSH ซึ่งมีความไวเพียง 83.98% และ ความจำเพาะ 100%*

สรุป *: จากงานวิจัยฉบับนี้แสดงให้เห็นว่าอุบัติการณ์ของภาวะ T_3 toxicosis มีค่าสูงถึง 16.2% ทำให้ควรเลือกการตรวจธัยรอยด์ฮอร์โมนด้วย FT_3 และ TSH เป็นลำดับแรก ในกรณีที่สงสัยภาวะต่อมธัยรอยด์เป็นพิษ*