Effects of Quetiapine on Thyroid Function Tests in Schizophrenic Patients

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Abstract

To investigate the effects of quetiapine on thyroid function tests in newly diagnosed schizophrenic patients. Thirty subjects with schizophrenia, were treated openly with quetiapine .Diagnosis of schizophrenia was made according to DSM-IV criteria of American Psychiatric Association. Another thirty healthy individual participated in the study as a control group. Thyroid data, consisting of values for thyroid-stimulating hormone (TSH), total triiodothyronine (TT3), and total thyroxine (TT4). TSH, TT3, and TT4 were measured by radioimmunoassay. Measurements of patient's thyroid data were done before and after 3 months of therapy (Suggested period of the research) with quetiapine and at the start of the research for the controls. Comparison of TSH, TT3 and TT4 of the control group and those of patients before treatment shows a non significant differences for all parameters. Comparison between TSH, TT3 and TT4 values before and after treatment with quetiapine shows only a significant reduction of TT4 values ($P<0.001$). This study shows that 3 months therapy with quetiapine leads to a reduction of TT4 concentration in the serum of schizophrenic patients.

تأثير الكواتيابين على فحوصات وظائف الغدة الدرقية في مرضى انفصام الشخصية

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المستخلص

الاهداف. لتحري تأثيرات الكواتيابين على فحوص وظائف الغده الدرقيه في مرضى الفصام المشخصين حديثا. المرضى وطرق العمل. ثلاثون مريضا من مرضى الفصام تمت معالجتهم بصوره مفتوحه بالكواتيابين. تشخيص الحالات بالفصام تم وفق معاييرالتصنيف الامريكي للامرض النفسيه-الطبعة الرابعه للجمعيه النفسيه الامريكيه. ثلاثون من الاشخاص الاصحاء تم اشراكهم في هذه الدراسه ايضا كمجموعة ضبط. النتائج تضمنت قيم الثايروكسين الكلي، التراي ايودوثايرونين الكلي والهرمون المحفز للغده الدرقيه. تم اجراء القياسات قبل اعطاء الكواتيابين وبعد ٣ أشهر من العلاج المستمر(الفتره المقترحه للبحث) وكذا في البدايه لمجموعة الضبط. النتائج. مقارنة قيم الثايروكسين الكلي، التراي ايدوثايرونين الكلي والهرمون المحفز للغده الدرقيه عند مجموعة الضبط والمرضى قبل العلاج اظهر وجود فروق غير معنويه في كل هذه القيم.بمقارنة قيم المفردات المذكوره اعلاه في المرضى قبل وبعد فترةالعلاج كان هنالك انخفاض معنوي في الثايروكسين الكلي. الاستنتاج.اظهرت هذه الدراسه ان العلاج بالكواتيابين لمدة ٣ أشهر قد يؤدي الى انخفاض في تركيز الثايروكسين الكلي عند مرضى الفصام.

Introduction

Quetiapine is a novel dibenzothiazepine antipsychotic developed by Zeneca Pharmaceuticals in 1985. It is marketed under the trade name Seroquel (1). Quetiapine was approved in September 1997 by the US Food and Drug Administration (FDA) and has since been introduced in Canada, most Western European countries, Japan as well as in 70 other countries worldwide for the treatment of schizophrenia and other psychiatric illnesses (2). The primary indications are adult schizophrenia and related psychoses in adults and elderly (3, 4). Other indications, such as treatment of moderate to severe manic episodes, treatment of aggressive behavior in children and adolescents, and behavioral disturbances in patients with dementia, have also been explored and have been successfully carried out. More recent data point to good efficacy of quetiapine in the treatment of depressive episodes in the context of bipolar disorder(5). Many drugs affect tests of thyroid function through alterations in the synthesis, transport and metabolism of thyroid hormones, as well as via influences on thyrotrophin (TSH) synthesis and secretion. Despite effects on circulating thyroid hormone and TSH levels, few drugs result in important changes in clinical thyroid state, but difficulty in interpretation of thyroid function tests often results. Commonly prescribed drugs including anticonvulsants, NSAIDs, beta adrenoceptor antagonists, steroid hormones and heparin may result in abnormal thyroid function tests in the absence of clinical features of thyroid dysfunction. In contrast, lithium and iodine containing drugs including radiographic contrast agents and amiodarone, may result rarely in overt thyroid disease (6). In psychiatry, the only drugs which are studied and found to affect thyroid function tests including lithium (7), Fluoxetine (8), clomipramine (9), desipramine (10). Recently, quetiapine, an antipsychotic drug have received a good attention and few authors have tests its effects on thyroid function during treatment of schizophrenic patients. This new field of research need further work in order to support the findings of this authors. Thus the present study was designed to investigate the effect of quetiapine on thyroid function tests in a number of schizophrenic patients.

Patients and Methods

Thirty subjects with schizophrenia but without a history of thyroid treatment or antipsychotic drug, were treated openly with quetiapine in doses ranged between 200to 400 mg daily. Diagnosis of schizophrenia was made according to DSM-IV criteria of American Psychiatric Association. Another thirty healthy individual participated in the study as a control group. Scizophrenic patients were collected from private clinic during the period from January/ 2010 to January /2011 .Thyroid data, consisting of values for thyroid-stimulating hormone (TSH), total triiodothyronine (TT3), and total thyroxine (TT4). TSH was measured by Immunoradiometric assay (IRMA) using commercial kits (Immunotech. France) (11).TT3, and TT4 were measured by radioimmunoassay by using commercial kits (Immunotech. France)(11). Measurements of patient's thyroid data were done before and after 3 months of therapy (Suggested period of the research) with quetiapine (Seroquel tablet-Astra Zeneca) and at the start of the research for the controls. Student unpaired t-test was used to compare between data of the controls and of the patients before and after therapy. Paired t-test also used to compare between of the patients obtained before and after therapy. Values less or equal to 0.05 considered significant.

Results

Table 1 shows comparison between ages, TSH, TT3, and TT4 values of the controls and patients before treatment. No significant differences obtained for all parameters. Table 2 shows comparison between TSH, TT3 and TT4 values before and after treatment with quetiapine. A significant reduction of TT4 values were obtained after 3 months therapy with quetiapine ($P<0.001$), and a non significant differences obtained for TSH and TT3, indicating that these 2 parameters were not affected by quetiapine.

Comparison between TSH, TT3 and TT4 values of the controls and of the patients after therapy with quetiapine revealed a significant difference for TT4 value only ($P<0.001$).

Discussion

The present study showed that the administration of quetiapine for 3 months to schizophrenic patient results in a significant reduction of the concentration of TT4. This indicate that quetiapine therapy may have a hypothyroidism effect . Review of literature revealed the presence of 3 articles that deals with the effects of quetiapine on thyroid function tests. In one study A 46-year-old African-American woman diagnosed with schizoaffective disorder, bipolar type, was suboptimally responsive to olanzapine treatment. Transition from olanzapine to quetiapine was initiated and, approximately two months after adding quetiapine to a standing pharmacotherapeutic regimen, the patient developed an elevated thyroid-stimulating hormone (TSH) concentration of 8.45 microU/L. A diagnosis of hypothyroidism was subsequently made, treatment with levothyroxine was initiated, and the patient's thyroid function became stable (12). In a 6-week double-blind study, inpatients with a recent exacerbation of schizophrenia were randomly assigned to treatment with paliperidone extended-release, quetiapine, or placebo. Mean changes in T4, T3, and TSH levels, respectively, at monotherapy phase endpoint were, for the paliperidone extended-release group, 0.04 µg/dl, –0.04 ng/ml, and 0.03 µIU/ml; for the quetiapine group, –1.87 µg/dl, –0.24 ng/ml, and 0.12 µIU/ml; and for the placebo group, 0.27 µg/dl, 0.00 ng/ml, and –0.17 µIU/ml (13). In another study Thyroid function was assessed in 38 adult DSM-IV-diagnosed schizophrenia patients after 6 weeks of prospective, double-blind, randomized treatment with quetiapine (400 mg/day), risperidone (4 mg/day), or fluphenazine (12.5 mg/day). Little change was noted in thyroid function during the 6 weeks of treatment, except for a significant decrease in TT(4) values for those taking quetiapine . Clinically, however, no patients demonstrated any signs or symptoms of hypothyroidism during the study, nor were any significant changes in the free thyroxine index or TSH levels noted (14). The mechanism involved in the reduction of TT4 concentration by quetiapine is unclear and another researches needed to support our finding and to clarify the mechanism by which quetiapine reduce TT4 concentration. Many commonly used drugs affect the regulation of thyroid function either by a direct effect on thyroid function (mostly suppression) such as amiodarone and lithium, or drugs which may cause analytical interference (increased FreeT4 by displacement) as heparin and NSAIDs, or by drugs which increase metabolism of thyroxin (cytochrome P450 inducers) as phenytoin and carbamazepine (15).

Conclusion

This study shows that 3 months therapy with quetiapine leads to a reduction of TT4

concentration in the serum of schizophrenic patients.

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Table(1):- Control and Baseline patient's characteristics (Mean±SD).

Parameters	Control	Baseline patient's characteristics	P=value
Age (year)	28.23±5.11	28.83±4.44	NS
TSH (mIU/L)	2.75±0.23	2.70±0.29	NS
TT4 (nmol/L)	117.82±17.50	114.55±14.90	NS
TT3 (nmol/L)	2.35±0.35	2.43±0.30	NS

NS = Not significant using Unpaired t-test

Table (2):- Comparison between baseline and after therapy parameters (Mean±SD).

Parameters	Baseline	After Treatment	P=value
TSH (mIU/L)	2.70±0.29	2.70±0.24	NS
TT4 (nmol/L)	114.55±14.90	102.15±9.29	< 0.001
TT3 (nmol/L)	2.43±0.30	2.43±0.29	NS

NS = Not significant using paired t-test

Table (3):- Comparison between control and after therapy parameters(Mean±SD).

Parameters	Control	After Treatment	P=value
TSH (mIU/L)	2.75±0.23	2.70±0.24	NS
TT4 (nmol/L)	117.82±17.50	102.15±9.29	< 0.001
TT3 (nmol/L)	2.35±0.35	2.43±0.29	NS

NS = Not significant using Unpaired t-test