

Thyroid Dysfunction in Chronic Schizophrenia Within a State Psychiatric Hospital

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Abstract

Objectives: This study seeks to determine the prevalence and pattern of thyroid dysfunction in a group of adult psychiatric inpatients with chronic schizophrenia. We also hypothesize that raised thyroid hormones are associated with more severe psychopathology. **Methods:** Thyroid function tests were performed on 189 patients and the Brief Psychiatric Rating Scale (BPRS) was administered by a single rater on all patients. **Results:** There was a high prevalence of (36.4%) thyroid function test abnormalities but all patients except 1 were assessed to be clinically euthyroid. Free thyroxine (fT4) and triiodothyronine (fT3) were significantly higher in patients with mild (BPRS score, 10-20) and major syndrome (BPRS score, equal or above 21) compared to no syndrome (BPRS score, 0-9). No correlation was found between thyroid hormones and neuroleptic use. **Conclusion:** Although thyroid function test abnormalities are common in patients with chronic schizophrenia, clinical thyroid illness was absent. This calls for caution in the use and interpretation of thyroid function tests in patients with chronic schizophrenia.

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Key words: Adults, Inpatients, Prevalence, Tests

Introduction

Thyroid dysfunction can give rise to various psychiatric symptoms.^{1,2} While there is a persistent interest in the role of thyroid axis in affective disorders,³ there is limited data on the interaction of thyroid dysfunction with psychotic disorders such as schizophrenia. Studies on abnormalities of thyroid function in acutely admitted patients with schizophrenia have yielded conflicting results on the levels of the various indices like thyroxine (T4), free thyroxine (fT4) and thyroid stimulating hormone (TSH).⁴⁻⁶ In comparison, literature on the thyroid status in patients with chronic schizophrenia is scanty and there is no reported data in our local population. It has been suggested that dopamine, which is increased in schizophrenia, may be inhibitory to TSH secretion.⁷ Treatment with neuroleptics, which are dopamine blockers, has been reported to lead to increases in TSH level or subclinical hypothyroidism.⁸

This study seeks to¹ determine the prevalence and pattern of thyroid dysfunction in an adult psychiatric inpatient population with chronic schizophrenia and² we also hypothesize that raised thyroid hormones are correlated with more severe psychopathology.

Materials and Methods

One hundred and eighty-nine inpatients at Woodbridge Hospital who fulfilled the DSM-IV criteria⁹ for schizophrenia were included in the study. The diagnosis was verified in each case by the consensus of 2 psychiatrists (KS and SAC). Patients with an established history of thyroid dysfunction, significant current medical or surgical illnesses and current lithium therapy were excluded. The study protocol was approved by the hospital's ethics committee and written informed consent was obtained from all patients after a detailed explanation of the study procedures.

Free thyroxine (fT4), triiodothyronine (fT3) and TSH were measured from venous blood samples using micro-particle enzyme immunoassays. The normal ranges for fT4, fT3 and TSH were 8.7 to 26.1 pmol/L, 5.8 to 8.7 pmol/L and 0.52 to 5.04 mIU/L, respectively.

The Brief Psychiatric Rating Scale (BPRS)¹⁰ was administered by a single rater (WML) who was blind to the results of the thyroid function. Each patient was interviewed and examined for any clinical manifestations of either hyperthyroidism or hypothyroidism. Details of the patients' current medications were recorded and the daily neuroleptic

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dosages were converted to chlorpromazine equivalents (CPZ eq).¹¹

Data were analysed using the Statistical Package for Social Sciences (SPSS) version 8.0 software. Normality of quantitative data was checked using the Kolmogorov-Smirnov 1-sample test. The parametric 2 sample *t*-test was used to determine the significance of the differences of fT3, fT4 and TSH levels between the different BPRS scores when normality assumptions were satisfied, otherwise Mann Whitney U-test was utilised. Spearman's correlation coefficient was used to present association between the variables. *P* value <0.05 was considered to be statistically significant.

Results

Of the 189 patients, 153 (81%) were males and 36 (19%) were females. There were 177 (93.7%) Chinese and 12 (6.3%) Malay patients. Their mean age (SD) was 55.6 (8.8) years, with a range of 33 to 83 years. The average duration of illness was 32.1 (8.9) years, with a range of 9 to 52 years. The mean (SE) number of neuroleptics was 1.62 (0.05), with a range of 0 to 4; while the mean (SE) daily neuroleptic dose was 446.6 (36.6) CPZ eq mg.

One hundred and twenty-two (64.6%) patients had normal thyroid function test results (fT4, fT3 and TSH). Sixty-seven (36.4%) of the patients had some biochemical abnormalities of thyroid function indices (Table I) and all of these patients except 1 were assessed to be clinically euthyroid. The majority (26.5%) had the "sick euthyroid syndrome", i.e., normal TSH and fT4 but low fT3.

One hundred and seventy (93.1%) patients had normal TSH alone (median, 1.31 mIU/L; range, 0.53 to 4.31 mIU/L). Their mean age (SD) was 55.9 (8.9) years (range, 33 to 83 years) and 35 (19.9%) were females. Low TSH levels were detected in 11 (5.8%) patients (median, 0.37 mIU/L; range, 0.01 to 0.52 mIU/L). Their mean age (SD) was 51.2 (7.4) years (range, 43 to 65 years) and 1 was female. One male patient had low TSH level with raised fT3 and fT4 which

TABLE I: PROFILE OF THYROID DYSFUNCTION IN CHRONIC SCHIZOPHRENIA

Thyroid function indices	No. (%)
low TSH, normal fT4, low fT3	2 (1.1)
low TSH, normal fT4, fT3	7 (3.7)
low TSH, normal fT4, raised fT3	1 (0.5)
low TSH, raised fT4, fT3	1 (0.5)
normal TSH, low fT4, normal fT3	1 (0.5)
normal TSH, normal fT4, low fT3	50 (26.5)
normal TSH, normal fT4, fT3	122 (64.6)
normal TSH, normal fT4, raised fT3	2 (1.1)
normal TSH, raised fT4, normal fT3	1 (0.5)
raised TSH, normal fT4, low fT3	2 (1.1)

TABLE II: CORRELATION BETWEEN THYROID HORMONES AND PSYCHOPATHOLOGY

	TSH	fT4	fT3
BPRS (0 – 9) (n = 5)	2.56 (1.04 – 5.29)	11.4 (9.13 – 13.05)	5.2 (4.2 – 6.4)
BPRS (10 – 20) (n = 81)	1.23 (0.36 – 4.31)	13.13 ^a (9.36 – 20.9)	6.7 ^c (3.1 – 8.7)
BPRS ≥21 (n = 90)	1.29 (0.1 – 5.05)	13.05 ^b (8.63 – 61.85)	6.5 ^d (3.8 – 33.3)

The values are median (range).

P values compared to BPRS (0-9) group using Mann Whitney U-test:

^a*P* = 0.033, ^b*P* = 0.013, ^c*P* = 0.009, ^d*P* = 0.030

was consistent with hyperthyroidism. He was treated and subsequently referred to the endocrinologist for review and follow-up.

The patients were divided into 3 groups ("no", "mild" and "major" syndromes) according their BPRS scores. The TSH levels were not significantly different amongst the 3 groups. However, the fT3 and fT4 were both significantly higher in those with "mild" and "major" syndromes (Table II).

There was no significant gender differences for the thyroid function test abnormalities. Neither was there any significant correlation between thyroid dysfunction and duration of illness, number of neuroleptics and daily chlorpromazine equivalents of neuroleptic medications.

Discussion

Our current study revealed a high prevalence (36.4%) of thyroid function test abnormalities among patients with chronic schizophrenia. Similar high prevalence (40%) was also noted by Othman et al.¹² In comparison with acute admissions, investigators found abnormal thyroid function tests in up to 38% of patients; with elevated values more common than low values.^{13,14} Low TSH level was found in 5.8% of this study population. Comparatively, Siris et al¹⁵ noted that 36% of patients with schizophrenia and post psychotic depression had a blunted TSH response; whereas, Othman et al¹² reported that 17% of the patients in their study sample had low TSH levels. Previous studies suggested that a reduced TSH response to TRH may be associated with response to neuroleptics in some patients with psychosis, in particular better efficacy^{16,17} or a more rapid neuroleptic response.¹⁸ However, the precise mechanism underlying the altered activity of the hypothalamic-pituitary-thyroid axis is still not entirely clear.

There is a dearth of data correlating thyroid dysfunction with psychopathology. In this study, fT4 and fT3 but not TSH were significantly higher in patients with higher

BPRS scores. Earlier studies found significantly increased rates of thyroid dysfunction in patients with schizophrenia (paranoid type) as opposed to undifferentiated type.¹⁹ Baumgartner et al²⁰ found elevated T4 levels to be significantly and positively correlated with the severity of the patients with acute illness but this was not so in patients with schizophrenia who were in remission. Increased dopamine levels, which is inhibitory to TSH secretion,^{21,22} could possibly account for the higher thyroid hormones in the patients with minor and major syndrome as rated by the BPRS.

Raised TSH with normal fT4 levels were uncommon and found in only 2 patients (1.1%). This is consistent with the findings of Othman et al.¹² Although it has been suggested that significant augmentation of the TSH response could occur after neuroleptic treatment,⁵ treatment with antipsychotics is associated with a variety of findings ranging from decreases,²³ no change²⁴ to increases in TSH levels.²⁵ Dopamine receptor density was found to be increased in patients on neuroleptic treatment.²⁶ In this study, there was no significant correlation between thyroid dysfunction and the mean daily neuroleptic dosage or number of neuroleptics. Differences in the demographic and clinical profiles of the study populations could have contributed to the inconsistent results.

Thyroid function tests are not infrequently done in acute psychiatric inpatient admissions.^{27,28} However, there is no consensus on the routine use of thyroid function tests in these patients.²⁹ The pattern of its use in chronic inpatients has never been fully studied. Although thyroid function abnormalities were present in 36.4% of patients in our study, all the patients except 1 were assessed to be clinically euthyroid. Attia et al³⁰ noted that the low prevalence of thyroid disease in psychiatric inpatients and the absence of clinical features suggesting thyroid illness accounted for the low yield of true-positive results and the same is likely to apply to our study population. A substantial proportion (26.5%) of the patients were also noted to have normal TSH and fT4 but low fT3, which is likely to be due to the sick euthyroid syndrome. Failure to recognise this may lead to unnecessary investigations, referrals or treatment leading to potentially undesirable effects on the patient and increased costs of health care.³¹

Conclusion

Despite the relatively high rate of thyroid function abnormalities, none of the patients except 1 exhibited any clinical features of such states. The apparent relationship of fT3 and fT4 with the severity of psychopathology suggests that these indices may be markers of the state of psychosis. The underlying mechanisms and their relationship to antipsychotic use await further research.

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