Original Article

Comparison of Alopecia severity and blood level of testosterone in men suffering schizophrenia with control group

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Abstract

Background: Testosterone causes Alopecia that is related to functional testosterone and end organ sensitivity to testosterone. Studies conducted on the relationship of schizophrenia and testosterone have reported different findings. This study was designed to measure the extent of Alopecia in schizophrenic patients which is one of the most important signs of sensitivity to Androgens.

Materials and Methods: In a cross-sectional study, 98 schizophrenic patients and 95 person of normal population encountered to study in two groups considering inclusion criteria and completing a consent form, in the psychiatric ward of Noor Hospital in Isfahan, Iran. Meanwhile, the record of necessary demographic information a blood sample was taken from every selected person to measure the blood level of testosterone. The severity of Alopecia was measured using Hamilton and Norwood criterion in a blindness condition. Collected data were analyzed using SPSS 19 software and statistical tests of χ^2 and logistic Regression.

Results: The mean blood level of testosterone in both studied and control groups were 458.80 ± 103 and 476.34 ± 108, respectively, having no significant difference ($P > 0.05$). There was no significant relationship in both groups between Alopecia severity and the blood level of testosterone. And in comparison of two groups, providing Androgenic Alopecia with a degree higher than three in Hamilton Scale, schizophrenia risk decreases 8.627 times.

Conclusion: Sensitivity to Androgens and Alopecia probably plays a protective role against schizophrenia, and if Alopecia rate exceeds the rate of grade 2 Hamilton, the risk of schizophrenia decreases 8.62 times.

Key Words: Alopecia, schizophrenia, testosterone

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INTRODUCTION

Schizophrenia is a clinical but deeply destructive mental syndrome with variable psychopathology, which affects cognition, emotion, perception and other aspects of the behavior. Schizophrenia usually begins before the age of 25, remains constant forever and none of the social classes are immune from encountering it.

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Short attention and social isolation involving these patients due to lack of public awareness towards this disorder, hurts them and their families in most cases. Although schizophrenia is described as a single disease, it is probably composed of a group of disorders having a heterogeneous causality and involving patients whose clinical appearances, therapeutic responses and prognosis are not the same.[1,2]

Appearance of Schizophrenia is attributed to several reasons and factors. There are numerous reports having cited hormonal differences between schizophrenic patients and normal controls.[1,2] Onset of schizophrenia symptoms in adolescence shows its relationship with sex hormones.[3] Some data indicate the reduction of concentration of luteinizing hormone and follicle-stimulating hormone in schizophrenic, which may be correlated with the age of disease onset and its duration. Slow release of prolactin and growth hormone in response to gonadotrophin-releasing hormone may be associated with negative symptoms.[1,4,5] Studies on the role of sex hormones in schizophrenia have shown that estrogen probably prevents schizophrenia but plays no role in its treatment. Estrogen and progesterone may have protective effects on neurons. High prevalence of psychosis in Turner syndrome during which there is no estrogen in the fetal period confirms this point.[6] Recent animal studies show that free testosterone may influence the effects of neurotransmitters and neuropeptides by passing blood-brain barrier.[3]

Studies conducted on the relationship of schizophrenia and testosterone have reported different findings.[3,7-10] Studies conducted on the relationship of testosterone and De Hydro Epi Andestrone and De Hydro Epi Andestrone sulfate level with schizophrenia has also had different results.[3,11-14] Some studies have reported an inverse relationship between testosterone level and negative symptoms of schizophrenia.[3,15-17]

Several factors affect the serum level of androgens in schizophrenic men.[3] Gray's study showed that testosterone level decreases with age and begins to fall in the fifth decade of life.[18] Testosterone level in young men has much fluctuation during the day so that it reaches the highest and the lowest amount at 8 am and in the evening, respectively.[19] The incidence of primary and secondary sexual traits is the direct effect of testosterone. Body muscularity, increase of testicles' diameter and size and growth of (head) hairs are all physiological complications of testosterone in the body. Testosterone causes Alopecia in front of the head. Those not having functional testosterone ever encounter Alopecia.[20]

Baldness in men is not a disease, but is physiological reactions induced by androgens in genetically susceptible men and the prevalence of androgen-dependent Alopecia in normal population is 50%.[21] Inheritance pattern has probably been polygenic. Hair thinning begins between the ages of 12 and 40. Progress and different patterns of Alopecia are classified by Hamilton.[22]

Given that many studies conducted on blood testosterone level and its relationship with positive and negative symptoms of schizophrenia have shown different results, and none of them are about the comparison of physiological effects of testosterone in body and regarding the instability of testosterone level in schizophrenic patients' blood and given that lack of Alopecia can be a symptom of the low amount of Androgen in blood or lack of sensitivity to these hormones in receptor level, this study was designed and implemented with the aim to measure the extent and pattern of Alopecia in schizophrenic patients which is one of the most important signs of sensitivity to Androgens. We decided to assess the level of schizophrenic patients' sensitivity to testosterone directly and the efficiency level of androgens in schizophrenic patients and its possible relationship with disease's appearance indirectly by investigating Androgenic alopecia and its relationship with the amount of blood testosterone.

MATERIALS AND METHODS

It is a descriptive-analytical and cross-sectional study. The studied individuals were 18-65-year-old male patients being hospitalized in the psychiatric ward of Noor Hospital in Isfahan, Iran. Based on the diagnosis of a psychiatrist in attendance, they were affected to schizophrenia, and this diagnosis was confirmed during a complementary renewed interview based on Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision DSMIV-TR. In the next step, referring to the patient and his family, and explaining the research project, its objectives and procedures for the patient and family, the project executors tried to satisfy them to participate in the study, and the candidate for entering the study (inclusion), if a written consent form was completed by the patient or a key member of his family.

Inclusion criteria include: Being male, suffering from schizophrenia disease, consent to participate in the study, lack of humor disease, not assisting organic disorders, drug addiction and lack of case history of treatments for Alopecia, lack of the history of severe diet and Anorexia Nervosa, not using Cytotoxic drugs, Heparin, Warfarin, vitamin A, lack of the history of

thyroid problems, lack of having concurrent medical illness, lack of the history of cancer, radiotherapy and chemotherapy, lack of addiction to Trichotillomania, no topical burns in head, lack of the history of using drugs affecting Alopecia including: Aminosalicylic acid, Enalapril, Amphetamines, Etretinate, Bromocriptine, Levodopa, Captopril Lithium, Carbamazepine, Metoprolol, Cimetidine, Propanolol, Coumadin, Pyridostigmin Danazol, Trimethadione and valproate sodium. At each stage of the study, participants were allowed to exit the study, if they were disinclined to cooperate.

Meanwhile, the record of necessary demographic information in this study, a 2-cc blood sample was taken from every selected person at 8 am and was sent to the laboratory to measure the blood level of testosterone. Then using Hamilton and Norwood criterion, the severity of Alopecia in the patient was measured and recorded in coded questionnaires by one of the project executors unaware of the study objectives. Hamilton criterion is widely used to assess the severity of Androgen Alopecia in men. In 1975, Dr. Uttar Norwood devised the standard classification of baldness with the male pattern based on previous works of Doctor Hamilton. Now the validity of this test is accepted, and it is used worldwide.[23-25]

He divided baldness with the male pattern (Androgenetic Alopecia) into two groups of normal form and type A. in the normal form, Alopecia begins from two regions: In front of the head (temples) and head peak, and these two bald areas gradually incorporate, and in type A, Alopecia begins from the front and gradually advances towards the rear. Type A is less common than normal form.[21]

In this test, 7 steps are defined for determining the severity of Alopecia [Figure 1], Step 1: No Alopecia is observed and the person has normal hair pattern, Step 2: Hair on the front side of the head becomes triquetrous due to margents' Alopecia, Step 3: Has the same pattern as step 2, but the shed area has expanded further towards the Frontal-temporal part of the head, Step 4: Shed areas of the head have completely expanded towards the Frontal-temporal part, and a separate Alopecia is begun from the upper back of the head, Step 5: The Alopecia pattern of step 4 is extended and the density of remained hair has significantly decreased in these areas, Step 6: The narrow strip of hair separating the bald part of the back and front of the head in stages 4 and 5 is vanished, and no hair is visible in scalp from front to back, Step 7: Alopecia has extended from back to down and from sides to upper part of the earlobe.

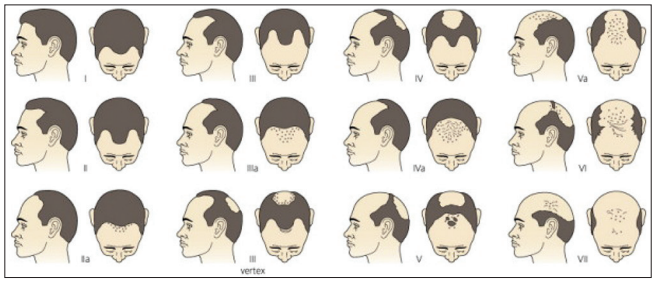

Figure 1: Visual pattern of hamilton-norwood scale for determination of Androgenic Alopecia severity in men

In this study, the scoring method for identifying the severity of Alopecia is determined based on the above definition and observation and comparison of hair pattern of patients participating in the project with visual patterns defined in Figure 1.

Control group was selected by age and sex matching through the relatives of patients hospitalized in Psychiatric Ward of Noor Hospital, having mental health and no history of drug addiction and use of drugs affecting Alopecia and no known chronic diseases, and blood sampling and measuring the severity of Alopecia was done in blind-making conditions.

Collected data were extracted from questionnaires and were analyzed using SPSS 19 software and statistical tests of χ^2 and logistic Regression.

RESULTS

Ninetyeight schizophrenic patients with an average age of 31.84 ± 7.68 and average disease duration of about 2 years in the study group and 95 subjects with an average age of 32.82 ± 7.82 participated in this study. The mean blood level of testosterone in both studied, and control groups were 458.80 ± 103 and 476.34 ± 108, respectively, having no significant difference with $P > 0.05$. The comparison of Alopecia severity in both groups is shown in Table 1. Ninety eight schizophrenic patients participated in the study, 77 cases (78.6%) were of Paranoid type, 10 cases

Table 1: Comparison of the frequency and the percent of Alopecia severity in two groups based on hamilton-norwood patterns

Alopecia severity	Study group		Control group	
	Frequency	Percentage	Frequency	Percentage
Step 1	63	64.3	33	33.7
Step 2	25	25.5	29	29.6
Step 3	7	7.1	13	13.3
Step 4	2	2	9	9.2
Step 5	1	1	7	7.1
Step 6	0	0	4	4.1
Step 7	0	0	3	3.1

P value<0.001

(10.2%) of disorganized type, 7 cases (7.1%) of catatonic type and four cases (4.1%) of undifferentiated type. Despite the high blood level of testosterone in patients suffering from disorganized type in comparison with control group and other subgroups of subject group, Alopecia level and blood testosterone level in different sub-types of schizophrenia had no significant difference ($P = 0.640$).

Seventeen cases of study group's individuals were new cases of having received no antipsychotic drug before hospitalization. Mean testosterone in these people had no significant difference in the control group and other patients. These patients were like other patients respecting Alopecia status, but the average of their Alopecia severity was less than the control group.

Testosterone level of recipients of Risperidone, olanzapine and Thiothixene in the study group was significantly less than control group ($P = 0.009$).

Results based on logistic regression analysis showed that there is no significant relationship in both studied and control groups between Alopecia severity and the blood level of testosterone. And in comparison of the study and control groups, providing Androgenic Alopecia with a degree higher than three in Hamilton Scale, schizophrenia risk decreases 8.627 times, indicating that higher severity of Alopecia is discussable as a protective factor against to schizophrenia.

DISCUSSION

Previous studies on the testosterone level in schizophrenic patients have shown diverse results.[7-10] Generally in this study, no significant relationship was obtained between blood testosterone level and schizophrenia disease, and the mean blood level of testosterone of the study group had no significant statistical difference with the individuals of control group ($P = 0.999$). The mean blood level of testosterone in the disorganized subgroup was more than other subgroups and control group. Given the inverse relationship between testosterone level and negative symptoms of schizophrenia in previous studies[3] and creation of obvious and positive symptoms of psychosis after the overuse of exogenous testosterone,[1,2] it seems that blood level of testosterone has direct relationship with disorganized symptoms (e.g., the patients of disorganized subgroup) and an inverse relationship with negative symptoms in patients suffering from schizophrenia.

Androgenic Alopecia level has been reported 50% in the normal population.[21] In this study, the overall prevalence rate of androgen-dependent Alopecia was reported 63% in control group and there was no significant relationship between the amount and the pattern of Alopecia with blood testosterone level in control group's individuals ($P = 0.679$). The overall prevalence rate of Alopecia in the study group was 33%, and no significant relationship was also observed between blood testosterone level and Alopecia rate in this group ($P = 0.157$). But in the comparison of both study and control groups, Androgenic Alopecia level in patients' group was less than control group quite significantly ($P < 0.001$). These findings demonstrate that schizophrenic people encounter Androgenic Alopecia less than normal subjects. The testosterone level of human blood is not the effective factor on Alopecia, but the existence of Testosterone and its transformation to De Hydro Testosterone in skin and inherent allergy to Androgens are determiners of Alopecia.[21] Patients participating in this study were being treated with different drugs of typical and atypical antipsychotics, and blood testosterone level in patients treated with Risperidone, olanzapine and Thiothixene were significantly lesser than the control group and other patients. However, none of these patients had significant difference in Alopecia compared to other patients. This finding confirms that testosterone level has had no direct impact on the rate of Alopecia, and no drug has caused a significant difference of Alopecia in the study and control groups. Given that 17 cases of 98 patients participating in the project were new schizophrenic patients and had received no medication, statistical analysis on the difference of Androgenic Alopecia rate and testosterone level in these patients compared to other patients and control group showed that these patients were not different from other patients respecting Alopecia and their testosterone level was the same as other patients, so we can infer that the rate of Alopecia in schizophrenic patients is probably an independent subject from the disease duration and the reception of antipsychotic drugs. Although the prevalence of schizophrenia is the same in both sexes, the course of disease is more severe in men, starts earlier and has more severe negative symptoms and eventually has a worse prognosis.[2] Early detection of at-risk-individuals and the reduction of the duration of untreated psychosis (DUP) can have a very important role in reducing the negative consequences of the illness in long-term.[1,2]

In this study, the analysis of obtained information shows that sensitivity to Androgens, and Alopecia probably plays a protective role in schizophrenia disease, and if Alopecia rate exceeds the rate of grade 2 Hamilton, the risk of schizophrenia decreases 8.62 times. In the same manner, in the case of lack of sensitivity of susceptible people to schizophrenia disease to endogenous Androgens and lack of Alopecia,

the risk of disease affection increases. The finding with clinical application in this study can be described such that considering the pattern of Alopecia as a predictor symptom of the probability of schizophrenia addiction in at risk people can probably increase the coefficient of early detection of disease and proportionally decrease the probability of the outlast of DUP and its complications.

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