Original Article

Biochemical changes in Schizophrenics

Inter-Relationship of Circulating Biochemical Markers of Oxidative Stress and Thyroid Hormones in newly Diagnosed Schizophrenics: Perspective study from Local Population of Punjab Pakistan

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ABSTRACT

Objective: Current study was conducted to determine the fluctuations of various circulating biomarkers including thyroid hormones, hepatic enzymes, oxidative stress markers as well as electrolytes in schizophrenics.

Study Design. Cross Sectional Study.

Place and Duration of Study: This study was conducted at Psychiatric Clinic of Jinnah Hospital, Mental Hospital from Jan. 2013 to Oct. 2013.

Materials and Methods: Seventy five acute schizophrenics and twenty five healthy individuals were selected for this study. Patients with chronic infections, diabetic history, liver disease or any other history of drugs including smoking and/or drinking alcohol were excluded from the study.

Results: Elevated levels of oxidative stress in the form of malondialdehyde (MDA) (7.8±2.71*) were observed in schizophrenics. Similarly raised levels of T3 (6.9±1.31*) and T4 (61.2±15.44*) were found in patients as compared to control. Electrolytes like Na, K, Ca and Mg showed alterations in the serum of both patients and control.

Conclusion: All the circulating biochemical markers were statistically significant (P<0.05). It is concluded that lipid peroxidation may has association with thyroid hormones and electrolytes. Moreover, alleviated concentration of anti-oxidant biomarkers like SOD, catalase and GSH may play a central role in schizophrenics and anti-oxidant therapy may be useful for the management of this psychiatric disorder.

Key Words: Oxidative Stress,Thyroid Hormone,Schizophrenia,Anti-Oxidant,Malondialdehyde,SOD,Catalase, GSH

INTRODUCTION

Schizophrenia is one of the most important mental disorders associated with dysfunction in brain structure and function, neurological abnormalities as well as physical anomalies. Long term memory and working memory are affected due to brain abnormalities. Schizophrenia usually characterized by disturbances in social behavior, emotional reactions and thinking associated with hallucination as well as illusions. Association of schizophrenic patients has been proposed with malnutrition, immune activation, obstetric complications and maternal exposure to stress. Alterations in the level of various neurotransmitters like dopamine in schizophrenic patients have been associated with delusions and hallucinations.

One of the important factors related to the pathological condition is oxidative stress in the biological system and it is also associated with patients suffering from schizophrenia [1](Akiibinu et al., 2012; [2]Ong et al., 2010). Similarly, alterations in thyroid hormones are common in mental disorders (Akiibinu et al., 2012; [3](Yazici et al., 2002), because particular concentration of thyroid hormones is crucial for maturation and development of central nervous system.

Current study was conducted to determine the fluctuations of various circulating biomarkers including thyroid hormones, hepatic enzymes, oxidative stress markers as well as electrolytes in schizophrenics.

MATERIALS AND METHODS

Seventy five (75) individuals suffering from acute schizophrenia, attending Psychiatric clinic in Jinnah Hospital, Lahore were included in this study. Only those patients were included that were not taking any treatment for schizophrenia. Patients with chronic infections, diabetic history, liver disease or any other history of drugs including smoking and/or drinking alcohol were excluded from the study. Moreover, twenty five (25) healthy individuals served as control group.

Following parameters were estimated

I-Lipid profile (Total Chol., Tg, HDL and LDL)

II-Electrolytes profile (Ca, K, Mg and Na)

III-Stress biomarkers including malondialdehyde (MDA)[4](Ohkawa et al., 1979), superoxide dismutase (SOD)[5] (Kakkar et al., 1984), catalase (Aebi, 1974), reduced glutathione (GSH) [6](Moron et al., 1979).

IV- Thyroid hormones (T3, T4 and TSH) were evaluated by commercially available enzyme linked immunosorbent assay (ELISA) kits.

Statistical Analysis: Data processed through independent student t-test by using SPSS version 17. P-value less than 0.05 was considered statistically significant for comparison of control and schizophrenic groups.

RESULTS

In case of thyroid hormones, the levels of T3 (6.9±1.31) and T4 (61.2±15.44) were raised in schizophrenics while TSH (0.28±0.10) was decreased as compared to control group (1.1±0.31; 48.2±10.0 and 1.5±0.32) respectively and were statistically significant (P<0.05).

Table No, 1: Serum circulating biomarkers of schizophrenicsand controls

Parameters	Control (n=25)	Schizophrenics (n=75)	P-value (<0.05)
ALT	24.00±5.69	31.75±19.73	.028
AST	20.25±5.21	29.50±9.32	.011
ALP	55.83±6.28	169.16±13.53	.023
TB	1.01±0.07	1.89±0.02	.041
TCh	4.44±0.37	5.60±0.41	.004
Tg	1.24±0.15	1.81±0.11	.030
LDL	2.31±0.15	3.18±0.52	.005
HDL	1.73±0.17	1.18±0.04	.001
SOD	0.73±0.025	0.06±0.05	.016
GSH	9.77±1.17	7.24±0.94	.005
Catalase	4.27±0.73	2.77±0.83	.033
MDA	3.71±0.91	7.8±2.71	0.03
Ca^{++}	12.03±3.26	13.34±3.67	.036
Na^{+}	143.15±8.26	177.78±2.88	.013
K^{+}	5.07±1.02	1.99±0.03	.000
Mg++	3.45±0.18	1.89±.54	.058
TSH	1.5±0.32	0.28±0.10	0.032
T3	1.1±0.31	6.9±1.31	0.021
T4	48.2±10.0	61.2±15.44	0.04

P value <0.05 (significant)

ALT=IU/L, AST=IU/L, ALP=IU/L, TB (Total Bilirubin)=mg/dl, TCh (Total cholesterol)=mg/dl, Tg (Triglycerides)=mg/dl, LDL=mg/dl, HDL=mg/dl, MDA=nM/ml, SOD=ng/ml, GSH=mg/dl, CAT=µM/mol of protein, Na^{+}=132-142 mEq/L, K^{+}=4.0 - 4.7 mEq/L, Ca^{++}=9-11 mEq/L, Mg^{++}=1.8-3 mg/dL, TSH=mIU/L, T3=ng/ml, T4=nmol/L

From the results presented in Table-01 shows that all the tested circulating biochemical markers e.g. alnine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin exhibited highly significant (P=.05, .028, .011, .023 and .041 respectively) differences not only between the study groups but also between within the same group. The highest values of ALT (31.75 IU/L), AST (29.50 IU/L and TB (1.89 mg/dl) were recorded in schizophrenics patients respectively.

The results depicted in Table-01reflecting that the lipid profile (TCh, Tg, LDL and HDL) of schizophrenics patients versus control differed significantly (P=.05, .044, .030, .007 and .001 respectively). An increasing trend of TCh (5.60 and 5.18 mmol/L), Tg (1.81 and 1.85 mmol/L) and LDL (3.18 and 4.88 mmol/L) was observed both in schizophrenics patients versus control but a decreasing trend of HDL was recorded in both the studied groups (1.18 and 1.22 mmol/L) respectively.

Data in Table-01regarding stress biochemical markers SOD (Superoxide dismutase), GSH (Glutathione) and CAT (Catalase) shows highly significant pattern between and within the studied groups. The consistent decreasing trends in case of Glutathione from groups A-B were recorded (9.77, 7.24 and 5.04 µg/dl) respectively. Catalase levels were also shows the consistent decreasing trend (4.27, 2.77, and 3.74 µmol/mol of protein) in different studied groups (A-B). The lowest value (0.06 ng/ml) of SOD was recorded in group B (Schizophrenicspatients) as compared to control (0.73 ng/ml). Data depicted Table-01regarding electrolytes profile of schizophrenics verses control shows highly significant differences between and within the studied groups.

DISCUSSION

Nearly 1% of the world population has been suffering from schizophrenia (Ong et al., 2010). Investigations have revealed that reactive oxygen species (ROS) are the major role player in pathogenesis of schizophrenia along with the alleviation in enzymatic and non-enzymatic anti-oxidants in the biological system. Particularly, hydrogen peroxide (H_2O_2) has been found to be an important component of the thyrocytes, in normal physiological conditions, for the oxidation of iodide into iodine accomplished by thyroperoxidase [7](De Deken et al., 2002; [8]Schweizer et al., 2008). Higher level of oxidative stress has been observed by the increase of MDA (7.80±2.71) in the patients suffering from schizophrenia as compared to control (3.71±0.91) group. Results of oxidative stress are in agreement with [9] Chittiprolet al., (2010) and Akiibinu et al., (2012). The levels of MDA were decreased after the treatment in schizophrenic patients (Chittiprol et al., 2010).

As far as anti-oxidative system is concerned, various enzymatic and non-enzymatic anti-oxidants are involved for the maintenance of normal physiology of biological system. The levels of anti-oxidants are altered in pathological state as in case of schizophrenia

[10](Gama et al., 2006; [11]Dadheech et al., 2008; [12]Padurariu et al., 2010). Most contrasting investigations have been reported in case of schizophrenia as compared to other psychiatric disorders. In current study, the levels of anti-oxidants (enzymatic and non-enzymatic) including SOD, GSH and catalase were decreased in patients as compared to control group (Table-01). Previous investigations elaborate different findings about anti-oxidant levels in schizophrenics. Increased activities of SOD and lipid peroxidation were reported by various investigators (Gama et al., 2006; [13]Kunz et al., 2008; Padurariu et al., 2010). In case of catalase, the results of current study are not in agreement with the previous one. [14]Miljevic et al., (2010) reported no significant change in schizophrenic when treated with clozapine.

Schizophrenia could be explained on the basis of electrolytes like sodium, potassium, calcium and magnesium. The alterations and/or imbalance were observed in the patients suffering from schizophrenia. The raised levels of sodium (177.78±2.88) and calcium (13.34±3.67) were observed while decreased levels of potassium (1.99±0.03) and magnesium (1.89±0.54) were found in patients as compared to control group (Table-01). The results of current study are contradicted with the previous studies conducted by [15](Sethi and Sethi) (1971) and [16](Bhatia et al., (1987) in case of potassium and magnesium. According to their findings the levels of these two electrolytes were increased in patients. On the other hand, raised levels of sodium and calcium are in agreement with the previous findings of Bhatia et al., (1987), [17](Hoagland (1955) as well as [18]Alexander et al., (1978).

In case of thyroid hormones, the levels of T3 and T4 were raised in schizophrenics while TSH was decreased as compared to control group and were statistically significant ($P<0.05$). The results of thyroid hormones are in agreement with Akiibinu et al., 2012. According to the previous findings the levels of thyroid hormones (total T3 and free T3) were significantly raised in schizophrenics [19](Yazici et al., 2011). MDA was significantly correlated with T3 in patients suffering from schizophrenia (Akiibinu et al., 2012).

CONCLUSION

All the circulating biochemical markers were statistically significant ($P<0.05$). It is concluded that lipid peroxidation may has association with thyroid hormones and electrolytes. Moreover, alleviated concentration of anti-oxidant biomarkers like SOD, catalase and GSH may play a central role in schizophrenics and anti-oxidant therapy may be useful for the management of this psychiatric disorder.

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