Plasma Amine Oxidase Activity in Some Psychiatric Patients

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Abstract

This research is directed to measure the level of the scarcely studied enzyme plasma amine oxidase (PAO) in schizophrenic patients (type I and type II), major depressive patients, and Bipolar disordered patients against a matched normal control subjects to study the correlation between the enzyme activity and many demographic and clinical variables. 107 psychiatric patients were studied (52 schizophrenics, 26 major depressives and 29 bipolar patients with psychotic features) and 30 normal control subjects. A structured interview was applied to collect the data and diagnosis according to DSM- III R, then schizophrenics were subtyped using the Scale for assessment of Negative Symptoms (SANS) into 33 type I and 19 type II. Depressive symptoms were assessed by Zagazig Depression Scale (ZDS). The plasma level of (PAO) was determined by the method of McEwen and Cohen (1963). Results showed significant lower level of (PAO) among patients than normal controls. No significant difference between the four patient groups. (PAO) level showed no significant correlation with hallucinations; depression; type of onset or duration of illness, even when dividing patients into two cohorts (those with PAO level within normal versus those with less than normal range) no significant difference was found in relation to any of the studied parameters.

Introduction: Since the early description of decreased platelet monomine oxidase (MAO) in chronic schizophrenics by Murphy and Wyatt (1972) several articles have been published in this area (Vieira et al.,1989) which presented some contradictory findings. That casted doubt on the role significance of the alternation in platelets MAO and led to the analysis of other enzyme systems (Wyatt et al., 1980 and 1982).

Benzylamine oxidase, also known as plasma amine oxidase (PAO) has been less studied and the clinical and physiological significance of this enzyme requires further education (Buffoni, 1983 and Callingham and Barrrand 1987).

Lower than normal (PAO) activity in schizophrenics has been reported in several studies (Meltzer and Arora, 1980 and Freeman et al. 1980), however there was considerable overlap in values between patients and normal control subjects.

The relation between (PAO) activity and the psychiatric disorders other than schizophrenia was less studied. Meltzer et al (1980) carried out a study in which PAO activity was determined in 70 normal controls and 76 psychiatric patients including schizophrenics (acute and chronic); manic; major psychotic depressives and major non psychotic depressives. They found that PAO activity was lower in all diagnostic groups, but results were statistically significant only for acute schizophrenics.

Increased (PAO) activity has been reported in depressed women by Klaiber et al. (1972), but Gershon et al. (1977) found no significant difference in (PAO) activity between patients with primary affective illness and normal controls. Thus discrepancy exists although the studies were few.

Aim of the work

1- To analyze PAO activity in schizophrenic patients and bipolar disorder with

psychotic features, major depression and normal control.
2- To study the relationship between the enzyme activity and many demographic and clinical variables.

Material and Methods:

Subjects

I- Patients:
The patients were selected from the outpatient psychiatric clinic and inpatient psychiatric department of Zagazig University Hospital. The total number of patients was 107 with the following diagnoses:

52 schizophrenics; 26 with major depression and 29 with bipolar disorder with psychiatric features according to the DSM-III-R(1987) criteria. Patients in clinical recovery were diagnosed according to the symptoms of the last psychotic state. Schizophrenic patients were classified according to Crow's classification (1982) into :-
1- Type I with favorable course, one or more psychotic states florid reversible positive symptoms, good premorbid adjustment and good response to neuroleptics, 33 type I patients were included in the study .
2- Type II with elevated percentage of negative symptoms, poor premorbid adjustment and poor response to neuroleptics, 19 type II patients were included in the study.

II- Control group :
30 normal subjects (free from neurotic psychotic symptoms and signs as well as from medical; surgical and drug abuse factors) were included in the study

Methods:

1- A semi-structured psychiatric interview especially designed for the study was applied to all patients for the purpose of collecting data and diagnosing patients according to DSM-III-R criteria.
2- Positive and negative psychotic schizophrenic symptoms were assessed using the Scale for Assessment of Positive Symptoms (SAPS) (Andreasen, 1983) and the Scale for Assessment of Negative Symptoms (SANS) (Andreasen,1983
3- The Zagazig Depression Scale (ZDS) (Fawzi et al., 1983):-
This is a self rating scale for measuring depression presented in the form of 52 questions written in colloquial Arabic, the answers for each question is either "Yes" or" No", involving the symptoms of depression. These are: depressed mood; guilt feelings; suicidal tendency; early insomnia; interrupted sleep; late insomnia; work and interests; retardation; irritability; psychic tension; gastro-intestinal symptoms; general somatic symptoms; libido; hypochrondriasis; loss of insight and loss of weight.
4-Biochemical methods :-
-Blood was collected by venipuncture in the morning 9-12 AM., plastic syringe was used and 9 ml blood was introduced in a propyle polyethylene centrifuge tube previously siliconized containing 1 ml of 3.8% sodium citrate to prevent coagulation.
-Plasma was isolated within 3 hours of venipuncture by centrifuging and then kept frozen for no more than two weeks to be used for benzylamine oxidase assay.
-Enzyme activity was determined using 0.3 ml plasma according to the technique of McEwen and Cohen (1963) based on the oxidation of benzylamine followed by extraction of benzyladehyde by cyclohexone.
5- Statistical analysis:-
"t" test; Chi-square test and one way analysis of variance (ANOVA) to look for the significant differences between patients and control group.

Results:

1- The comparison between patients and control subjects (table 1) revealed a highly significant difference regarding (PAO) activity where the mean±SD 20.05 ±11.46 and 34.48±19.17 respectively and t =3.93 and p<0.0005.
2- The comparison between the four patient groups (table 2) revealed the following :-
A- The depressed patients were younger in age than bipolar patients (F=3.4S, p<0.05).
B- Highly significant differences as regards (residence; marital status; socio-professional adjustment; age at onset ;type of onset and duration of illness) were found between the 4 groups.
C- No significant difference was found in relation to sex; life events and plasma amine oxidase (PAO) activity.

3- (tables 3 and 4) show no statistically significant relation was found between PAO activity and depressive symptoms; hallucination; type of onset or duration of illness. When we classified patients into those within normal PAO level versus those with less than normal level; we found no statistically significant difference between the two groups of patients regarding demographic and some clinical characteristics (table 4).

Discussion: During the past two decades evidence has accumulated suggesting a link between mental disorders and the metabolism of biogenic amines. One of the most extensively studied subjects is the enzyme involved in their metabolism, mono amine oxidase (MAO) (Vieira et al., 1989).

Biochemical MAO is a general name for two types of enzymes, the first is mitochondria bound MAO (MAO A and MAO B) which was studied extensively in most psychiatric disorders to the extent that the general name MAO is used in psychiatric literature to refer to the mitochondria bound form of the enzyme (McIlwain and Bachelard, 1985). In contrast the soluble plasma amine oxidase enzyme (PAO) has received little attention and psychiatric literature on it is scarce (Baron et al.; 1983; Gruen et al., 1985 and Vieira et al., 1989).

To our knowledge after manual and computer assisted search (Medline)- our

Table (1) comparison between psychiatric patients and normal control

	Patients (N=107)	Control (N=30)	t (x^2)	P
Age Mean ±SD	28.2±8.22	26.9±8.63	0.955	NS
Sex Male(%) Female(%)	58 (54.2%) 49 (45.8%)	28 (60%) 12 (40%)	(0.339)	NS
PAO Mean±SD	20.05±11.46	34.48±19.17	3.39	<0.0005

Table (2) Comparison between the four patient groups

	Type I schiz. (N=33)	Type II schiz. (N=19)	Bipol. Dis. (N=29)	Major Dep. (N=26)	(F) X^2	P
Age Mean±SD	27.64 ±7.52	31.05 ±8.15	26.69 ±8.7	32.65 ±6.99	(3.45)	<0.05*
Sex Male (%) Female (%)	21(63.6%) 12(36.4%)	11(57.9% 8(42.1%)	12(41.4%) 17(58.6%)	14(53.4%) 12(46.1%)	3.18	NS
Martial status Single (%) Married (%) Divorced and widowed (%)	23(69.7%) 7(21.2%) 3(9.1%)	14(73.7% 2(10.5%) 3(15.8%)	16(55.2%) 11(37.9%) 2(6.9%)	2(7.7%) 24(92.3%) - --	41.76	<0.005
Residence Urban (%) Rural (%)	18(54.5%) 15(45.5%)	16(84.2%) 3(15.8%)	9(31%) 20(69%)	10(38.5%) 16(6.5%)	14.84	<0.005
Social prrofes-sional adjustment Good (%) Poor (%)	20(66.7%) 11(33.3%)	3(15.8%) 16(84.2%)	18(62.1%) 11(37.9%)	1557.7%) 11(42.3%)	14.21	<0.005
Age at onset <20 y >20 y	22(66.7%) 11(33.3%)	11(57.9%) 8(42.1%)	12(41.1%) 17(58.6%)	6(23.1%) 20(76.9%)	12.3	<0.01
Life events at on-set Present Abscent	14(42.4%) 19(57.6%)	7(36.8%) 12(63.2%)	10(34.5%) 19(65.5%)	15(57.7%) 11(42.3%)	3.46	NS
Type of onset Acute Gradual	23(69.7%) 10(30.3%)	10(52.6%) 9(47.4%)	23(79.3%) 6(20.7%)	5(19.2%) 21(80.8%)	23.32	<0.005
Duration of illness <5y >= 5 y	14(42.4%) 19(47.6%)	3(15.8%)1 16(84.2%	20(68.9%) 9(31.1%)	10(61.5%) 16(38.5%)	15.07	<0.005
PAO Mean±SD	17.33 ±11.5	23.56 ±13.5	22.7 ±12.3	18.7 ±7.3	1.84	NS

study is the second in the published literature to study and compare PAO activity in both schizophrenic and mood disordered patients in addition to normal controls being preceded only by the work of Meltzer et al. (1980).

The use of benzylamine as a substrate for the measurement of "PAO" activity was firstly introduced by McEwen and Cohen (1963) and it is still known to be the best substrate for "PAO" (Vieira et al. 1989).

Also the technique of MeEwen and Cohen is an excellent method for PAO activity measurement as reported by Meltzer and Arora (1980); Meltzer et al. (1980) and Freedman et al. (1981). The subtract is very sensitive and the technique could be used to measure PAO activity in plasma or in serum (McEwen and Cohen 1963).

Some Limitations

Patients on whom the study was carried out were:

1- Mostly chronic or subchronic receiving the classical psychotropic drugs, consequently we were not able to have patients on and off medications to exclude the possible effects of psychtropics drugs on "PAO" activity. However "PAO" activity was found to be non-significantly reduced after 3 months of neuroleptic intake in an unpublished study by Baron and associated (Baron et al., 1983).

2- Also patients were mostly from the socieconomically compromised strata in the Egyptian society. So we can not claim

Table(3) Relationship of PAO activity to some psychiatric symptoms

	Mean (PAO)level	SD	t	P
Depression				
Depressed (>10 on ZDS)	19.34	7.89	0.774	NS
Non depressed	21.05	13.96		
Hallucination				
Hallucinating pts	19.25	11.596	1.312	NS
Non-hallucinating pts	22.15	10.76		
Type of onset				
Acute	18.99	11.49	1.294	NS
Gradual	21.85	11.19		
Duration of illness				
<=2y	12.51	11.63	0.749	NS
>2y	19.65	11.28		

Table (4) Comparative analysis by X2 test of 11 charactristics in 2 sub-group patients (those with PAO activity within the normal range versus those with PAO activity less than normal range)

Items of comprison	Cohort A (patients with PAO within normal range) N=55		Cohort A (patients with PAO less normal range) N=52		X^2	P
	No.	%	No.	%		
Age at onset <20 y >20 y	26 29	47.3 52.7	18 34	34.6 65.4	1.786	NS
Sex Male Female	32 23	58.2 41.8	26 26	50 50	0.73	NS
Diagnosis Type I Type II B.D. Major depression	16 13 14 12	29.1 23.6 25.5 21.8	17 6 15 14	32.7 11.5 28.8 26.9	2.69	NS
Type of onset Acute Gradual	29 26	52.7 47.3	32 20	61.5 38.5	0.879	NS
Family history of mood disorder Present Abscent	15 40	27.3 72.7	19 33	36.5 63.5	1.08	NS
Family history of schizophrenia Present Abscent	17 38	30.9 69.1	8 44	15.4 84.6	3.513	NS
Number of flareups <3 >=3	25 30	45.5 54.5	23 29	44.2 55.8	0.0136	NS
Activity of psychosis at sampling Active Inactive	32 23	58.2 41.8	39 13	75 25	3.62	NS
Life events Present Abscent	26 29	47.3 52.7	20 32	38.5 61.5	0.879	NS
Social prrofessional adjustment Good Poor	22 33	40 60	23 29	44.2 55.8	0.186	NS
Length of illness <5y >=5y	23 32	41.8 58.2	28 24	53.8 46.2	1.536	NS

that our results could be generalized.

Discussion:

- When the patients "PAO" level was compared to that of the control subjects, a very highly significant difference was found ($p<0.0005$) (table I) i.e. "PAO" activity was significantly lower in psychiatric patients than normal controls, a finding that is in accordance with several previous studies such as the studies of Freedman et al. (1981) and Gruen et al. (1985) and of Kalber et a. (1972) and Gershon et al. (1977).

When "PAO" activity of the four patients' group was compared to each other (table II), a higher activity was found in type II schizophrenia followed by bipolar patients the major depressives and the lowest level type I schizophrenia, however the difference was not statistically significant, Meltzer et al. (1980) also reported a non-significant difference between schizophrenic, manic and depressives patients.

No correlation was found between "PAO" level and many demographic and clinical characteristics of the patients as shown in (table 3 & 4), however Vieira et al. (1989) found correlation between "PAO" activity and type of onset whether acute or gradual; presence or absence of life events at onset of the disease and whether poor or good socio-professional adjustment. This discrepancy may be due to the inclusion of mood disordered patients in our study and not only schizophrenic patients as in the study of Vieira et al. (1989).

Based upon our results and the results of the previously cited studies, we may speculate that low plasma amine oxidase activity may be a biological marker of some psychiatric disorders and specifically to type I schizophrenia, however we found a marked overlap in "PAO" level between patients and the normal control subjects. Also we failed to delineate the characteristics of the patients with low "PAO" level.

Our recommendation to researchers interested in our topic is to study the level "PAO" in other psychiatric disorders i.e. anxiety disorders; somatoform disorders.....etc. and to conduct a longitudinal study that might permit them to observe "PAO" level changes over time in individual patients either with changes in their symptomatology or their medication status.

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نشاط انزيم امينو اوكسيداز لدى بعض المرضى النفسيين

تهدف هذه الدراسة لقياس انزيم "البنزيل امين اوكسيداز" فى البلازما عند بعض المرضى النفسيين (مرضى الفصام ومرضى الإكتئاب الجسيم و مرضى الاضطراب الوجدانى ثنائى القطب المصحوب بإعراض ذهانية) ومقارنته بمجموعة من الأصحاء كمجموعة ضابطة وكذلك محاولة التعرف على الأرتباط بين مستوى الانزيم و بعض الاعراض النفسية.

شملت الدراسة ١٣٧ شخصا منهم ٥٢ مريضا بالفصام و ٢٦ مريضا الإكتئاب الجسيم و ٢٩ مريضابالاضطراب الوجدانى ثنائى القطب و٣٠ شخصا طبيعيا كمجموعة ضابطة من المترددين على العيادة النفسية ومن القسم الداخلى بمستشفيات جامعة الزقازيق.

أجريت مقابلة إكلينيكية لجميع المرضى بهدف جمع المعلومات و تشخيص المرض طبقا للتقسيم الأمريكي الثالث المعدل (١٩٨٧م) وقسم مرضى الفصام الى مجموعتن "ذوى الأعراض الإيجابية" وكان عددهم ٣٣ و"ذوى الأعراض السلبية" وكان عددهم ١٩ وذلك حسب مقياس أندريسون و طبق مقياس الزقازيق للإكتئاب على كل المرضى وأخيرا مستوى الانزيم كيميائيا فى الدم بعد ذلك و كانت اهم نتائج الدراسة:

١- هبوط مستوى الانزيم فى البلازما عند بعض المرضى النفسيين " كمجموعة واحده " عنه عند المجموعة ضابطة هبوطا ذا دلالة إحصائية عالية.
٢-عدم وجود فروق ذات دلالة إحصائية بين مجموعات المرضى الأربعة بالنسبة لمستوى الانزيم .
٣- عدم وجود ارتباط ذو دلالة إحصائية بين مستوى الانزيم و العديد من الاعراض المختلفة.

فى النهاية نوصى بقياس الانزيم لدى مرضى نفسيين اكثرعددا وبتشخيصات اخرى كما نوصى بقياس مستوى الانزيم على فترات متباعدةلدى نفس المريض لمحاولة إيجاد علاقة بين تغير اعراض المرضى و تغير مستوى الانزيم.

مستشفيات الطب النفسى بالمعادى

د. محمد فؤاد أبو المجد

مصحة النيل بالمعادى

٤٠ أ طريق مصر - حلوان الزراعى
ت. ٣٥٠١٤٣٣ - ٣٥٠١٥٤٢

مستشفى قصر المعادى

كورنيش النيل بالمعادى

ت. ٣٥٠٢٢١ - ٣٥٠١٠٥١