Erciyes Tıp Dergisi 13: 346-352, 1991

PLATELET MAO-B ACTIVITY AND SERUM INORGANIC PHOSPHATE LEVEL IN MAJOR DEPRESSION AND DYSTHYMIC DISORDER (*)

Seher Sofuoğlu*, Pakize Doğan**, Mustafa Baştürk***, Gürsel Tanrıkulu****, Tuncay Besim*****

Summary: Platelet MAO-B activities and serum inorganic phosphate levels were measured in 31 depressed patients (12 of them major depression, 19 of them with dysthymic disorder) and 24 healthy control subjects. The male patients in the major depression and combined groups had significantly higher MAO-B activities both than those of female patients in the same groups and those of control males while no difference was present between healthy female and male control subjects. The female patients in the dysthymic disorder and combined groups had higher enzyme activities than those of the control females. There was no significant difference in serum inorganic phosphate levels between the patient and control groups. The results of this study support the hypothesis that platelet MAO-B activity may be a biological marker of depression but contradict the idea that higher MAO-B activity which represent lower dopaminergic activity would be associate with higher serum inorganic phosphate level.

Key words: Major depression, dysthymic disorder, MAO-B, inorganic phosphate

Major depresyon ve distimik bozuklukta platelet MAO-B aktivitesi ve serum inorganik fosfat seviyesi

Özet: 31 depresyonlu hastada (12 major depresyon, 19 distimik bozukluk vakası) ve 24 sağlıklı şahısda platelet MAO-B aktivitesi ölçüldü. MAO-B aktivitesi major depresyon grubu ile kombine gruptaki kadınlarda hem aynı gruptaki kadınlara hem kontrol erkeklere nazaran yüksek bulundu. Sağlıklı kadın ve erkekler arasında ise bu bakımdan bir fark yoktu. Distimik grupta ve kombine grupta kadın hastalar kontrol kadınlara nazaran daha yüksek enzim aktivitesi gösterdiler. Serum inorganik fosfat seviyesi bakımından hasta ve kontrol grupları arasında fark yoktu. Bu çalışmanın bulguları platelet MAO-B aktivitesinin major depresyon için bir biyolojik işâretleyici olabileceği hipotezini desteklemekte, düşük dopamin aktivitesini temsil eden yüksek MAO-B aktivitesinin, yüksek serum fosfat seviyeleri ile birlikte bulunacağı fikrini ise naksetmektedir.

Anahtar Kelimeler: Major depresyon, distimik bozukluk, MAO-B, inorganik fosfat

---

(*) 27th National Congress of Psychiatry and Neurological Sciences. Mersin 15-21 Oct, 1989

* Erciyes University School of Medicine. Associate Professor of Psychiatry

** Erciyes University School of Medicine. Professor of Biochemistry

*** Erciyes University School of Medicine. Assistant Associate Professor of Psychiatry

**** Erciyes University School of Medicine. Doctoral Fellow in Biochemistry

***** Erciyes University School of Medicine. Resident in Psychiatry

Monoamine oxidase (MAO) is a mitochondrial enzyme present in all tissues and responsible for the oxidative deamination of monoamines (catecholamines and indoleamines). Therefore, it participates in the regulation of intraneuronal levels of these brain neurotransmitters. In human brain, there are at least two different forms of MAO according to its substrate specifity: MAO-A and MAO-B. Platelets contain MAO-B only (15).

The kinetics of platelet MAO are believed to be similar to that of central MAO and therefore, its values may reflect the MAO-B activity of brain. Based on this idea, platelet MAO-B activity has been used as an indirect functional indicator of monoaminergic neurotransmission (2,8,15). In addition, it has previously been suggested that peripheral catecholaminergic activity was inversely correlated with serum inorganic phosphate concentration (10).

In this study, we aimed at evaluating catecholaminergic activity indirectly by measuring platelet MAO-B activity and serum inorganic phosphate level, and also testing the hypothesis that platelet MAO-B activity might be a biological marker for depression.

METHODS

Subjects. The current study included 31 hospitalized patients (17 females, 14 males) mean (±SEM) age being 37.65±2.35 years (range 17-63 years); 12 of them had major depression (MD) and 19 dysthymic disorder (DD). Mean (±SEM) age of the patients was 41.58±4.43 years (range 19.63 years) and 35.36±2.52 years (range 17-58 years) in the MD (4 females, 8 males) and DD (13 females, 6 males) groups respectively. Our control group comprised 24 physically-mentally healthy subjects (6 females, 18 males) mean (±SEM) age being 31.50±1.49 years (range 18-46 years).

The patients were diagnosed according to DSM-III criteria (American Psychiatric Association 1980) by two psychiatrist and all were free of psychotropic medication for at least one week (5,6). Subjects taking estrogens, insulin, nitroglicerine, guanetidine, L-dopa or epinephrine were excluded from the study in order to eliminate their influence upon MAO activity (2,10). Subjects with migraine, diabetes mellitus, cirrhosis, malignancies, epilepsy, Huntington's disease, vitamin B6 or iron deficiency (2), protein- caloric malnutrition (6) were also excluded, and subjects with renal or hepatic failure which may affect serum inorganic phosphate level (10) were not included in the study.

MADRS (Montgomery-Asberg Depression Rating Scale)(13) and CAS (Clinical Anxiety Scale)(20) were used to evaluate the severity of depression and anxiety.

Biochemical Procedure. Five milliliters of venous blood was drawn from each subject, and platelet rich plasma (PRP) was obtained on the same day. PRP suspensions were disrupted by six cycles of freeze-thawing and homogenized by a motor-driven homogenizer, and MAO-B activity was assayed by a modification of the method described by Mc Ewen (11). Briefly, fifty microliters of PRP homogenates, 2.65 ml of 0.2 M phosphate buffer (pH=7.2) and 0.3 ml of 8 mM buffered benzylamine (pH=7.2) in a total volume of 3 ml were incubated at 37 oC for one hour. The product was determined spectrophotometrically as described previously (11).

Serum inorganic phosphate level was determined by Kuttner-Lichtenstein's method (4).

All measurements were double-checked.

Statistical Evulation. Data were analysed using one-tail analysis of variance (ANOVA) covarying for age and sex, Spearman's rank-order correlation, Student's t and Mann-Whitney's u tests.

RESULTS

Severity of Clinical Symptomatology

MADRS and CAS scores were higher in the MD group than in the DD one (t=3.98 p<0.01 and t=2.61 p<0.01 for MADRS and CAS respectively). No correlation was present between enzyme activity and MADRS and CAS scores in all groups.

Platelet MAO-B Activity

A. Platelet MAO-B activity without consideration of gender differences

Mean (±SEM) values of MAO-B activity in the patient and control groups were represented in table I.

An overall ANOVA indicates significantly higher MAO activity was in MD, DD and combined groups compared to controls (The comparisons are as follows: Major depression-Control: F=4.48 df=11/23 p<0.05, Dysthymic disorder-Control: F=5.81 df=18/23 p<0.05, Combined-Control: F=4.99 df=30/23 p<0.05). No significant difference in MAO-B activity is observed between the MD and DD groups. There was not significant difference between the DD and combined groups either. There was no correlation between MAO-B activity and age in the groups.

B. Platelet MAO-B activity in consideration of gender differences

Mean (±SEM) values of MAO-B activity in the female and male groups were shown in table II. The following results were obtained by an overall ANOVA test:

Comparisons to the Control group

a. Major depression group: The MAO-B activity was found to be significantly higher in males of the MD group than both in females of the same group and in males of the control one (Comparisons: Males in major depression group-Females in major depression group: F=3.57 df=7/3 p<0.05,

TABLE I. Platelet MAO-B Activity and Serum Inorganic Phosphate Levels in Patients and Controls

Groups	Inorganic phosphate level (mg/dl)	MAO-B activity (Units/mg protein)
Major depression (n=12)	2.73 ± 0.16	0.095 ± 0.010*
Dysthymic disorder (n=19)	2.74 ± 0.12	0.096 ± 0.009*
Combined *** (n=31)	2.73 ± 0.01*	0.095 ± 0.006*
Control (n=24)	3.05 ± 0.10	0.072 ± 0.003

Results are represented as mean ± SEM

Significances: Compared to control; *p<0.05, **p<0.005.

*** Combined group= Major depression group + Dysthymic disorder group.

TABLE II. Platelet MAO-B Activity and Serum Inorganic Phosphate Level in the patient and Control Groups

	Platelet MAO-B Activity (units/mg protein)		Inorganic Phosphate Level (mg/dl)	
	FEMALES	MALES	FEMALES	MALES
GROUP	$\bar{X} \pm$ SEM	$\bar{X} \pm$ SEM	$\bar{X} \pm$ SEM	$\bar{X} \pm$ SEM
Major depression	0.006 ± 0.009 (n=4)	0.111 ± 0.0010 (n=8)[a,b]	3.22 ± 0.34 (n=4)	2.48 ± 0.11 (n=8)
Dysthymic disorder	0.095 ± 0.010 (n=13)[b]	0.099 ± 0.007 (n=6)[a]	2.63 ± 0.09 (n=13)	2.72 ± 0.25 (n=5)
Combined	0.088 ± 0.010 (n=17)[b]	0.115 ± 0.007 (n=14)[a,b]	2.77 ± 0.12 (n=17)	2.70 ± 0.16 (n=14)
Control	0.074 ± 0.007 (n=6)	0.070 ± 0.007 (n=18)	3.05 ± 0.25 (n=6)	2.98 ± 0.11 (n=18)

a: $p<0.05$ compared to females in the same group by ANOVA

b: $p<0.05$ compared to control subjects by ANOVA

Males in major depression group-Males in control group: $F=4.0$ $df=7/13$ $p<0.05$).

b. Dysthymic disorder group: It was observed that the MAO-B activity values were higher in males of the DD group than in females of the same group ($F=8.0$ $df=12/5$ $p<0.05$), and it was also higher in females of the DD group than in females of the control one ($F=7.89$ $df=12/5$ $p<0.05$).

c. Combined group: MAO-B activity values were significantly higher in males of the combined group than both in females of the same group and in males of the control group (Comparisons: Males-Females in the combined group: $F=2.47$ $df=16/13$ $p<0.05$, Males in the combined group-Males in the control group: $F=2.71$ $df=13/17$ $p<0.05$). It was found that MAO-B activity values were significantly higher in females of the combined group than in females of the control one ($F=6.7$ $df=16/5$ $p<0.05$).

There was no significant difference in MAO-B activity in comparisons between Major depression-Dysthymic risorder, Major depression-Control, Dysthymic disorder-Control and Combined-Control groups.

The only statistically significant relationship found was a negative correlation between age and MAO-B activity in females of the MD group ($r= -0.893$ $p<0.05$). No correlation was present between MAO-B activity and serum inorganic phosphate levels in the groups.

Serum Inorganic Phosphate Level

It was observed that there was no statistically significant difference in inorganic phosphate levels in all groups in or without consideration of gender differences. There was not significant correlation between age and inorganic phosphate level in the groups either.

DISCUSSION

In this study, without the consideration of gender differences platelet MAO-B activity was found to be lower in the major depression, dysthymic disorder and combined groups than in the control one. There are some reports demonstrating contradictory results such as an increase (2,14,15) or a decrease (7,16) in platelet MAO activity in depressed patients when

compared to healthy controls.

While we found no difference in MAO-B activity in healthy female and male control subjects, we observed higher enzyme activity in male patients of the two depression groups (the MD group and the combined group) than those in female patients of the same groups and the control males. Furthermore, males of the dysthymic disorder group showed higher MAO-B activity than those of females in the same group. In a previous study, it was reported that there was no difference in platelet MAO activity between depressed females and males while healthy women had higher enzyme activity than those of male counterparts (15). It was also reported that depressed females and higher MAO activity when compared to male patients (8). Although our results were contradictory to the previous reports in the literature, these results obtained from the males supported the idea that higher MAO-B activity observed might be a useful marker for monoaminergic activity in depression since there were no alterations in MAO activity which could be induced by mentrual cycle in men.

In this study, we found significantly higher MAO-B activity in females of the DD and combined groups when compared to those in control females. This result was consistent with the finding of presence of higher MAO activity in depressed females than in healthy females in the literature (18) but the latter study had been done just in postmenopausal female patients. Our findings need further replication because the number of female patients in our study was limited and comparisons were done regardless their ovulation cycles.

In previous studies, while Poirier (15) has reported no difference in platelet MAO activity between the subtypes of depression Schatzberg (17) has observed higher levels of MAO in psychotic depressed patients than in their nonpsychotic counterparts. In our study, we found no difference in MAO-B values in subtypes of depression considering and without consideration of gender differences. Our data were consistent with the finding of Poirier, et al (15). These results support the idea that major depression and dysthymic disorder could have been sharing the same biological substrate.

We did not observe any relationship between platelet MAO-B activity and severity of clinical symptomatology; But in some previous studies, a positive correlation between severity of anxiety and peripheral catecholaminergic activity in depression has been reported (6,8,10). It has also been demonstrated that severity of depressive symptoms was positively correlated with MAO enzyme activity (6,8,15). Limited size of our sample might have caused such a relationship to escape from our observation or platelet MAO activity is in fact, a "trait marker" rather than a "state marker" as previously suggested by some authors (6,17).

We did not find any relationship between platelet MAO-B activity and age in patients, except in females of the major depression group. In this group MAO-B activity was significantly but inversely correlated with age only in female patients. It has been suggested that although platelet MAO activity is determined by heredity it also increases with age (2,18). It has been reported that, regardless of sex, there was no correlation between this enzyme activity and age (6,15). Our findings contradicted the results of other studies in which MAO activity had been reported to be correlated with age in depressed female patients (1). There is another study which reported a positive

correlation between MAO activity and age in depressed female patients who were above 65 only (15). If MAO activity decreasing with age leads to an increase in tendency towards depression, needs to be evaluated in various age groups.

We found no difference in serum inorganic phosphate levels between the patient and control groups. Previously it has been reported that high catecholamine levels might be related to low phosphate levels. Additionally, it has been demonstrated that infusion of catecholamines reduced inorganic phosphate levels and rised anxiety scores (10). The negative correlation between catecholaminergic activity and phosphate level has been explained by the probable mechanism that beta-adrenergic receptor mediated stimulation of muscle glycogenolysis which depletes intracellular phosphate causes a transcellular shift from plasma into muscle cells (12). We did not find such a relationship between the two parameters. Platelet MAO-B has been suggested to be selectively DA-degradating enzyme (10). Our failure to confirm that kind of correlation between dopaminergic activity that is represented by platelet MAO, and serum inorganic phosphate level may be ascribe to the limited size of our sample or circadian variation of phosphate level (9). If the latter possibility is valid, our finding will just show that there is no relationship in time of obtaining blood samples. Furthermore, depending on the presence of a negative correlation between phosphate level and age in dysthymic female patients, we consider that the relationship should be found out in various age groups.

In conclusion, our findings supported the hypothesis that MAO-B activity might be a biological marker of depression but did not confirm the idea that higher MAO-B activity would be associated with lower phosphate levels depending on the negative correlation between dopaminergic activity and serum phosphate levels.

References

1. Alexopoulos,GS, Lieberman,KW, Young,RC, Shamoian,CA. Platelet MAO activity age at onset of depression in elderly depressed women. ***Am J Psychiatry*** *141: 1276-1278,1984.*

2. Alexopoulos,GS, Young,RC, Lieberman,KW, Shamoian,CA. Platelet MAO activity in geriatric patients with depression and dementia. ***Am J Psychiatry*** *144:1480- 1483,1987.*

3. American Psychiatric Association. DSM-III: ***Diagnostic and Statistical Manual of Mental Disorders.*** *3rd ed. APA, Washington, DC, 1980,pp 205-241.*

4. Frankel, S: Electrolytes. In Frankel S, Retiman S, Sonnenwirth AC (eds): ***Grandwohl's Clinical Laboratory Methods and Diagnosis.*** *7th ed, Saint Louis, CV Mosby Co, pp 692-693,1971.*

5. Friedman E, Shopsin B, Sathananthan G, Gershon S. Blood platelet monoamine oxidase activity in psychiatric patients. ***Am J Psychiatry*** *131:1392-1394,1974.*

6. Georgotas A, McCue RE, Friedman E, Hapworth WE, Kim OM, Cooper TB, Chang I, Stokes PE. Relationship of platelet MAO activity to characteristic of major depressive illness. ***Psychiatry Res*** *19:247-256,1986.*

7. Goltfrias CG, von Knorring L, Oreland L. Platelet monoamine oxidase activity in mental disorders. II Affective psychoses and suicidal behavior. ***Neuro-Psychopharmacol*** *4:185-192,1980.*

8. Khan A, Lee E, Dager S, Hyde T, Raisys V, Avery D, Dunner D. Platelet MAO-B

activity in anxiety and depression. **Biol Psychiatry** 21:847-849,1986.

9. Kreisberg RA. Phosphorus deficiency and hypophosphatemia. **Hosp Pract** 12:121, 1977.

10. Maddock RJ, Moses JA, Roth WT, King R, Murchison A, Berger PA. Serum phosphate and anxiety in major depression. **Psychiatry Res** 22:29-36,1987.

11. McEwen CM Jr. Monoamine oxidase (human serum or plasma). In Colowick SP, Kaplan NO, eds. **Methods in Enzymology.** Vol XVII, Part B. New York, Academic Press, pp 692-693,1971.

12. Massara F, Camanni F: Propranolol block of adrenaline-induced hypophosphathemia in man. **Clin Sci** 38:245-248,1970.

13. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. **Br J Psychiatry** 134:134-138,1979.

14. Oreland L, Wiberg A, Asberg M, Traskman L, Jostrand S, Thoren P, Bernsson L, Tybring G. Platelet MAO activity and monoamine metabolytes in cerebrospinal fluid in depressed and suicidal patients and in healthy controls. **Psychiatry Res** 4:21-29,1981.

15. Poirier MF, Loo H, Mitrani N, Benkelfat C, Askienazy S, Le Fur G. Platelet MAO activity in clinical subtypes of depression and DST supression. **Acta Psychiatr Scand** 75:456-463,1987.

16. Furinski S, Hauptmann M, Zaluska M. The activity of blood platelet monoamine oxidase in endogenous depression. **Biol Psychiatry** 14:575-580,1980.

17. Schatzberg AF, Rotschild AJ, Langlais PJ, Lerbinger JA, Schildkraut JJ, Cole JO. Psychotic and nonpsychotic depression: II platelet MAO activity, plasma catecholamines, cortisol and specific symptoms. **Psychiatry Res** 20:155-164,1987.

18. Schneider LS, Severson JA, Pollock V, Cowan RP, Sloane B. Platelet monoamine oxidase activity in elderly depressed outpatients. **Biol Psychiatry** 21:1360-1364,1986.

19. Silverman LM, Cristenson RH, Grant GH. Amnioacids and proteins. In Tietz NW, ed. **Textbook of Clinical Chemistry.** Philadelphia, WB Saunders Co, pp 583-584, 1986.

20. Snaith RP, Baugh SJ, Clayden AD. The clinical anxiety scale: Derived from the Hamilton rating scale. **Br J Psychiatry** 141:418-423.