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Age and Sex Related Alterations in Serum and Platelet Monoamine Oxidase

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Summary: The process of aging presents itself with various alterations in physiological events. Although the turnover of catecholamines increases with aging, there is a lack of response to catecholamines in target tissues. One of the key enzymes in catecholamine metabolism is monoamine oxidase. It has been suggested that tissue and serum monoamine oxidase activities show pathological alterations in various diseases while physiological fluctuations can also be detected in normals. The aim of this study is to determine the sex and age related changes of platelet and serum monoamine oxidase in healthy volunteers.

In this study, 75 healthy volunteers of different ages (21–80 a) and sexes (40 females, 35 males) were included. Serum and platelet monoamine oxidase determinations were performed spectrophotofluorometrically by *Tufvesson*'s (Scand J Clin Lab Invest 1970; 26:151–4) and *Kraml*'s (Biochem Pharmacol 1965; 14:1684–6) modified methods, respectively.

While there was no significant difference in serum monoamine oxidase activities related to age and sex, platelet monoamine oxidase manifested a significant increase in females compared to males ($p < 0.05$) and the mean values in both sexes showed an increase with age ($p < 0.001$).

The results of this study imply that platelet monoamine oxidase shows an age related increase which is more prominent in females.

Introduction

The process of aging, which has been an extensive area of investigation during recent years, manifests itself with various alterations in physiological events. It has been shown that with aging, the turnover of catecholamines increases, however, there is a lack of response to catecholamines in target tissues. The increases in the activities of the enzymes involved in catecholamine metabolism are held responsible for these changes (1–6).

One of the key enzymes in catecholamine metabolism is monoamine oxidase (EC 1.4.3.4) which is an oxidoreductase that deaminates monoamines such as adrenaline, noradrenaline and dopamine (7–8). There are two types of monoamine oxidase, one being a FAD containing enzyme (intracellular) located in the outer membrane of the mitochondria of many tissues such as platelets (8–12) and the other, a Cu^{2+} and pyridoxal phosphate containing enzyme found in serum (13). It has been suggested that while tissue and serum monoamine oxidase activities manifest abnormal alterations in various disease states (13–26), physiological fluctuations may also be detected in normals (8, 27–30). The objective of this study has been to investigate the sex and age related fluctuations of platelet and serum monoamine oxidase in healthy volunteers.

Materials and Methods

Cases

In this study, conducted in the Hospital of Ege University School of Medicine with the permission of the Ethics Committee, 75 healthy volunteers of different ages (21–80 a) and sexes (40 females, 35 males) were included. These volunteers were taking no medication or alcohol. They neither smoke nor suffer from any disorder.

Reagents and solutions

All reagents were analytical grade and purchased from Sigma Chem. Co. (St Louis) and Merck Darmstadt (Germany).

Assay

For serum monoamine oxidase determinations, 3 ml venous blood, after coagulation, was centrifuged at 1500 *g* for 15 minutes to obtain the serum. For platelet monoamine oxidase determinations, 10 ml venous blood samples were collected in polypropylene test tubes containing 0.5 ml of 50 g/l Na_2EDTA. For platelet isolation, *Corash*'s platelet isolation method modified by *Glover* et al. (19) was applied. The sample was centrifuged at 320 *g* for 10 min and the platelet-rich plasma withdrawn and re-centrifuged at 2500 *g* for 15 min. The platelet pellet was resuspended and washed in 1 ml of 0.15 mol/l NaCl and re-centrifuged at 2500 *g* for 15 min. The pellet was resuspended in 1 ml of 0.15 mol/l NaCl and used for the measurement of monoamine oxidase. Platelet protein concentrations were assayed by the method of *Lowry* et al. (31).

Serum and platelet monoamine oxidase determinations were performed spectrophotofluorometrically (with the Aminco-Bowman spectrophotofluorometer) using *Tufvesson*'s (32) and *Kraml*'s (33) modified methods, respectively. The principle of both of these as-

says is based on the spectrofluorometric measurement of the fluorescence of 4-hydroxyquinoline formed by the oxidative deamination of kynuramine via monoamine oxidase. The amount of 4-hydroxyquinoline formed is directly proportional to the monoamine oxidase activity of the sample.

Statistical analysis

For statistical analysis, variance analysis (F test-one way ANOVA) and the *Student* t test were used.

Results

The mean platelet monoamine oxidase activities in different age groups and sexes are presented in table 1. As

Tab. 1 Platelet monoamine oxidase activities in different age groups and sexes.

Age groups (a)	Platelet monoamine oxidase activities (nmol/h · mg protein)			
	Females		Males	
	n	$\bar{x} \pm SD$	n	$\bar{x} \pm SD$
21–30	6	5.61 ± 1.45	6	3.85 ± 0.78
31–40	5	5.92 ± 1.11	5	2.92 ± 0.87
41–50	10	5.29 ± 1.48	5	3.87 ± 1.45
51–60	9	7.81 ± 1.40	7	7.76 ± 4.52
61–70	5	13.30 ± 4.31	6	7.92 ± 1.22
71–80	5	19.80 ± 4.50	6	9.55 ± 1.15

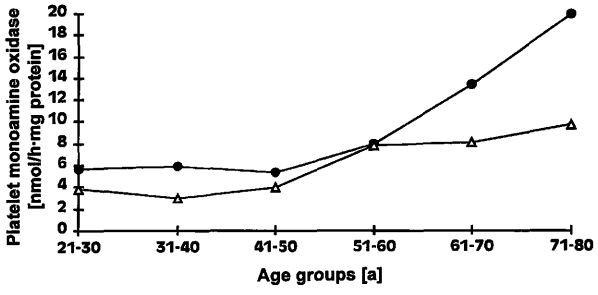

Fig. 1 Age-related changes in the mean values of platelet monoamine oxidase activities in different age groups in both sexes.
−●− female
−△− male

may be observed in figure 1, mean platelet monoamine oxidase activities increase with age (for females $p < 0.001$, for males $p < 0.005$).

The mean platelet monoamine oxidase activity of females (8.80 ± 5.43 nmol/h · mg protein) is significantly higher than that of males (6.18 ± 3.32 nmol/h · mg protein) ($p < 0.05$). The mean serum monoamine oxidase activity is 17.27 ± 6.97 mU/l for females, while it is 18.21 ± 7.03 mU/l for males. Although serum monoamine oxidase activity is higher in males than in females, the difference is not statistically significant (fig. 2).

The results of the age-related changes in serum monoamine oxidase activities in both sexes are presented in table 2. As may be observed in figure 2, serum mono-

Tab. 2 Serum monoamine oxidase activities in different age groups and sexes.

Age groups (a)	Serum monoamine oxidase (mU/l)			
	Females		Males	
	n	$\bar{x} \pm SD$	n	$\bar{x} \pm SD$
21–30	6	16.28 ± 3.94	6	17.13 ± 6.17
31–40	5	17.56 ± 3.12	5	14.58 ± 3.08
41–50	10	14.53 ± 4.24	5	16.31 ± 2.41
51–60	9	19.60 ± 11.1	7	21.01 ± 6.54
61–70	5	15.56 ± 4.16	6	19.93 ± 9.95
71–80	5	21.14 ± 6.49	6	18.92 ± 7.88

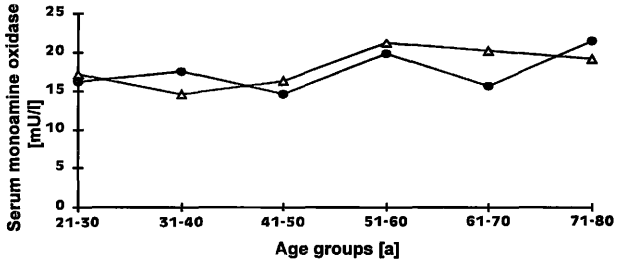

Fig. 2 Age-related changes in the mean values of serum monoamine oxidase activities in different age groups in both sexes.
−●− female
−△− male

amine oxidase activities do not change related to age in either females or males.

Discussion

The results of the studies investigating the age and sex related changes in platelet and serum monoamine oxidase activities reveal contradictory data. *Robinson* et al. (4) in serum and platelets, *Tryding* et al. (26) in serum, *Murphy* et al. (34) and *Bagdy & Rihmer* (35) in platelets and *Benedetti* et al. (5) in brain tissue noted an increase in monoamine oxidase activity with age. Meanwhile, *Baron* et al. (36) in platelets and *Tryding* et al. (26) in serum showed that monoamine oxidase activities were higher in females than in males. These investigators proposed that the higher activity of the enzyme in females is the result of the interaction between female sex hormones and monoamine oxidase (26, 36). However, in concordance with our results, most of the studies assaying serum monoamine oxidase activities reveal no significant differences related to age and sex (8, 27–30).

In our study, when the relationship between platelet monoamine oxidase activity and age was investigated, it was seen that in correlation with *Robinson*'s et al. (4), *Murphy*'s et al. (34) and *Bagdy*'s & *Rihmer*'s (35) findings there was a significant correlation between aging and enzyme activity. Regardless of sex, mean platelet monoamine oxidase levels in different age groups manifested a significant increase with age ($p < 0.001$). When

the females and males are evaluated separately, it is observed that platelet monoamine oxidase activities also increase with age in both sexes ($p < 0.001$ in females and $p < 0.005$ in males) (fig. 1).

It is observed that in all of the age groups mean platelet monoamine oxidase levels are higher in females than males. This increase in females is significantly higher in all groups ($p < 0.05$) except between the ages of 41–50 and 51–60 (tab. 1). Especially, the striking increase related to monoamine oxidase in females after the age of 60 is interesting. Our findings related to monoamine oxidase activity in females points to a possible link between female hormonal status and monoamine oxidase. However, this link is still obscure. Previously, *Holzbauer & Youdim* (37) have observed a stimulating effect of progesterone on uterine, ovarian and adrenal monoamine oxidase activity. The information available being incomplete, it is not possible to draw any general conclusion (4, 34, 37). Further research in this area should be continued.

As to serum monoamine oxidase activity, no significant correlation between enzyme activity and sex is noted. Mean serum monoamine oxidase values are higher in males than in females but this increase is not statistically significant (tab. 2). Our results, related to serum monoamine oxidase activity, age and sex are in correlation with the previous studies (8, 27–30).

As a result, it is concluded that platelet monoamine oxidase activity increases with age, this change being more prominent in females.

Further detailed studies revealing the interaction between platelet monoamine oxidase activity and biogenic amine metabolism are necessary in order to elucidate the role of biogenic amines in the process of aging.

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