

STUDIES ON PLASMA HISTAMINASE LEVELS IN NORMAL AND ALLERGIC INDIVIDUALS

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Lahiri (11) in 1965 reported a distinct increase in plasma histaminase activity in tropical eosinophilia. He also found a correlation between the absolute eosinophil count and plasma histaminase level. It has long been suspected that allergy is a possible aetiological factor in tropical eosinophilia. Hence we decided to investigate plasma histaminase levels in other instances where allergy and eosinophilia are likely to coexist. Schoen and Pizer (5) had demonstrated that in one of their cases of eosinophilia, cigarette smoking appeared to be the cause of the same. Chronic allergic rhinitis is a condition associated frequently with a high incidence of nasal polyps and Kameswaran and Kameswaran (8) have already reported that in these polyps histamine content is high compared to other tumours in the nose.

Therefore we have in our present study estimated absolute eosinophil counts and plasma histaminase levels in a series of diagnosed cases of allergic rhinitis and also in a series of established chronic smokers and compared the values with those obtained in normal, male and female non-smokers.

MATERIALS AND METHODS

Blood samples were collected in heparinised syringes by venepuncture and centrifuged and plasma separated. Histaminase activity was estimated by the method of Kapeller Adler (7) and has been expressed in permanganate units (p.u.) per millilitre of plasma. Total and differential counts were determined and absolute eosinophil counts were calculated and have been expressed as thousands per cubic millimetre.

RESULTS

Mean values for plasma histaminase obtained from 25 apparently healthy male non-smokers were much lower than similar values obtained for a series of 21 healthy female non-smokers, (Table I) even though there was no significant variation in the mean absolute eosinophil counts.

TABLE I

Mean Plasma Histaminase level and Mean Eosinophil count in normal adults

	Mean Plasma Histaminase (p.u./ml. Plasma)	Mean Absolute Eosinophil count (Thousand/cmm.)
Men-25	0.132	0.443
Women-21	1.052	0.345

Statistical evaluation :

Test applied 't'-- non paired obs.

For Histaminase levels

t OBSD-3.438
t EXP (.05)-2.025
t OBSD t EXP

For Eosinophil count.

t OBSD-0.654
t EXP (.05)-2.05
t OBSD t EXP.

*Inference :—*Mean Eosinophil count for normal men and women is likely to be the same and the absolute eosinophil count is free from the influence of sex. Women are likely to have increased mean plasma histaminase level.

Histaminase values were estimated in 16 normal women medical students at regular intervals during a single menstrual cycle. The mean values show that there is a tendency for the histaminase value to be high during the earlier part of menstrual cycle which drops to lower levels towards the later phase even though it remains higher than values obtained for normal men (Table II).

TABLE II
Plasma Histaminase levels during different weeks of Menstrual Cycle in normal Women

Sl.No.	Ist week	IInd week	IIIrd week	IVth week	
1.	0.6	0.5	0.5	0.7	
2.	0.5	1.5	0.3	0.2	
3.	0.4	0.2	0.4	0.3	
4.	0.5	0.4	0.2	0.4	
5.	0.4	0.5	0.7	0.5	
6.	0.2	0.2	0.1	0.1	
7.	0.8	0.2	0.7	0.2	
8.	0.2	0.4	0.4	0.2	
9.	0.2	0.5	0.7	0.6	
10.	0.7	0.3	0.4	0.2	
11.	1.3	0.5	0.2	0.4	
12.	0.3	0.1	0.3	0.2	
13.	0.5	0.2	0.3	0.2	
14.	0.8	0.4	0.2	0.1	
15.	0.5	0.1	0.5	0.4	
16.	0.5	0.2	0.5	0.4	
Mean		0.525	0.394	0.4	0.319

Statistical Inference : The difference is highly significant and the plasma histaminase levels vary widely between weeks.

Hence for purposes of comparison with values obtained in probable allergic cases only male patients were chosen. 20 cases of chronic allergic rhinitis were studied before and after treatment. In this series mean absolute eosinophil count and mean plasma histaminase level are both slightly higher before treatment than values obtained in apparently normal males. (Tables III and IV). In a series of smokers also there is an apparent increase in the absolute eosinophil count and also in plasma histaminase activity (Tables V and VI).

TABLE III
Mean Plasma Histaminase level and mean eosinophil count in allergic rhinitis in men

	Mean Plasma Histaminase level (p.u./ml. plasma)	Mean Absolute Eosinophil count (thousand/cmm.).
Normal	0.132	0.443
Before Treatment	0.355	0.505
After Treatment	0.130	

Statistical evaluation :

Test applied 't' (Paired observations)

Inference :

In allergic rhinitis plasma histaminase is likely to be raised and we can reasonably state that treatment has its own significant effect on plasma histaminase level.

After treatment there is a fall in plasma histaminase levels.

TABLE IV

Plasma Histaminase levels in allergic rhinitis cases. Before and After Treatment

Case No.	Pasma histaminase (p.u./ml. plasma)	
	Before Treatment	After Treatment
1.	0.2	0.2
2.	0.2	0.2
3.	0.3	0.1
4.	0.4	0.1
5.	0.2	0.1
6.	0.2	0.1
7.	0.3	0.1
8.	0.3	0.2
9.	0.3	0.1
10.	0.6	0.2
11.	0.2	0.3
12.	0.7	0.3
13.	0.7	0.1
14.	0.3	0
15.	0.2	0.2
16.	0.3	0.1
17.	0.5	0.1
18.	0.8	0
19.	0.2	0.1
20.	0.2	0

In smokers both the plasma histaminase levels and absolute eosinophil counts are higher than normal.

TABLE V

Mean Plasma Histaminase level and mean absolute Eosinophil count in male smokers and non-smokers

	Mean Plasma Hista- minase level (p.u./ ml. plasma)	Mean Absolute Eosinophil Count (thousand/cmm.)
Normal	0.132	0.443
Smokers	0.315	0.679

Statistical evaluation :

Test applied 't' —nonpaired observation
t —OBSD —4.01
t —EX (.05) —2.024
t —OBSD —t expected

Inference : Smokers have a raised plasma histaminase level.

TABLE VI
Plasma Histaminase levels and absolute Eosinophil counts in smokers

Case No.	Plasma Histaminase (p.u./ml plasma)	Absolute Eosinophil count (thousand/cmm.)
1.	0.2	0.168
2.	0.1	0.540
3.	0.2	0.666
4.	0.2	0.178
5.	0.2	1.183
6.	0.2	0.924
7.	0.1	0.298
8.	0.3	0.756
9.	0.4	1.680
10.	0.1	0.196
11.	0.3	0.392
12.	0.8	0.408
13.	0.4	2.475
14.	0.4	0.609
15.	0.5	0.106
16.	0.4	0.224
17.	0.3	0.282
18.	0.1	1.485
19.	0.4	0.498
20.	0.7	0.504

DISCUSSION

The significant difference in plasma histaminase activity between apparently healthy normal male and female adults is interesting and requires further study. Already, Kim (9) has reported a clear sex difference in the histamine metabolism of albino rats after a study of urinary excretion of free histamine. He has suggested that this difference is primarily due to the fact that male and female rats handle "formed-histamine" in a different manner and that there is a greater amount of conjugated histamine excreted by the male while a greater amount of free histamine is excreted by the female rat. Gustafsson *et al.* (4) found no sex difference in the total urinary histamine excretion in male and female rats. If this difference in the pattern of histamine excretion in the urine is a reflection of the histamine content in the blood it would indicate that the male rat conjugates histamine rapidly and therefore there is likely to be more free histamine in circulation in the female. If the same conditions exist in humans as in rats then this could act as stimulus for histaminase production and could account for a higher plasma histaminase level in the female. Raised histaminase levels have been reported during pregnancy in the plasma, lymph and placenta in some species [Swanberg (13) Carlsten (3); and Wicksell (15 and 16)]. Kapeller Adler (6) has also reported that *in vitro* natural oestrogens activate histaminase and androgens inactivate histaminase activity. It may be that Progesterone hormones are similar to androgens in the effect on histaminase activity. This may account for the higher values in the earlier phase of the menstrual cycle and the progressive reduction towards the end. The continuous presence

of some oestrogens in circulation may account for the elevated values obtained in females even though there is a relative difference during the different weeks of menstrual cycle. What role the sex hormones play in normal metabolism of histamine and what changes occur during the menstrual cycle and pregnancy are aspects which require further investigation.

As the results reported above indicate clearly a sex difference in plasma histaminase levels it was realised that comparisons could be made strictly amongst individuals of one sex only. So care has been taken to select cases of allergic rhinitis amongst males only. Histaminase levels have been estimated both before and after treatment with various steroids either alone or with antihistamines. Though the values obtained in smokers and in cases of allergic rhinitis before treatment are low compared to Lahiri's (11) results in tropical eosinophilia for both absolute eosinophil counts and for plasma histaminase levels still the mean values are higher than normal. After treatment only histaminase levels were estimated and this seems to be lowered. When an analysis is made for the different sexes separately there appears to be raised plasma histaminase levels in cases of allergic rhinitis also in men.

In the study of smokers and non-smokers there appears to be a correlation between the degree of smoking and eosinophil count and plasma histaminase level. The difference is more significant in plasma histaminase value than in eosinophil count.

Deschienes and Poiner (1955) demonstrated eosinophilia in guineapigs after an injection of tobacco extract. Schoen and Pizer (5) observed eosinophilia in a chain smoker the cause of which could not be traced to anything other than smoking because in this case abstinence from smoking rapidly brought down the eosinophil count. As referred by Silvette *et al.* (12) in an editorial in Medical Times as early as 1917 "inhalation of the combustion products of tobacco affords a very direct mode of access of antigen to the blood". Therefore it has been suggested that it is reasonable to suppose that the inhalation of tobacco protein is capable of producing an allergic effect (12).

In chronic allergy of this type in smokers there is likely to be release of histamine and a raised histamine level in plasma which may probably act as a stimulus for production of more histaminase. Moreover in conditions where allergy is suspected as an aetiological factor as in tropical eosinophilia and worm infestation marked eosinophilia has been found to occur in clinical studies. Broome and Archer (1) and Esch F. Tawbert (14) have reported that eosinophils may themselves contain in addition to histamine anti-histamine like component also. If this antihistamine like component is similar to histaminase then it could diffuse into the plasma and account for the enhanced plasma histaminase activity in eosinophilia. There is also a possibility that after antigen-antibody reaction, as a result of cell damage along with the release of histamine there may be release of other cell constituents some of which may be activators of plasma histaminase.

SUMMARY

Plasma histaminase level and eosinophil count have been estimated in a series of apparently normal men, women, cases of allergic rhinitis and smokers.

Plasma histaminase activity is higher in females than in males, even though the absolute eosinophil counts are about the same. It is highest in the 1st week of the menstrual cycle and progressively falls to lower levels towards the later phase of menstrual cycle.

The absolute eosinophil counts and plasma histaminase levels in cases of chronic allergic rhinitis are slightly higher than normal and show a tendency to fall with antiallergic treatment.

There is a mild eosinophilia and correlated increase in plasma histaminase levels in chronic smokers. The possible relationship between eosinophilia and smoking with that of raised histaminase levels has been discussed.

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