

SHORT COMMUNICATION

THE ROLE OF IMIPRAMINE HYDROCHLORIDE ON PLASMA TRANSAMINASE AND GLUCOSE LEVEL ON RATS UNDER ALTITUDE STRESS

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Summary: The effect of exposure of albino rats to simulated high altitude stress of 5000 metres for 3 and 6 hrs on plasma transaminases, non-protein nitrogen (NPN), total protein percentages and blood sugar levels have been studied both with and without the administration of an anti-stress drug Imipramine HCl at 2.0 mg/kg body weight. The drug appears to have a slight hepatotoxic effect.

Key words: Imipramine hydrochloride plasma transaminase plasma glucose
altitude stress

INTRODUCTION

The level of the transaminases in plasma and tissues, changes under various experimental and clinical stress and exercise as well as under pathological conditions. Transaminase activity in the urine has been utilized as an index of liver and kidney damage (14). Andreotti *et al.* (1) reported transient increase in serum glutamic-oxalacetic (GOT) and glutamic-pyruvic transaminase (GPT) levels during a boxing match. Lending *et al.* (9) found that exposure of puppies under reduced atmospheric pressure conditions for 3 hrs produced no significant effect on the plasma GOT level. Exposure of heat stress and muscular exercise also increased the serum GOT and GPT levels of dogs as compared to their corresponding controls (2). Nerdrum and Berg (11) reported an increase in serum GOT level 10 mins after brief exertion falling to normal within 45 mins. Vanlerenberghe *et al.* (13) found that rats subjected to hypoxia showed a marked increase in serum GOT and GPT levels.

In the present investigation, the effect of exposure of albino rats to a simulated high altitude condition on plasma transaminases, non-protein nitrogen (NPN), total protein percentages and blood sugar levels have been studied, both with and without the administration of an antistress drug, Imipramine HCl, at 2.0 mg/kg body wt. The aim of administration of Imipramine HCl was to assess its efficacy as an antistress drug. Previously our similar studies in this laboratory with methylamphetamine (4) and DOPA (5) have shown that both these drugs increase serum transaminase and NPN levels quite significantly as compared to sea level controls.

MATERIALS AND METHODS

Male albino rats, weighing approx. 200 g were divided into six groups of ten or more animals each. The drug, Imipramine hydrochloride, was given to the animals i.p. at a concentration of 2.0 mg/kg body wt. 30 mins prior to drawing of blood or subjecting them to stress. The stress involved keeping the animals in a vacuum chamber for 3 and 6 hrs at 350 mm. Hg. After the stress period, the animals were quickly anaesthetized with ether and blood was drawn by cardiac puncture into a bottle containing a suitable anticoagulant. For control animals also ether anaesthesia was used for drawing of blood so, any effect, due to ether is eliminated.

Total duration from taking out of high altitude chamber to collection of blood was approx. 5 mins. Transaminase in blood was estimated colorimetrically according to the method of Reitman and Frankel (12). Non-protein nitrogen (NPN) in blood was estimated by method of Folin and Wu (6). Total protein was estimated by Micro-Kjeldahl method (8). Blood sugar was estimated by method of Folin and Wu (7). Groupings of the animals and their respective treatment were as follows :—

- Group I Without drug and without stress (under room condition).
- Group II Without drug and with stress for 3 hrs.
- Group III Without drug but with stress for 6 hrs.
- Group IV With drug but without any stress.
- Group V With drug and with stress for 3 hrs.
- Group VI With drug and with stress for 6 hrs.

RESULTS AND DISCUSSION

The data recorded in the Table I shows that exposure of rats to an altitude stress of 5000 metres for a period of 3 hrs caused a highly significant rise in serum GOT, GPT and blood glucose and a highly significant fall in serum total protein level. Similar changes in serum GOT and GPT levels under different types of stress have also been reported by Andreotti *et al.* (1), Bedrak (2) and Vanlerenberghe *et al.* (13) Increase in the serum enzyme levels may be due to cellular damage or due to increased capillary permeability (15). In the present investigation, it is observed that when the exposure of the rats to the stress of high altitude was prolonged to 6 hrs, the blood glucose and serum GPT levels did not differ significantly from those of control group, while the serum GOT remained slightly elevated and serum total protein decreased to a small extent. Cellular damage is thus ruled out in the present study and the changes observed after an exposure of 3 hrs are most likely due to increased capillary permeability, the latter returning to nearly normal value because of acclimatization to the high altitude during the exposure for 6 hrs. Similarly, the changes in the blood glucose and total protein levels during the exposure to high altitude for 3 hrs and 6 hrs may also be explained as due to the stress of acute exposure and the relief of stress due to acclimatization.

When the drug Imipramine is administered to the rat maintained at sea-level, it causes a highly significant rise over the control group in serum GOT and NPN levels and a slight rise

TABLE I: Changes in serum transaminases, NPN, total protein and blood glucose levels of albino rats under administration of drug (Imipramine Hydrochloride) and/or subjection to simulated altitude stress of 5000 metres for 3 and 6 hours.

Group	Treatment	SGOT in I.U./litre mean±S.E.	SGPT in I.U./litre mean±S.E.	NPN mg% mean±S.E.	Glucose mg% mean±S.E.	Total protein g/100 ml mean±S.E.
I	No drug+No stress (Control)	36.6±2.3	6.9±1.7	34.6±5.5	91.5±10.7	6.1±.25
II	Stress of 3 hrs+No drug.	66.9±3.8**	31.0±1.6**	46.2±4.5@	158.2±12.3**	5.3±.12**
III	Stress of 6 hrs+No drug.	46.1±3.0*	10.7±0.9@	44.1±4.2@	88.4±10.4@	5.5±.12*
IV	Drug+No Stress	55.5±4.5**	17.1±4.1*	61.4±2.8**	129.2±7.7*	5.9±.12@
V	Drug+Stress of 3 hrs.	62.8±3.0**	23.1±3.0**	50.3±2.1*	92.3±7.4@	5.2±.25*
VI	Drug+Stress of 6 hrs.	100.1±14.9**	15.3±4.0@	45.5±4.6@	96.9±2.2@	5.2±.09**

Max. level of significance : P < .05
 Highly significant : **
 Significant : *
 Non-Significant : @

in blood glucose and serum GPT levels. An elevation of SGOT is observed in cases of muscle damage, e.g., acute myocardial infarction and trauma and unless there is an associated hepatic damage, SGPT remains normal (3). The cardiotoxic activity of antipsychotics has been reported by Nemeč (10) and our results show that the drug imipramine has cardiotoxic, nephrotoxic and slight hepatotoxic property in addition to its hyperglycaemic action. When the animal, after treatment with imipramine is exposed to the stress of high altitude for a period of 3 hrs, it is observed that, in addition to serum GOT, the serum GPT is also elevated highly significantly over the control figures, while there is a slight elevation of serum NPN, a fall in serum total protein levels and a fall of blood glucose to the normal level. It is evident that under conditions of high altitude, the drug imipramine retains its cardiotoxic property while there is a modification of its nephrotoxic and hyperglycaemic activity due to which the serum NPN remains slightly elevated over that for the control group and the blood sugar returns to normal. On prolonged exposure for a period of 6 hrs after treatment with imipramine the nephrotoxicity and hepatotoxicity of the drug are lost while the cardiotoxic activity is elevated.

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REFERENCES

1. Andreotti, D. A. Bencini and G. Nuzzaci. Modification of glutamic — Oxalacetic and glutamic pyruvic transaminase activities in serum of boxers. *Boll. Soc. ital. biol. Sper.*, **35** : 1348-50, 1959.
2. Bedrak, E. Blood serum enzyme activity of dogs exposed to heat stress and muscular exercise. *J. Appl. Physiol.*, **20** : 587-90 1965.
3. Cantarow, A. and M. Trumper. *Clinical Biochemistry*, 6th Edition, p. 450-451, W.B. Saunders & Co., London, 1962.
4. Chatterjee, A.K., S.K. Dighe, R.C. Naithani, A. Ghose and Bal Krishna. The role of methylamphetamine on plasma transaminase level under altitude stress. *Jap. J. Pharmacol.*, **22** : 871-3, 1972.
5. Chatterjee, A.K., S.K. Dighe, R.C. Naithani and A.S. Sachan. The role of DL—Dihydroxy phenyl alanine (DOPA) on plasma transaminase level under altitude stress. *Jap. J. Pharmacol.*, **23** : 269-71, 1973.
6. Folin, O. and H. Wu. A system of blood analysis. *J. Biol. Chem.*, **38** : 81-110, 1919.
7. Folin, O. and H. Wu. A system of blood analysis. Supplement I. A simplified and improved method for the determination of sugar. *J. Biol. Chem.*, **41** : 367-74 1920.
8. Hawk's *Physiological Chemistry*, 14th Edition p. 1081, McGraw Hill New York, 1964.
9. Lending, M., L.B. Slobody and J. Mestern. Effect of prolonged hypoxia on cerebrospinal fluid and glutamic—oxalacetic transaminase (GOT) and lactic dehydrogenase (LDH). *Neurology*, **11** : 520-7 1961.
10. Nemeč, J. Cardiotoxic effects of tricyclic antipsychotics. Comparison of some newer derivatives from the 10, 11-dihydrodibenzo/b f/thiepin group with perphenazine and amitriptyline. *J. Eur. Toxicol.*, **6** : 224-31 1974.
11. Nerdrum, H.J. and K.J. Berg. Changes of serum glutamic-oxalacetic transaminase and serum lactic dehydrogenase on physical exertion. *Scand. J. Clin. Lab. Invest.*, **16** : 624-9, 1964.
12. Reitman, F. and S. Frankel. A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. *Am. J. Clin. Pathol.*, **28** : 56-63, 1957.
13. Vanlerenberghe, J., C. Voisin, F. Guerrin and C. Bel. Variations of plasma transaminases in rats kept in a confined atmosphere. *Compt. Rend. Soc. Biol.*, **159** : 1164-6 1965.
14. Vorobeva, R.S. and I. Khazanova. Transaminase activity in urine as an index of liver and kidney damage. *Khim Faklory Vneshn Sredy i ikh Gigien Znachenic Sp. Moscow*, 54-5 1965; *Chem Abstr.*, **65** : 4408f.
15. Wotton, I.D.P. *Microanalysis in Medical Biochemistry* p. 109, J.A. Churchill Ltd., London 1964.