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Isoniazid-Associated Uric Acid Retention in the Lizard, Uromastix HardwickII

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ABSTRACT

A study has been made on the reduction of uric acid excretion following oral administration of 0.06 mg Isoniazid (INH) per day for 5, 10 and 15 days to 3 batches of Uromastix hardwickii respectively. The rise of uric acid concentration in the blood was 60 per cent higher on day 5; and about 4 and 5 times greater than controls on day 10 and 15 respectively due to increased reabsorption or decreased excretion of uric acid from tubular fluid.

Keywords: *Uric acid retention, Isoniazid, lizard.*

I. INTRODUCTION

Isoniazid (INH) is known for its dose-related hypersensitivity and mediated toxicities.

Neurotoxicity including psychosis, confusion, coma and convulsions have been observed in patients treated with high concentration of the drug [1, 2]. Peripheral neuritis is dose-related [3]. However, the toxicity, due to frequent and slow inactivation of the drug, is preventable by simultaneous administration of pyridoxine hydrochloride [4].

Among the miscellaneous reactions in common laboratory tests are Coombs' (direct), hyperglycemia (glycosuria) LE cells and presence of methemoglobin. INH is known to increase blood ammonia [5,6]. INH increases erythrocyte permeability with increase in span of treatment in Uromastix hardwickii [7]. Also the drug has been shown to shorten the survival of erythrocytes and resulting hemolytic anemia [8]. In another study INH showed severe adverse effects on Packed Cell Volume (PCV) [9] and differential leucocytes cellularity of the lizard [10].

Evidently, INH is also responsible for urinary retention [11]; but its effect on blood uric acid remains to be worked out in Uromastix hardwickii. Therefore, in this investigation, attempt has been made to show the effect of administration of therapeutic doses of isoniazid on the blood uric acid level in the scaly tailed lizard.

II. MATERIALS AND METHODS

Design of Experiment

There were altogether 6 groups each consisting of 5 lizards. Group I, III and V were kept as control. Whereas, group II, IV and VI served as tests.

Drug Information

The INH dose is determined by the 6-hr serum level and adjusted accordingly. All routes of administration are feasible, but the drug is usually given by mouth. It is readily absorbed when administered either orally or parenteraly. Peak plasma concentration of 3 to 5 µg/ml develops 1 to 2 hours after oral ingestion of usual doses.

There is a genetic variation in the metabolism of this drug in man; which significantly alters the plasma concentrations achieved and as well as the half-life of INH in the circulation. But half-life of the drug may be prolonged in the presence of hepatic insufficiency.

The average active concentration of INH in the presence of rapid inactivators in circulation is about 30 to 50 per cent and much less is present in persons who acetylate the drug slowly. The half-life of INH varies from less than 1 hour to more than 3 hours. The mean half-life in rapid acetylators is approximately 80 minutes; while a value of 3 hours is a characteristic of slow inactivators [12].

Drug Administration

Test individuals of group II received a daily dose of 0.06 mg INH/day for 5 days; but individuals of test IV received the same dose daily for 10 days and individuals of group VI also received 0.06 mg of INH per day for 15 days.

Control individuals of group I received a 'sham' dose of 0.06 ml pyrogen free distilled water per day for 5 days; of control III for 10 days and individuals of group V daily for 15 days.

Collection of Blood

For uric acid estimation, blood sample of each individual of comparable groups was collected prior to start of drug

administration to obtain 0-day value. Blood samples of group I and II were drawn on day 5; blood samples of group III and IV were collected on day 10 and blood samples of group V and VI were obtained on day 15. Blood uric acid values were measured by using commercially available biochemical kit and absorbance was read on spectrophotometer.

III. RESULTS AND DISCUSSION

Animals belonging to different lots were obtained at different periods of times. Fig.1 indicates the amount of uric acid present in the blood of controls and tests. Uric acid mean values of control groups of day 5 to day 10 and day 15 showed increase inspite of 'sham'treatment. This increase in concentrations of uric acid in controls is indicative of desert adaptation. In nature, Uromastix collects urinary excretion in its bladder and reabsorbs water along with some amount of uric acid. However, test values were higher when compared with controls (Fig., 1). The mean test values on day 5 to 10 and day 10 to 15 showed 4.82 mg /100 ml to 6.64 mg /100 ml and 7.9 mg /100 ml of serum uric acid respectively.

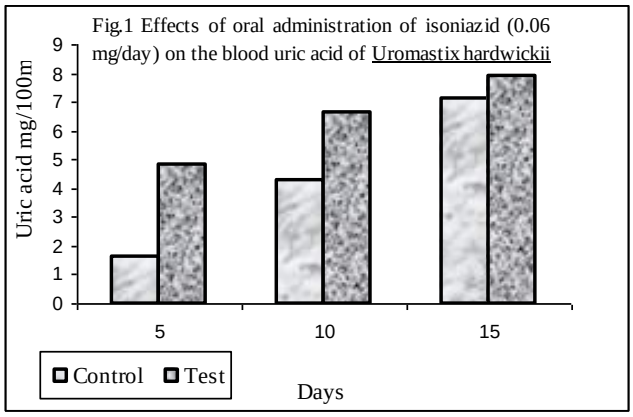

Fig.1 Effects of oral administration of isoniazid (0.06 mg/day) on the blood uric acid of Uromastix hardwickii

Rise in serum uric acid was 50 per cent more than control on day 5; about 3 times more than that of control values on day 10 and 15. Whereas, uric acid retention in this study was 3, 4 and 5 times greater in tests on day 5, 10 and day 15 respectively.

The mechanisms through which drugs inhibit carrier-mediated transport have been studied extensively [13]. General metabolic inhibitors have played an important role in experimental studies. Excreted uric acid is largely reabsorbed in man by active transport and thus the amount that is really excreted is small; and fraction of that which is filtered. In lizards as in all species, excreted uric acid is transported by carrier-mediated mechanisms and not by diffusion. In Uromastix hardwickii the site of transport is possibly located in the proximal tubules, including both the convoluted and straight positions.

A drug may either increase or decrease the excretion of uric acid [14]. Though, the paradoxical effect results from differences in the sensitivity of the reabsorptive and secretory mechanisms for urates to drug [15]. Probenecid increases the urinary excretion of uric acid by inhibition of reabsorption [16].

There is considerable evidence that higher concentrations of uric acid in Uromastix blood are due to the dominant action of INH. However, it is difficult to say that INH decreases the reabsorption or inhibits the excretion of uric acid via tubular fluid in this lizard.

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