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Isoniazid-Associated Uric Acid Retention in the Lizard, *Uromastix hardwickii*

R. HASAN*, S. MALIK, G. YASMEEN AND M. AHMAD

Department of Physiology, University of Karachi, Karachi-75270, Pakistan.

Reduction in uric acid excretion was observed following oral administration of 0.06 mg isoniazid per day for 5, 10 and 15 days to three groups of *Uromastix hardwickii* lizards. The rise of serum uric acid levels in the treated groups was 60 per cent higher on day 5, and about 4 and 5 times greater than in control groups on day 10 and 15 respectively. The rise in serum uric acid levels may be attributed to increased reabsorption or decreased excretion of uric acid in the kidneys of isoniazid-treated lizards.

Key words: Uric acid retention, isoniazid, lizard

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.

MATERIALS AND METHODS

Design of experiment: There were altogether 6 groups each consisting of 5 lizards. Groups I, III and V were kept as control while groups II, IV and VI served as tests.

Drug information: The INH dose is determined by the 6 h 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 parenterally. Peak plasma concentration of 3 to 5 μg/ml develops 1 to 2 h 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. The half-life of the drug may be prolonged in hepatic insufficiency.

The average active concentration of INH in the presence of rapid inactivators in circulation is about 30-50% and much less is present in persons who acetylate the drug slowly. The half-life of INH varies from less than 1 h to more than 3 h. The mean half-life in rapid acetylators is approximately 80 min; while a value of 3 h 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 in individuals of test IV received the same dose daily for 10 days and individuals of

*Author to whom correspondence may be addressed.

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.

RESULTS AND DISCUSSION

Animals belonging to different lots were obtained at different periods of times. Fig.,1 indicates the amount of uric acids present in the blood of controls and test. 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 hardwickii* collects urinary excretion in its bladder and reabsorbs water along with some amount of uric acid.

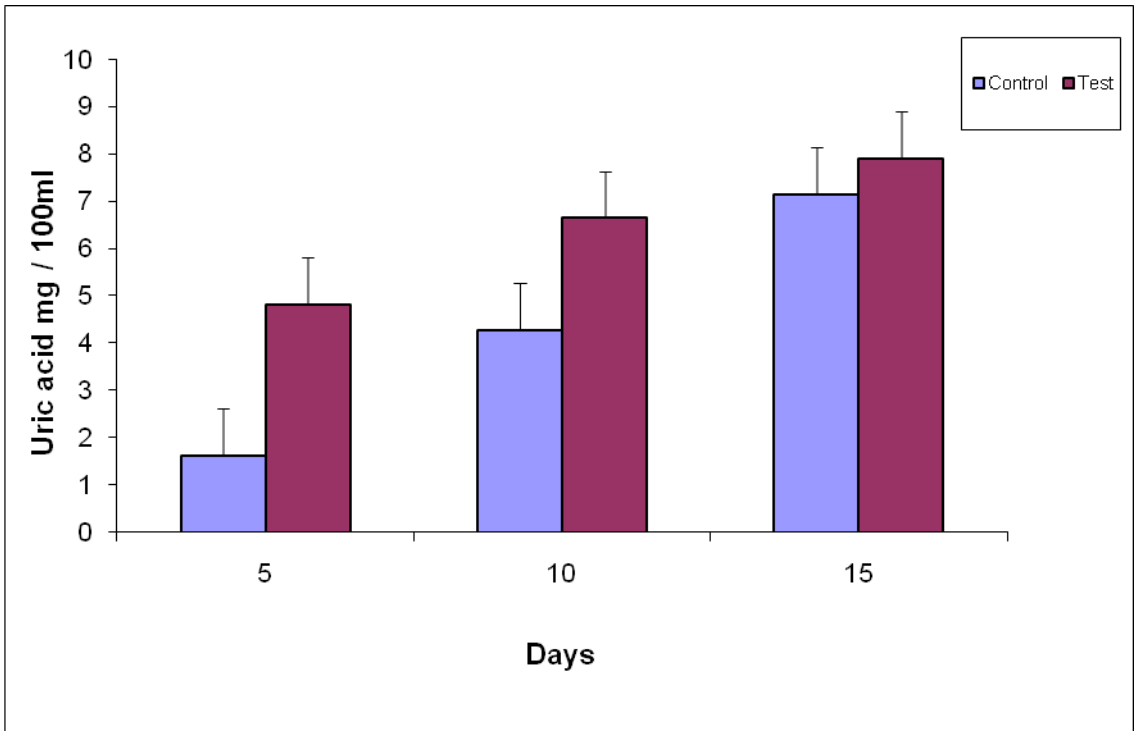

Figure 1. Blood levels of uric acid in the test and control *Uromastix hardwickii* lizards.

However, test values were higher when compared either with controls (Figure 1) or mean test values of 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 respectively.

The rise in serum uric acid levels in the isoniazid-treated lizards was 50% more than in the control group on day 5, and about 3 times more than that of control values on days 10 and 15. Whereas, uric acid retention in this study was 3, 4 and 5 times greater in the test groups 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 mechanism 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 hardwickii* 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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