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ORIGINAL ARTICLE

EXPERIMENTAL STUDY OF ANTIMONY INDUCED RENAL TOXICITY IN RABBITS

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ABSTRACT

Background and Objectives: Contamination of the environment, food and water with antimony compounds may affect human health through the persistent exposure to small doses over a long period. This study was carried out to demonstrate the dose related effects of antimony on renal tissues of rabbits.

Material and Methods: The study was carried out on 40 healthy rabbits, weighing 1.5 kg average, divided into 4 groups, each group having 10 animals with one control group. Group I animals were injected with antimony sodium tartrate of ½ MLD 6 mg/kg body weight I/V at interval of 2 days for 12 weeks. The experimental dose of 1.71 mg/kg body weight was injected I/V at interval of 4 days to group II animals. Those of group III were injected 2ml of specific bovine albumin 30% (Dade, USA) followed by schedule of group II animals. Group IV (control group) animals were injected I/V with distilled water. Animals were sacrificed and renal biopsies were taken for microscopic evaluation of any pathological changes.

Results and Conclusions: Main morphological changes were seen in proximal convoluted tubules and glomeruli (H&E, PAS). A total of 10% glomeruli showed focal hypercelluarity of mesangial and endothelial cells, increase in mesangial matrix, leading to mesangial widening and vascular congestion along with protein casts. Mild to moderate degree of nephrocalcinosis was seen. On the other hand distal convoluted tubules did not reveal any change. This study indicated the toxic effects of antimony on renal tissue of rabbits predominantly involving the glomeruli with some degree of epithelial degeneration in the proximal convoluted tubules. Hyaline casts in the renal tubules were also prominent feature. It is concluded that the antimony has toxic effects on the renal tissue, so preventive measures should be taken to avoid long term exposure in the industries and for therapeutic uses.

Key words: Antimony, Renal cortex, Glomeruli, Rabbits, Bovine Serum.

INTRODUCTION

Effects of antimony on various organs of rats have been conventionally described by many authors.[1-3] Man has always been exposed to heavy metals in the environment. Antimony is a major environmental toxin due to its presence in air, water food and soil.[4] Antimony and its compounds are used in manufacturing of paints, coatings, rubbers, insecticides, colored printing inks and glass.[5] Antimony toxicity occurs either due to occupational exposure or during therapy.[6] Antimony has been mostly used for the treatment of leishmaniasis and schistosomiasis[7]. Metallic contamination of food and water lead to first incidence of metal toxicity.[8,9] In this study, in addition to direct toxic effects of antimony, its effects were also seen in immunologically altered state of rabbits by injecting bovine albumin at interval of 04 days for 12 weeks.

MATERIALS AND METHODS

This study was carried out on 40 healthy rabbits with average weight of 1.5 kg. They were housed individually in well aerated metal cages at 26 – 28°C room temperature. Their diet consisted of seasonal vegetables and grains.

The antimony was used as Antimony sodium tartrate $NasbOC_4H_4O6$ (BDH, U.K). Its minimum lethal dose (MLD) was calculated as follows:

MLD = 12 mg/kg.

½ MLD = 6 mg/kg.

Experimental dose calculated for antimony as sodium tartrate = 1.71 mg/kg body weight. Stock solution of antimony sodium tartrate 2% solution prepared by dissolving 1 gm antimony tartrate in 50ml of distilled water. The rabbits were divided in 4 groups each group composed of 10 animals.

Group 1: Animals were given ½ MLD, 6 mg/kg of antimony sodium tartrate I/V at interval of two days for 12 weeks.

Group II: Animals were injected with experimental dose of 1.71 mg/kg body weight of antimony sodium tartrate at interval of 4 days for 12 weeks.

Group III: Animals were injected I/V with 2.0 ml of

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specific bovine albumin (30%) (DADE USA) followed by injections scheduled in group II.

Group IV (Control Group): Received only I/V injections of distilled water.

All the animals were sacrificed at the end of experiment after 12 weeks by anaesthetizing them with ether. Kidneys were dissected out by giving midline incision on anterior abdominal wall. Capsule was gently stripped off. One of the kidney was cut longitudinally whereas other transversely and tissues were preserved in 10% formalin solutions. Sections were prepared and stains used included haematoxylin and eosin (H&E), Periodic acid Schiff (PAS), Methenamine silver (MS) and reticulin stain (RS).

RESULTS

Group I: On gross examination kidneys appeared slightly smaller and rather pale with normal cortico medullary pattern.

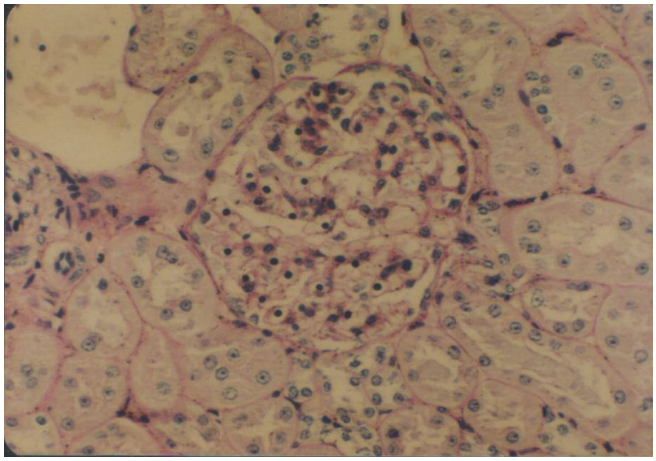

Fig. 1: *Photomicrograph showing focal mesangial hypercellularity of the glomeruli in group I animal. H & E × 340. Four animals revealed mild degree (+) of focal proliferation of endothelial cells along with focal hypercellularity of mesangial cells in 3 of them, involving most of the glomeruli There was significant increase in the amount of mesangial matrix leading to mesangial widening in 4 animals.*

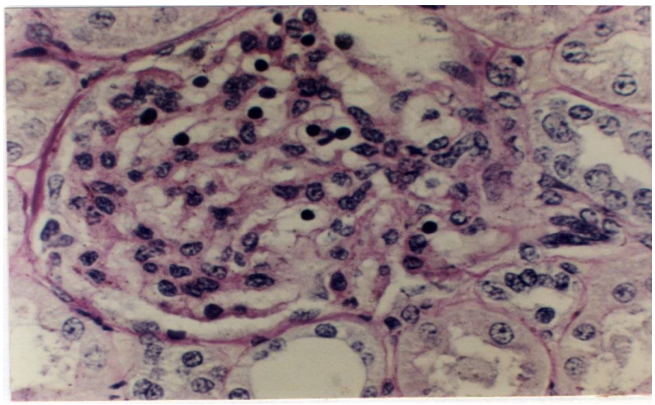

Fig. 2: *Photomicrograph showing an increase in mesangial matrix and cellularity along with mesangial widening in group I animal P.A.S. × 580.*

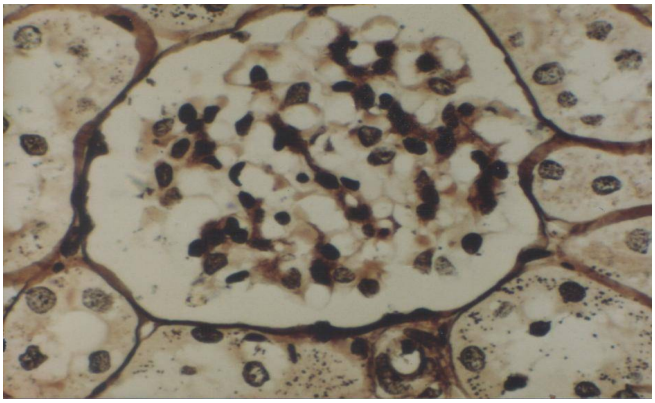

Fig. 3: *Photomicrograph showing expanded measangium containing silver positive matrix in group I animal. Methenamine Silver ×. 640.*

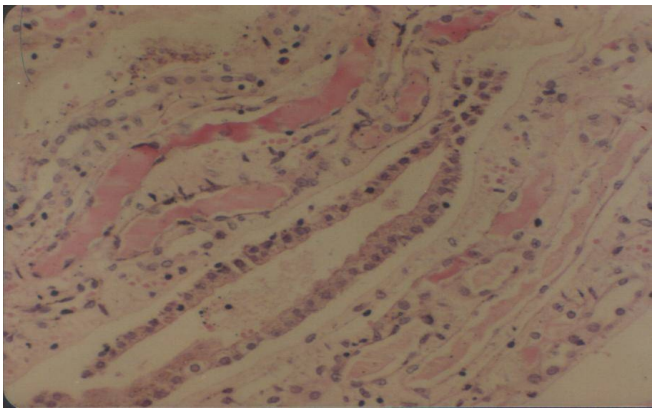

Fig. 4: *Photomicrograph of Group I animal showing protein casts in distal tubules H & E × .540.*

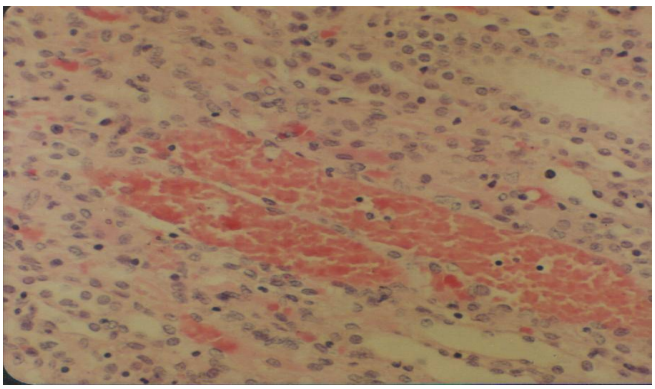

Fig. 5: *Photomicrograph showing interstitial vessels with sludging of red blood cells and early thrombus formation. H & E × 390.*

Microscopically 5 animals showed moderate degree (++) of focal hypercelluarity of the mesangial cells in 10% of glomeruli.

Basement membrane remained unremarkable on PAS & MSS.

Seven animals showed vascular congestion in glomeruli.

Proximal convoluted tubules revealed mild degree (+) of granular degenerative changes in epithelial cells along with protein casts in three animals of group I. No change in distal convoluted tubule was seen.

Five animals showed peripheral tubular focal nephrocalcinosis (mild to moderate degree). No remarkable change seen in interstitial stroma of any of the animals.

Group II, Gross: kidneys are normal in size, shape and colour with normal corticomedullary pattern.

Microscopic examination of the 5 animals showed mild to moderate focal proliferation of mesangial cells and increase in mesangial matrix.

20% of glomerular capillaries showed marked congestion (+++).

Five animal showed protein casts in proximal convoluted tubules.

Distal convoluted tubules revealed apoptosis and nephorocalcinosis.

Extra glomerular blood vessels appeared normal except in 4 animals which showed vascular congestion, sludging of RBCs with thrombus formation in small and medium sized blood vessels. No change was seen in interstitial stroma.

Group III, Gross: Kidneys appeared slightly smaller, pale with normal corticomedullary pattern. Microscopic examination showed mild focal mesangial cell proliferation. There was increase in amount of mesangial matrix in 3 animals with PAS positive material.

No significant change in epithelial or endothelial cells of glomeruli was noted. There was severe degree of glomerular congestion in two animals.

Protein filtrate seen in Bowman's space along-with sludging of RBC's in glomerular capillaries was observed.

Distal tubules showed protein casts and degenerative.

Group IV: Microscopically, no significant change was seen in renal tissue. Kidneys were normal in size and shape with normal corticomedullary pattern.

DISCUSSION

Antimony sodium tartrate is a known toxic metal present in air, water, food and soil as well as in the manufacturing of rubber, glass, paints, coatings, and coloured printing inks.[8] Antimony has now created environmental pollution, due to increase in industrial applications.[9] The nephrotoxicity of antimony has been suggested by many authors.[10] As regards to therapeutic application, potassium antimony tartrate was put into use in the treatment of schistosomiasis and Leeishmaniasis.[7,11] Most of the heavy metals are nephrotoxic particularly causing tubular necrosis.[12] It is known that even relatively low doses of a variety of metals can produce various renal abnormalities.[13]

Chronic low level antimony exposure remains our major health problem especially in industrial workers; therefore current study was designed to evaluate the effects of antimony administration on structure and function of kidneys of rabbits.

In this study, rabbits were used as a mammalian model for studying, as they are easily available and easy in handling. It is known that human and rabbits normally do not have detectable proteinuria.[14] Therefore presence of significant quantities of urinary proteins is considered pathological.[15]

Microscopic examination of renal tissue revealed significant glomerular congestion which was seen of moderate to severe degree in 50% of animals of various groups. Among group I, animals moderate degree (++) of focal hypercellularity of mesangial, endothelial and epithelial cells were seen in most of glomeruli along with significant increase in mesangial matrix leading to mesangial widening, whereas in group II and III mild degree (+) of mesangial cell proliferation was seen with no significant change in endothelial and epithelial cells of glomeruli. One animal of group III revealed a renal infarction while no such change was seen in group I and II animals.

The proximal convoluted tubules demonstrated granular degenerative changes of mild degree (+) in less than half of animals in group I, II and III along with presence of protein casts. An interesting feature was the presence of focal nephrocalcinosis in animals of group I and II. Although not much experimental work has been carried out on antimony, Maher[16] reported renal damage after antimony administration. Patients treated with antimonials in high doses reported fatty degeneration of kidneys,[17] whereas no such change was observed in the present study.

It is ***concluded*** that antimony has proven to be toxic on the structure and function of renal tissue of rabbits. Based on the results of present study, preventive measures should be taken to avoid the long term exposure in different industries and also when it is used for therapeutic purposes.

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