LEAD INDUCED EFFECTS ON RENAL ALKALINE PHOSPHATASE WITH ROLE OF ZINC IN ALBINO RATS

NAHEED KHAN, IMTIAZ WAGGAN, FARRUKH MUSTAFA AND KHALIDA PERVEEN
Dow Medical College, DUHS, Karachi, Pakistan

ABSTRACT:
Kidneys are adversely affected by a wide variety of therapeutic agents and chemicals including the environmental pollutants such as Lead. The nephrotoxic effects of lead have been widely studied. The proximal tubular cells are especially vulnerable to lead induced damage to membrane structure and function, characterized by enzymuria and inhibition of certain renal enzymes. Alkaline phosphatase activity is also known to be suppressed which has been evaluated in the present study by enzyme histochemistry. Moreover Zinc, an essential micronutrient has been used to minimize the effects of lead.

Keywords: Lead, nephrotoxicity, alkaline phosphatase, zinc, proximal tubules.

INTRODUCTION

The increasing use of therapeutic agents and chemicals for the last few decades has considerably increased the possibility of damage to the kidneys (WHO, 1991). Nephrotoxic effects of analgesics, antibiotics, anticancer agents, various household, industrial and environmental chemicals have been investigated.

Lead environmental pollution is a major concern for public health (Oliveira et al., 2009). Several sources of lead poisoning have been identified in humans. The most common are the leaded gasoline, batteries, paints, ceramics, soldering, and building materials (ATSDR, 1999), improperly glazed containers (Klaasen, 2001), gunshot wounds with retained lead pellets or particles, and a variety of folk remedies and cosmetics (Meyer et al., 2008; Woolf et al., 2007).

Besides having detrimental effect on other organ systems it is also capable of inducing nephrotoxicity (WHO, 1991) as kidneys form major route of its excretion (Noorafshan, 1998). Autopsy studies of lead exposed humans showed that among soft tissues, liver is the largest repository followed by kidney (Sharma et al., 2010).

It is suggested that the mechanism involved in lead induced toxicity is the metal-induced reactive oxygen species (Ercal et al., 2001) which are the initiators of peroxidative damage to the membranes (Adegbesan and Adenuga, 2007; Sandhir et al., 1994) and cause impaired membrane function, impaired structural integrity and inactivation of a number of membrane bound enzymes (Sidhu et al., 2004). Lead-induced impairment of proximal tubular function manifests as enzymuria (ATSDR, 1999) and inhibition in the activities of certain renal enzymes which were also observed in lead administered rats.

The effects of lead were also studied on isolated brush-border enzymes such as alkaline phosphatase, that showed a decline upon its administration (Sivaprasad et al., 2004). A study by Flora et al (1983) showed that the oral administration of lead acetate significantly enhanced the urinary excretion and a corresponding decrease in renal activities of Alkaline Phosphatase. Alkaline phosphatase helps in ionic movement across the cell membrane and is also associated with

*Correspondence to: e-mail: drnkhan@yahoo.com
Lead induced effects on renal alkaline phosphatase and absorption processes of the cell (Bansal and Roy, 1997).

Adequate supply of essential micronutrients in the diet is known to minimize the effects of lead. Amongst them zinc seems to have the maximal effects in lowering the ill effects of lead (D’Souza et al., 2003). Dose dependent effects of zinc supplementation as a chelator in lead treated rats was reported (Flora et al., 1994).

Zinc supplementation could significantly compete for and effectively reduce the availability of binding sites for lead uptake (Batra et al., 1998). Zinc is an essential mineral found in almost every cell (Office of Dietary Supplement – National Institute of Health, 2002), and plays a biochemical role by stabilizing membrane structure, thus reducing per oxidative damage to cell.

The pre-treatment with an essential metal could prevent the appearance of signs of toxic metal induced tissue injury (Afonne et al., 2002) in experimental animals. A study of zinc deficient patients receiving zinc supplementation showed increases in alkaline phosphatase activity that paralleled the degree of zinc repletion. Important zinc containing metalloenzymes in humans include alkaline phosphatase (Milne, 2001).

MATERIALS AND METHODS

The study was carried out on a total of 36 active, young adult Albino rats in the Department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi

At the onset of experimental study, the animals were divided into three groups comprising 12 rats each; on the bases of drugs they received. The drugs were injected intraperitoneally to ensure uniform absorption.

- Group-A rats served as control, received injection normal saline 1 ml intra-peritoneally daily for 6 weeks.
- Group-B rats received Injection Lead Acetate (Merck, Germany) at a dose of 8 mg/kg body weight intra-peritoneally daily for 6 weeks.
- Group-C rats received Injection Zinc Chloride (Merck, Germany) at a dose of 0.21mg/kg body weight intra-peritoneally two hours before administration of Lead Acetate at a dose of 8 mg/kg body weight intra-peritoneally daily for 6 weeks.

The animals were sacrificed under ether anesthesia at the end of experimental period. The kidneys were obtained and were fixed in 10% formalin for 24 hours, after which processing, sectioning and staining with Gomori’s Calcium phosphatase methods were done. The method was applied for the histochemical study of enzyme Alkaline Phosphatase.

OBSERVATIONS AND RESULTS

The present study was designed to observe the lead induced nephrotoxicity with role of zinc in albino rats. The histochemical observations of renal Alkaline phosphatase were based on the study of sections, stained with Gomori’s Calcium Phosphate method.

The Gomori’s Calcium Phosphate stained sections of group A rats showed the sites of enzyme activity of alkaline phosphatase in the renal proximal tubules in the form of brownish black deposits. The deposits were seen regularly and evenly arranged within the tubules (Fig. 1).

The Gomori’s Calcium Phosphate stained sections of group B rats for alkaline phosphatase showed decreased enzyme activity in tubules. The brownish black deposits were decreased as few clumps, irregularly distributed in renal tubules (Fig. 2).

The Gomori’s Calcium Phosphate stained sections of group C rats for alkaline phosphatase showed an increase activity of enzyme in the tubules, which is comparable to
control. The blackish brown deposits were seen in the tubules quite regularly arranged (Fig. 3).

**DISCUSSION**

It was thought worthwhile to carry out a study using experimental induction of nephrotoxicity in albino rats by administration of lead. Moreover attempts have been made to study the protective effects of zinc on lead induced nephrotoxicity.

The histochemical study was done to observe the effects of lead on activity of enzyme alkaline phosphatase. The study of Gomori’s Calcium Phosphatase stained
sections of group-B showed a decreased amount of brownish black deposits in the proximal tubules and hence a decrease activity of enzyme alkaline phosphatase as compared to corresponding controls. This could be correlated with the study of Flora et al. (1983) according to which the oral administration of lead acetate enhanced the urinary excretion and decrease the renal activities of alkaline phosphatase. It is also in agreement with the study of Wapnir et al. (1979) who observed that administration of lead acetate intraperitoneally for six weeks to rats decreased the alkaline phosphatase activity in kidney homogenates. A marked inhibition of alkaline phosphatase in kidneys is also observed in other species such as Heteropneustes fossilis (Sastry and Agrawal, 1979).

These histochemical findings led us to conclude that such changes in the activity of phosphatases could be an adaptation to the metabolic, structural, and functional alterations in the organelles of the renal cells due to lead intoxication (Sivaprasad et al., 2004).

The study of Gomori’s Calcium Phosphate stained sections in group-C revealed a greater number of deposits as compared to group-B, thus showing an increase in alkaline phosphatase activity. This could be attributed to the fact that alkaline phosphatase is a zinc-dependent enzyme and zinc supplementation showed an increase in alkaline phosphatase activity (Milne, 2001).

CONCLUSION

It is concluded from this study that higher lead levels reduces the activities of renal alkaline phosphatase in experimental rats, and a pretreatment with zinc improves activity of renal alkaline phosphatase.

REFERENCES


