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Lipid peroxidation and some oxidative stress enzymes in aluminium acetate intoxicated albino mice

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Abstract

The purpose of this study was to investigate the effect of intraperitoneally administered aluminium acetate on lipid peroxidation and some oxidative stress enzymes in different tissues like brain, liver, kidney, heart, muscle and testis of albino mice. Exposure to sublethal dose (3.5 mg/kg body weight) of aluminium acetate has revealed significant variations in the present study. Under experimental conditions, the levels of XOD increased and it is more in double and multiple dose animals. Significant change was observed in double and multiple dose administered mice. Where as in double dose aluminium acetate administered mice, the consistent elevation has been recorded. Significant increase was observed in multiple dose aluminium acetate administered mice. Such dose dependent elevation has been recorded under aluminium acetate in the present investigation.

Keywords: Different tissues of albino mice, aluminium acetate, detoxification enzymes, lipid peroxidation.

Introduction

Aluminium (Al) is an important element with known toxicity in the human body, mainly in the central nervous system (Amal A Fyiad, 2007). The toxic consequences in human after aluminium exposure are well established (Nayak, 2002). Trace elements enter the body either by direct absorption via the air or drinking water or via by the food chain. Loss of appetite and subnormal growth are common manifestations of most trace element deficiencies and excesses. The general mechanism of metal action is by influencing the enzymes present in the body. Metals that enter the body get distributed to all parts of the body and causes toxicity. Exposure of cells to oxygen radicals may cause lipid peroxidation in cell membranes which in turn may generate species that damage cell proteins and promote their degradation (Kelvin & Goldberg, 1987). The animals protect themselves against toxicity by adopting various detoxification and defense mechanisms. The mechanism responsible for oxygen toxicity include the generation of super oxide anion (O^2-), hydroxyl ion (OH^-), hydrogen peroxide (H_2O_2) and lipid peroxidation. Xanthine oxidase pathway is the important one of free radical production. Mammalian cells possess both non-enzymatic and enzymatic antioxidant defense to cope up with oxygen free radicals. The enzymatic parameters include superoxide dismutase, catalase etc. Organisms under oxidative stress are capable of inducing antioxidant enzymes (Venkataiah, 1995). When the production of reactive oxygen species exceeds the ability of the antioxidant system, it results in oxidative stress. Lipid peroxidation is associated with cellular injury and is commonly used as an indicator of oxidative damage in cells and tissues. During lipid peroxidation polyunsaturated fatty acids in membrane are degraded to a variety of aldehydes of which the amount of malondialdehyde is most frequently used as a measure for the extent of lipid peroxidation in biological samples (Comporti, 1985). Aluminium salts administered by different routes can produce toxic effects in animal models (Liu *et al.,* 1996) some of which involve alterations in enzymatic activities (Zatta *et al.,* 1995). Aluminium acetate is harmful by inhalation, in contact with skin and if swallowed it causes possible risk of irreversible effects. In the present study aluminium acetate induced alterations

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in LPO and oxidative stress enzymes have been studied in different tissues of mice.

Materials and Methods

Healthy adult albino mice of same age group 60 ± 2 days and weight (25 ± 5g) were taken from veterinary college, Bangalore, India and maintained at laboratory conditions (26 ± 2°c, 12 h light and 12 h darkness). Toxicity of aluminium acetate was evaluated as per Finney (1964) and the LD_{50} was found to be 35 mg/kg body weight (John Sushma and Jayantha Rao, 2005). Ten-fold lower concentration of LD_{50} (3.5 mg/kg body weight) was selected as sublethal dose and it was given intraperitoneally. Adult animals were divided into four groups, the first group of animals were considered as controls. To the animals of second group single dose (1st day) of aluminium acetate was given. To third and fourth group of animals double (1st and 3rd days) and multiple doses (1st, 3rd, 5th and 7th days) were given. After stipulated time control and experimental animals were dissected and the tissues like brain, liver, kidney, heart, muscle and testis were isolated for biochemical analysis. Xanthine oxidase activity was estimated by the dye reduction method of Srikanthan and Krishnamurthy (1955). Superoxide dismutase activity was measured as the inhibition of photoreduction of nitroblue tetrazolium (NBT) by the enzyme as per the method of Beachamp and Fridovich (1971). Catalase activity was measured following the method of Chance and Machly (1955). The lipid peroxides were determined by the TBA method of Hiroshi *et al*. (1979).

Results

In the present investigation, profound changes were observed in all the enzymes related to detoxification mechanism (Fig. 1 to 4). Under experimental conditions, the levels of XOD increased (Fig.1) and it is more in double and multiple dose animals. In the case of single dose of aluminium acetate administered mice non-significant change in SOD (Fig.2) was recorded. However, in both double and multiple doses the experimental mice tissues have recorded significant change in superoxide dismutase activity.

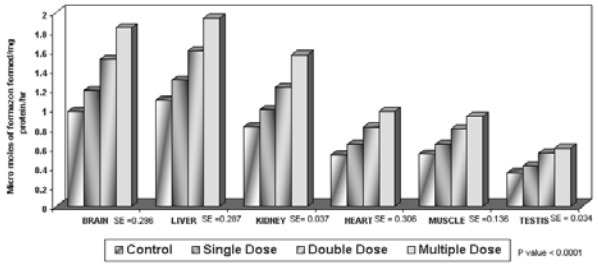


Fig.1: Changes in xanthine oxidase activity in different tissues or albino mice exposed to aluminium acetate

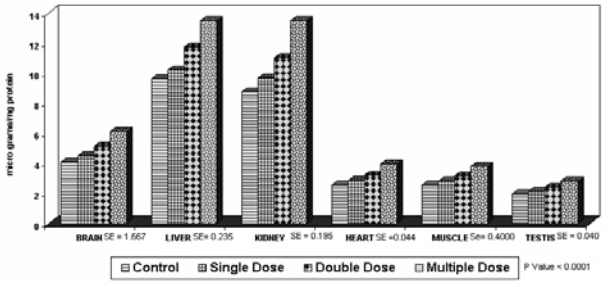


Fig.2: Changes in superoside dismutase activity in different tissues of albino mice exposed to aluminium acetate.

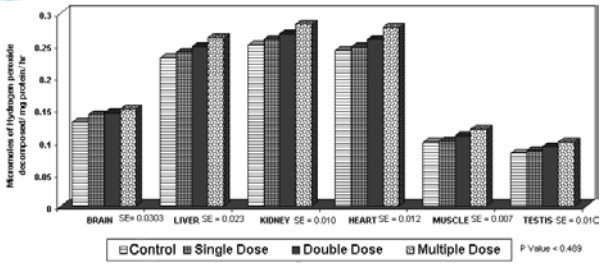


Fig.3: Changes in catalase activity in different tissues of albino mice exposed to aluminium acetate.

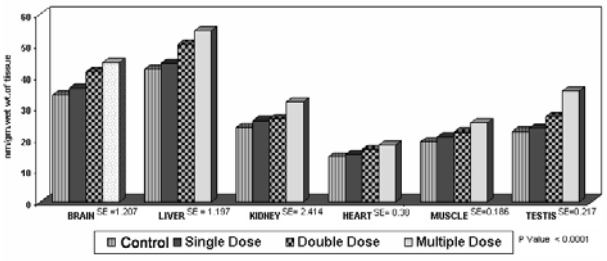


Fig.4: Changes in malondialdehyde content in different tissues of albino mice exposed to aluminium acetate.

This change in superoxide dismutase activity is maximum in multiple dose animals when compared to single and double doses. The catalase activity both in control and experimental tissues was recorded. In case of single dose aluminium acetate administered mice, only brain and kidney tissues

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have shown significant increase but the rest of the tissues have recorded non-significant increase in catalase activity. In both double and multiple doses aluminium administered mice, the consistent elevation has been recorded (Fig-3). The malondialdehyde formation or lipid peroxidation was enhanced as a function of aluminium acetate administration in experimental mice tissues. The tissues of double and multiple doses aluminium acetate administered mice tissues have recorded significantly increased levels of malondialdehyde (MDA) in the tissues which is an index of rate of lipid peroxidation (Fig-4). Dose dependent elevation has been recorded under aluminium intoxication in the present investigation.

Discussion

Under aluminium acetate stress increased xanthine oxidase activity might be due to conversion of xanthine dehydrogenase to xanthine oxidase. For the nitrogen balance of the tissue, xanthine oxidase is produced when the native form of xanthine dehydrogenase is altered either by sulphydryl oxidation or by limited proteolysis (Dellacorte & Stripe, 1972). The elevated levels of xanthine oxidase leads to the formation of superoxide anion (O^{2-}) in the tissues of mice in response to aluminium acetate treatment. The increased activity of SOD may be to detoxify the superoxide anion radicals produced from XOD reaction in order to arrest the radical damage to cellular organization. Enhancement of XO may lead to the accumulation of intermediate toxic compounds such as hydrogen peroxide and hydroxyl radicals, since SOD activity is increased as well (Moumen *et al.*, 2001). A significant increase in lipid peroxidation and decrease in the activities of antioxidant enzymes, SOD and catalase was observed (Dua *et al.,* 2001) in cerebrum, cerebellum and brain stem of rat exposed to aluminium phosphide. Aluminium influences the activity of superoxide dismutase which plays a major part in the destruction of oxygen free radicals in the body and the other oxidative enzymes, peroxidase and catalase (Serra *et al.,* 1991). Increased catalase activity might be due to its active involvement in decomposition of hydrogen peroxide (H_2O_2) generated during dismutation of superoxide anion radicals by SOD. This is in consonance with the reports of (Pritosos *et al.,* 1985, 1986). For dismutation of superoxide anion to hydrogen peroxide and oxygen , SOD is necessary, where as the activity of the enzyme catalase decomposes hydrogen peroxide to water and oxygen. The elevated levels of SOD, under aluminium acetate toxicity might result in increased formation of hydrogen peroxide. Hence in aluminium acetate treated mice, the role of catalase in the decomposition of the hydrogen peroxide has been studied. Lipid peroxidation in the biological system is known to produce cellular damage in brain (Slater, 1979). The concentration of lipid peroxidation products increased in the aluminium lactate exposed brain of rat (Yuki Ogasawara *et al.,* 2003). The elevated levels of xanthine oxidase might result in generation of free radicals of oxygen and there by increased lipid peroxidation. The in vivo effects of aluminium on lipid peroxidation were studied in mouse brain homogenates and purified brain sub cellular fractions (Patricia *et al.,* 1993). Aluminium induced a significant increase in lipid peroxidation in hippocampus and frontal cortex (Nedzvetsky, 2006). Oxidative damage to brain cell components may be an important mechanism mediating the neurotoxicity of aluminium. Aluminium exposure promotes oxidative stress in different neural areas and acts as a pro-oxidant (Esparza *et al.,* 2003). The dietary Al-intoxication can increase brain lipid peroxidation rates in mice. The increase in lipid peroxidation rates in brain membranes contribute to the etiology of aluminium neurotoxicity. Lipid peroxidation was influenced by aluminium ingestion (Sugawara and Sugawara, 1992). Aluminium acetate induced alterations were observed in different regions of brain of albino mice by selecting specific enzymes like SOD, Catalase, XOD and Lipid peroxidation (John Sushma *et al.,* 2006). Thus these parameters have shown dose dependent elevation in different tissues of albino mice.

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