EFFECT OF LEAD ON MALE REPRODUCTION IN EXPERIMENTAL ANIMAL MODEL

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ABSTRACT

Introduction: In early 1960’s, there is a first evidence of the toxic effects ionizing radiation on elevated oxygen levels in aerobes and proposed that oxygen toxicity is due to free radical formation. An alteration between oxidants and antioxidants in favour of the oxidants, potentially leading to damage is termed “oxidative stress”. Lead and cadmium do not have any detectable beneficial biological roles rather it produces detrimental effects on biochemical, physiological and behavioral dysfunctions. Even a little lead poisoning can cause serious health problems, and at very high levels, it can be fatal. Mainly it affects the heamopoeitic system, Liver, Kidney, Cardiovascular system and reproductive system. Methodology: Experimental rats, injected intraperitoneally with lead acetate for 15 days at the dosage of 50, 100 mg/kg/day body weight and compared to control rats injected with deionized distilled water instead. At the end of study tests were removed and right tests was used for testicular antioxidant Malandeadaldehyde (MDA) levels estimation by Thiobarbituric acid reactive substance assay and left tests was used for histopathological analysis. Unpaired t test and ANOVA was used for statistical analysis. Results: The MDA (nmole/gm tissue) levels in control, lead 50mg, lead 100mg groups were 12.16±0.4, 17.06±0.16 and 18.11±0.13. Histopathology examination Lumen showing decreased sperm count and maturation. Some of the lumens showing absence sperm maturation. Conclusion: Study on lead-exposed rat testis have shown that reduction of spermatogenesis formation and sperm maturation. Increased MDA levels indicate that it may be due to oxidative stress. The toxicity of lead was noted at level ≥50mg/kg.

Keywords: Lead, Lipid peroxidaon, Male reproduction, Testicular histology

INTRODUCTION

Infertility is defined as one year of unprotected intercourse without pregnancy [1-3]. It affects approximately 15% -30% of all couples trying to conceive [1, 4, 5]. Of all the cases of human infertility 20% are due to male factor [6]. Several studies have examined the relationship between stress and sexual behavior in male rats. Increasing evidence suggests that the cumulative damage caused by reactive oxygen species contribute to numerous diseases [7].

In the late 1950’s, free radicals and antioxidants were almost unheard of in the clinical and biological sciences but chemists had known about them for years in the context of radiation, polymer and combustion technology. In early 1960’s, there is a first evidence of the toxic effects ionizing radiation on elevated oxygen levels in aerobes and proposed that oxygen toxicity is due to free radical formation [8]. Various forms of physical, psychological, environmental and heavy metals are believed to produce free radicals. Recently, oxidative stress has become the focus of interest as a potential cause of male infertility. Many industrial chemicals are known to have a negative impact on human reproduction, particularly exposures to heavy metals such as aluminum, Cd2+, Fe2+, Chromium (Cr3+), Ni2+ and Pb2+ [9]. Several studies have examined the relationship between stress and sexual behavior in male rats. Increasing evidence suggests that the cumulative damage caused by reactive oxygen species contribute to numerous diseases [7].

Normally, equilibrium exists between reactive oxygen species (ROS) production and antioxidant scavenging activities in the male reproductive organs [10]. Testicular membranes are rich in polyunsaturated fatty acids and thus susceptible to peroxidation injury, it leads to decrease sperm production and maturation [11]. Lead and cadmium do not have any detectable beneficial biological roles rather it produces detrimental effects on biochemical, physiological and behavioral dysfunctions. Even a little lead poisoning can cause serious health problems, and at very high levels, it can
be fatal [12]. Mainly it affects the haemopoietic system, Liver, Kidney, Cardiovascular system and reproductive system.

To better understand the disease progression experimental animal models are required [13]. Rats were enable us to obtain answers in a short period of time, since 10 days in the life of a rat are approximately equivalent to 1year of human life [14, 15].

The threshold level has been difficult to establish due to the selection of the exposure indicator and the reproductive endpoints. So in the present study was undertaken to study the effect of lead in testicular tissue antioxidant status and histological changes.

MATERIALS AND METHODS

Study design: An experimental animal based study

Ethics approval: The study was approved by the institutional animal ethics committee

Animal: Adult male albino rats weighing 220 – 250 g and aged 10-12 weeks old were obtained from authorized animal breeding centre. The animals were kept in wire bottomed cages in a room under standard conditioan of illumination with a 12 - h light-dark cycle at 25 ± 1° C. They were provided with tap water and balanced diet ad libitum. The study was approved by the IAEC authorities and it followed the CPCSEA rules on animal protection.

Sample size: In each group n=6

Drug preparation: Lead was obtained from the authentic distributor. Drugs were dissolved in isotonic saline solution and injected intra peritoneally

Grouping: Rats were randomly divided into 3 groups

Group 1: Control received normal saline

Group 2: Received lead 50mg/kg

Group 3: Received lead 100mg/kg

Methodology: Experimental rats (Group 2,3) injected intraperitoneally with lead acetate for 15 days at the dosage of 50, 100 mg/kg/day body weight and compared to control rats injected with normal saline.

Animal sacrifice, collection and preparation of samples: At the end of the study each animal was sacrificed by cervical dislocation.

Tissue preparation: The testicular tissue was transferred into 10% w/v of Phosphate buffer (pH 7.4). The tissue was homogenized using a manual homogenizer. The broken cells debris were removed by centrifugation 3,000rpm for 10min. The obtained supernatant were divided into aliquots and stored in -80°C. The level of Lipid peroxidation (MDA) was measured by Thiobarbituric acid reactive substance assay (TBARS) by Burge Aust [16].

Histopathological examination: Tissue specimens from testes of all experimental rats were collected at the end of the study and fixed in neutral buffered formalin, processed by conventional method, embedded in paraffin, sectioned at 4-Sum and stained by Haematoxylin and Eosin [17].

Statistical analysis: To analysis unpaired t test and ANOVA was applied.

RESULTS

<table>
<thead>
<tr>
<th>Group</th>
<th>Testicular MDA levels (nmole/gm tissue)</th>
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<tbody>
<tr>
<td>Control</td>
<td>12.2±0.41</td>
</tr>
<tr>
<td>Lead 50mg/kg/day</td>
<td>17.01±0.15***</td>
</tr>
<tr>
<td>Lead 100mg/kg/day</td>
<td>18.09±0.1*** $</td>
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</table>

*Comparison with normal group, $ comparison with low doses vs High dose lead

DISCUSSION

In the present study MDA levels were increased. This probably reflects the increased in lipid oxidation due to either increased production of free radicals or decreased antioxidant defense mechanism or both.

Histopathological results: Microscopically testes of stress group marked necrosis of spermatogonial cells seminiferous tubules associated with incomplete spermatogenesis and Azoo Spermia. Degeneration of germ cells lining seminiferous tubules.

There are a number of mechanisms by which exposure to lead may reduce male fertility [18]. The lead con-
centration in the tissue could affect hormone receptor kinetics, enzyme activities and hormone secretion. Although environmental exposure to lead may impair spermatogenesis, as shown in several animal studies [19].

Direct toxic effects on sperm and gonads have been observed in animal tests. Lead and other cations (mercury, copper) may cause a partial replacement of zinc which is essential for sperm head chromatina stabilization it may lead to decreased fertility or DNA damage in the fertilization process [20].

Male rats exposed with lead PbB 15–23 µg/dl have been observed in genomic expression in 2-cell embryos fathered by male rats. Interestingly, fertility was reduced only at a higher PbB level (27–60 µg/dl). It suggest an effect on the regulation of gene transcription or translation rather than direct genetic damage to the male germ cell [21].

CONCLUSION

Study on lead-exposed rat testis have shown that reduction of spermatogenesis formation and sperm maturation. Increased MDA levels indicate that it may be due to oxidative stress. The toxicity of lead was noted at level ≤50mg/kg.

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REFERENCES


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