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Effect of Aluminum-Containing Antacid on Sperm Parameters And testicular Structure in Male Rats

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Abstract: Aluminum compounds are used in many pharmaceuticals. Antacid as aluminum hydroxide [Al $(OH)_3$] was tested for its effects on the sperm parameters and testis of rats at dosage of 18 mg/kg/day. Mature male rats were treated orally for 30 days. The sperm parameters in epididymis were counted and testes were examined. Results obtained showed that $Al(OH)_3$ caused significant ($P < 0.05$) decrease in sperm concentration, sperm motility percent and sperm viability percent compared to the control group, while abnormal sperm morphology percent were increased. In addition, the exposure of rats to $Al(OH)_3$ caused obvious histopathological changes in the testes. It can be concluded that high antacid intake for long period can be effective on reproductive system.

Keywords: Antacid, $Al(OH)_3$, Sperm parameters, Epididymis, Testis, Rat.

Introduction

Aluminum (Al), as metal, is used extensively and various salts of aluminum are widely used in foods, fluids, add medications[1]. Aluminum salts, particularly $Al(OH)_3$, are commonly used as antacid drugs. $Al(OH)_3$ is also used as a buffer with aspirin to reduce the gastric irritation caused by this analgesic compound. Oral aluminum and carbonate are used extensively in the therapeutic management of the hyperphosphatemia in patients with chronic renal failure[2].

The absorption of aluminum from small intestine following the oral intake constitutes the main route of entry for this metal into the blood stream. On the other hand, increases in serum and tissue aluminum concentrations have been recognized as complications in patients with chronic renal failure on long-term treatment with dialysis[3]. Thus, apparently at some level of exposure between 125 and 1000 mg/day, the body may absorb aluminum faster than it can excrete it and aluminum may begin to accumulate[4]. Aluminum concentrations have been measured in various tissues, especially in the blood, skeleton, liver, and testes [5, 6, 7, 8, 9, 10]. The toxic effects of different metals depend on dose, duration, and route of administration in male human and various animal species[11].

Adverse effects of aluminum compounds administration on the male reproductive system in mammals have been reported in numerous studies[12, 13, 14, 15, 16, 17]. Moreover, the toxic effects of aluminum exposure on male reproductive system and probable mechanisms of toxicity have been summarized by Pandey and Jain [18]. However, there is limited information on Al $(OH)_3$ toxicity following oral exposure. For this reason, the aim of this work was to study the effects of Al $(OH)_3$, that used as antacid, on the sperm parameters and testicular tissue in albino male rats.

Materials and Methods

Experimental animals

White albino male rats (Sprague-Dawley rats), weighing 200-250 g were supplied by the animal house at the Faculty of Science/University of Kufa. The rats were housed in standard plastic cages in an environmentally controlled room before and during the experiment. Housing was under constant temperature (22-25 C). The animals were maintained on an *ad libitum* diet of commercial chow and tap water. The rats were acclimated to laboratory conditions for 14 days before the initiation of the study.

Experimental procedure

Two groups of 20 rats were used for the experiment. Males were randomly divided into groups, each composed of 10 mice. Al $(OH)_3$ was provided by the Merck Company (Darmstadt, FRG). Animals in treated group were given by gavage a daily dose of 18 mg/kg/day (equal to 1 gm/day for human) of Al $(OH)_3$ (which is a main constituent of antacid (dissolved in distilled water for 30 days, while control group received a daily dose of 1 ml normal saline.

At the end of experiment, epididymis and testis were removed from the body. Spermatozoa were obtained from the tail of epididymis to be used for semen analysis. Sperm function test was estimated which include: sperm concentration, sperm motility percent, sperm viability percent, and abnormal sperm morphology percent. Sperm parameters were assessed according to WHO laboratory manual [19]. Histological examination was done by fixing the testes in Bouin's fluid overnight, and processed for routine paraffin embedding. The testes were cut into 5-µm sections and stained with hematoxylin-eosin stain [20]. Sections of the testes were examined by light microscopy.

Statistical analysis

Data were analyzed using one-way analysis of variance (ANOVA-test). Data are presented as means ± SE. Least significant difference (LSD) test was used to compare the significant differences between means. The SPSS (Statistical Packages for the Social Sciences) program (V.14) was used.

Results and Discussion

In this investigation, treatment of male rats with $Al(OH)_3$ significantly ($P < 0.05$) decreased sperm concentration, motility (%), and viability (%) while increased abnormal sperm (%) as compared to control groups (Table 1).

Table 1: Effect of oral administration of antacid [$Al(OH)_3$] for 30 days on cauda epididymal sperm analysis.

	Sperm count (million/mm^3)	Sperm motility (%)	Sperm viability (%)	Abnormal sperm (%)
Control	88.33 ± 1.52	82.17 ±2.67	90.75 ±2.65	11.50 ±0.33
$Al(OH)_3$	43.00* ±0.34	*55.22 ±0.88	*60.20 ±3.93	20.00 * ±1.20

- Data are expressed as mean ± standard error.
* Significant difference at ($P<0.05$).

On the other hand, observation of treated testes with antacid revealed several alterations of testicular tissue whereas the microscopic examination of the control group revealed normal histologic criteria (Figures1-4).

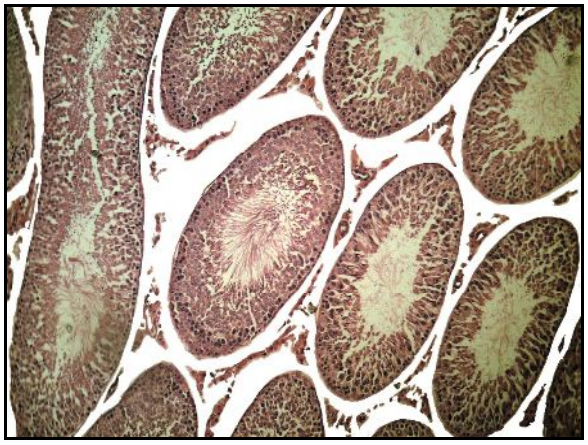

Figure 1: Normal histological section of testis from control group.

(H.&E.,100 X)

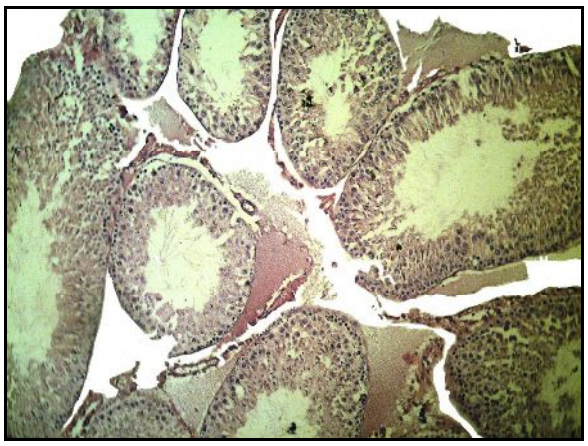

Figure 2: Histological section of testis from antacid [$Al(OH)_3$] treated group showing few sperms in the lumen of seminiferous tubules increased amount of interstitial tissue.

(H.&E., 100 X).

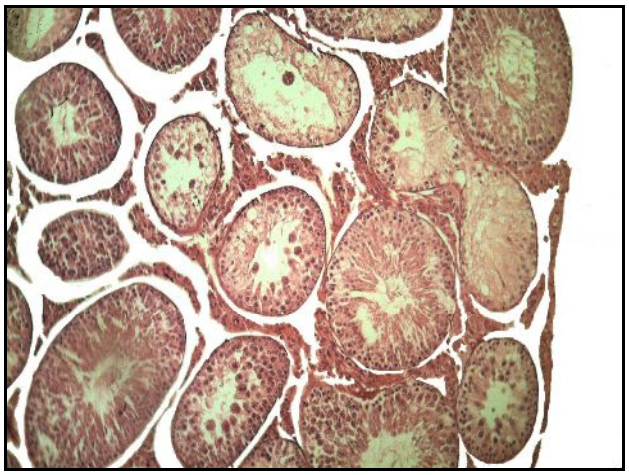

Figure 3: Histological section of testis from antacid [$Al(OH)_3$] treated group showing severe damage within the seminiferous tubules. (H.&E.,100 X).

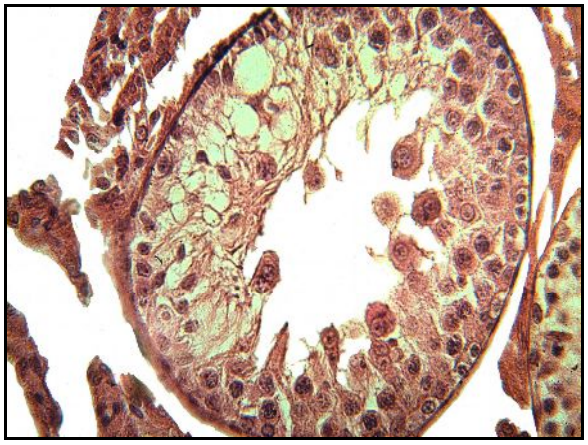

Figure 4: Histological section of testis from antacid [$Al(OH)_3$] treated group showing clear degeneration in germ cells lining seminiferous tubule with formation of giant cells.

(H.&E., 400 X)

Histological alterations represented by irregularity of germ cell layers, marked distorted seminiferous tubules with degeneration of spermatogenic cells and necrotic debris in the tubules, appearance of multinucleated giant cells, congestion of interstitial blood vessel, interstitial edema, abnormal distribution of spermatozoa in the lumina.

Aluminum compounds have many medical implications as, antacids, phosphate binders, buffered aspirins, vaccines, antiperspirants and allergen injection [21]. In healthy subjects, absorption of aluminum by gastrointestinal tract following oral doses of aluminum-containing salts is associated with a rise in serum concentration that is followed by a rapid increase in urine excretion [22]. Aluminum ingestion in excessive amount leads to accumulation in target organs and has been associated with damage of testicular tissues of both humans and animals.

Johri *et al*. [15] noted that the oral administration of aluminum hydroxide to male rabbits at the dose level of 5.0 mg/rabbit/day for 60 days caused body weight loss and decreased the weight of testis, epididymis, seminal vesicle and prostrate in a significant manner. Also, they suggested that the chronic use of aluminum hydroxide caused anti-fertility implication in male rabbit. Besides, the present findings for microscopic examination of treated rats revealed the occurrence of some giant cells in the lumen of seminal tubules. Chinoy *et al*. [23] suggested that giant cells could be the result of faulty or failed chromosomal replication or cell division. Overall, the increased oxidative stress, alteration in spermatogenesis as well as in steroidogenesis, alterations in membrane function, disruption in cell signaling and the impairment of blood testis barrier, affect on the endocrine system might be the various possible mechanisms of aluminum induced male reproductive toxicity [18].

In conclusion, long-term intensive antacid administration in our experimental model caused adverse effects on certain reproductive parameters like sperm count motility, viability and morphology ,and histology of testis . It is likely that intensive therapy with antacids may have a similar effect in man. Therefore, it would seem advisable to avoid the consumption of high doses of aluminum-containing compounds. Although the knowledge of aluminum toxicity has markedly improved in recent years, few studies were carried out concerning the antacid [$Al(OH)_3$] toxicity following oral exposure. Consequently, further investigations are necessary to evaluate toxicity of antacid on reproductive performance of male mammals.

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