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Effects of Sodium Fluoride on Liver and Kidney in Rabbits

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Abstract

Sodium fluoride (NaF) in the form of mouthwashes, toothpaste, fluoridated water, and tablets was used for the protection from caries

Aims: to study effects of sodium fluoride on liver and kidney in rabbits. Materials and Methods: Twelve healthy male rabbits were involved. Control group: six rabbits were kept on a standard diet and water with no any treatment. Treatment group: another six rabbits were treated by NaF at the dose of 20 mg/kg/day dissolved in 400 ml of distill water. At the end of 30 days of treatment, five ml of blood samples were taken from each animal . Serum analysis was done by colorimetric Assay kit for total antioxidant capacity(TAC), Malondialdehyde (MDA), alkaline phosphatase (ALP), Aminotransferases (AST and ALT), Creatinine and urea. Results: there were significant differences between the control and treatment groups. Significant reduction in TAC with a significant increase in MDA, ALP, AST, ALT, creatinine, and urea in the treatment group compared to the control group. Conclusion: (NaF) at the dose of 20 mg/kg/day for 30 days can result in a significant change in serum biochemical markers of liver and kidney in rabbits.

Keywords: Sodium fluoride; liver; kidney; total antioxidant capacity TAC; malondialdehyde MDA; alkaline phosphatase ALP; urea; creatinine.

1. Introduction

The extensive fluoridation of drinking water and the widespread use of fluoride in oral health products such as toothpaste, this assessment would be highly significant if valid. To get a better understanding of these claims, researchers looked at human exposure levels as well as animal experiment findings, with a specific emphasis on developmental toxicity and the molecular pathways by which fluoride can cause damage[1] Fluoride causes an increase in oxidative stress and a decrease in antioxidant function. The classification of fluoride as a pollutant rather than a helpful ingredient or drug is a good place to start looking at fluoride's negative effects. Fluoride deficiency has already been recognized as a medical condition. [2, 3] It also plays no significant effects in the growth and development of the human body [4].

exposure to high levels of fluoride is toxic and deleterious to human health, leading to a condition called fluorosis [5]. It results in teeth mottling and crippling skeletal deformities with damage to liver, lung, kidney, blood, nerves, brain and gastrointestinal system [6] [7]. High levels of serum fluoride damage the kidney[8] while long term drinking of fluoridated water can be a risk factor in development of type 2 diabetes [9] Fluoride also appears to be mutagenic, genotoxic and causes chromosomal abnormalities [10].

Consequently, it act against the most essential metabolic pathways of the living tissues [11, 12 13,14,15]. The precise mechanisms by which fluoride exerts its effects are unclear [16,17].

Fluoride also can cause induction of malondialdehyde formation at therapeutic concentrations, but higher concentrations of NaF were not, so greater malondialdehyde levels were obtained with less fluoride. Shivarajashankara et al. (2001) showed that rats who drink 100 ppm fluoride (as NaF) with water for 4 months have decreased activity of erythrocyte superoxide dismutase but increased levels of malondialdehyde in erythrocytes, brain, and liver [18]. So fluoride action on oxidative stress could clarify its harmful effect on the tissues. From another point of view, Na+, K(+)-ATPase which is available in major salivary glands of animals [19], exerts a major role in usual developmental and functional processes and it is damage is involved in higher risk of metabolic, pulmonary, cancer, and

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cardiovascular diseases. Excessive fluoride exposure is considered a problem in many countries due to unwarranted fluoride consumption, affecting about 200 million people around the world [20]. While full epidemiological and clinical information about the dental consequences of fluoride ingestion has previously been provided, there is still work to be done on the site of action and non-dental effects of fluorides, including histopathological effects. More research is needed to investigate these connections. The clinician is in charge of reducing the risk of fluoride toxicity. The causes of fluoride's toxic effects are poorly understood [21].

This study aims to investigate the serum biochemical changes including total antioxidant capacity(TAC), Malondialdehyde (MDA), alkaline phosphatase (ALP), Aminotransferases (AST and ALT)), Creatinine, and urea.

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2- Experimental

This research was approved by the scientific committee/department of Dental Basic Science /College of Dentistry /University of Mosul under the UoM. Dent/A.L.37/21 license.

This research involved twelve mature healthy male local rabbits "10-12" months old with a bodyweight of "1.0-1.5" kg. Animals were kept indefinitely indoors "the animal house" of the University of Mosul's College of Dentistry. They were housed in groups and subjected to a photoperiod interval of light from 6:00 to 18:00 h and dark from 18:00 to 6:00 h. The animals were served a standardized diet of tap water twice a day. Before they were slaughtered, they were subjected to regular veterinary examinations by a veterinarian. The animals were sacrificed after one month of care, and 5 ml of venous blood were obtained from each rabbit during sacrifice, kept for 30 minutes at room temperature, and then centrifuged for 10 minutes at 3000 rpm. Separated serum samples were collected and processed at -20 ˚C till the time of analysis.

All animals were split into two classes at random: Control group "6 animals": The rabbits were fed a normal diet and given no treatment. Treatment group "6 animals": The rabbits were given 20 mg/kg/day sodium fluoride (NaF) dissolved in 400 ml purified water, then all animals were sacrificed on the 31st day.

Biochemical Analysis

After 30 days of the study, all animals were sacrificed. Serum biochemical markers were measured by colorimetric Assay kit for both T-AC (Elabscience, Cat.No.E-BC-K136-S, TBA method) and MDA(Elabscience, Cat.No.EBC-K025-S, TBA method)., alkaline phosphatase (ALP), Aminotransferases (AST and ALT) Creatinine and urea (BIOLABO SAS,Kinetic method .

3- Result and Discussion

Independent test showed highly significant difference between control and treatment groups for all serum biochemical marker. Table (1).

Table (1): Independent Samples t-test comparison for all serum biochemical markers between the Control & Treatment groups.

Serum markers	Animals No.	Mean ± SD		Independent Samples t-test	P value
		Treatment	Control		
TAC	6	4.461 ± 1.095	6.226 ± 1.659	2.173	0.05*
MDA	6	5.267 ± 1.083	1.773 ± 0.457	6.675	0.000**
ALP	6	88.245 ± 6.387	31.927 ± 2.998	19.554	0.000**
GOT	6	108.233 ± 13.327	56.560 ± 8.095	8.117	0.000**
GPT	6	56.5833 ± 3.553	41.350 ± 1.562	9.615	0.000**
Creatinine	6	1.583 ± 0.117	0.7167 ± 0.133	11.993	0.000**
Urea	6	31.833 ± 2.742	21.617 ± 0.752	8.799	0.000**

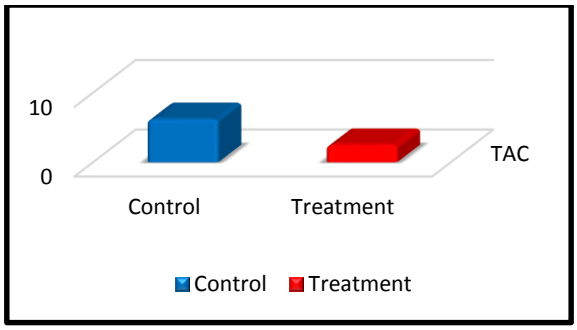

Figure (1) Total antioxidant capacity in control group was higher than in treatment group .

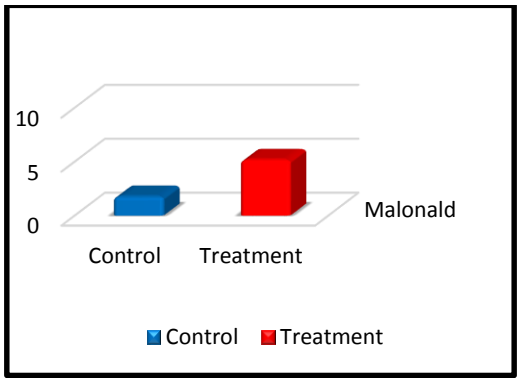

Figure (2). Malonaldehyde in treatment group higher than control group .

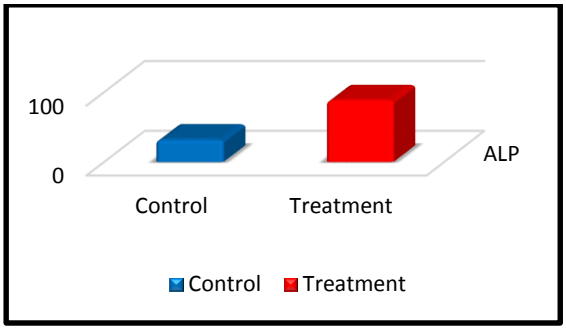

Figure (3) Alkaline phosphatase in treatment group more than control one

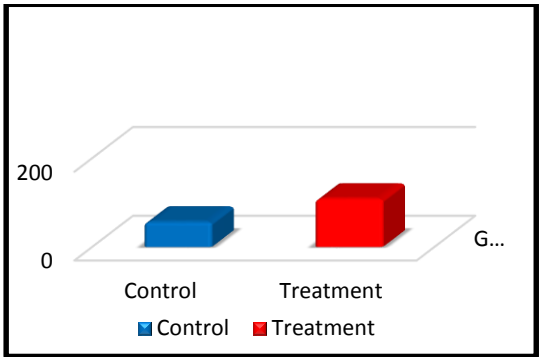

Figure (4): Liver enzyme aspartate aminotransferase AST\GOT, higher in treatment group than control group.

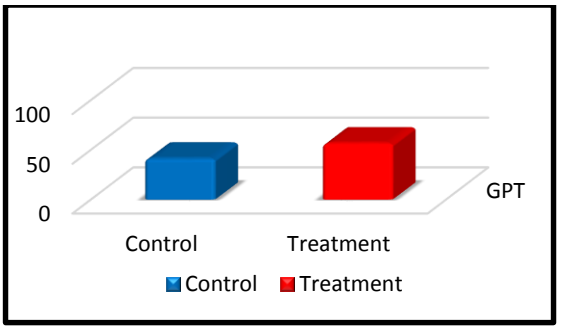

Figure (5): Liver enzyme Alanine aminotransferase ALT\GPT higher in treatment group than control group .

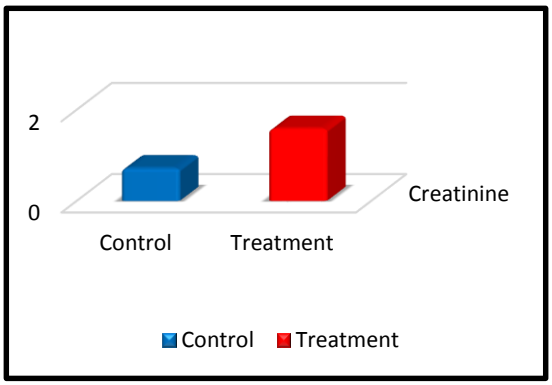

Figure (6) Kidney function test show higher creatinine

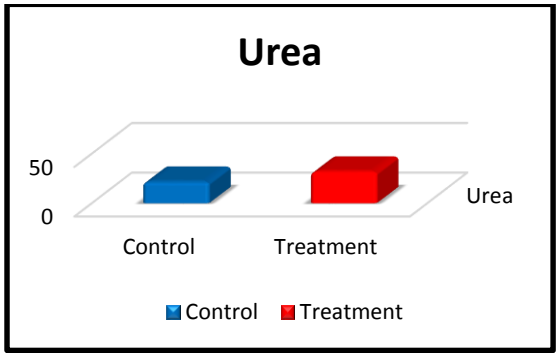

Figure (7) Kidney function test show higher urea

Biological human screening has been used as a way to assess health harm in communities all around the world by evaluating a variety of biomarkers that offer knowledge about the vulnerability of producing toxic symptoms as a result of some kind of exposure [22]. Moreover, according to previous studies, a rabbit model is a suitable research model because this animal is closer in phylogenetical manner to humans than are lab. rodents and they need easy handling and are small but large enough to tolerate nonlethal tracking of biochemical changes [23,24].

Although topical fluoride is thought to help prevent dental caries, long-term exposure to systemic fluoride has been linked to health problems like dental and skeletal fluorosis.[25]. Fluoride side effects are linked

to the amount of fluoride absorbed daily as well as the amount of fluoride contained in the body. Understanding fluoride metabolism and its functional definition is critical for preventing or reducing the harmful effects of chronic fluoride toxicity. [26] Fluoride can lead to the formation of free radicals and reactive species, causing a redox imbalance, both of which can lead to cytotoxicity. As a mechanism of action, fluoride toxic effect is thought to cause oxidative harm [27]. Fluoride absorbed destroys DNA inside nucleus, causes loss of mitochondrial function, and alters the intracellular redox state, resulting in membrane lipid and protein oxidation [28]. According to current studies, fluoride can create ROS and result in cellular harm in animals [27]. Fluoride lowers glutathione levels, increases MDA levels, and inhibits the actions of certain antioxidant enzymes. It reduces the ability of cells to scavenge ROS by inhibiting ATPase activity. This results in ATP loss and a decrease in their ability to scavenge ROS. Fluoride causes mitochondrial depolarization, which enhances ROS synthesis and oxidative stress, leading to apoptosis and cell death [29].[30,31]. This suggests that improvements in redox homeostasis, as well as oxidative and nitrosative pathways, are essential in fluoride action [32]. Exposure to NaF also increased ALP activity [33]. The exact mechanism underlying fluoride's stimulatory Urea 0 20 40 Control Treatment Urea Control Treatment effect on ALP release is likely to be related to the mechanisms underlying fluoride's enhancement of bone formation as well as its destructive effects throughout the liver and kidney [34].

Fluoride can boost protein and mRNA expression in chronic fluorosis rats' liver cells. This signaling pathway is essential in the pathogenesis of fluorosis-induced liver damage. [19]. The in vivo experiment showed that overexpression of Gli1 would induce early osteogenic differentiation in a Runx2-dependent manner, which increases ALP activity to a certain degree. The researchers believe that when fluorine is present, Ihh stimulates Gli2, and then transcribes the signal into the nucleus, causing Runx2 speech. Furthermore, it interacts with Ihh to facilitate ALP behavior enhancement [35].Hepatic lesions may be to blame for the increased behaviors of the GGT, AST, and ALP in this sample. The increased amounts of creatinine and urea in the treated groups in this sample could be attributed to renal lesions [36].

Parameters responsible for normal liver and kidney functions have been changed due to exposure to increased NaF level, including enlarged oxidative stress, changed levels of hepatic enzymes, histological and morphological

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