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The effect of silver nanoparticles and thioacetamide on blood urea nitrogen and creatinine in male laboratory mice

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Abstract

Today, with the help of nanotechnology, new ways of treating specific diseases have been added. Nanoparticles due to very small size and large surface can penetrate cells and tissues and to affect them. Since ancient times, silver has been used, due to antimicrobial properties. Silver nanoparticles have the ability to destroy microorganisms but may also have many side effects. The aim of this study was to investigate the effect of silver nanoparticles on renal function in the male balb/c mice in compare whit thioacetamide. In this study, animals were divided into four groups, the first group received food and water. The second and third groups received 50 mg/kg thioacetamide and 3000 ppm silver nanoparticles respectively, and the last group received a combination of silver nanoparticles and thioacetamide. Then, the blood was taken from heart and changes in creatinine and BUN were measured by a spectrophotometer. Silver nanoparticles led to significant increases in BUN and creatinine levels compared with the control group. But thioacetamide increased slightly BUN levels, and creatinine levels did not changed. The combination of nanosilver and thioacetamide has also led to increased BUN and decreased creatinine in the fourth group. According to the survey results silver nanoparticles and thioacetamide can lead to renal dysfunction, but the cellular destruction caused by oxidative stress in the last group with combination of silver nanoparticles and thioacetamide were more than other groups.

Introduction

Silver nanoparticles show different physicochemical characteristics compared with other nanoparticles and their biological activities are compared with metals. Also, their high ration of surface to volume lets them to be faced with their environment in larger values (Peijneburg and Herberts, 2009).

Antimicrobial material such as nanosilver becomes more important over the time due to their wide range of application. Despite wide use of nanosilver products, a few related studies have determined the Bun and creatinine are two important factors to identify kidney function [Ref]. concentration of these factors in blood serum is increased by renal damages therefore, evaluator changes of these two factors can provide important information about doing this investigation compared with normal levels of these two factors in kidney of male mice that was conducted by biochemical tests of blood serum and microscopic researches on tissue for comparing the toxic effects of silver nanoparticles and thioacetamide on kidney.

The aim of this study is effect of Silver Nanoparticles and Thioacetamide on Blood Urea Nitrogen and Creatinine in Male Laboratory Mice

Materials and methods

Materials

In this research, 32 male mice weighting 28-30 gr were produced from Islamic Azad University, Shahr-e-Kord branch and were maintained in animals' room under standard conditions (12 hours in darkness and 12 hours under light, temperature by 25^0C and suitable humidity).

Methods

The animals were fed unlimitedly then; mice were randomly divided into four groups and were maintained in separate cages. The first group received water and food as control group. The second group was injected by thioacetamide (with dose of 50 mg/kg) in three consecutive days. The third group also received a nanosilver solution with dose of 3000 ppm within 20 servings once two days and ultimately, the fourth group received silver nanoparticles through intraperitoneal injection within 20 servings once two days and then, they received three servings of intraperitoneal injection of thioacetamide with dose of 50 mg/kg once two days. Then, the mice were anesthetized by chloroform and blood was taken from their heart. Blood samples were collected and kept under laboratory temperature for 45 minutes. After clotting, serum was separated by centrifugation, and BUN and creatinine were measured using spectrophotometer (D20/20) with wavelengths of 475 nm and 500 nm respectively to evaluate and compare kidney function in different groups.

In order to analyze the data SPSS15 software was used. After doing ANOVA test, LSD test was used for more accurate investigation of differences. Significant level of means difference was considered $P<0.05$.

Results

Amount of BUN and creatinine

The results of measuring the amount of BUN and creatinine showed that, there is a significant difference ($P>0.05$) in all groups except nanosilver and thioacetamide groups before and after thioacetamide injection. $P<0.05$ means that, the difference has been increased significantly in the group, and mean of BUN is not same before thioacetamide in the six groups ($P=0.0005$) as well as after thioacetamide ($P<0.05$) (Table 1).

Also, comparison of mean of creatinine between all groups demonstrates significant difference before and after thioacetamide injection but, among the six groups, significant difference is only observable before thioacetamide ($P<0.05$) (Table 2).

Creatinine in different groups

Table 1. Mean of creatinine in different groups before and after thioacetamide injection and results of ANOVA test.

Table 1. Mean of BUN in different groups before and after thioacetamide injection and results of ANOVA test.

Groups	Before thioacetamide Mean± Standard deviation	After thioacetamide Mean± Standard deviation	Significant level
Control	21±1	26.5±5.5	0.09
Thioacetamide	23.7±2.5	28.5±4.9	0.09
Nanosilver	38.3±3.2	40±1.6	0.18
Combination	23.67±2.52	31.8±3.35	0.01

Table 2. Mean of creatinine in different groups before and after thioacetamide injection and results of ANOVA test.

Groups	Before thioacetamide Mean± Standard deviation	After thioacetamide Mean± Standard deviation	Significant level
Control	0.06±0.37	0.09±0.33	0.56
Thioacetamide	0.06±0.37	0.02±0.22	0.005
Nanosilver	0.06±0.43	0.05±0.26	0.004
Combination	0.1±0.50	0.07±0.24	0.005

Discussion and conclusion

Thioacetamide injecting on BUN of kidney has had destructive effect and has caused to increase this valuable factor of kidney correct function.

Ahmad *et al.* (2002) indicated that, damage resulted from thioacetamide represents tissue toxicity has been done by xenobiotic. Nitrogen is naturally transported from blood into the nephrons but, when capillaries and nephrons cells are damaged, nitrogen enters serum (Ahmad *et al.,* 2002).

Kim *et al.* (2002) showed that, thioacetamides used by cytochrome enzymes P450 present in microsomes are metabolized and are converted to thioacetamide –S by oxidation. Thioacetamide –S generates stress and causes to damage cells and their apoptosis and finally necrosis (Bruck, 2001). Results of research about making the renal toxicity by thioacetamide are similar with the results of this study. Nanosilver has been reported as a high toxic material compared with other materials, and this toxicity is along with free oxygen species production (Khodadadi *et al.,* 2012). Silver nanoparticles can destroy many microorganisms, so, they can have side effects and tissue diseases just like many medicines because, after entering the body, they are metabolized in liver and are sent to the kidneys to be excreted, therefore, liver and kidney are affected more than other tissues (Moaddab *et al.*, 2012). Another effect of nanosilver is to release free oxygen along with oxidative stress which has been observed as damaging and destructing the embryonic layer, damage to mitochondria and reduced glutathione levels (Akradi *et al.*, 2012). According to the authors' belief, absorbed nanosilvers are boned with proteins of plasma in organs such as liver, kidney, heart, brain, lungs and stomach and by folding change, the third and fourth structures of necessary proteins of these organs result in fundamental changes in them (Chanch *et al*, 2006). In current study, the effect of nanosilver on kidney shows that, although nanosilver has caused to increase BUN and creatinine, after being toxic by thioacetamide, it has caused BUN to stay constant and to decrease creatinine. Considering these two factors it can be concluded that, despite theories of some scientists about safety of silver nanoparticles, this particles can be harmful for kidney.

Therefore, according to conducted researches in this field and available evidences, the mechanism of this

damage can be considered so that, this nanoparticle leads to release free radicals and reactive oxygen species (ROS), and extreme ROS accumulation can begin inflammatory reaction and mitochondrial damage. Consequently, GSH level decreases as a result of generated inflammation, therefore, cellular planned death factors like cytochrome C is released and cell death occurs.

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