Gazi University Journal of Science
GU J Sci
28(4):541-544 (2015)

Lead Nitrate Induced Toxic Effects on Small Intestine Tissues in Diabetic and Non-Diabetic Rats: Role of Sodium Selenite

Çağlar ADIGÜZEL[1, ♠], Yusuf KALENDER[1]

[1]*Gazi University, Faculty of Science, Department of Biology, Teknikokullar, 06500 Ankara, Turkey*

Received: 17/11/2014 Revised: 09/04/2015 Accepted: 09/11/2015

ABSTRACT

In this study, diabetic and non-diabetic male rats were given to sodium selenite (Se), lead nitrate (LN) and sodium selenite plus lead nitrate through gavage. LN caused to histopathological changes in small intestine tissue of non-diabetic LN and non-diabetic sodium selenite+LN groups. We observed that supplementation of sodium selenite has protective role on histopathological changes in small intestine tissue when the non-diabetic sodium selenite+LN group compared with non-diabetic LN group. In diabetic control group, histopathological changes in small intestine tissue were detected. Treatment of LN to diabetic rats caused seriously histopathological alterations. Sodium selenite treatment didn't show preventive effect on LN-induced toxicity in diabetic rats.

Keywords*: Lead nitrate, sodium selenite, small intestine, histopathology, diabetes mellitus*

1. INTRODUCTION

Metals are a major class of known or suspected carcinogens [1]. Especially in developing countries, Lead (Pb) is one of the effective toxic heavy metal that has been found in environment and biological systems [1,2]. It is known that caused many histopathological alterations in several tissues like liver, kidney and brain [3]. It has been shown that lead exposure resulted in increased oxidative stress. Heavy metal toxicity has been related to generation of reactive oxygen species (ROS) [4,5]. Many researchers have reported that lead exposure could induce pathological changes and also oxidative stress in experimental animals [3]. After absorption, Pb is also distributed to soft tissues and bone [4]. Pb is lead to many toxicological effects such as hematological and neurological damages [5.6].

Selenium (Se) is an antioxidant for animals and human and its various forms have important roles in several biochemical and physiological process. Sodium selenite, a common dietary form of Se, has anticarcinogenic and antimutagenic effects. It is frequently used against Se deficiency [6]. Recent studies show that Se protects tissues from heavy metal induced oxidative damage [5].

Diabetes mellitus (DM) is a chronic metabolic disorder that continues to present a major worldwide health problem [7]. Additionally, it is known that sodium selenite is a common dietary form of selenium [8].

In the present study, we determined the possible adverse effects of lead nitrate on the small intestine tissue of diabetic and non-diabetic male rats and assess whether these effects can be ameliorate by co-administration

♠Corresponding author, e-mail: *cglr.adiguzel@gmail.com*

with sodium selenite. To achieve this aim, diabetic and non-diabetic rats were given lead nitrate and sodium selenite by oral gavage for 4 weeks, histopathological changes were assessed.

2. MATERIAL AND METHODS

2.1. Animals

Male Wistar rats (weighing approximately 200-250 g) were procured from the Gazi University Laboratory Animals Growing and Experimental Research Center. Animals were housed in plastic cages, fed a standard laboratory diet and water *ad libitum*. Rats were exposed to a 12 h light/dark cycle, and maintained at 20±2 ºC. The animals were quarantined for 10 days before beginning the experiment. All rats were handles in accordance with the standards guide for the care and use of laboratory animals. The Gazi University Committee on the Ethics of Animal Experimentation approved all animal experiments (Protocol no: G.Ü.ET – 11.028).

2.2. Chemicals

Lead nitrate (99% purity), streptozotocin (STZ, %99 purity) and sodium selenite (99% purity) were supplied by Sigma-Aldrich (Germany). All other chemicals used were analytical grade and also were obtained from Sigma-Aldrich (Germany).

2.3. Animal Treatment Schedule

Eight groups were formed for this study. In each group there were 6 animals. Groups' names were control, sodium selenite, LN, sodium selenite+LN, STZ+control, STZ+sodium selenite, STZ+LN, STZ+sodium selenite+LN.

All rats were treated for 28 days. During the experimental period 1ml/ kg b.w (body weight) distilled water for control groups, 1mg/ kg b.w sodium selenite for sodium selenite treatment groups and 22,5 mg/kg b.w (1/100 LD_{50}) LN [9] for LN treatment groups were given to rats daily via gavage.

DM was induced using an intraperitoneal injection of STZ at a single dose of 55 mg/kg. STZ was prepared in sodium citrate buffer at 4.5 pH. Two days after injection, the blood glucose levels were measured from the tail with a glucometer. Rats whose blood glucose levels were 300 mg/dl or higher, they were approved to be diabetic and selected for diabetic groups [10].

At the end of the 4^{th} week (28 days) of treatment, the rats in each group were sacrificed and dissected. The small intestine tissues were quickly taken to light microscopic investigations.

2.4 Light Microscopic Examination

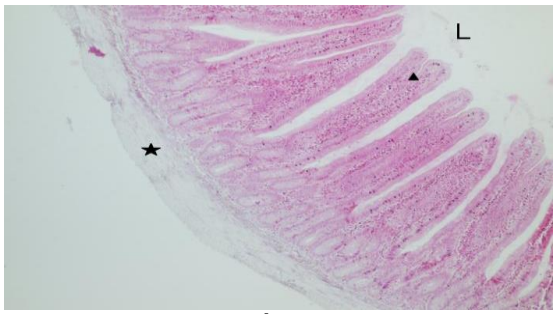
The tissues from each rat were dissected and then fixed in Bouin. After, small intestine samples dehydrated in ascending grades of ethanol and embedded in paraffin. Sections of 6-7 µ thickness were taken from paraffin blocks and stained with hematoxylin and eosin (H&E) and examined by light microscopy (Olympus BX51, Tokyo, Japan) and photographed with a camera (Olympus E-330, Olympus Optical Co., Ltd., Japan).

3. RESULTS

3.1. Light Microscopic Results

In our study histopathological examination of diabetic and non-diabetic rat small intestine were investigated using light microscope. The histological examination of the small intestine tissues of the control and sodium selenite (Figure 1) treated rats showed normal structure. Rats treated with LN alone exhibited necrosis and degeneration like dilatation of villi (Figure 2). Sodium selenite treatment reduced these pathological changes however we shown that separating from basal membranes (Figure 3).Diabetic control and sodium selenite treated (Figure 4) rats showed degeneration in epithelium. In diabetic LN and diabetic LN plus sodium selenite groups showed that seriously necrosis and degeneration in epithelium and also infiltration (Figure5-6).

Figure 1. Small intestine **s**ections of control rats X100,



H&E. L:Lumen, ▲: villi, ✶: muscle

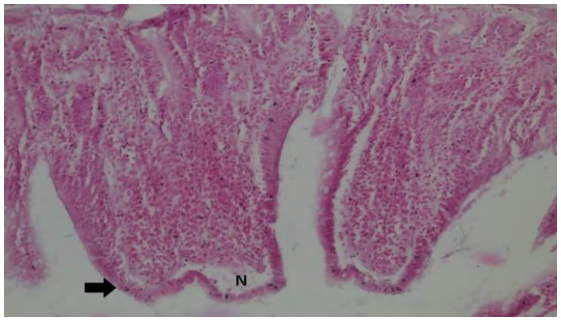


Figure 2. Small intestine sections of LN treated rats, X200, H&E. Dilatation of villi (➡), necrosis (N).

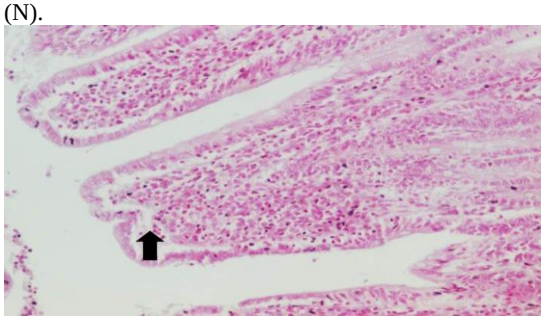


Figure 3. Small intestine sections of LN+sodium selenite treated rats, X200, H&E. separating from basal membrane ⬆

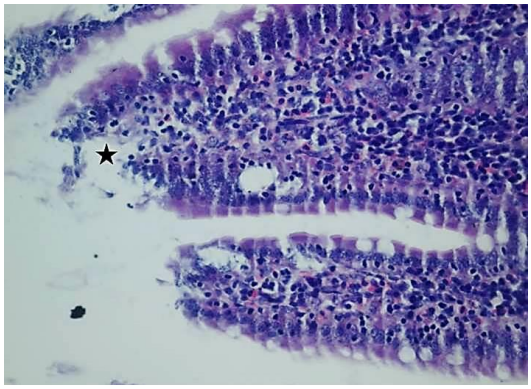


Figure 4. Small intestine sections of diabetic sodium selenite rats, X200, H&E. Degeneration in epitelium ✱

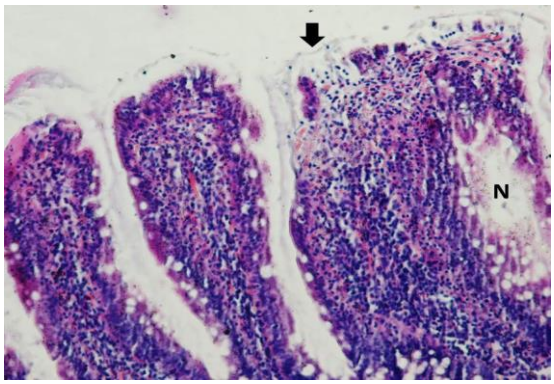


Figure 5. Small intestine sections of diabetic lead nitrate treated rats, X200, H&E. Degeneration in epitelium ✱ and N: necrosis

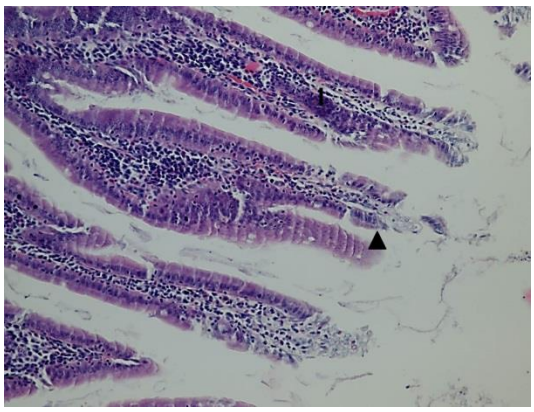


Figure 6. Small intestine sections of diabetic lead nitrate+sodium selenite treated rats, X200, H&E. degerenation ▲, infiltration ⬆

4. DISCUSSION

Lead is an important environmental toxicant that induces a broad range of dysfunctions [11]. It is reported that lead cause alter serum testosterone level and also sperm quality in rats [12]. Among environmental toxins, Pb is especially ominous because it cannot be converted into harmless forms by biological processes. There are many studies which have indicated that Pb exposure could cause biochemical and physiological dysfunctions in experimental animals and humans [13]. Thinking of the relationship between oxidative stress and Pb toxicity, caution has been focused on substances that have antioxidant specialities for show effects against Pb caused toxicity [14]. Lead is an important environmental toxicant that induces a broad range of dysfunctions [11]. The oral LD_{50} of LN for male rats is 2250mg/kg body weight [9]. In the present study, LN was given at 1/100 of oral LD_{50} and none of the rats died during the experimental period.

Diabetes mellitus remains one of the leading cause syndromes [15]. The production of reactive oxygen species (ROS) is central to the pathogenesis of diabetes [16]. Various studies have shown that oxidative stress mediates diabetes-induced alterations in various tissues [17].

Liu et al., reported that Se supplements could alleviate toxic effect of lead in their study [18]. Furthermore, some researchers shows that selenium inhibit the absorption of lead in intestinal system [19]. Selenium may therefore play a protective role on toxicity caused by lead.

It is reported that lead causes pathological effects on several tissues [20]. In our study, we showed that both diabetic and non-diabetic groups there are many histopathologic changes like necrosis, infiltration. In this study, because of lead induced toxicity histopathological changes were shown. Therefore, we can say that LN causes cellular toxicity in small intestine tissues and diabetes cause more pathological changes than non-diabetic groups.

In the present study, it is evident that lead nitrate caused histopathological changes in small intestine tissues both diabetic and non-diabetic rats. Sodium selenite prevents this toxicity in non diabetic groups but not prevent diabetic groups.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

[1] Tokar, E.J., Diwan, B.A., Waalkes, M.P., "Early life inorganic lead exposure induces testicular teratoma and renal and urinary bladder preneoplasia in adult metallothionein-knockout mice but not in wild type mice", Toxicology, 276, 5-10. (2010).

[2] Liu, M., Xu, Y., Chen, Y., Li, J., Zhao, F., Zheng, G., Jing, J., Ke, T., Chen, J., Luo, W., "The effect of sodium selenite on lead induced cognitive dysfunction", Neurotoxicology 36: 82-88 (2013).

[3] El-Neweshy, M.S., El-Sayed, Y.S., "Influence of vitamin C supplementation on lead-induced histopathological alterations in male rats", Exp. Toxicol. Pathol. 63: 221-227 (2011).

[4] Jihen, E., Imed, M., Fatima, H., Abdelhamid, K., "Protective effects of selenium (Se) and Zinc (Zn) on cadmium (Cd) toxicity in the liver of the rat: Effects on the oxidative stress", Ecotox. .Environ. Safe. 72: 1559-1564 (2009).

[5] Kalender, S., Uzun, F.G., Demir, F., Uzunhisarcikli, M., Aslanturk., A., "Mercuric chloride-induced testicular toxicity in rats and the protective role of sodium selenite and vitamin E". Food Chem Toxicol, 55: 456-462 (2013).

[6] Sakr, S.A.R., Mahran, H.A., Nofal, A.E., "Effect of selenium on carbimazole induced testicular damage and oxidative stress in albino rats", J. Trace Elem. Med. Biol. 25, 59–66 (2011).

[7] Farokhi, F., Farkhad, N.K., Togmechi, A., Band, K.S., "Preventive effects of *Prangos ferulacea (L.)* Lindle on liver damage of diabetic rats induced by alloxan", A. J. P. 2(2), 63-71 (2012).

[8] Shilo, S., Aronis, A., Komarnitsky, R., Tirosh, O., "Selenite sensitizes mitochondrial permeability transition pore opening in vitro and in vivo: a possible mechanism for chemo-protection", Biochem J, 370: 283-290, (2003).

[9] Sharma, V., Sharma, A., Kansal, L., "The effect of oral administration of *Allium sativum* extracts on lead nitrate induced toxicity in male mice", Food Chem. Toxicol. 48, 928-936 (2010).

[10] Schmatz, R., Mazzanti, C.M., Spanevello, R., Stefanello, N., Gutierres, J., Corrêa, M., da Rosa, M.M., Rubin, M.A., Schetinger, M.R.C., Morsch, V.M., "Resveratrol prevents memory deficits and the increase in acetylcholinesterase activity in streptozotocin-induced diabetic rats", Eur. J. Pharmacol. 610, 42- 48 (2009).

[11] Narayana, K., Al-Bader, M., "Ultrastructural and DNA damaging effects of lead nitrate in the liver", Exp. Toxicol. Pathol. 63: 43-51, (2011).

[12] Allouche, L., Hamadouche, M., Touabti, A., "Chronic effects of low lead levels on sperm quality, gonadotropins and testosterone in albino rats", Exp. Toxicol. Pathol 61: 503–510, (2009).

[13] Liu, C., Ma, J., Sun, Y., "Quercetin protects the rat kidney against oxidative stress mediated DNA damage and apoptosis induced by lead". Environ. Toxicol. Pharmacol. 30, 264-271 (2010).

[14] Dewanjee, S., Sahu, R., Karmakar, S., Gangopadhyay, M., "Toxic effects of lead exposure in Wistar rats: Involvement of oxidative stress and the beneficial role of edible jute (*Corchorus olitorius*) leaves", Food Chem. Toxicol. 55, 78-91 (2013).

[15] Abdul-Hamid, M., Maoustafa, N., "Amelioration of alloxan-induced diabetic keratopathy by beta-carotene", Exp. Toxicol. Pathol 66, 49-59 (2014).

[16] Shirpoor, A., Ansari, M.H., Salami, S., Pakdel, F.G., Rasmi, Y., "Effect of vitamin E on oxidative stress status in small intestine of diabetic rat", World Gastroentero13: 4340-4344, (2007).

[17] Mykkanen, H.M., Humaloja, T., "Effect of lead on the intestinal absorption of sodium selenite and selenomethionine (75Se) in chicks", Biol Trace Elem Res 6: 1-7, (1984).

[18] Liu, M., Xu, Y., Chen, Y., Li, J., Zhao, F., Zheng, G., Jing, J., Ke, T., Chen, J., Luo, W., "The effect of sodium selenite on lead induced cognitive dysfunction", Neurotoxicology 36: 82-88 (2013).

[19] Manna P., Sinha M, Sil P.C., "Amelioration of cadmium-induced cardiac impairment by taurine", Chem.Biol.Interact.174: 88–97 (2008).

[20] El-Naggar A.M,. Mahmoud S.A. Tayel S.I., "Bioaccumulation of Some Heavy Metals and Histopathological Alterations in Liver of *Oreochromis niloticus* in Relation to Water Quality at Different Localities along the River Nile, Egypt", World Journal of Fish and Marine Sciences. 1 (2): 105-114, (2009).