

RESEARCH ARTICLE

Acute exposure of cadmium induced hypoglycemia in mice

ADON Mousan Arsène*¹, N'GUESSAN Assue Adja Julien^{1,2}, KONAN Kouassi Martin^{1,2}, DOSSO Mireille¹, DJAMAN Allico Joseph^{1,2}

¹Cell Biology Unit, Pasteur Institute of Côte d'Ivoire (IPCI) 01 BP 490 ABIDJAN 01

²Laboratory of Biochemical Pharmacodynamics, Félix Houphouët-Boigny University (UFHB) 22 BP 582, Abidjan 22, Côte d'Ivoire

Received on: 30/10/2017, Revised on: 30/11/2017, Accepted on: 29/12/2017

ABSTRACT

Cadmium (Cd) is one of the most toxic environmental pollutants, causing a number of adverse health effects in humans. The main objective of this study was to evaluate the effect of cadmium on the pancreas. Mine male mice were divided into three groups: the control (Ctrl-) group, the STZ-treated diabetic control group and the Cd-treated experimental group.

STZ-treated mice which received a single dose of ip injection of 8 mg/kg of body of STZ dissolved in a freshly prepared solution of sodium citrate used as a positive control for diabetes and the control non treated mice received distilled water during the experiment. Cd-treated group had distilled water enriched with cadmium. This experiment was conducted for seven days.

Exposure of the mice to the cadmium caused a significant decrease in the animals' body weight and decrease in the blood glucose level. Our results suggest that cadmium exposure induced a sever hypoglycemia

Key words: Cadmium, hypoglycemia, pancreas, body weight

INTRODUCTION

Cadmium (Cd) is a toxic, natural, and non-essential heavy metal widely distributed in the earth's crust. It has many industrial applications, for example, it is used in alloys, color pigments, electroplating, and rechargeable nickel-cadmium batteries [1]. In mammals, the main sources of cadmium exposure are water, contaminated food, cigarette smoke, and industrial pollutants [2,3]. Although cadmium accumulates preferentially in the liver, kidneys, and bones, pancreas is also an important target organ [4,5].

The pancreas is a single organ consisting of two distinct parts: the exocrine pancreas and the endocrine pancreas [6]. The exocrine tissue produces pancreatic juices, which participate in digestion, while the endocrine tissue composed of four different cell types (alpha, beta, delta, and pancreatic polypeptide) [7, 8], secreting glucagon and insulin into the blood to regulate blood glucose [9,10]. Pancreas dysfunction can induce either hyperglycemia or hypoglycemia. Diabetes is a chronic disease affecting approximately 382 million people worldwide which represents 8.3% of the world's population [11]. In 2013, it caused

5.1 million deaths, that is, one person died of diabetes every six seconds [11]. This is a chronic hyperglycemia that occurs when the body is unable to produce enough insulin or use insulin effectively [11, 12, 13]. Insulin is an hormone secreted by pancreatic β -cells, which allows glucose in food to enter the cells of the body, where it is converted into the energy necessary for the proper functioning of muscles and tissues [11].

In contrast to diabetes, hypoglycemia is an abnormally low blood sugar concentration of less than 0.70g / l that exposes the subject to potential danger [14]. It is caused by either an excess of insulin or a defect in glucose production. While many environmental risk factors for diabetes have been identified, such as obesity, diet, and lifestyle, some experimental studies suggest that cadmium exposure may be associated with an increased risk of developing diabetes. . However, these experimental data are contradictory because other studies have shown that cadmium can also improve the ratio of glucose-stimulated insulin release [15, 16].

The objective of this study is to evaluate the effects of acute Cd exposure on mice.

***Corresponding Author:** ADON Mousan Arsène, **Email:** arsenemadon@gmail.com

MATERIAL AND METHODS

Animals and maintenance

Nine adult male mice in good health, weighing around 20g, raised at the Institute Pasteur animal facility in Côte d'Ivoire (IPCI) were used in this study.

The animals were housed in groups of 3 mice per cage in a room maintained between 22 - 24 °C, of stable humidity, provided with a ventilation system and a system regulating periods of darkness. (12h) and light (12h). Animals had ad libitum access to food (granulated, FACI, Abidjan) and water.

Experimental protocol

Nine male mice (*Musculus Abbinos*) were divided into three groups of three each: the control (Ctrl-) group, the STZ-treated diabetic control group and the Cd-treated experimental group. The STZ-treated mice which received a single dose of ip injection of 8 mg/kg of body of STZ dissolved in a freshly prepared solution of sodium citrate used as a positive control for diabetes and the control non treated mice received distilled water during the experiment.

The Cd-treated group had distilled water enriched with cadmium (50 mM). This experiment was conducted only for seven days. The weight and blood glucose of all animals were measured every three days and this during the entire period of treatment that last 7 days. Blood glucose levels were measured from blood collected from the tail vein using an Accu Chek Active® (Roche, Germany) blood glucose meter.

RESULTS

Effect of Cd on the body weight

At the end of these 7 days of treatment, a slightly increased of the body weight was observed in the control mice however, the STZ-treated group had a lost in their average body weight with no significant difference when compared to the untreated control mice.

The Cd-treated mice showed a highly decreased body weight when compared to both diabetic STZ-treated and the control non treated mice. This decrease remains statistically insignificant compared to untreated mice. The Cd group showed a clear decrease in body weight compared to the control group.

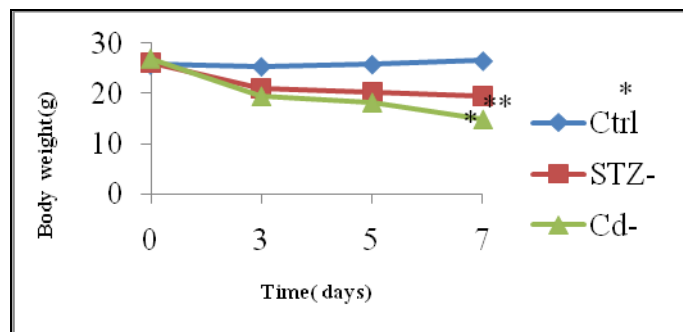


Figure 1: Effects of cadmium on body weight non-diabetic mice. n = 3; data are expressed as mean \pm SE. * P < 0.05, ** P < 0.01 compare to Control

Effect of Cd on blood glucose

By the end of the treatment, a highly significant increase in the blood glucose level of the STZ-treated group was observed when compared to the control non treated mice. However a highly reduced blood glucose level was observed in the Cd-treated mice when compared to the STZ-treated diabetic mice or even to the control non treated mice.

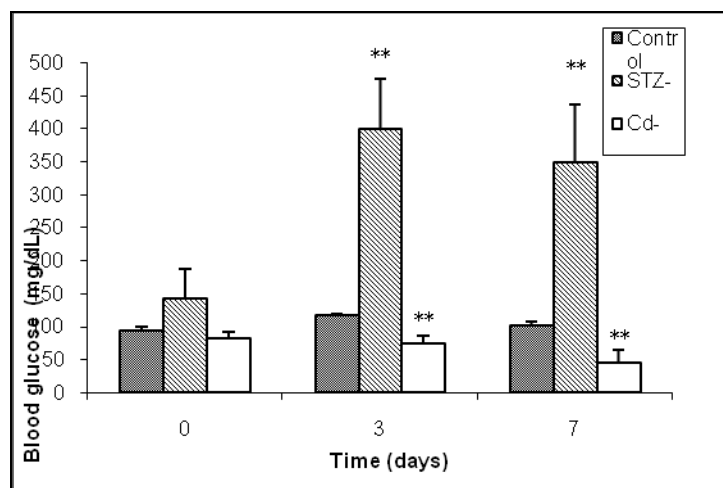


Figure 2: Effect of cadmium on blood glucose in non-diabetic mice, n = 5; data are expressed as mean \pm SE. ** P < 0.01, compare to Control.

DISCUSSION

Cadmium (Cd) is one of the well-known, highly toxic environmental and industrial pollutants, capable to cause a number of adverse health effects and diseases in humans [15]. In this study, the effect of an acute administration of Cd on the body weight and blood glucose of mice was evaluated. At first, our study revealed that an acute administration of 50 mM of cadmium causes a significant decrease in the body weight of the mice compared to the controls (p < 0.05). This may be due to an increase in lipid and protein degeneration caused by cadmium toxicity [17]. On the other hand, cadmium reacts with several nutrients [18]. Indeed, several studies suggest a competition between Cd²⁺ and Ca²⁺, Mg²⁺, and Zn²⁺ at the level of different metabolisms [19,

²⁰. This can lead to poor assimilation of food by the body ^[21, 22]. Our results are consistent with several other studies such as that published by ^[23] in rats. Secondly, our results revealed that there is no implication of cadmium exposure and the occurrence of diabetes. On the contrary, our results show a significant decrease in the blood glucose levels in the cadmium-treated mice when compared to first the STZ-treated diabetic control mice and even to the non-treated normal control mice ($p < 0.05$). Unlike the STZ that is known to induce hyperglycemia, our study demonstrated that acute administration of cadmium induced hypoglycemia in mice.

CONCLUSION

Our experimental study revealed that there is no association between acute cadmium exposure and the occurrence of diabetes. Cadmium at this concentration is not a risk factor in the genesis of diabetes. Acute administration of cadmium rather induced a severe hypoglycemia in mice.

ACKNOWLEDGEMENTS

We thank the Institut Pasteur of Cote d'Ivoire (IPCI).

CONFLICT OF INTEREST

The authors state that they have no financial interest and no conflict of interest.

REFERENCES

- Jarup L. (2003). Hazards of heavy metal contamination. *Br Med Bull* 68: 167–182.
- IPCS (1992). Environmental Health Criteria 134. Cadmium. World Health Organization, Geneva.
- Bernard A (2008) Cadmium & its adverse effects on human health. *Indian J Med Res* 128: 557–564.
- Inaba T, Kobayashi E, Suwazono Y, Uetani M, Oishi M, et al. (2005). Estimation of cumulative cadmium intake causing Itai-itai disease. *Toxicol Lett* 159: 192–201
- Lei LJ, Jin TY, Zhou YF (2005). The toxic effects of cadmium on pancreas. *Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi* 23: 45–49
- Githens, S. (1988). The pancreatic duct cell: proliferative capabilities, specific characteristics, metaplasia, isolation, and culture. *J Pediatr Gastroenterol Nutr* 7, 486-506.
- Dorrell C, Abraham SL, Lanxon-Cookson KM, Canaday PS, Streeter PR, et al. (2008) Isolation of major pancreatic cell types and long-term culture-initiating cells using novel human surface markers. *Stem Cell Res* 1: 183–194.
- Pitocco D, Zaccardi F, Di Stasio E, Romitelli F, Santini SA, et al. (2010) Oxidative stress, nitric oxide, and diabetes. *Rev Diabet Stud* 7: 15–25.
- Idelman, S., Verdeti, J., (2000). *Endocrinologie et communication cellulaire*. Ed. Sciences, France, pp: 281-425.
- Grimaldi, A., (2005). *Traité de diabétologie* Ed. Flammarion, Paris, pp: 1-116
- FID(2013). *Atlas du diabète de la federation international du diabetes*. Sixième édition.
- Rodier M. (2001). Définition et classification du diabète. *Médecine Nucléaire - Imagerie fonctionnelle et métabolique*, vol.25 - n°2 : 5-18.
- Sharma B., Viswanath G., Salunke R., Roy P., (2008). Effects of flavonoid-rich extract from seeds of *Eugenia jambolana* (L.) on carbohydrate and lipid metabolism in diabetic mice. *Food Chemistry* 110: 697–705.
- ADAWH (2005). American Diabetes Association Workgroup on Hypoglycemia. Defining and reporting hypoglycemia in diabetes. *Diabetes care* , 28:1245-1249.
- Kai-Chih Chang, Ching-Cheng Hsu, Shing-Hwa Liu, Chin-Chuan Su, Cheng-Chieh Yen, Ming-Jye Lee, Kuo-Liang Chen, Tsung-Jung Ho, Dong-Zong Hung, Chin-Ching Wu, Tien-Hui Lu, Yi-Chang Su, Ya-Wen Chen, and Chun-Fa Huang (2013). Cadmium Induces Apoptosis in Pancreatic β -Cells through a Mitochondria-Dependent Pathway: The Role of Oxidative Stress-Mediated c-Jun N-Terminal Kinase Activation *Journal List PLoS One* .8(2);
- Jacquet, M. Cordier, M. Lenon, J. Arnaud, H.-F. Isabelle, M. Osman, C. Cottet , K.Couturier , E. Fontaine , J.M. Moulis , C. Demeilliers (2014). Effet de l'ingestion de faibles doses de cadmium sur le fonctionnement pancréatique. *Nutrition Clinique et Métabolisme* 28(1) : 573-574.
- Erdogan Z, Erdogan S, Celik S, Unlu V (2005). Effects of ascorbic acid on

- cadmium-induced oxidative stress and performance of broilers. *Biol. Trace. Elem. Res.* 104:19-31.
18. Solomons, N.W., Viteri, F., Shuler, T.R., Nielsen, F.H. (1982). Bioavailability of nickel in man effects of foods and chemically defined dietary constituents on the absorption of inorganic nickel. *Nutr.* 12 (1):39-50.
 19. Sugiwaru, N. (1977). Inhibitory effect of cadmium on calcium absorption from the rat duodenum. *Arch. Environment Contamination. Toxicology.* 5: 167-175
 20. Washko, P.W., Cousins, R.J. (1977). Metabolism of Cd¹⁰⁹ in rats fed normal and low-calcium diets. *Toxicology Environmental Health* 1: 1056-1066.
 21. Nielsen, F.H., Shuler, T.R., McLeod, T.G., Zimmerman, T.J. (1984). Nickel influences iron metabolism through physiologic, pharmacologic and toxicology mechanism in the rat. *Nutrition* 14: 1280-1288.
 22. Smialowicz, R.J., Rogers, R.R., Riddle, M.M., Leubke, Fogelson, L.D., Rowe, D.G. (1987). Effects of manganese, calcium, magnesium, and zinc on nickel induced suppression of murine natural killer cell activity. *Toxicology Environmental. Health* 20: 67-80.
 23. Rana, S.V., Rekha, S., Seema, V. (1996). Protective effects of few antioxidants on liver function in rats treated with cadmium and mercury. *Indian Journal of Experimental Biology* 34: 177-179.