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Dissertation

Title *Experimental Investigation on the Relationship between Lead Exposure, Thyroids and Systemic Toxicity in Health and Diabetes*

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Defense Date 26 April 2015

Abstract

Lead exposure can cause multiple systemic toxicities, particularly affecting the hematopoietic, nervous and renal systems. However, its effects on the thyroid functions are not well elucidated and the published studies are controversial. In addition, although there are several experimental thyroid models, each one of them has its own limitations. Accordingly, in this dissertation, we investigated the possible relationship between lead exposure, thyroid functions and short-term systemic toxicity in two animal models, namely normal (non-diabetic) and diabetic animals. We also investigated the possibility of developing a hormonal thyroid model. In the non-diabetic model, Wistar rats were divided into five groups and treated for five days. The four treatment groups received 1, 25, 50, or 100 mg/kg of lead acetate trihydrate intraperitoneally (i.p.), respectively. The control group received i.p. injections of distilled water. As for the diabetic model, diabetes was induced with an i.p. injection of 60 mg/kg streptozocin (STZ). Six weeks later, lead exposure experiments started. Here, four groups were studied i.e. a control; and 25, 50 and 100 mg/kg lead acetate groups. In each model, the measured blood lead levels correlated very well with the administered doses of lead acetate. Treatment of the animals with lead acetate resulted in significant weight loss in both models. Lead exposure caused a dose-related increase in thyroid stimulating hormone (TSH) in non-diabetic and diabetic animals. Although, thyroxine (T4) and triiodothyronine (T3) levels remained within normal range in non-diabetic animals, their levels were reduced in diabetic animals. The highest dose of lead (100 mg/kg) significantly increased white blood cell counts and caused a significant decrease in the number of platelets in non-diabetic animals. In addition, C-reactive protein levels increased significantly in response to lead exposure in this model. Moreover, there was a significant increase in lactate dehydrogenase (LDH), aspartate aminotransferase, total bilirubin, and urea levels; following lead exposure in non-diabetic animals. On the other hand, lead exposure in diabetic animals increased urea levels and caused a significant decrease in creatinine levels in plasma. While the concentrations of malondialdehyde were not affected, glutathione stores were depleted in response to lead exposure in the diabetic animals. In the last stage, we tried to develop a new experimental thyroid model, based on the use of hormones. In this regard, animals were treated for five days with either thyrotropin-releasing hormone (TRH) or octreotide (OCT) to induce hyperthyroidism or hypothyroidism, respectively. Although there were no effects on T4 and T3 levels, TRH was effective in causing an increase in TSH levels. However, TRH also elevated LDH levels. The use of TRH did not cause any other side effects on the tested parameters, which included weight change, oxidative stress markers and renal and hepatic functions. In comparison, OCT failed to affect TSH, T4 and T3 levels, at the dose and treatment duration that we used. In conclusion, short-term lead exposure in healthy and diabetic animal models affected the functions of the anterior pituitary and thyroid glands, caused oxidative stress, liver and kidneys toxicity and induced systemic inflammation. In addition, we found that TRH has a potential to induce hyperthyroidism in experimental animals. Keywords: lead; rat; diabetes; thyroid; experimental model and systemic toxicity.