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RENAL AND HEPATIC EVALUATION DUE TO CADMIUM EXPOSURE IN RABBITS

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ABSTRACT

Cadmium is nowadays regarded as an environmental pollutant. Epidemiological studies have demonstrated the association between its exposure and functional alterations, due to high atmospheric levels, because it is not biodegradable and for its longlasting persistence. The aim of this study was to screen and analyze the renal and hepatic functionality due to drinking water pollution (well source) in a rabbit farm near the industrial zone in Mexico City. Five periods were sampled, in which 6 rabbits were randomly selected, collecting 4 mL of blood from the marginal auricular vein in tubes with and without anticoagulant. The first samples were taken when the rabbits aged 8 weeks and on days 15, 30, 45 and 60. Samples were centrifuged and serum obtained to determine ALT (alanine aminotransferase), AST (aspartate transferase), GGT (gamma glutamyl transferase), urea, creatinine, hematocrit and total proteins, comparing the results to previously reported ones in the literature. An initial ALT activity of 63 ± 8.87 U/L was found, in the first period 93 ± 12.62 U/L, in the second, 95 ± 6.11 U/L, in the third, 112 ±10.58 U/L, and in the fourth, 68 ± 19.55 U/L. Regarding GGT and AST, values were reported within normal ranges. Urea showed an increasing value up to 29 ± 3.18 mmol/L, with an initial value of 20 ± 7.30 mmol/L. Creatinine initial concentration was 111 ± 13.57 µmol/L increasing up to 118 ± 8.99 µmol/L in the last period. Hematocrit significantly decreased from 42 ± 4.31% down to 30 ± 13.23 % in the fourth period. Total proteins slightly increased from 6.2 ± 0.46 to 6.5 ± 1.06

g/dL in the last period. These parameters show that rabbits which have been exposed to cadmium suffer physiological changes that may permanently alter hepatic and renal funcion.

Key words: Bioaccumulation, cadmium, physiopathology, pollute, toxicity.

Introduction

Due to natural causes as well as to anthropogenic activities, there is important pollutant production nowadays. When they are eliminated to the environment without previous treatment, they may accumulate or scatter to different places. Such is the case for cadmium (Cd), lead (Pb), arsenic (As) and mercury (Hg) which have been referred as capable of producing irreversible damages to organisms which have been exposed to them, in which slight cellular damages have been produced (in red blood cells, white blood cells and platelets) or mortality reported. Exposure continues and the quantity of substances in water, air and soil determine the extent of the physiological problems in animals, meanwhile the route of exposure as well as their susceptibility determine the course of the lesions due to environmental pollution.

Cadmium (Cd) in particular, as an environmental pollutant, can provoke functional alterations in organisms which have consumed contaminated food. In herbivores, an important source for cadmium intoxication is the ingestion of forages or soil. In humans, the main source of exposure is occupational, in which renal disfunctions, osteomalacia and osteoporosis are found. Other processes which have been chronically identified are proteinuria, hepatic damage, emphysema (when inhaled), neurologic deterioration, testicular, pancreatic, adrenal disfunction and anemia, and in laboratory animals carcinogenic effects have been reported (ATSDR, 2012).

It is one of the most toxic elements. Its accumulation is gradual and increases with age. Intestinal absorption is due to the divalent metal transporter (DMT-1) located in the duodenum, erythrocytes, liver and proximal convoluted tubules. It is an Fe transporting protein with great affinity towards Cd. When Fe and Zn ingestion is decreased, DMT-1 expression increases, increasing the intestinal absorption of Cd and therefore its toxicity. The aim of this study was to

screen through clinical enzymology the renal and hepatic function in rabbits, due to the detection of cadmium in drinking water in a rabbit farm near the industrial zone of Mexico Valley, where respiratory problems and renal ilnesses with no aparent cause were found.

Material and Methods

In a rabbit farm near the industrial zone in Mexico Valley, with a population of 40 animals, cases of respiratory disease as well as sudden death in stage of completion were previously reported. Food was based on commercial feed and water from a near well. Cadmium concentration in water was 16,5 g/kg. When direct information was gathered, growth, bone and dehydration were detected. Six rabbits meant for human consumption were sampled to demostrate and assess physiological alterations in liver and kidney, by collecting blood samples with and without anticoagulant in different periods. The first one was taken when the rabbits aged eight weeks, and then on days 15, 30, 45 and 60. Each sample was centrifuged and divided for analysis through colorimetric methods using an spectrophotometer with specific reactives for ALT, AST and urea at a wavelength of 340 nm. For GGT the Szazs/Persijn method was used at 405 nm; for creatinine the absorbance was read at 510 nm (Clinical Chemistry-Instrumentation Laboratory®). Total protein measurement was performed in plasma using a refractometer (Veterinary Refractometer 10436, Reichert® g/%).

Results and Discussion

The results obtained for ALT were: during the first period 63 ± 8.87 UL, 15 days afterwards 93 ± 12.62 UL, for the third one 112 ±10.58 UL, and during the rest, the enzyme decreased (Table 1). Increasing ALT values show specific hepatic lesion due to degeneration changes up to necrosis, which is different from the increase in AST values that show hepatocelular or muscular (either skeletal or cardiac) lesion. A GGT increase in values may indicate hepatic disease. In this research, its values were stable during the sampling periods, just as what happened with AST.

Urea gradually increased, from 20 ±7.30 mmol/L up to 29 ±3.18 mmol/L. For creatinine the initial value was 111 ±13.57 µmol/L and increased up to 118 ± 8.99 µmol/L in the last period. Hematocrit decreased from 42 ± 4.31% to 30 ± 13.23 % in the fourth period and total proteins showed a slight increase from 6.2 ± 0.46 up to 6.5±1.06 g/dL on the last period (Table 1).

Table 1. Enzymatic values for renal and hepatic evaluation in rabbits.

Parameter / Period	**Day 0**	**Day 15**	**Day 30**	**Day 45**	**Day 60**	**Reference values**
ALT (U/L)	63 ± 8.87	93 ± 12.62	95 ± 6.11	112 ± 10.58	68 ± 19.55	79
AST (U/L)	55 ± 7.23	43 ± 11.36	49 ± 5.79	49 ± 5.20	42 ± 4.58	47
UREA (mmol/L)	20 ± 7.30	21 ± 2.76	26 ± 3.06	24 ± 1.66	29 ± 3.18	3.45 ± 0.85
CREATININE (µmol/L)	111 ± 13.57	103 ± 9.04	106 ± 10.64	122 ± 13.52	118 ± 8.99	70.7-227.2
GGT (U/L)	12.17 ± 0.75	7.67 ± 1.37	7.00 ± 0.89	8.33 ± 2.08	7.00 ± 0	9
HEMATOCRIT (%)	42 ± 4.31	42 ± 1.94	39 ± 3.21	40 ± 2.00	30 ± 13.23	40.5 ± 2.11
TOTAL PROTEINS (g/dL)	6.2 ± 0.46	6.3 ± 0.06	6.6 ± 0.36	7.2 ± 0.35	6.5 ± 1.06	5.7 ± 0.6

Regarding the enzymatic values in the rabbits, it can be assumed that pollutant effects such as the ones produced by cadmium may be altering the optimal functionality of these animals, and that the presence of pathologies in the farm may not only be due to cadmium exposure but to the existence of other elements that may be harmful to the rabbits' health.

When cadmium is metabolized in the liver, it joins to low molecular weight proteins (<10kD) named metallothioneins (MT), distributed all over the organism, cysteine rich, with high reactive and storage affinity which participate on free radical elimination, and cellular repairing and regeneration. An increase in Cd intracellular levels rises MT expression, therefore increasing susceptibility in toxicity regarding these kinds of metals. It may also join to albumin in circulation, and is transported to the liver where it may join to glutathione (GSH) and metallothionein-1 (MT1) (Liu, 2001).

There was no severe damage in the renal system that could cause proteinuria, maybe due to the fact that the evaluation period was too short to provoke tubule lesions, which may be found in chronic cases and to the quantity of Cd consumed as well.

Cd-MT1 complex is secreted via bilis and reabsorbed in blood through enterohepatic circulation. It is a low molecular weight complex, which can be totally reabsorbed in the S1 segment of the proximal convoluted tubule by endocytosis which can be clinically evaluated through the damages it causes.

Conclusions

The parameters found in the rabbits exposed to cadmium show that they suffer physiological changes which may permanently alter hepatic and renal functionality. ALT and urea levels progressively rise, indicating important hepatic and renal damage due to cadmium exposure.

References

1. ATSDR. 2012. Resumen de Salud Pública. Cadmio EE.UU. http://www.atsdr.cdc.gov/es/phs/es_phs5.pdf.

2. KANEKO, J.J. 2008. Clinical Biochemistry of Domestic Animals, 6th ed. Blood Analyte Reference Values in Small and Some Laboratory Animals. Elsevier. UK.

3. Liu Y., Liu J., Klaassen C.D. 2001. Metallothionein-null and wild-type mice show similar cadmium absorption and tissue distribution following oral cadmium administration. *Toxicol Appl Pharmacol, 175*, 253-9.

4. Olayemi, F.O. and Nottidge, H.O. 2007. "Effect of Age on the Blood Profiles of the New Zealand Rabbit in Nigeria". *African Journal of Biomedical Research, 10*, 73-76.

5. SCHALM'S Veterinary Hematology. 2010. Weiss D.J. and Wardrop K.J. editors. 6th ed. Reference Erythrocyte Parameters of the New Zealand White (NZW) Rabbit (*Oryctolagus cuniculus*). Wiley-Blackwell. USA.

6. Thrall M.A., Baker D.C., Campbell T.W., DeNicola D., Fettman M.J. 2006. Veterinary hematology and clinical chemistry. Blackwell, USA.