

SERUM CHOLESTEROL, TRIGLYCERIDES AND GLUCOSE CONCENTRATION AFTER MANGANESE EXCESS IN WISTAR RATS

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Abstract

The study followed to appreciate serum cholesterol, triglycerides and glucose concentration after manganese excess. For the experiment we used Wistar adult rats and we administrated manganese as gavage. The administrated manganese was as manganese chloride solutions in two different doses of manganese: $RDI \times 2$ – for E_1 group, and $RDI \times 4$ – for E_2 group (RDI – Recommended Daily Intake) for a short period of time. Over-doses of manganese intake increased the serum glucose comparing to control group with 15.81mg/dL for E_1 , and 44.16mg/dL for E_2 , and serum cholesterol concentration with 0.80mg/dL for E_1 and 5.60mg/dL for E_2 . The triglycerides concentration decreased in both experimental groups with 35.40mg/dL for E_1 and 50.80mg/dL for E_2 compared with the control group.

Keywords: *manganese, gavage, rat, glucose, cholesterol, triglycerides.*

Introduction

Manganese (Mn) is an essential trace element for growth, reproduction, skeletal structure, milk production and has vital functions in organism. Also manganese can influence the carbohydrate, lipid, and protein metabolism. Almost half of the total amount of manganese from organism (about 15-20mg) is found in bones and the remainder quantities are found in liver, pancreas, kidney and pituitary and adrenal glands (Aspects sanitaires et nutritionnels des oligo-éléments et des éléments en traces, 1997). Usually, the

manganese is found in mitochondrial cells as superoxide dismutase with manganese - an antioxidant enzyme (Gârban, 1999).

The homeostasis of manganese in organism is realized mainly by excretion via bile and intestinal tract as feces, and then by absorption. After absorption the manganese goes to liver, kidney and other organs and then is taken by transmangamin – a transporter globulin protein – into the blood (Haas, 1992). Absorption is low because only about 15 – 30% from ingested Mn is efficient utilized. The process of manganese absorption in the blood form intestine may be influenced by Mn level in organism, presence of other elements in food (zinc, cobalt, iron, calcium), alcohol, lecithin, soy protein, the chemical form of administered manganese and others aspects. For a better absorption, manganese has to be administrated in absence of other elements from food and in its protein-chelated form. An excess of Mn lead to iron and copper deficiency and large amounts of calcium and/or phosphorus will interfere with manganese absorbtion.

Experimental

The study followed the serum concentration of glucose, cholesterol and triglycerides after manganese administration to rats for a short period of time. Experiments were performed on 10 Wistar strain adult rats (females and males) for each group, with an average weight of 100 ± 10 g. We used three groups of animals: one control group (C) and two experimental groups (E₁ and E₂). After anaesthesia of the animals with Ketamina (i.m.), a total amount of 1mL solution/100g body weight (b.w.) was administered by gavage on days 4th and 7th of experiment (Vincu et al., 2000). To C group we administrated tap water, to those in group E₁ – MnCl₂ solution (two times the RDI for manganese for humans, i.e. 0.214mg x 2/b.w.) and to animals in group E₂ – MnCl₂ solution (four times the RDI for manganese for humans, i.e. 0.214mg x 4/b.w.) – Devlin, 1992; Derek, 1995.

On the 15th day of experiment, after anaesthesia the blood samples were taken from all experimental animals for biochemical analysis of glucose, cholesterol and triglycerides from serum.

The obtained data were statistically preceded and mean values (X) and standard deviations (SD) were calculated for each metabolite.

Results and Discussions

Manganese is involved in many enzymatic processes, as synthesis of fatty acids and cholesterol, mucopolysaccharide synthesis (in bones, collagen), synthesis of glycoproteins - which coat body cells and protect against invading viruses, synthesis of L-dopamine, synthesis of glucose from non-carbohydrate substances (gluconeogenesis), and others. Many of the metabolic functions – in which manganese is an important cofactor – can use magnesium and manganese interchangeably (www.superlife.co.uk/healthlife.htm; Expert Group on Vitamins and Minerals Meeting, Review of Manganese, 2002).

Generally, manganese is not a toxic element, but if it is inhaled as powder, can become toxic for organism. Manganese is considered the less toxic element when is orally administrated. The quantum of absorbed manganese is smaller when is administrated as manganese chloride, sulfate or oxide compared to manganese citrate, gluconate, ascorbate or aminoacid chelates. Manganese administrated as Mn^{2+} is more toxic then Mn^{3+} for organism. Also, the absorption of manganese is inversely related to the level of iron and calcium in the diet. Usually, highest tissue concentrations of manganese are found in the liver, kidney, pancreas, and adrenals (European Commission, Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Manganese, 2000).

After gavage administration of $MnCl_2$ solutions, for a short period of time, we observed an increase of blood glucose level in experimental rats (Table 1).

Experimental researches using Wistar strain rats showed that gavage ingestion of manganese over-doses rise the concentration of blood glucose in relation with the administrated doses.

Other studies in this field presented that manganese excess is used for diabetic persons because its hypoglycemic effect in time. Diabetic people have low concentration of manganese in blood. Manganese supplementation (3 – 5 mg manganese daily) for a long period of time caused severe hypoglycemia at insulin-dependent diabetic people. Other reports showed that manganese supplementation had no effect on blood glucose level (Rubenstein et al., 1962).

Cholesterol, Triglycerides and Glucose Concentration after Manganese Excess in Wistar Rats

Table 1. Concentration of blood glucose level in rats after an excess of manganese.

Specification	n	Serum concentration of glucose (mg / dL)
		$\bar{X} \pm DS$
Group C	10	158.44 ± 45.75
Group E ₁	10	174.25 ± 56.57
ΔX_1		+ 15.81
Group E ₂	10	202.60 ± 46.94 ^{**}
ΔX_2		+ 44.16

n – number of experimental animals; ** P < 0.01.

Our results showed that, in a very short period of time, gavage ingestion of manganese in excess has hyperglycemic effect. The mechanism of this process could take in view the period of time from ingestion to the moment of quantitative analyses, the presence of other substances from water and food, the chemical form of administered manganese, and doses of administered manganese. Also, other experimental studies demonstrated that excess of manganese altered the carbohydrate metabolism with variation of blood glucose level.

The increase of glucose concentration in blood for experimental animals compared to control animals was gradually, thus for E₁ group after administration of MnCl₂ solution with RDIx2 manganese concentration, the glycemia rise with 15.81mg/dL, but for rats from E₂ group after MnCl₂ administration with RDIx4 manganese concentration, the glycemia rise with 44.16mg/dL.

Baly and his work group in 1985 found that Sprague-Dawley strain rats had high blood glucose level after 2 hours from intraperitoneally injection with 40 mg manganese/Kg b.w. (administered as manganese chloride). The increased blood glycemia was associated with a decrease of plasmatic insulin. This was caused by manganese distribution in tissues, because manganese was rapidly concentrated in pancreas (after 15 minutes) and liver (after 45 minutes). In 1990 the same work group demonstrated that manganese

deficiency influences the glucose transport in blood and of course, the homeostasy of glucose (Baly et al., 1990).

But, administration of manganese chloride also modifies the lipidic anabolism and catabolism, with modification of biochemical blood tests. Thus, we evaluated the concentration of blood cholesterol and triglycerides in experimental rats (Table 2).

Table 2. Cholesterol and triglycerides concentration in rats blood after manganese excess

Specification	Serum lipid concentration (mg / dL)			
	n	Cholesterol	n	Triglycerides
		$\bar{X} \pm DS$		$\bar{X} \pm DS$
Group C	10	55.60 ± 8.63	10	98.80 ± 18.04
Group E ₁	10	56.40 ± 15.56	10	63.40 ± 21.93*
ΔX_1	+ 0.80		- 35.40	
Group E ₂	10	61.20 ± 15.05	10	48.00 ± 14.39**
ΔX_2	+ 5.60		- 50.80	

n – number of experimenta animals; * P < 0.05; ** P < 0.01.

Experimental results for manganese administration in excess for E₁ animals demonstrate that seric cholesterol level increases compared to concentration of cholesterol in control animals from 55.6 to 56.4mg/dL, respectively with 1.44%. But at a double concentration of manganese (RDIx4) in E₂ group, the cholesterol blood level is higher than for E₁ rats (from 55.6 to 61.2mg/dL, respectively 10.07%).

In the case of triglycerides quantum in blood we observed that an excess quantum of manganese induces a decrease of triglycerides blood level for bouth experimental groups of animals.

Researchers demonstrated that metabolic processes involved lipids are influenced by the presence of manganese. The cholesterol and fatty acids (compounds of triglycerides) synthesis need manganese, but over-doses or low quantum modify the concentration of these lipids in blood and different organs.

Cholesterol, Triglycerides and Glucose Concentration after Manganese Excess in Wistar Rats

Manganese being necessary in cholesterol and fatty acids synthesis, is also important to sex hormone formation and thus its involved in normal sexuality and reproduction too (Haas, 1992). In optimal supplements manganese can help lower high cholesterol and triglycerides, stabilizing LDL cholesterol and decreasing its atherogenic potential to create blockages (<http://www.herbalhut.com/.htm>).

One study of Jenkins and Kramer (1991) using preruminant calves assessed the manganese excessive effect on plasma, heart and liver lipids. For this the calves were fed with milk replacer containing 40ppm Mn for control animals, and two high doses of 200ppm and 1000ppm Mn for experimental animals. For both two higher Mn intakes there was no effect on lipid classes in liver and heart, except for elevated triglycerides in liver and lower sphingomyelin in heart in the case of calves fed with milk replacer containing 1000ppm of Mn. Also, at 1000ppm of Mn intake and not at 200 ppm, obvious increases occurred in plasma total lipids, phosphatidylcholine, cholesterol, cholesterol esters, sphingomyelin, and triglycerides. The authors suggesting that very high excess of Mn interfered with hepatic desaturation and elongation of the essential fatty acids.

Conclusions

Manganese is an essential element for human and animal organism. Many metabolic processes need manganese and several diseases have been associated with deficiency or excess of manganese. Researchers try to establish the border between manganese essentiality and toxicity, and also they try to explain the mechanisms of action having in view the causes and effects.

Followed the experimental results we can conclude that the effects of over-doses manganese are influenced by the experimental animals, the concentration of administrated manganese, chemical form of manganese, administration method, and the period of time for the experiment.

After excess of manganese gavage ingestion as $MnCl_2$ for a short period of time, the blood glucose level is increased for experimental animals compared to control, in relation with administrated doses. Also, concentration of cholesterol is higher after ingestion of

manganese over-doses, while triglycerides blood level decrease in experimental rats compared to control rats for a short-term experimental period.

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Cholesterol, Triglycerides and Glucose Concentration after Manganese Excess in Wistar Rats

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