Distribution of Nickel in Rat Organs after an Administration of Nickel (II) Chloride

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Abstract
The aim of this study was to find the distribution of nickel chloride (II) in selected rat organs after an experimental administration. Forty Wistar male rats were divided into three experimental and one control groups (10 rats each). Animals in group A were intraperitoneally dosed with NiCl2 at a single dose of 25 mg/kg b.w., in group B with 35 mg/kg b.w., and killed 48 hours after nickel (Ni) administration. Rats in group P were dosed orally with Ni (100 mg/l) in drinking water for 90 days. Ten males served as the control group (C) without Ni administration. Distribution of Ni was evaluated in kidneys, muscle (m. quadriceps femoris), liver and testis by electro thermal atomic absorption spectrophotometry. The significant increase in Ni concentration was found in the kidney in group A ($p<0.05$) and group B ($p<0.001$) when compared with control. Significantly lower level of nickel was found in muscle in group B ($p<0.05$) and group P ($p<0.01$) in comparison with the control one. The testis level of nickel significantly increased in group B ($p<0.05$) in comparison with controls. The nickel levels in liver were not significantly changed. The results indicate that kidney is the organ with the highest level of nickel. However, elevated nickel levels in testis may suggest the relation between the metal and reproductive functions in males.

Keywords: distribution, nickel, organs, rat

1. Introduction

Nickel (Ni) is the 24th most abundant element and the earth's core is composed of 6 % of this metal. It is used in stainless steel products, nickel plating, to color ceramics, in batteries and other industrial applications [1]. Anke et al. [2] discussed the nickel essentiality for living systems and stated that low nickel offers reduce growth particularly during an intra-uterine development. Nickel deficiency is accompanied by histological and biochemical changes and reduced iron resorption and leads to anemia. Nickel therefore performs a vital function in metabolism. However, the increasing utilization of heavy metals in modern industries leads to an increase of nickel in the environment. Nickel accumulation in the environment may represent a serious hazard to human health. Food is the major source of exposure to nickel but only about 1% is absorbed after the nickel intake in food. A human study shows that 40 more nickel was absorbed from the gastrointestinal tract when $NiSO_4$ (nickel sulphate) was given in the drinking water than when it was given in food [3]. When administered in water, significant elevations in nickel levels were found in the small intestine of mouse after 8 weeks of exposure. In the kidneys, the nickel levels were only significantly higher than controls after 20 weeks of administration [4]. Nickel concentrations in Atlantic salmon muscle and gills exposed to metal mixture (Cu, Zn, Ni, Cr, Cd, Pb) significantly increased [5]. Organs as the gonads,

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bones, and brain may show high metal levels, while the muscles, comparing to the other tissues, usually show low concentrations of metals but are often examined for metal content due to their use for human consumption [6].

Toxic effects depend on the chemical species, their physical form as well as on their concentration and exposure pathway. The most common harmful health effect in the general population is allergic contact dermatitis elicited by prolonged skin contact of sensitized individuals with nickel [7]. Nickel also causes lung fibrosis, kidney and cardiovascular system damage, reproductive toxicity and carcinogenesis [8-13].

2. Materials and methods

Forty males of Wistar rats were divided to four groups, nickel-treated groups (A, B and P) and control group (C), each containing 10 males. The males were housed in a plastic cages and kept under standard animal room conditions at 12:12 light/darkness regime and 22°C±2 of temperature and 55%±10 of relative humidity in an accredited experimental facility (SK PC 50004), handled in accordance with the standard guide for the care and use of laboratory animals. The animals had unlimited access to drinking water and feed. The rats in the nickel–exposed groups A and B were dosed intraperitoneally with a single nickel dose of 25 and 35 mg $NiCl_2$/kg bw, respectively. Rats in group P were given drinking water treated with $NiCl_2$ at the concentration of 100 mg/L for three months. Ten males served as the untreated control group without nickel treatment. The rats were sacrificed and dissected and 48 hours (group A and B) after the injection, and after 3 months of peroral intake (P) of nickel, the tissue samples of liver, kidney, muscle (*m. quadriceps femoris*) and testis were taken for Ni analysis. Nickel levels in tissues were measured using the electrothermal atomic absorption spectrophotometry (Varian SpectrAA 20 BQ GTA 96) in EL s.r.o. (Spisska Nova Ves, Slovakia). From final data, basic characteristics were calculated (mean, standard deviation, coefficient of variance) and analysis of variance between the groups by Scheffe test was completed by using statistical software SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

3. Results and discussion

The results of the analyses of the kidneys, liver, testis and muscle samples are summarized in tables 1 to 4. We have found the highest nickel amount in kidney after the intraperitoneal administration. Liver, kidney and gonads are extremely sensitive to concentrations of contaminants which already at a low dose exhibit structural change or functional disorders [14]. The average content of nickel in group B significantly increased ($p<0.001$) when compared to control group. The difference between group A and the control one was also statistically significant ($p<0.05$). Nickel level in kidney of group P with the per oral administration of nickel in comparison with group of higher Ni dose (group B) was also significantly lower ($p<0.001$) (Table 1).

Ishimatsu et al. [15] point to the fact that after 24 hours, 10-34% of a single per oral dose of nickel is absorbed. The highest concentrations were recorded in the lungs and the lowest amount in the liver and kidney. The authors state that 80-90% of the total quantity of nickel accumulated in the body appeared in the kidney. The authors further argue that the transfer and distribution of nickel compounds applied *per os* is very closely related to the solubility of compounds of nickel which decreases in the following order: $[Ni(NO_3)_2 > NiCl_2 > NiSO_4] >> [NiS > Ni_3S_2] > NiO$. In our experiment, nickel chloride has been used and it is well soluble. Solubility of nickel compounds is the most important factor which determines the harmful effect of nickel in the animal organism.

In the long-term experiment (group P) we have seen a lower nickel level in the kidney. Our results do not correspond with the results of Severa et al. [16]. Authors found the highest concentrations of nickel in liver during the per oral application of nickel sulphate. In males the levels decreased as follows: liver>kidney>blood (serum, plasma) >testes and in females: liver>kidney=blood =serum=plasma>urine>ovaries.

Muscle tissue, or meat, is an essential part of the human diet. In this respect, it is important to monitor the contents of xenobiotics in the muscles. On the other hand, the muscle does not represent a high risk in terms of affecting the health of consumers because it is not characterized by the high bioaccumulation of metals [6, 18].

As can be seen from table 2, the analysis of muscle samples showed that the nickel levels in

all experimental groups was lower than that of the control group. A significant decrease in the levels of nickel was found in groups B ($p<0.05$) and P ($p<0.01$) when compared to control. Svobodová et al. [19] analyzed the contents of Cd, Pb, Cr, Ni and Cu in the muscle tissue of carp. The measured values were below the limit except of nickel. The nickel content was above 0.5 mg/kg.

The lowest levels of nickel have been found in the liver (Table 3). A slight, insignificant increase in the liver concentration of nickel was found in the group with higher nickel intraperitoneal dose (group B), and decrease in groups A and P in comparison with the control one. Our results are identical to the results of Obone et al. [17] who found the highest values in the kidneys, the lowest levels in testicles, lungs brain, spleen and the lowest values in liver after the application of 0.1% solution of the NiS (223.5 mg Ni/L). The study which investigated metal contamination in cattle offal from an agricultural area in Zambia, where inorganic fertilizers, agricultural lime, and pesticides are routinely applied, recorded 0.594 mg/kg in the liver [21]. The results are similar to those in our experiment in group B (0.54 mg/kg) and the control (0.50 mg/kg). The nickel content in the testes is shown in table 4. The single intraperitoneal administration of 35 mgNi/kg bw caused the significant increase in metal concentration in testis of experimental rats when compared to that of the control. Per oral administration of nickel did not change the nickel level in the testis as we have found the same Ni level like in the control testes. The metal amount in testes of rats in per oral group (P) was significantly lower than in group with the higher Ni dose (group B). Severa et al. [16] and Obone et al. [17] point out that the testicles belong to the organs in which the accumulation of nickel does not appear. Contrary to these findings, Sunderman et al. [3] noted in a higher accumulation of nickel in testes than in the liver. The results obtained in our experiments are in accordance with the findings of these authors, because acute exposure to nickel has increased the accumulation of this metal in the testis and its level ranged from 0.22 to 0.61 mg/kg depending on the dose and method of administration. As a result of dietary supplementation of 50 and 500 mg Ni/kg to rabbits, Ni accumulated in the kidneys (4.9 and 17.1 vs. 1.9 mg/kg), ribs (10.3 and 10.4 vs. 9.1 mg/kg), heart (1.4 and 2.5 vs. 1.0 mg/kg) and liver (1.3 and 2.2 vs. 0.9 mg/kg), as compared to the control animals [20].

Table 1. Nickel concentrations in kidney (mg/kg)

Group	X±SD	Differences
Control	0.17±0.12	
A (25 mgNi/kg bw, i.p.)	2.48±83	A:C*
B (35 mgNi/kg bw, i.p.)	9.71±4.45	B:C***, B:A***
P (100 mgNi/L)[1]	0.24±0.14	P:B***

[1]$NiCl_2$ administered in drinking water, i.p.=intraperitoneal administration

* $p<0.05$, *** $p<0.001$, X - arithmetic mean, SD-standard deviation

Table 2. Nickel concentrations in muscle tissue (mg/kg)

Group	X±SD	Differences
Control	1.18±0.79	
A (25 mgNi/kg bw, i.p.)	0.83±0.42	NS
B (35 mgNi/kg bw, i.p.)	0.29±0.09	B:C*
P (100 mgNi/L)[1]	0.20±0.12	P:C**

[1]$NiCl_2$ administered in drinking water, i.p.=intraperitoneal administration

* $p<0.05$, ** $p<0.01$, X-arithmetic mean, SD-standard deviation, NS=not significant

Table 3. Nickel concentrations in liver (mg/kg)

Group	X±SD	Differences
Control	0.50±0.34	
A (25 mgNi/kg bw, i.p.)	0.29±0.16	NS
B (35 mgNi/kg bw, i.p.)	0.54±0.20	NS
P (100 mgNi/L)[1]	0.30±0.21	NS

[1]$NiCl_2$ administered in drinking water, i.p. intraperitoneal administration

X-arithmetic mean, SD-standard deviation, NS=not significant

Table 4. Nickel concentrations in testis (mg/kg)

Group	X±SD	Differences
Control	0.22±0.19	
A (25 mgNi/kg bw, i.p.)	0.38±0.25	NS
B (35 mgNi/kg bw, i.p.)	0.61±0.19	B:C*
P (100 mgNi/L)[1]	0.22±0.17	P:B*

[1]$NiCl_2$ administered in drinking water, i.p.=intraperitoneal administration
* $p<0.05$, X-arithmetic mean, SD-standard deviation, NS=not significant

4. Conclusions

This study demonstrates the dose- and route of administration-dependent accumulation of nickel in tissues of rats. The highest nickel levels were found after the intra peritoneal administration of metal at a dose of 35 mg/kg bw in the kidneys. The lowest levels of nickel were recorded in testes, muscle tissue and liver. Per oral long-term administration of nickel did not elevate the metal concentration in tissues, suggesting that nickel ingested orally is not accumulated in animal tissues.

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