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Effect of high doses of ochratoxin A (OTA) on magnesium concentration in the skin of experimental animals

Present progress and development of new technologies lead to the occurrence of disturbances in the ecological chain. This is the consequence of the introduction of harmful chemical compounds and biotoxic substances into the links of the ecological chain. What happens is soil impoverishment with elements important for the organism, especially magnesium but also other microelements, e.g. selenium and zinc. As a result, there occur deficits of these elements in nourishment. A low level of magnesium is characteristic of the majority of developed countries (1). It is known, that mitoxins (especially aflatoxins) and nitrosoamines have carcinogenic effect through disturbance in antioxidative processes (1). A decrease in antioxidants, including magnesium, constitutes also a risk of vascular diseases. In the genetic aspect, this risk is also increased by the deficits of α-tocopherol, selenium, taurine, magnesium and other natural antioxidants (9).

Environmental pollution with mycotoxins is becoming one of the most important problems of ecoprophylaxis. One example of these compounds is ochratoxin A (OTA). It is produced among others by the strain *Aspergillus ochraceus* and *Penicillium viridicatum* (15) while storing crops and their products (13) as well as herbs, spices and grapes. It also occurs in fodder presses or in slaughterhouses during the production of pork, especially pluck and sausages (14). Ochratoxin A may occur in beer, wine and coffee (6, 7). OTA has a nephrotoxic, carcinogenic and immunotoxic effect (14, 15). Researchers look for compounds that could minimize the harmful effect of OTA. It seems that such a compound could be aspartame, which acts both *in vivo* and *in vitro* (6).

In previous studies of experimental animals we have found that administration of magnesium chloride caused a decrease in the concentration of chromium Cr^{6+} in the skin (4), which is a strong carcinogen with exposed animals. Following this trail, we were also conducting further observations of the magnesium concentration in the skin, depending on the OTA dose and the dose of the administered magnesium chloride (3, 5). These observations used very high, daily (d) doses of OTA, i.e. 1 mg/kg^{-1} of body mass and low doses of $MgCl_2$ – 5 mg/kg^{-1} b.m. Such concentration of $MgCl_2$ is the best tool to determine magnesium deficits during its oral administration (8).

MATERIAL AND METHODS

The experiment was conducted on male rats of the Wistar race weighing 150–170 g. For the period of 30 days the exposed group II was orally administered OTA in the dose of 1 mg/kg^{-1} b.m. The next group, group III received OTA in the same high dose, but apart from that animals were given $MgCl_2$, also orally, in the dose of 5 mg/kg^{-1} b.m.. In the control group I the animals were given vehiculum. On completion of the experiment the animals were decapitated and the obtained skins were defatted and mineralized. The element was denoted by the method of spectrophotometry of atomic absorption on apparatus AAS-3 (10). Statistical data were worked out by the t-Student test. The results are shown in Table 1.

Table 1. Magnesium concentration in the skin under the influence of high doses of ochratoxin A (OTA)

30-day experiment	Studied groups		
Group number	I	II	III
Application type	control	OTA	OTA + $MgCl_2$
Daily doses/body mass	0	1 mg/kg^{-1}	1 mg/kg^{-1} + 5 mg/kg^{-1}
Mg concentrations in the skin μg/g^{-1}	262.8 ± 20.9	346.9 ± 16.5	277.1 ± 10.7
Trial number	11	12	13
Statistical significance vs. control* group II vs. /III^{o}	-	$p< 0.001^{*o}$	ns* $p< 0.001^{o}$

*No significance

RESULTS

The results of the conducted observations are shown in Table 1. The concentration of magnesium in the skin of animals from the control group I was 262.8 ± 20.9 μg/g^{-1}. After administration of OTA in the concentration of 1 mg/kg^{-1} b.m. for 30 days, the magnesium concentration in the skin tissue of the exposed group II (OTA) reached the value of 346 ± 16.5 μg/g^{-1} and it was significantly higher than in the control group I ($p<0.001$). With simultaneous OTA application in the concentration of 1 mg/kg^{-1} b.m., and b.m. in the group III (OTA + $MgCl_2$), the concentration of magnesium in the skin of animals from the group III (OTA + $MgCl_2$) was higher (not significantly) than the concentration of this element in the control group I, and it was significantly lower than the concentration of magnesium in the group II, exposed only to OTA ($p<0.001$).

DISCUSSION

In previously conducted experiments (5) it was found that exposure to low doses of OTA 25μg/kg^{-1} body mass, caused a significant increase in magnesium concentration in the skin of exposed animals ($p<0.02$). Simultaneous administration of $MgCl_2$ in the dose of 5 mg/kg^{-1} b.m . and OTA in the concentration 25 μg/kg^{-1} b.m. caused a slight increase in the magnesium concentration in the skin, statistically insignificant for the control group. Whereas administration of medium doses of OTA i.e. 50μg/kg^{-1} b.m., using the same procedures during the experiment, caused a significant ($p<0.001$) increase in magnesium concentration in the skin of rats – experimental males (3). Simultaneous application of higher doses of magnesium chloride (than in this study), i.e. 250 mg/kg^{-1} b.m. and simultaneously of OTA 50 μg/kg^{-1} b.m. caused (3) statistically significant lowering of magnesium

concentration in the skin ($p<0.05$). simultaneous administration of OTA 50 $\mu g/kg^{-1}$b.m. and vitamin E 100 mg/kg^{-1} b.m. also caused significant lowering of magnesium concentration in the skin of experimental animals (3). In other research it was found that administration of sex hormones and vitamin E in the dose of 100 mg/kg^{-1} b.m., was reducing the effect of hormone activity and it was lowering the magnesium concentration in tissues (12).

It is not clear why during administration of OTA in small doses 25 $\mu g/g^{-1}$ b.m. to experimental animals, there is lowering of magnesium concentration in kidneys, liver and brain (11). Perhaps this is related to the time of OTA deposition in the organs. Isotope ^{14}C-OTA is maintained in the blood and skin of experimental animals (2).

CONCLUSIONS

1. In the group of male rats exposed to high doses of ochratoxin (OTA) 1 mg/kg^{-1} b.m. for 30 days, there is a significant increase in the magnesium concentration in the skin, in comparison to control.

2. Exposure to high doses of OTA with simultaneous supplementation with small doses of magnesium (5 mg/kg^{-1} b.m.), causes statistically insignificant increase in the magnesium concentration in the skin in comparison to control group.

3. Magnesium concentration in the skin of animals exposed to OTA is significantly higher than with rats, which apart from OTA were at the same time given magnesium chloride in small doses.

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SUMMARY

Oral administration of high toxic doses 1 mg/kg^{-1}/b.m. of ochratoxin A (OTA) for 30 days to male rats of the Wistar race, caused a significant increase in magnesium concentration in the skin. Simultaneous application of OTA in the same dose, during the same period with simultaneous oral supplementation of $MgCl_2$ 5 mg/kg^{-1} b.m., caused an insignificant increase in magnesium concentration in the skin. However, it was significantly lower than in the group which was given only OTA. Magnesium values in both studied groups were higher than in the control group. However, only the magnesium concentration in the skin of animals exposed only to OTA, was higher in comparison to the control group and it significantly differed statistically ($p<0.001$).

Oddziaływanie wysokich dawek ochratoksyny A (OTA) na stężenie magnezu w skórze zwierząt doświadczalnych

Podawanie wysokich toksycznych dawek 1 mg/kg^{-1}/m.c. ochratoksyny A (OTA) doustnie w okresie 30 dni samcom szczurów rasy Wistar powodowało istotny wzrost stężenia magnezu w skórze. Aplikowanie OTA w tej samej dawce w tym samym okresie przy suplementowaniu doustnym $MgCl_2$ 5 mg/kg-^{1} m.c. powodowało nieistotny wzrost koncentracji magnezu w skórze szczurów. Była ona jednak znamiennie niższa niż w grupie, w której podawano tylko OTA. Wartości magnezu w obu badanych grupach były wyższe niż w grupie kontrolnej. Jednakże tylko stężenie magnezu w skórze zwierząt eksponowanych wyłącznie na OTA było wyższe w stosunku do grupy kontrolnej i różniło się znacząco statystycznie ($p<0,001$).