INFLUENCE OF ZEARALENONE ON PLASMA CATECHOLAMINES IN RABBITS

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Abstract

The effect of low dose (10 ng/kg b.w.) of mycotoxin zearalenone on plasma catecholamine levels in female rabbits was studied. The toxin was administrated orally for 14 d in a dose of 10 ng/kg b.w. A significant increase in dopamine, norepinephrine and epinephrine levels was observed at 24 and 72 h after the mycotoxin administration. The increase in epinephrine level lasted for 336 h until it returned to the control values. It may be concluded that the mycotoxin changes the levels of plasma catecholamine in female rabbits by oestrogenic effect.

Key words: rabbits, catecholamines, zearalenone.

Mycotoxins are a diverse group of relatively small molecules produced by fungi. They elicit a wide range of toxic responses in animals and humans (2, 4). In farm animals, mycotoxin contamination reduces growth efficiency, lowers feed conversion and reproductive rates, impairs resistance to infectious diseases, reduces vaccination efficiency, and induces pathologic damage in the liver and other organs (2, 3). Studies on structure, activity, and relationship among F2 toxins provide information how one of them - zearalenone interacts with oestrogen receptors (10).

Catecholamine level in the blood plasma reflects the activity of the adrenergic nerve system. Both the norepinephrine and dopamine are released from the presynaptic endings of vascular neurons of the sympathetic system and from the adrenal gland (12). F2 toxin belongs to the toxins with strong oestrogenic effect. Its higher doses can intervene in the course of ovulation, implantation and foetal development. Considering our previous works (7, 8), where we found pronounced changes in plasma catecholamines after hyperoestrogenization, we have intended to study the oestrogenic effect of zearalenone on the grounds of changes in blood plasma catecholamines in rabbits.

Material and Methods

Thiry 1-year-old female Chinchilla giant rabbits, weighing 3.4 ± 0.5 kg were used in the experiment. Experimental animals were divided into 3 groups. The control intact group (n=10) was given 1 ml of sterilized distilled water by a probe. The first experimental group (n=10) was administrated daily 10 ng/kg b.w. of zearalenone (Sigma) in 1 ml/kg b.w. of 8% ethanol by a probe per os. To eliminate the effect of ethanol, the „sham“ control group was (n=10) given only 1 ml/kg b.w. of 8% ethanol by the same way. Blood was collected from the v. auricularis marginalis before the first administration (0 h) and then at 24, 72, 168 and 336 h of the experiment. The blood testing was carried out in the same time in the morning. Glutathion was used as an antioxidative agent (0.05 mol.l⁻¹) and the tubes were centrifuged at 4°C for 20 min. The clear unhaemolysed plasma was stored for short time at -70°C until processed. Catecholamines were determined in duplicate samples by the radioenzymatic method according to Johnson et al. (5) using 50 nM of plasma. The radioactivity of catecholamine derivatives was measured on scintillating spectrophotometer Packard Tri Carb in ¹¹C H canal. The sensitivity of the method was from 0.37 to 4.00 pmol.ml⁻¹ for norepinephrine and epinephrine and from 0.53 to 4.00 pmol.ml⁻¹ for dopamine. A coefficient of variation for dopamine was 4.1% and 4.2% for norepinephrine and epinephrine. The levels of catecholamine in the blood plasma were expressed as means ± S.E.M. and statistically evaluated by the unpaired t-test.

Results

The rabbits receiving F2 toxin (Fig. 1) had significantly higher levels of dopamine (P < 0.001) 24 and 72 h after the administration of the toxin in comparison with the intact and „sham“ control groups. At other time intervals, the levels remained on a significantly higher level compared to control values (P < 0.05). Norepinephrine (Fig. 2) increased markedly at
24 h (P < 0.001) and 72 h (P < 0.01) after application of zearalenone. At 168 h and other time intervals, it remained on the elevated levels compared to the control values (P < 0.05). No marked differences were found between the „sham” control and intact control groups in plasma norepinephrine and dopamine contents. Epinephrine (Fig. 3) showed a different time dependence: it increased at 24, 72 and 168 h after application of F<sub>2</sub> toxin, and the increase lasted for 336 h until it returned to the control values.

**Fig. 1.** The effect of zearalenone on the levels of plasma dopamine in control samples from the intact (IC) and „sham” (SH) control rabbits at 0, 24, 72, 166 and 336 h (E) after zearalenone administration (n = 15). The results are given in p.mol.ml<sup>-1</sup>. Significant differences: ** P < 0.001; * P < 0.01
IC – 1 ml of distilled water; SH – 1 ml of 8% ethanol/kg b.w.; E – 10 g of F<sub>2</sub>/kg b.w.

**Fig. 2.** The effect of administration of F<sub>2</sub> toxin on the levels of plasma norepinephrine in control samples from the intact (IC) and „sham” (SH) control rabbits at 0, 24, 72, 166 and 336 h (E) after zearalenone application (n = 15). For other details see Fig.1.

**Fig. 3.** The effect of administration of zearalenone on the levels of plasma epinephrine. For other details see Fig.1.

**Discussion**

Mycotoxin represents one of negative factors influencing health of animals. The effect of aflatoxins and ochratoxins are quite well known. Recently, in tense attention has been paid to fusariotoxins including zearalenone. Even low doses (1 ppm) of this toxin lead to fertility disorders in swine and cattle (2, 10). Higher doses (50 – 100 ppm) affect conception, ovulation, implantation, foetal development, and viability of newborns (13).

Blood catecholamines participate in the regulation of some physiological mechanisms and represent a sensitive indicator of release of norepinephrine and epinephrine from synaptic neurons and adrenal glands and reflect the activity of the peripheral adrenergic system. The release of catecholamines as the hormones from adrenal glands causes increase in their levels in blood (12).

Changes in levels of plasma catecholamines (14) may reflect transient (physical and psychical stress, action of some short-acting medicines) or permanent changes (hypertension, diabetes mellitus, circulatory or tumourous growth) and the condition of adrenergic receptors of blood capillaries and the heart. The levels of plasma catecholamines in females are significantly affected by the phase of natural oestrous cycle, the phase of controlled oestrous cycle after application of hormonal superovulatory preparations (7, 8), or at the parturition (11). A marked increase in levels, particularly of norepinephrine and dopamine during ovulation (P < 0.001), was recorded in our experiments (8, 9). After application of zearalenones in female rats, there were observed constant oestus, pseudopregnancy and infertility (13). Zearalenones act as oestrogens because they are able to adopt a conformation which sufficiently resembles 17β-Estradiol and other natural oestrogens contract permits binding to the oestrogen receptors. The exposure of laboratory animals to various stressful situation results in many times increased
catecholamine content in circulating blood, excretion of catecholamines to urine and expression of sources by catecholamines synthesizing enzymes in the adrenal medulla as well as in the peripheral sympathetic ganglia (12). The effect of mycotoxins on the central and peripheral catecholaminergic system has been studied to relatively small extent. According to Chi et al. (1), mycotoxin is a stressor which alters the dynamics of changes in catecholamines in the blood of turkeys. Various acute stressful stimuli have been shown to alter catecholamine dynamics. Mycotoxins caused inflammation, contact erosion, and irritation which can be considered as the chemical stress. Acute temperature stress increased the turnover rate of catecholamines in turkeys (1).

The administration of zearalenone in our experiment had a more pronounced effect on plasma dopamine which showed a significant increase (P < 0.001) at 24 and 72 h after its administration. The increase in dopamine and norepinephrine concentration observed in plasma of sheep 24 and 72 h after the administration of F1 toxin is considered to be related to the increase in oestrogens in the plasma at the given time (8, 9). This suggestion is supported by findings of Miyake et al. (6) who reported changes in the levels of catecholamines in the plasma of women after direct administration of oestrogens. From our results and from the literature data (1) we can conclude that the short-term oral administration of zearalenone causes damage to peripheral adrenergic system which is involved in the regulation of some endocrine processes.

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References