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Inoffensivity of imupurin in pregnancy

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Abstract

Background: Determination of imupurin inoffensivity on embryogenesis, organogenesis and teratogenesis in rats.
Material and methods: The study of immupurin's safety during pregnancy was performed on 60 rats, divided into 4 groups. Animals from the control group were given 2 ml of physiological solution (NaCl, 0.9%), and those from the experimental groups – 2 ml of imupurin suspension, internally, 1000 mg / kg in different periods of pregnancy, to investigate embryotoxic, teratogenic and fetotoxic effect. The fetuses were monitored during the postnatal period, from birth to the age of 2 months, with appreciation of the physical development, the behavior and coordination of newborn movements, the evolution of body mass in dynamics, the teeth eruption, the appearance of the hair cover, the opening of the eyes, the ability to feed individually after removal from the female.
Results: The studies have shown that the pre-implantation and post-implantation indices in the control group were 4.1 and 3.8 respectively, and in experimental groups were 4.4 and 3.3. The number of live fetuses in the investigated groups was 12.1±1.5, which did not differ from the control group, whose live fetuses were 12.3±1.9. Postnatal period indices (teeth eruption, hair cover, and eye opening) were similar in all investigated groups and corresponded to the age of the rats.
Conclusions: Imupurin has been shown to have no embryotoxic, fetotoxic and negative effects on the postnatal period and may be recommended in pathologies accompanying pregnancy.

Key words: entomotherapy, imupurin, fetotoxicity, pregnancy embryotoxicity.

Introduction

Pathologies of allergic and immune genesis are nowadays widespread due to advanced technologies, also of using synthetic substances in the pharmaceutical, food and agricultural industries, and immunomodulatory drugs become a goal for many researchers [1, 2]. The fact that insects can produce substances that modulate the basic mechanisms of human immunity has been the basis for the synthesis from insects of new preparations with different pharmacological properties such as entomological preparations [3, 4, 2, 5], which by their lipoprotein and polysaccharide composition can be considered as compounds with an important immunostimulatory potential [6, 7].

Imupurin, an entomological preparation obtained from butterflies, species *Lepidoptera*, the *Lemantria* family [6, 3, 4] , due to the immunogenic amino acids and oligopeptides from its composition possesses marked immunomodulatory properties that are capable to stimulate immune system [7,8,9] . It is recommended for complex treatment of pathologies developed due to immune system disorders [8, 9, 10].

Pregnancy, physiological condition characterized by additional efforts of woman's immunity [11], which on the one hand must adapt to the new conditions of embryo and fetus presence, on the other hand, the immune system must provide effective protection against infections or reactivation of existing pathologies of the mother [12]. It is important to remember that pregnancy pathologies and a range of illnesses occurring during pregnancy evolve with more peculiarities and require medical treatment that needs double attention because the drugs can act on both the mother and the fetus [13]. In these situations, preparations which do not possess embryotoxic, fetotoxic or teratogenic effects are preferred.

Based on the above, we intend to investigate the embryotoxic, fetotoxic and teratogenic properties of imupurin in view of its inoffensivity in pregnancy [14].

Material and methods

Investigations of embryotoxicity, fetotoxicity and teratogenicity of imupurin were performed according to contemporary recommendations [15,16].

In the study were used 60 matured, reproductive age albino rats with a mass of 170-230 g, divided into four groups.

The studied substance (imupurin) was given endogastral, 1000 mg per kg. The frequency of administration was once daily at the same time, according to the following schedule: Group No 1 was intact and served as a control; they were given the saline sol. NaCl, 0.9% – 2 ml, internal use. The females from the group No 2 received imupurin from the 1st the day of pregnancy to the 6th, group No 3 – from the 6th day to the 16th, group No 4 – from the 16th day to the 20th day (tab. 1). Animals were monitored daily.

Table 1

Groups	Days of administration			
	Amount of the administered substance (mg) in suspension in 2 ml volume	1-6	6-16	16-20
I (control) (24 rats)	2 ml of saline solution, NaCl, 0.9%	+	+	+
II (12 rats)	Imupurin 1000 mg per kg	+	-	-
III (12 rats)	Imupurin 1000 mg per kg	-	+	-
IV (12 rats)	Imupurin 1000 mg per kg	-	-	+

Postnatal development of newborns was studied 24 hours from birth to 2 months old, and were appreciated the physical development, newborns behavior and movements coordination, evolution of body mass in dynamics, teeth eruption, the appearance of the hair cover, the opening of the eyes, the ability to feed individually after removal from the female 25 days after birth.

Results

The supervision of animals during experiences has not found deviations of behavior during pregnancy in females included in the study, compared with the control group. After imupurin administration, the rats became more active for 10 minutes, with subsequent behavioral restoration, feeding and use of water was common without differentiation from the control group. Examination of the skin, mucous membranes and hair cover did not show pathological changes. Once every 7 days they were weighed. The body weight of females on the average increased to 30 g in all groups. On the 20th day the animals were euthanized by dislocation of the cervical vertebrae and were determinated the following indices: embryonic mortality in pre- and post-implantation periods, developmental malformations, general retention of the development of the fetuses. Pre-implantation mortality was determined by the difference between the number of yellow bodies in the ovaries and the number of places implanted in the uterus. Later we determined the post-implantation index – by the difference between the number of implanted places and the number of live embryos.

The analysis of the investigated indices did not reveal significant deviations in the females from imupurin lots compared to the control regarding the number of yellow bodies, the number of implant sites, the number of live and dead females, the number of resorptions (tab. 2). No significant differences were found between experimental and control groups in mortality determination in the pre-implantation and post-implant period.

The number of newborns from the females who received imupurin corresponds to the number of fetuses born from the control group's females.

Table 2

Influence of imupurin on the embryotoxicity, teratogenicity and fetotoxicity parameters

Investigation indices	Imupurin	Control
Number of pregnant females	26	30
Number of yellow bodies	13.3 ± 1.6	13.9 ± 2.4
Number of implant sites	12.7 ± 1.3	13.3 ± 2.3
Number of live fetuses	12.8 ± 1.5	12.7 ± 1.9
Number of resorbtions	0.2 ± 0.4	0.3 ± 0.5
Number of dead fetuses	0.2 ± 0.4	0.3 ± 0.7
Mortality at preimplantation stage (%)	4.4	4.1
Mortality at postimplantation stage (%)	3.3	3.8
Fetuses weight	3.2 ± 0.29	3.3 ± 0.25

The weight of the fetuses in the investigated groups did not differ from the control and constituted an average of 3.2±0.3. Also, there were no significant differences in the number of fetuses per female, which was 12.1±1.5 in the study groups which received imupurin, once daily, compared to the control group. The mortality cases of the fetuses were few – 3.3% in the investigated group and 3.8% in the control group. Mortality during pre-implantation and post-implantation is not statistically significant (tab. 2).

In all study groups were not detected disturbances in the development of embryo-amniotic fluid which was transparent; fetal membranes were normally developed, well vascularized, without sclerosis. At the opening of the fetal membranes and the umbilical cord section, appeared the spontaneous breath of the fetuses. The skin was rosy, eyes and ears – covered. No external abnormalities of the skeleton and internal organs have been detected in the morphological research of the fetuses.

The postnatal behavior of rats undergoing study did not differ from those in the control group. After euthanasia of newborns, development abnormalities were not detected.

All rats were removed from natural food on the 26th day of life. Adaptation to artificial foods was in the early hours. Analysis of postnatal indices did not reveal significant deviations regarding the detachment of the ear pavilion, the teeth eruption, the appearance of the hair cover, the opening of the eyes (tab. 3).

Table 3

Appearance indices

The studied indices	Time of appearance
Detachment of the ear pavilion	Day 4
Tooth eruption	Day 8
The appearance of the hair cover	Day 11
Opening of eyes	Day 15

Conclusions

1. Entomological preparation did not influence the behavior of pregnant females throughout the pregnancy.

2. Imupurin did not show embryotoxic, teratogenic and fetotoxic properties.

3. The postnatal development of fetuses born to females which have been given imupurin was similar to the animals in the control group.

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