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IMPORTANT REQUIREMENTS FOR STUDYING THE GENERAL TOXIC EFFECTS OF PHARMACOLOGICAL SUBSTANCES

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Abstract: The article provides an overview of methodological recommendations, rules and guidelines for conducting preclinical studies of the general toxic effects of pharmacological drugs based on international requirements for studies.

Keywords: Preclinical toxicological studies, laboratory animals, pharmacological substances, method.

INTRODUCTION: During preclinical toxicological studies, preliminary information about the toxicity of the drug being studied is obtained [1] and these data are used to determine the initial safe dose, dose range for clinical studies, and also to establish parameters for clinical monitoring of potential adverse effects. Significant phenomena and determining the feasibility and risk of conducting clinical trials of a medicinal product.

MATERIALS AND METHODS: Preclinical toxicological studies of pharmacological drugs include the study of general toxic properties and specific types of toxicity (allergenicity, immunotoxicity, mutagenicity, carcinogenicity, reproductive toxicity). The study of general toxic properties is mandatory both for pharmaceutical substances and for all dosage forms of a pharmacological substance, and allows you to solve the following problems:

– establish tolerable and toxic doses of a pharmacological substance;

– identify the organs and systems of the body that are most sensitive to the substance under study, the nature and degree of pathological changes, the reversibility of the damage caused;

– determine the dependence of toxic effects on the dose and duration of use of a pharmacological substance.

RESULTS AND DISCUSSION: There is no universal scope for preclinical toxicology studies, so study designs must be tailored to the specific substances being tested. Conducting toxicological studies in full is mandatory for the substance of the original pharmacological substance. When combining several pharmacological substances in one dosage form (fixed combination), the toxicity of the combination as a whole and each component separately is studied, if it has not previously been approved for use in practice. When changing the method of obtaining a pharmacological substance, a repeated toxicological assessment is carried out on animals of one of the most sensitive species, which is determined based on the data of initial studies [2].

Before conducting toxicological studies, you must have:

– characteristics of a pharmacological substance (draft regulatory documentation), according to which it is identified, limits for impurity content are established, and stability is determined. If the characteristics of a pharmacological substance change (for example, as a result of modification of the production method), it is necessary to evaluate the impact of this change in a comparative aspect with the data obtained from the study of the original substance;

– information on solubility, lipophilicity or hydrophobicity, crystal size of the pharmacological substance, as well as characteristics of solvents (if used),

– data characterizing the therapeutic (specific) activity of a pharmacological substance in an experiment on animals, indicating the type of models used, routes of administration, doses, methods and duration of use.

When conducting research, whenever possible, experiments on living organisms should be replaced by in vitro experiments on isolated tissues or other biological models. When researching

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living objects, it is necessary to minimize the number of animals involved in the study by standardizing experimental conditions, increasing the information content of methodological techniques, and eliminating factors that increase the scatter of experimental data; provide convincing reasons for the need for the planned experimental studies and the impossibility of replacing the animal with any model or alternative object; take the necessary measures to prevent animal suffering; It is imperative to provide proper care for animals, taking into account the peculiarities of their ethology [3].

Acute toxicity is a toxicometric characteristic of a pharmacological substance (or drug), manifested in its ability to cause death in animals with a single administration or when administered at short (no more than 6 hours) intervals during the day. In the process of studying acute toxicity, tolerable, toxic and lethal doses of a pharmacological substance are determined, the cause of death of animals is determined, and the clinical picture of intoxication is described.

The total duration of observation of animals during acute toxicity studies should be at least 2 weeks, and animals should be under continuous observation on the first day after administration. During the experiment, the general condition of the animals, the characteristics of their behavior, the intensity and nature of motor activity, coordination of movements, the presence and nature of seizures, skeletal muscle tone, reaction to tactile, pain, sound and light stimuli are regularly recorded. Frequency and depth of respiratory movements, heart rate, condition of hair and skin, color of mucous membranes, pupil size, tail position, amount and consistency of feces, frequency of urination and color of urine, food and water consumption, change body weight and other indicators that can be used to identify the toxic effect [3].

CONCLUSION: The use of new drugs in veterinary clinical practice presupposes the availability of proven data on their high degree of safety. Therefore, one of the most important stages of research, mandatory for pharmaceutical substances and drugs, is the study of their general toxic effect in preclinical conditions, including: determination of tolerable and toxic doses, identification of the most sensitive organs and systems of the body to the studied substance, nature and the degree of pathological changes, reversibility of the damage caused.

REFERENCES

1. Astakhova A.V., Lepakhin V.K. Adverse side reactions and drug safety monitoring. – M., 2014.
2. Belenky M. L. In the book: Elements of quantitative assessment of the pharmacological effect. – L., 2018.
3. Berezovskaya I.V. Classification of chemical substances according to parameters of acute toxicity for parenteral routes of administration. Chem.-pharm. magazine. – 2013. – T. 37. – No. 3.
4. Zapadnyuk I.P., Zapadnyuk V.I., Zacharia E.A., Zapadnyuk B.V. Laboratory animals. Breeding, maintenance, use in experiments, 3rd ed., revised. and additional – Kyiv: Vishcha School, 2013.