

THE DYNAMICS OF HISTOMORPHOLOGICAL CHANGES IN THE LIVER AFTER ACUTE CLOZAPINE POISONING

*Olga Romanova¹, Dmitriy Sundukov¹, Arkadiy Golubev^{1,2},
Vladimir Goshkoev¹*

¹ Peoples' Friendship University of Russia, Moscow, Russia

² Federal Scientific and Clinical Center for Resuscitation Research
and Rehabilitation, Moscow, Russia

INTRODUCTION. Clozapine is an atypical antipsychotic drug, which is widely used in medicine. It is metabolized in the liver [1,2].

Several studies have shown pathological changes in the liver in case of clozapine poisonings [3,4]. Morphological changes in the liver were studied presumably at late stages of the pathological process.

THE AIM OF THE STUDY. The aim of the study is to reveal morphological changes in the liver in acute clozapine poisoning 3 and 24 hours after the intoxication.

MATERIALS AND METHODS. We performed a comparative study of histological sections of the liver of outbreed male rats weighing 290–350 g. Study group 1 included 5 rats treated with clozapine oral dose of 150 mg/kg and decapitated 3 hours after the intoxication. Study group 2 included 5 rats treated with clozapine in the same dose and decapitated 24 hours after drug administration. Control group included 5 intact animals of the same sex and age. We used Fisher's ratio test to estimate the reliability of the difference between the groups. The presence of the sign was considered to be reliable if the sign didn't appear in one group and appeared in 4 or 5 cases in the other group.

RESULTS. No pathological changes were observed in the group of comparison (controls). 3 hours after clozapine administration we observed the following histological changes: venous plethora. 24 hours after the intoxication we observed venous plethora, which was more severe than 3 hours after the intoxication, lack of hepatocyte nuclei staining, vacuolization of the cytoplasm.

CONCLUSION. All these histomorphological changes among with the histomorphological changes and the results of chemical analysis can be used to diagnose clozapine poisonings and the cause of death. A morphometric analysis of liver tissue is to be performed for more definite diagnostics.

REFERENCES

1. DAIN J.G., NICOLETTI J., BALLARD F. Biotransformation of clozapine in humans. *Drug Metab. Dispos.* 1997; 25 (5): 603–609.
2. MASHKOVSKY M.D. Medicinal products. 16th ed. Moscow: Novaya Volna; 2014: 73–74.
3. ZIMINA L.N., MIKHAILOVA G.V., BARINOVA M.V., PAVLENKO E.YU., POLOZOV M.A., POPOV S.V., ROZUMNYI P.A., ILYASHENKO K.K., ERMOKHINA T.V. Morphological aspects of acute intoxication with Azaleptin. Forensic-medical expertise (Sudebno Meditsinskaya Ekspertiza). 2008; 51 (3): 8–10.
4. ZLATKOVIĆ J., TODOROVIĆ N., TOMANOVIĆ N., BOŠKOVIĆ M., DJORDJEVIĆ S., LAZAREVIĆ-PAŠTI T., BERNARDI R.E., DJURDJEVIĆ A., FILIPOVIĆ D. Chronic administration of fluoxetine or clozapine induces oxidative stress in rat liver: a histopathological study. *European Journal of Pharmaceutical Science.* 2014; 59 (1): 20–30.