

CLOZAPINE DISTRIBUTION IN ACUTE CLOZAPINE POISONING

**O.L. Romanova, D.V. Sundukov, A.M. Golubev,
M.L. Blagonravov**

*Peoples' Friendship University of Russia (RUDN University), Moscow,
Russia*

*V. A. Negovsky Research Institute of General Reanimatology,
Federal Research and Clinical Center of Intensive Care Medicine and
Rehabilitation, Moscow, Russia*

INTRODUCTION: Clozapine (Ileponex[®], clozaril) belongs to the so called *atypical* antipsychotics [1]. It is a highly lipophilic substance and it is metabolized in the liver [2]. Its main metabolites are norclozapine and clozapine-N-oxide [3]. Clozapine and its metabolites are capable of accumulating in body tissues including the liver, the lungs and others [4]. The distribution of clozapine and its metabolites between the liver, the kidney, the heart and the lung hasn't been studied before.

THE OBJECTIVES OF THE STUDY: The objectives of the study are to assess the distribution of clozapine and its main metabolites between the liver, the lung, the kidney and the heart in case of clozapine poisoning.

MATERIALS AND METHODS: The study was performed on 10 outbreed male rats aged 20 weeks. The weight of the rats was 290–350 g. The animals were divided into 2 groups (5 rats in each group): group 1 (clozapine, 3 hours), group 2 (clozapine, 24 hours). The animals were narcotized and after that clozapine was administered. The dosage of clozapine was 150 mg/kg. 3 and 24 hours after the drug administration the animals were euthanized. The samples of the lung, kidney, liver, heart tissue (about 2 g) were mixed with 5 ml of saline and homogenized on Ultra Turrax Tube Drive control «IKA» (Germany) within 2 minutes at 4000 rpm to obtain homogenate. Acetonitrile (CH₃CN) was added to 100 µl of the homogenate up to 500 µl, than mixed on Vortex, centrifuged on the Centrifuge 5425 «Eppendorf» (Germany) within 10 minutes. We performed a chemical analysis of the homogenates using the method of high performance liquid chromatography method with mass spectrograph detection (HPLC-MS/MS).

RESULTS: 3 hours after clozapine administration the concentration of clozapine decreased in the following sequence: lung-liver-kidney-heart; the concentration of norclozapine correspondently: kidney-lung-liver-heart. 24 hours after clozapine ad-

ministration the concentration of clozapine decreased in the following sequence: kidney-lung-liver-heart; the concentration of norclozapine correspondently: lung-kidney- liver-heart.

CONCLUSION: the results of the chemical analysis along with the results of histological study will help to determine the fact of clozapine poisoning and its exact time.

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