DETERMINATION OF S-OXIDE OF PROCHLORPERAZINE IN OBJECTS OF BIOLOGICAL NATURE BY THE CHROMATOGRAPHY METHOD

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Introduction. The growing use of neuroleptics leads to an increase in acute poisonings. According to statistics, the number of fatal overdoses is 18%. Such data make it necessary to search for new methods of diagnosis of poisoning by neuroleptics, in particular phenothiazines. Their main metabolite is S-oxides, but the issue of determining prochlorperazine in biological objects by metabolites is currently not enough studied.

Aim. The purpose of the research is to develop a technique for determining prochlorperazine S-oxide in urine by HPLC.

Materials and methods. Prochlorperazine S-oxide in urine was determined by HPLC. The research was carried out on a microcolumn liquid chromatograph Milichrome A-02 in the reversed-phase version on a sorbent with a grafted chemically non-polar phase - Nucleosil-100-5, C-18 (metal column size 2×75 mm). A UV spectrophotometer was used as a detector (the wavelength range was 190-360 nm). As an eluent, 0.2 M lithium perchlorate with 0.01 M phosphoric acid (pH 2.2) and acetonitrile was used, which was fed in a gradient mode 2-100% acetonitrile. The S-oxide of prochlorperazine was found by retention time.

Results and discussions. The S-oxide was obtained according to a known method in collaboration with professor Blazheyevskiy. 0.6423 g (0.002 mol) of prochlorperazine was dissolved in 5 ml of water, a peroxyacetic acid (0.316 mol) was added to the red color and left for 15 min. 4 ml of 0.19 M NaOH to pH 9 was added. Extraction was done in separator using 50 ml of diethyl ether. The separated organic phases were combined and evaporated to a dry residue in air stream and dissolved in ethanol. The yield of S-oxide was 93%. The structure was found by melting temperature and PMR spectroscopy data. Modeling of poisoning was done by saturating 10 ml of urine with 0.5 ml of an ethyl solution of S-oxide with 20 μg of the substance. For isolation, 0.1 M HCL was added to 10 ml of the urine mixture to pH 2 and extracted three times with diethyl ether in 5 ml portions. The aqueous layer was alkalized with a 50% NaOH to pH 11 and extracted three times with chloroform in 10 ml portions. The chloroform extractions were filtered through a filter with 1 g of anhydrous sodium sulfate into a 25.0 ml flask, the volume was brought up to the mark with chloroform. Then extract was analyzed by HPLC. The retention time of S-oxide was 10.70-12.18 min. The lower limit of the detectable concentration of S-oxide is 0.002 μg in 2 μl of sample (n=5; P=0.95). The RSD of the average when determining the S-oxide in a solution of 2 μg/ml does not exceed 2% (n=5; P=0.95).

Conclusions. The developed technique for determining prochlorperazine by the product of S-oxide metabolism by the HPLC method in urine can be used for the analytical diagnosis of acute poisoning with this drug.

Keywords: phenothiazines, S-oxides, HPLC, toxicology, poisoning.