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# Effects of cisplatine on the level of phospholipids in brain tissue of the rat

Niektóre aspekty działania cisplatyny na poziom fosfolipidów w tkance mózgowej szczura

Cisplatinum (cis-Diamminedichloroplatinum), being one of the cytostatics, is widely applied in the treatment of neoplasms. It is especially efficient in the treatment of cancer of ovary, testicle and others (2, 8). It is an alkyling drug and its mechanism consists in joining the alkyl active radicles. During this process many basic functions of the cell get disturbed. The cytostatics, besides having therapeutic properties, may be toxic for the normal tissues and changes protein synthesis, enzymes level or tissue respiration (7).

Considering the wide range of therapeutic function of cisplatinum and on the other hand its toxic function (e.g. nephrotoxic or ototoxic), it seemed reasonable to investigate the influence of cisplatinum on the phospholipids composition.

The aim of the study was to test the influence of cisplatinum on the phosphatidylethanolamine, phosphatidylserine and phosphatidylcholine levels in the brain tissue of rats.

#### MATERIAL AND METHODS

The experiments were carried out on 40 Wistar rats with body weight 200-250 g. The animals were divided into two groups: the experimental one and the control one, with 20 rats in each group. Cisplatinum (Rhone-Poulenc Rover Laboratoire Roger Bellon, France) dissolved in physiological saline was administered intraperitoneally in doses of 0.1 ml/square meter of the body surface. In order to state the dose of the drug, the body weight was converted into the surface, using Fischer formula (log S = 100 W x 0.425 +

log L, where S = body surface in  $m^2$ , W = body weight, L = body length) (3). The control animals were given intraperitoneally 0.1 ml/square meter of the body surface of physiological saline.

The experiments were carried out in three stages, each of them lasting five days. There was a 24-hour break in drug administration between the individual stages. After completing the cycle, the rats were anaesthetised with chloroform and decapitated. Then their brain tissue was sampled and homogenised according to Folch procedure (4) and the phospholipids were separated by a thin layer chromatography. Phosphorus content was assayed according to Bartlett (1).

The phosphatidylethanolamine, phosphatidylserine and phosphatidylcholine levels in the brain tissue of rats have been investigated.

Statistical analyses were performed by Student's t test for unpaired data with p < 0.05 as statistical limit.



Fig. 1. Changes in phosphatidylethanolamine level induced by cisplatine administration



Fig. 2. Changes in phosphatidylserine level induced by cisplatine administration



Fig. 3. Changes in phosphatidylcholine level induced by cisplatine administration

#### RESULTS

The carried out research confirms that cisplatinum, being administered intraperitoneally, causes changes in the phospholipids composition in brain tissue of rats.

In the cerebral hemispheres it was proved that the phosphatidylethanolamine level was decreased from 32.3% to 26.2%. (Fig.1)

Similar effect was observed with reference to phosphatidylserine: decrease from 16.6% to 11.1%, as compared with the control group. (Fig.2).

Figure 3 showed the phosphatidylcholine level in comparison with the control group got increased from 24.6% to 45.2%.

Though the biggest changes were confirmed in phosphatidylcholine, all of these changes were statistically insignificant.

#### DISCUSSION

The experiments prove that cisplatinum changes the composition of phospholipids in the brain tissue in rats. It is known that phospholipids are components of cellular membranes, and the lipophyl drugs, when dissolving in this layer, change the permeability of the cellular membrane. It causes the change of membrane transport and disturbance of cells functioning. Another mechanism of performance consists in joining the receptor and thus it reacts pharmacologically.

In the study of Giri inhibition of phosphatidylcholine and neutral lipids synthesis was proved in hamsters, to which other cytostatic - bleomycin had been administered intratracheally (5).

Gupta A. and his co-worker confirmed that in brain tissue of rats exposed to cadmium the phospholipids composition got changed (6).

Schiffer et al. showed that contrary to the effects exerted by cisplatinum on brain tumours, general clinical neurological condition of the rabbits to which intraarterial cisplatinum was administered was unaffected and histopathological examination of the rabbit's brain was normal (9).

It can be assumed that the observed changes in the phospholipids composition in the brain tissue of rats are caused by cisplatinum activity or by the changes of cellular membranes permeability or else by connecting it with the receptor.

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#### STRESZCZENIE

W pracy badano wpływ cisplatyny (podawanej dootrzewnowo) na skład fosfolipidów w tkance mózgowej u szczura. W homogenizatach tkanki mózgowej oznaczano poziom fosfatydyloetanolaminy, fosfatydyloseryny i fosfatydylocholiny.

Z przeprowadzonych doświadczeń wynika, że pod wpływem cisplatyny zmienił się skład fosfolipidów. Poziom fosfatydyloetanolaminy i fosfatydyloseryny zmniejszył się odpowiednio z 32,2% do 26,2% oraz z 16,6% do 11,1%. W przypadku fosfatydylocholiny wykazano wzrost z 24,6% do 45,2%. Obserwowane przez nas zmiany były nieistotne statystycznie.