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Topochemical Examinations of the Lungs of the Rat after Combined Administration of Serpasil and Deslanatoside. II. Morphological Examinations

Badania topochemiczne płuc szczura po skojarzonym podawaniu Serpasilu i Deslanatosidu. II. Badania morfologiczne

Топохимические исследования легких крыс после сопряженного применения Серпасила и Десланатосида. II. Морфологические исследования

Arterial hypertension often accompanies acute circulatory failure, with atrial fibrillation and in tachycardia. Nowadays, Serpasil is used to reduce blood pressure, while Lanatoside is irreplaceable in disturbances of heart rhythm. Although Serpasil is considered to be not very toxic, it may cause oligopnea which results in accummulation of musoc in the respiratory tract and in pulmonary oedema (12).

It should also be added, that some pathological conditions make treatment with cordial glucosides difficult (13). Wasyluk (13) emphasises, among others, the occurrence of respiratory insufficiency in tuberculosis and the use of cordial glucosides is sometimes made difficult here. Since respiratory insufficiency had been signalled after roserpine (7) and after Lanatoside (3), it was interesting to examine how combined effect of these two drugs would influence morphology of the lungs and especially mucous cells in the epithelium.

MATERIAL AND METHODS

Examinations were carried out on female white Wistar rats, sexually mature, with body weight 160 g. Observation took place in the spring months and the animals were fed with standard LSM feed. The animals were divided into 4 experimental groups:

Group I — animals which were given no drugs,

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Group II — animals which were given Serpasil in the dose of 0.5 mg/kg body weight for the period of 5 days,

Group III — animals which were given Serpasil in the dose of 0.25 mg/kg body weight for the period of 5 days,

Group IV — animals which were given Serpasil in the dose of 0.25 mg/kg body weight and Lanatoside in the dose of 0.4 mg/kg body weight.

Serpasil had been produced by CIBA and Deslanatoside by POLFA Warsaw. The drugs were administered by intraperitoneal route. After 5 days of the drugs administration the animals were killed by decapitation and their pulmonary tissue was collected for examinations. Sections were fixed in 10% formalin and embedded in paraffin (1). Staining was performed on 7 μ thick sections:

1) with hematoxyline and eosine according to Bagiński's method (1);
2) triplex staining according to Messon's method (1);
3) staining of neutral polysachrides with PAS method according to McManus's method (1).

STUDY RESULTS

Staining with hematoxyline and eosine

Group I. Survey staining with hematoxyline and eosine showed normal, conformable to literature structure of pulmonary parenchyma. The parenchyma had fine interalveolar septa, in the walls of which were visible cells of lymphatic tissue in moderate number. Alveoli of the lungs lined with pavement epithelium showed large air space. The wall of bronchi and bronchioles was characterized by typical columnar epithelium (Fig. 1). In the region of bronchial tree branching there was found a typical accummulation of lymphatic tissue.

Group II. In pulmonary parenchyma of most examined animals there occurred widening of interalveolar septa, with considerably increased number of lymphatic tissue. Air space of alveoli was diminished in some places (Fig. 2). In the region of bronchioles there were observed aggregates of lymphatic tissue which did not occur in control group. There was also observed congestion of interalveolar septa (Fig. 2).

Group III. The picture of pulmonary tissue in this group was approximal to control group. Interalveolar septa were delicate. Respiratory epithelium as well as the air space of lung alveoli did not show any differences as compared with control material. Only exceptionally in some animals there was observed widening of interalveolar septa. Lymphatic tissue occurred in the number and distribution characteristic of normal pulmonary parenchyma.

Group IV. In two rats from this group there was observed considerably bigger amount of lymphatic tissue. There were also found foci with widened and congested interalveolar septa. The wall of bronchi and bronchioles did not differ from control group.

Staining according to Masson's method

Group I. Trichromatic method of staining clearly showed very delicate connective tissular septa as well as epithelium of pulmonary alveoli. In interalveolar septa there were observed small numbers of blood morphotic elements. Bronchial and bronchiolal wall lined with columnar epithelium had clearly visible in this method layer of smooth muscular coat (Fig. 3).

Group II. In this method of staining clearly visible erythrocytes occurred in greater number in connective tissular septa giving picture of congestion. In some places there was observed increased quantity of connective tissue. In bronchi and bronchioles no significant differences in comparison with control group were observed. Like in survey staining there were found foci with greater number of phagocytary cells.

Group III. The structure of pulmonary parenchyma of animals from this group resembled that of control group. Staining did not show increased quantitiy of connective tissue or greater number of blood morphotic elements.

Group IV. In pulmonary parenchyma of animals from this group there were observed places considerably different than in control group (Fig. 4). On small flat surfaces of parenchyma there were observed considerably greater numbers of connective tissular elements in interalveolar septa and decreased air space of alveoli. In nearly all pulmonary parenchyma there occurred considerable congestion. No significant changes, however, were observed in bronchial and bronchiolal wall.

Staining of polysaccharides with PAS reaction, according to McManus's method

Group I. Glucoproteins occurred in membranes of alveolar walls and as mucous in beaker cells of columnar epithelium and mucous lining epithelium (Fig. 5).

Group II. In this group, in sites of widened interalveolar septa there occurred a great number of neutral glucoproteins. In columnar epithelium slightly more mucous cells occurred.

Group III. The number of neutral glucoproteins in pulmonary parenchyma of animals from this group was approximate to control group.

Group IV. In the group of animals which were administered Serpasil and Deslanatoside there occurred a visible increase of PAS positive substances in pulmonary parenchyma. In bronchi of the same parameters a greater number of mucous cells than in control group was observed. On the surface of columnar epithelium greater amount of mucous was left behind (Fig. 6).

DISCUSION

Roserpine and its derivatives are commonly used in medicine as a component of hypotensive mixtures. Physicochemical properties get combined with cytologic effect of this drug. Roserpine may combine with blood albumins (1, 3) or with very reactive cation imine group (–NH–), to react with phospholipids of cellular structures (2).

At the same time attention is turned by clinical reports to complications in treatment with digitaloid drugs in the respiratory tract of patients with previous disease of the tract (9). In pulmonary alveolus phospoholipids are primarily the surfactant and disturbances of alveolar surface tension. Defect of this barrier may lead to intraseptal oedemy (2).

In this study the focally observed widening of interalveolar septa and decrease of alveolar air space could point to defect of phospholipids of cellular structures. These changes were observed after a big dose of Serpasil or small dose of Serpasil given together with Lanatoside. Additionally, in animals after a big dose of Serpasil greater quantity of connective tissue was observed. The changes observed suggest that Serpasil as a derivative of roserpine may disturb calcium homeostasis while reacting with phospholipids of cellular structures.

It may be supposed that Deslanatoside has the action aiding Serpasil, since the reaction in the group after a big dose of Serpasil was approximate to the reaction after a small dose of Serpasil, but in conjuction with Deslanatoside. Widening of connective tissular septa, unless accompanied by an increase of connective tissue quantity, may be connected with defect of vascular wall, and in the first stage with their increased permeability. In the performed study, both after administration of Serpasil in big doses and after its administration together with Deslanatoside, there were observed numerous ecchymoses. It should be supposed that disturbances in calcium homoestasis and in electrolytic balance described by other authors (4, 8) also contributed to electrophisiologie changes of vascular properties. Komatsu goes further claiming that disturbances of electrolytic balance, changes in the amount of secreted catecholamines, damage of cellular absorption by inactivation of adenyl cyclase may directly affect proliferation and physiologic activity of cell.

In the present study time of experiment was rather too short to observe proliferation of cells, but there was observed a clear increase of cellular secretory activity manifested by increased quantity of PAS substance in endothelial lining and in epithelium of bronchi and bronchioles.

Klika (6) tells about the presence of PAS positive substances in basement membranes of alveoli and about mucocytes occurring in the epithelium and their role in pulmonary clearance. Like in this study, an increase of PAS positive substances after administration of Serpasil and Lanatoside had been observed by Podlewska and Wasyluk (12, 13).

Increase of quantity of PAS substances can hardly br associated, in this case, only with so-called „pulmonary clearance". One should rather agree with Carrier (4) that there takes place a change in the structure of membranes and a disturbance of metabolism of carbohydrates. This has been confirmed by studies of Głowacka (5), who observed accummulation of glycogen in oocytes after roserpine.

With mobilization of defense mechanisms will be connected an appearance of macrophages in greater quantity, which was observed in this experiment. Increased number of macrophages accompanied changes in interalveolar septa and numerous erythrocytes present there.

Summing up, it should be stated that administration of Serpasil in big doses as well as administration of Serpasil in combination with Deslanatoside causes slight, focal changes in the morphology of pulmonary epithelium in the form of widened interalveolar septa, diminished air space of pulmonary alveolus, focal ecchymoses, increased number of macrophages and PAS-positive substances.

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EXPLANATION TO FIGURES

Fig. 1. Group I (control). Rat's lung. Staining with hematoxyline and eosine. Magn. ca 200 ×.

Fig. 2. Group II (experimental). Rat's lung. Staining with hematoxyline and eosine. Magn. ca 200 ×.

Fig. 3. Group I (control). Rat's lung. Staining according to Masson's method. Magn. ca 200 ×.

Fig. 4. Group IV (experimental). Rat's lung. Staining according to Masson's method. Magn. ca 200 ×.

Fig. 5. Group I (control). Rat's lung. Staining with PAS method according to McManus's method. Magn. ca 200 ×.

Fig. 6. Group IV (experimental). Rat's lung. Staining with PAS method according to McManus's method. Magn. ca 200 ×.

STRESZCZENIE

Badano działanie Serpasilu jako często stosowanego leku obniżającego ciśnienie w połączeniu z Deslanatosidem. Badania histologiczne prowadzono na samicach szczurów białych rasy Wistar, dojrzałych płciowo, o m.c. ok. 160 g. Badania wykazały, że podawanie Serpasilu w dużej dawce oraz skojarzone z Deslanatosidem wywoływało niewielkie ogniskowe zmiany w morfologii miąższu płucnego w postaci poszerzonych przegród międzypęcherzykowych i zmniejszonej powierzchni powietrznej pęcherzyka. W miąższu płucnym obserwowano często wybroczyny krwawe, zwiększoną ilość makrofagów oraz znacznie większą ilość substancji PAS +.

РЕЗЮМЕ

В данной работе представлены результаты исследования Серпасила, понижающего давление крови и применяемого часто в сопряжении с Десланатосидом. Гистологические исследования велись на половозрелых белых самках крыс Вистар весом около 160 гр. Исследования показали, что применение большой дозы Серпасила, а также сопряжение с Десланатосидом, вызывало небольшие очаговые изменения в морфологии легочной паренхимы, проявляющиеся расширением междупузырьковых перегородок и уменьшением воздушной поверхности пузырьков. В легочной паренхиме часто замечались петехии, увеличение количества микрофагов и значительное увеличение вещества PAS +.

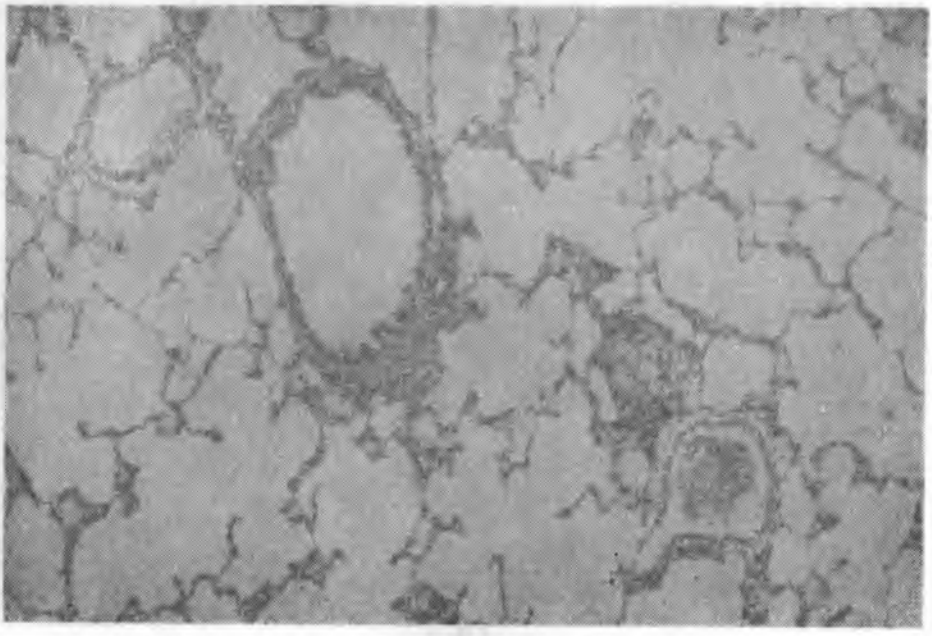

Fig. 1

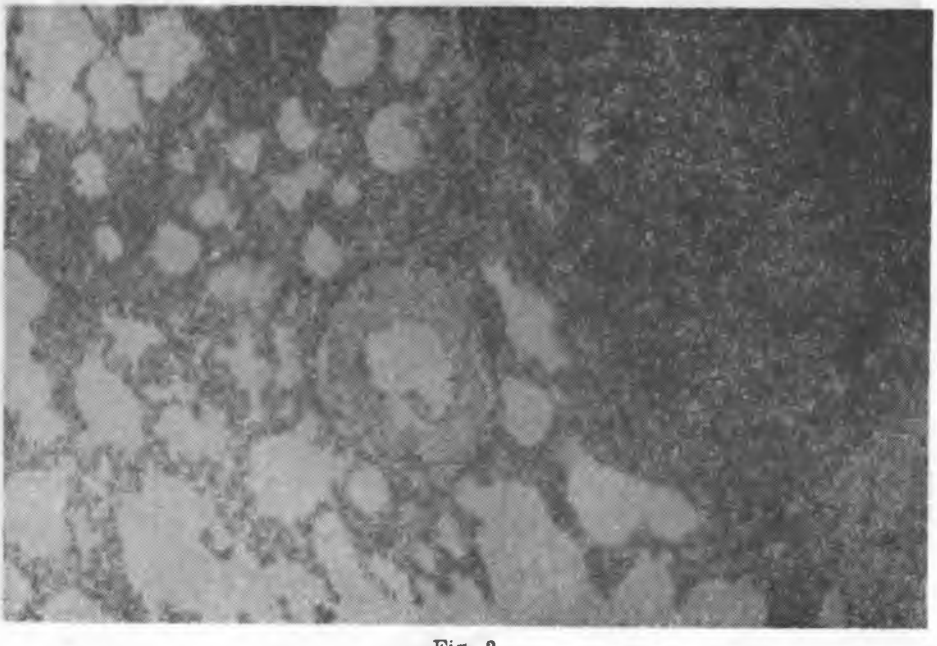

Fig. 2

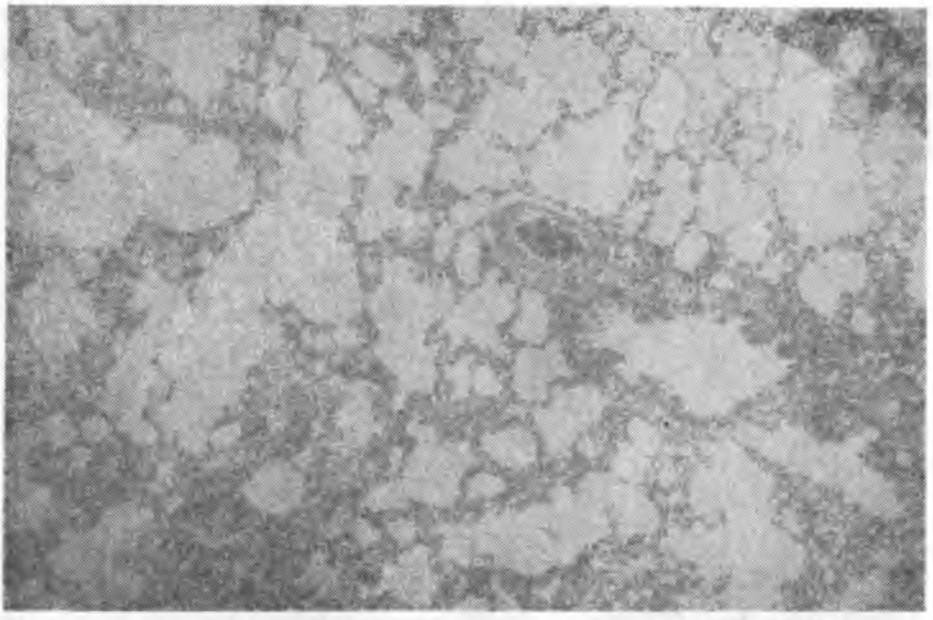

Fig. 3

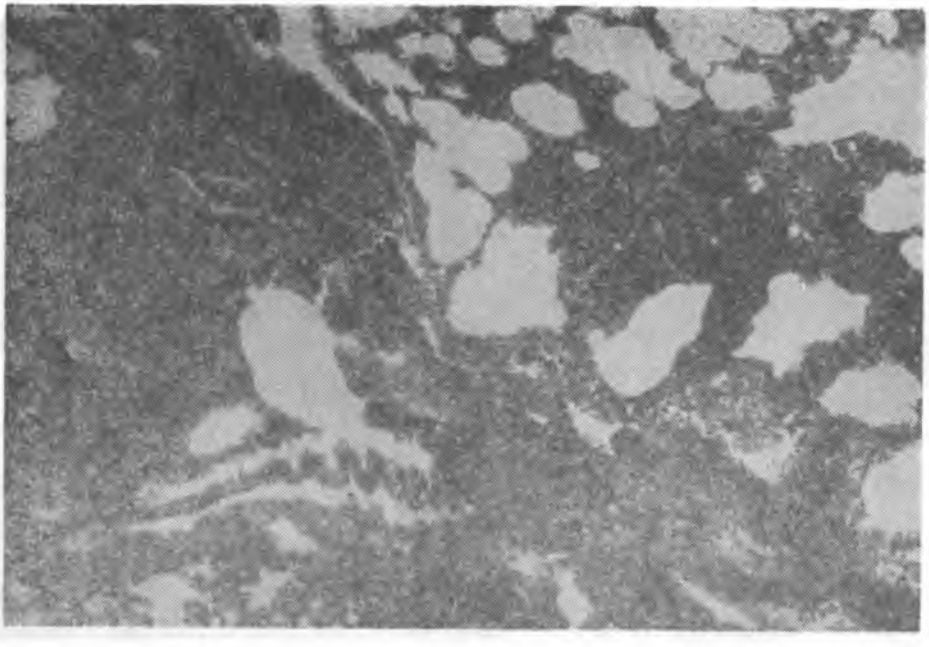

Fig. 4

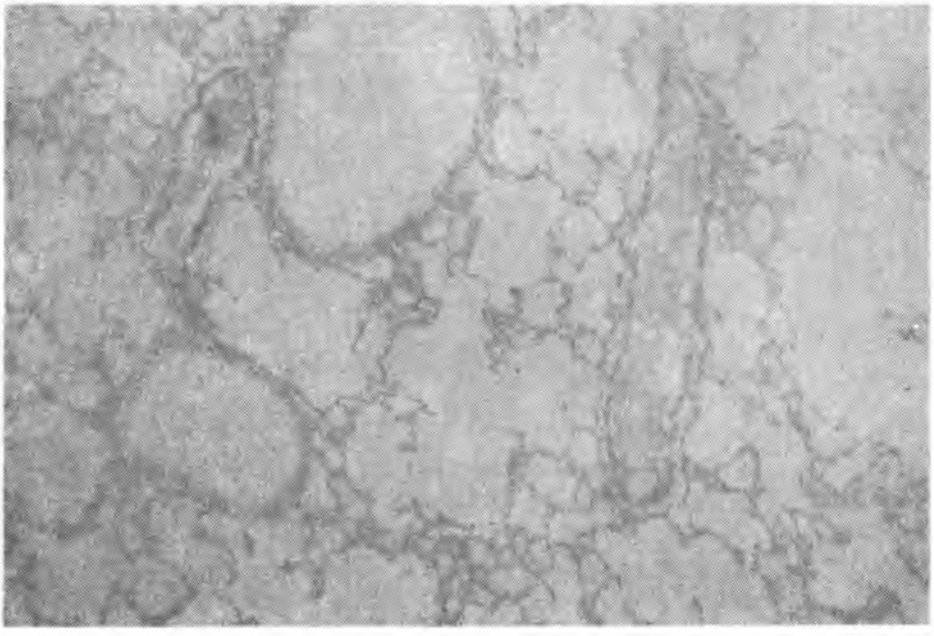

Fig. 5

Fig. 6