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Katedra i Zakład Histologii i Embriologii z Pracownią Cytologii Doświadczalnej. Akademia Medyczna w Lublinie
Kierownik: prof. dr hab. n. med. Irena Królikowska-Prasał

Jadwiga ROMANOWSKA, Krystyna CZERNY,
Ewa KIFER-WYSOCKA, Włodzimierz MATYSIAK

The Effect of Administering Dexamethasone on the Histochemical Reactions in Rats' Liver

Wpływ podawania Dexamethasonu na odczyny histochemiczne w wątrobie szczurów

Natural glucocorticoids, together with other hormones, are regulators of mature tissues' metabolism (17), they also play an important role during specified stages of embryogenesis (6, 15).

Dexamethasone (9-fluoro-16-methylo-prednisolon) is a synthetic derivative of Encortolon. It exerts an inhibitory effect in acute and chronic stage of inflammation, shows strong anti-allergic and immunosuppressive action (1, 11). Decomposition of glucocorticoids takes place mainly in the liver, where glucocorticoids are transformed into biologically non-active metabolites (2). Synthetic glucocorticoids display higher pharmacological activity and they differ from natural glucocorticoids as regards undesirable effects (3, 10).

The aim of the present paper was the appreciation of the effect of Dexamethasone on the morphology and histochemical reactions in rats' liver.

MATERIAL AND METHODS

The investigations were carried out on white rats of Wistar strain with 250—350 g of body mass. The experimental animals received Dexamethasone (tablets, „Polfa" — Poznań) in daily dose of 1 mg/kg body mass in the form of suspension, with stomach-pump, intragastrically. The three experimental groups (5 animals each) were formed: the Ist group received the drug only once, the IInd group — for 2 days, and the IIIrd group — for 7 successive days. The animals of the control group received distilled water. After 24 hrs since the last dose of the drug had been administered the liver segments were collected and on the sections there was carried out H+E (hematoxylin+eosin) staining, PAS reaction to polysaccharides after McManus, histochemical reactions to the activity of acid phosphatase after Gomori's method and to ATP-ase activity after Wachstein and Meisel's method.

RESULTS OF OWN INVESTIGATIONS

Staining with hematoxylin and eosin (H + E)

In comparison with the liver of control animals (Fig. 1), in the liver of the animals receiving the drug only once (the experimental group I) and for 2 days (the experimental group II), coarse granulations intensively staining with H + E occurred in the cytoplasma of hepatocytes. In the liver of the animals of the IInd experimental group, most often in the region of central veins, the widening of the sinusal vessels and the presence of erythrocytes in them was locally observed. In the animals receiving the drug for 7 successive days congestion of liver parenchyma was clearly marked (Fig. 2). In places of strong congestion the hepatocytic cytoplasma contained tiny vacuoles. Just as in the groups I and II numerous granulations intensively staining with H + E occurred in the cytoplasma of liver cells (Fig. 3).

PAS reaction to polysaccharides

Carrying out of PAS reaction showed, in the liver of the animals of the Ist and IInd experimental groups, very numerous granulations in the cytoplasma of liver cells, specially in the central and slightly peripheral parts of the lobule. In comparison with the liver of the control animals, PAS reaction was slightly more intensive (Figs. 4 and 5). In the liver of animals receiving Dexamethasone for 7 days PAS reaction was negative.

Acid phosphatase

The intensity of enzymatic reaction to acid phosphatase in the liver of animals from the Ist experimental group was similar as in the control animals (Fig. 6). In the animals from the experimental groups II and III reaction to acid phosphatase was uneven (Fig. 7): often weakened and locally, around portal spaces, concentrated granules of the product of the reaction were observed.

Adenosine-triphosphatase-ATP-ase

In comparison with the control preparations, in the liver of the experimental animals there was observed a subtle intensification of ATP-ase reaction in the walls of biliary canaliculi in the region of central veins as well as in the region of portal spaces of the liver (Figs. 8 and 9).

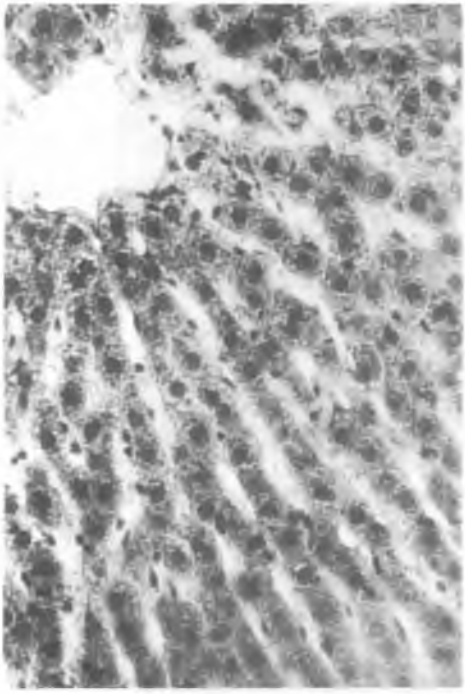

Fig. 1. Control group. A rat liver. Hematoxylin and eosin staining. Magn. ca 80×

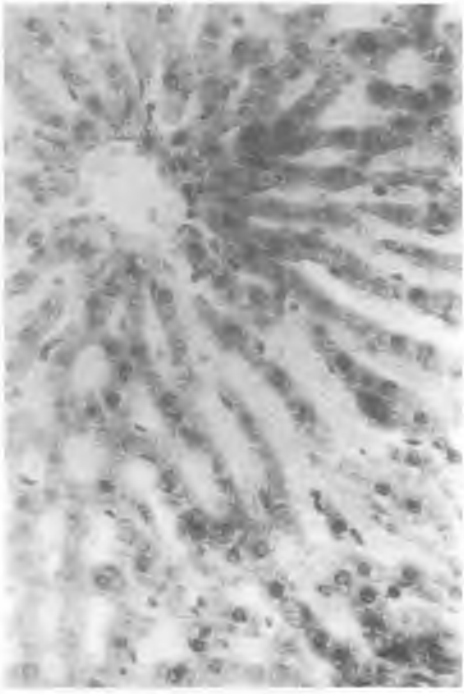

Fig. 2. Experimental group III. A rat liver. Hematoxylin and eosin staining. Magn. ca 80×

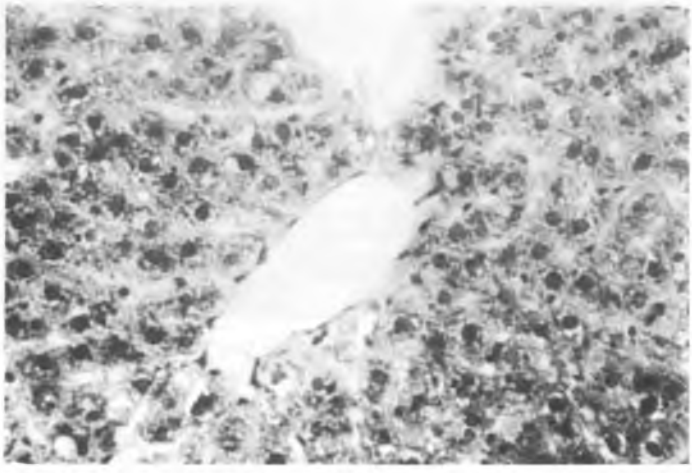

Fig. 3. Experimental group III. A rat liver. Hematoxylin and eosin staining. Magn. ca 80×

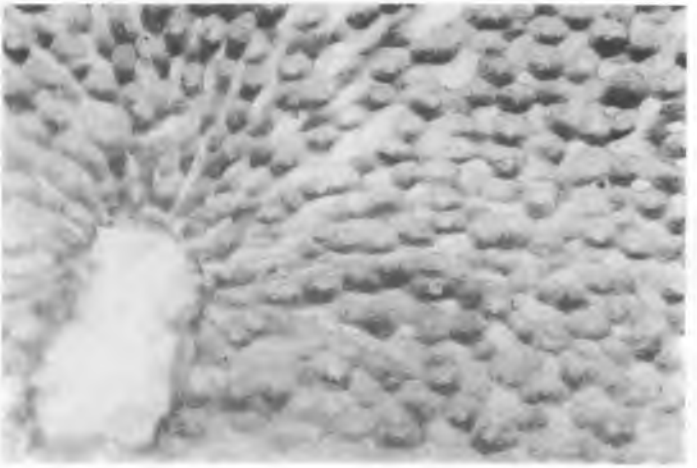

Fig. 4. Control group. A rat liver. PAS reaction, McManus method. Magn. ca 80×

Fig. 5. Experimental group II. A rat liver. PAS reaction, McManus method. Magn. ca 80×.

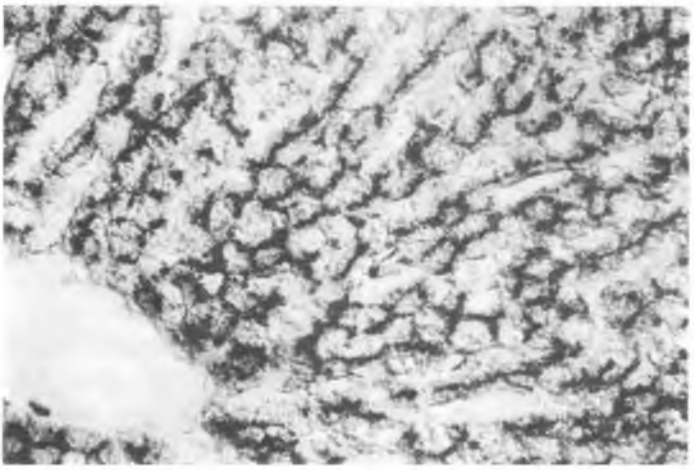

Fig. 6. Control group. A rat liver. Reaction to acid phosphatase activity, Gomori method. Magn. ca 80×

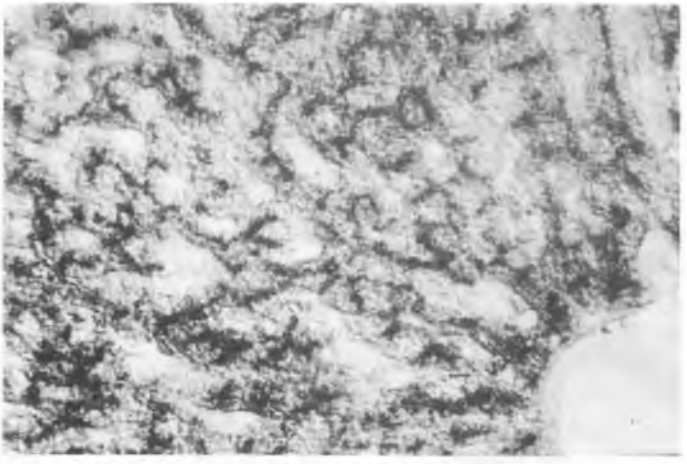

Fig. 7. Experimental group II. A rat liver. Reaction to acid phosphatase activity, Gomori method. Magn. ca 80×

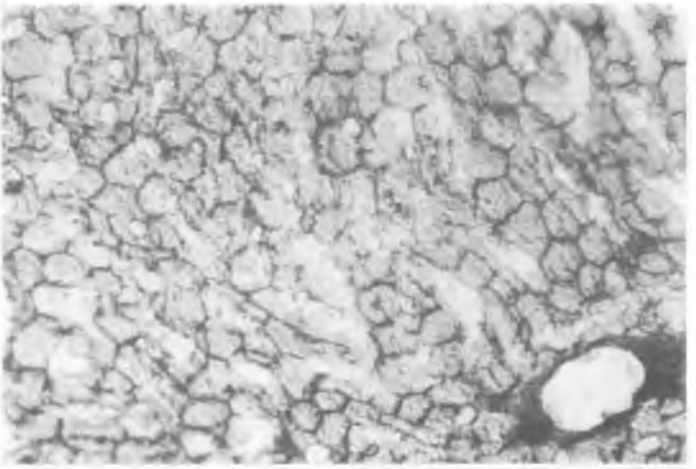

Fig. 8. Control group. A rat liver. Reaction to ATP-ase activity, Wachstein and Meisel method. Magn. ca 80×

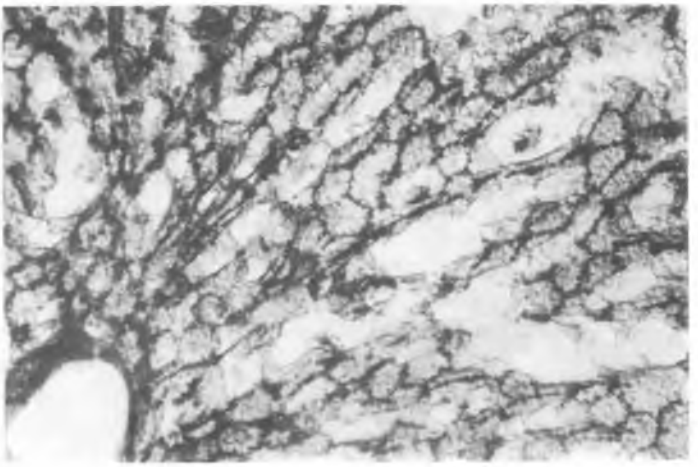

Fig. 9. Experimental group III. A rat liver. Reaction to ATP-ase activity, Wachstein and Meisel method. Magn. ca 80×

DISCUSSION ON THE RESULTS OF INVESTIGATIONS

Morphological and histochemical observations carried out on the liver of experimental animals subject to the action of Dexamethasone proved that significant changes were noticeable in the group of animals after 7 days of administration of the drug. There was found strong local congestion and widening of the sinusal vessels of the liver and numerous granulations staining with H + E in the hepatocytes' cytoplasma. There was not observed any increase of the liver cells.

It has been assumed that glucocorticoids, showing anabolic action on liver cells, stimulate the synthesis of enzymatic proteins and gluconeogenesis processes lead to an increased synthesis of glucogen (7). While carrying out the experiment, the attention was paid to the proceeding of PAS reactions in the liver. In the animals receiving Dexamethasone only once and for 2 days the intensity of PAS reaction was slightly increased in relation to the reaction in the sections of preparations coming from the control animals, whereas in the group of animals receiving Dexamethasone for 7 days — PAS reaction in the liver was negative. This suggests that in this case, probably, the synthesis of glucogen was inhibited. K u c z y ń s k a (9) states that the main reason of the lowering of the content of glucogen in hepatocytes is its intensified combustion in reparation processes taking place in the liver.

The danger of applying Dexamethasone has been pointed out recently, since treatment with this drug leads to the inhibition of ACTH secretion and to secondary adrenocortical insufficiency (16, 7, 4). This phenomenon is in many respects similar to the one which takes place after removal of pituitary gland or adrenal gland when a complete disappearing of glucogen in the liver can be observed (8). It was experimentally proved that Dexamethasone causes diabetes and it is accounted to be the antagonist of insulin (14). Dexamethasone damages mucopolysaccharides of the osseous tissue (5), causes a decrease in the content of PAS-positive substances in big salivary glands (13). In young tissues glucocorticoids inhibit biosynthesis of collagenic fibres, showing embryotoxic action (6, 12).

The mechanism of functioning of glucocorticoids has been still examined. These hormones, acting on target cells' receptors, affect changes in the structure and membranes organization, and by that they can modify cells' response to other hormones (14).

In our experiment changes in the activity of ATP-ase and acid phosphatase in rats' liver after administration of Dexamethasone were small. The action of glucocorticoids being the factors stabilizing lysosomal membranes which is connected with a decrease of the liberation of hydrolases to cytoplasma, and also the factors strengthening cytoplasmic membranes and reducing permeability of capillaries (18) is well-known.

Conclusions

1. It results from the carried out investigations that the administration of Dexamethasone in a daily dose of 1 mg/kg of body mass for 1, 2, 7 days evokes changes in the animals' liver, whose intensity is connected with the length of administration of the drug.

2. The administration of Dexamethasone in the afore-mentioned dose for 7 days causes significant disturbances in the content of PAS-positive substances in the animals' liver.

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STRESZCZENIE

Szczurom białym szczepu Wistar podawano Dexamethason (prod. „Polfa" — Poznań) w postaci zawiesiny, sondą, dożołądkowo, w dawce 1 mg/kg m.c. Zwierzęta grupy I doświadczalnej otrzymały lek jednorazowo, w grupie II lek podawano przez 2 dni, w grupie III — przez 7 kolejnych dni. Na skrawkach wątroby zwierząt kontrolnych i doświadczalnych wykonano: barwienie przeglądowe H+E, reakcję PAS na wielocukry, reakcje histochemiczne na aktywność fosfatazy kwaśnej i ATP-azy. Z przeprowadzonych badań wynika, że zmiany histochemiczne w wątrobie po podawaniu Dexamethasonu związane są z długością okresu podawania leku, a ponadto Dexamethason podawany w dawce 1 mg/kg m.c. przez okres 7 dni zaburza w sposób istotny zawartość substancji PAS-dodatnich w wątrobie szczurów.