

Department of Histology and Embryology with the Laboratory of Experimental Cytology
Medical University of Lublin

ALICJA ZARĘBSKA, MARTA LIS-SOCHOCKA, AGNIESZKA PEDRYCZ,
KRYSTYNA CZERNY, AGATA MAKAREWICZ

*Histological and morphological investigations of serous
parotid cells after experimental administration of Metizol*

Stimulative influence of thyroid hormones on serous parts of sublingual gland is known from long time (2). It was also proved that in parotid gland, like in thyroid gland, iodine is uptaken from blood and then metabolized (9). Finally iodine is discharged into saliva as iodides.

The purpose of our study was to show if Metizol used in the treatment of hyperthyroidism, has an essential influence on morphology and function of serous parotid cells. This drug inhibits creation peroxidase-iodine complexes and iodization of tyrosine in tyreoglobuline. It blocks tyroxin transformation into triiodothyronine peripherentially.

MATERIAL AND METHODS

The study was performed on white male Wistar rats with initial body weight about 300 g. Animals were divided into two experimental groups and two corresponding control groups (five animals in each group). Rats from experimental group I had administered by gastric tube Metizol (Polfa) dissolved in distilled water in the dose of 1 mg/kg of body weight every 21 days. Animals from experimental group II had administered Metizol in the same way every 42 days. Animals from the control groups were administered distilled water by gastric tube every 21 or 42 days.

After 24 hours from the last dose the animals were decapitated and sections of the right parotid gland were collected for investigation. Sections were fixed in Baker fluid, dehydrated in ethanol and paraffin embedded. For evaluation in light microscopy 7 μ m thick gland sections were stained with hematoxylin and eosin. Then the largest and the smallest nuclei diameters were measured and nuclear sections fields were counted, using formulas πr^2 for circle field and πab for elypse field.

Measurements were made in projection microscope at the magnitude 1000x. In parotid gland sections of every animal 100 nuclei were measured in gland follicles chosen at random. Results were statistically processed using t-Student test. Pictures were made in light microscopy from Nikon firm (LABOPHOT-2) using digital camera Coolpix 990 from Nikon firm.

RESULTS AND DISCUSSION

Tionamids (Metizol) are often used antithyroid drugs. Long-term therapy with these drugs could be the reason of side-effects. Usually they are small and transient – for example cutaneous rash, mild leukocytes (1). However, rare cases of cholestatic liver damage were also reported (7, 8).

In our studies we stated that 21-day administration of Metizol induced histological changes in numerous serous parotid follicles. Their cytoplasm was basophilic, but in the apical part, where secretion is collected, affinity to eosin was not observed. Sections fields of follicles were smaller than in control groups and more irregular in shape. Cell nuclei were with statistical significance bigger than in control animals (Fig. 2).

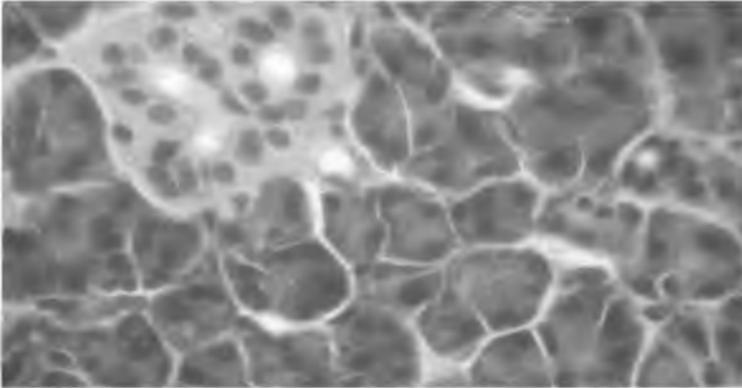


Fig. 1. Parotid gland of a rat from control group. Basal part of cells show basophilic character and apical part, containing secretion – acidophilic. H+E staining. Magn. 400x

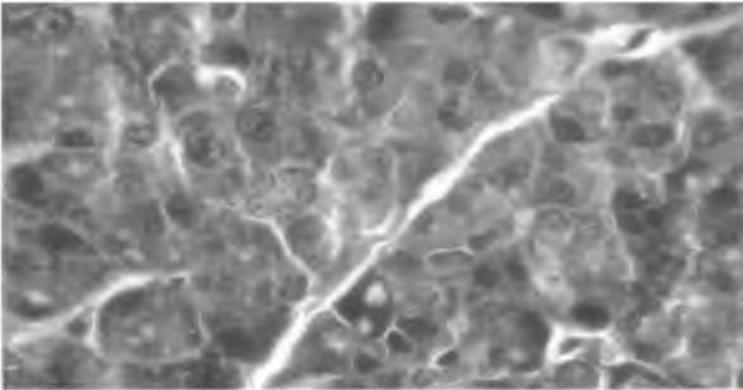


Fig. 2. Parotid gland of a rat from experimental group I. Larger than in control animals cell nuclei, irregular shape of follicles and smaller amount of secretion. H+E staining. Magn. 400x

Similar results with reference to mandibular gland and Loewenthal gland reported Sochocka et al. (3, 4) after 21 days of Metizol administration. Majewska and Matysiek observed after the same time of that drug administration the increased activity of hepatocytes (5) and changes in the histological structure of kidneys (6). Our remarks about parotid glands are the evidence of metabolism changes in cells of that organ.

Two times longer administration of the drug (42 days) induced changes similar to those in experimental group I. In that case in numerous serous parotid cells typical acidophilic secretion was not observed. However, cell nuclei had thick chromatin and were significantly smaller than in control animals. Follicles field section was also smaller and their shape was less regular. Moreover, in the cytoplasm of some cells there were observed “empty vacuoles” resembling lipid drops (Fig. 3).

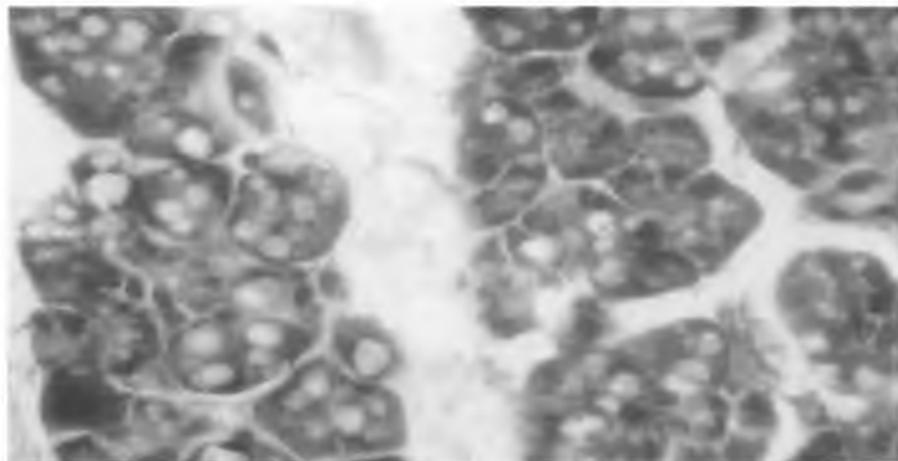


Fig. 3. Parotid gland of a rat from experimental group II. Smaller than in control animals cell nuclei contain thick chromatin. In numerous cells “empty vacuoles” are present, which resemble lipid drops. Serous follicles shape is less regular than in control group. H+E staining. Magn. 400x

Lack of typical secretion in the apical parts of cells, accompanied by a decreased nuclear activity, shows inhibition of cell metabolic process. The presence of lipid drops in some cells is a sign of fatty degeneration. Hepatic damage after Metizol with features of fatty degeneration is described by Schmidt et al. (7). Other authors also reported about cases of liver damage with cholestasis features (8).

It is supposed that side-effects of Metizol activity touch numerous organs.

Table 1. Mean fields of nuclear section in the serous cells of rat parotid after experimental administration of Metizol (in μ^2)

Groups	Mean value	Standard deviation	Differences between means	t-student test value
Control I	16.03	7.12	+6.60	7.14
Experimental I	22.63	5.90	p<0.001	
Control II	15.30	9.49	-5.25	6.55
Experimental II	10.05	3.84	p<0.001	

CONCLUSIONS

1. 21-day Metizol administration in the dose of 1mg/kg of body weight cause decreases secretion activity of parotid serous cells in rats.

2. 42-day Metizol administration in the dose of 1 mg/kg of body weight decreases secretion activity of rat parotid serous cells, and in some cells causes changes with fatty degeneration features.

REFERENCES

1. Bartalena L. et al.: Adverse effects of thyroid hormone preparations and antithyroid drugs. *Drug.-Saf.*, 15/1, 53, 1996.
2. Leblond C. P., Grad P.: Control of the serous acini of the rat submaxillary gland by the thyroid hormone. *Anat. Rec.*, 100, 750, 1948.
3. Lis-Sochocka M. et al.: Histological examination of the submandibular gland after experimental administration of Metizol. *Annales UMCS, D*, 57, 174, 2002.
4. Lis-Sochocka M. et al.: Histological examination of the Loewenthal gland after experimental administration of Metizol. *Annales UMCS, D*, 57, 181, 2002.
5. Majewska T., Matysek M.: Influence of Metizol on the liver of pregnant rats. *Annales UMCS, D*, 46, 129, 1991.
6. Matysek M., Majewska T.: Histological and histochemical investigations of the influence of Metizol on the function of the kidneys when given during pregnancy. *Annales UMCS, D*, 46, 133, 1991.
7. Schmidt G. et al.: Methimazole-associated cholestatic liver injury: case report and brief literature review. *Hepatogastroenterology* 33, 6, 244, 1986.
8. Schwab G. P. et al.: Methimazole-induced cholestatic liver injury, mimicking sclerosing cholangitis. *Langenbecks, Arch. Chir.*, 381, 4, 225, 1996.
9. Walker J. E. et al.: Handling of iodide chloride and pertechnate by salivary glands and the thyroid gland in man. *Alabama J. Med. Sci.*, 7, 323, 1970.

SUMMARY

White male Wistar rats were administered Metizol by gastric tube in the dose of 1 mg/kg of body weight for 21 days and 42 days. 7 μ m sections thick were stained with hematoxylin and eosin and then assessed in light microscopy, and also cell nuclei measurements were performed. It was stated that 21-day Metizol administration causes a significant increase of nuclear sections field and changes showing the decrease of metabolic activity of serous cells. 42-day drug administration causes a decrease of nuclear section field and in some cells changes with fatty degeneration features.

Histologiczne i morfometryczne badania komórek surowiczych przyusznicy szczura po doświadczalnym podawaniu metizolu

Szczurom białym – samicom rasy Wistar podawano sondą przez 21 dni i 42 dni Metizol w dawce 1 mg/kg m.c. Skrawki grubości 7 μ m barwione H+E oceniano w mikroskopie świetlnym, a także wykonano na nich pomiary jąder komórkowych. Stwierdzono, że 21-dniowe podawanie Metizolu powoduje statystycznie istotny wzrost powierzchni przekroju jąder komórkowych oraz zmiany wskazujące na zmniejszenie aktywności metabolicznej komórek surowiczych. 42-dniowe podawanie preparatu powoduje natomiast statystycznie istotne zmniejszenie powierzchni przekroju jąder komórkowych, a w niektórych komórkach zmiany o cechach zwyrodnienia tłuszczowego.