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Tissue and Cellular Changes of Rat Thyroid Gland After Morphine Administration

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Histological and ultrastructural changes in rat thyroid gland after morphine treatment (acute and chronic application) were investigated. The morphological study carried out indicated that single dose of morphine (50 mg/kg b.w.) stimulated the evacuation of thyroid hormones. The first signs of destruction also were shown to be present. The chronic effect during a long term treatment (4 months) resulted in functional exhaustion of the organ and considerable destructive damages in the thyroid structure both on its cellular an tissue components. The main ultrastructural changes included reduction of the endoplasmic reticulum and lysis of mitochondria.

Key words: thyroid gland, morphine, histological- ultrastructural changes.

Introduction

Many studies have provided a significant information about the effects of opiates on the CNS. The wide use of these drugs as analgesics and the increasing number of addicts suggest the investigation of its action on several endocrine organs. Acute administration of morphine stimulates the secretion of hypothalamic-pituitary-adrenal hormones, ACTH, beta-endorphine and corticosterone in the rat [13].

The possible role of endogeneous opiates and morphine on the secretion of thyroid stimulating hormone (TSH), thyroxine (T_4) and triiodthyronine (T_3) has been investigated in rats, mice, goats and men [3, 4, 5]. Previous studies have shown that administration of morphine inhibited TSH release in rats [4]. These results suggested that the inhibitory effect of morphine on both the basal and stimulated TSH levels may be mediated by the activation of opiate receptors, and opioid peptide neurones may to play a modulating role in the regulation of serum TSH. Sharp et al [11] reported that only high doses of morphine suppressed basal TSH level. The most probable explication of the inhibitory effect of morphine on serum TSH levels appeared to be that morphine reduced TRH (thyrotrophine-releasing hormone) in normal, cold-exposed and thyroidectomized rats [9]. The exact mechanism of morphine effect(s) on thyroid function is, however, unclear at present. The majority investigations presented biochemical study on serum levels of TRH, TSH, T_4 and T_3. Little is known about the structural changes in thyroid gland after morphine administration and this fact determined the aim of our investigation.

Material and Methods

Sexually mature 45-day female Wistar rats were treated with morphine according to the following diagram: 1st group — acute treatment with morphine in high dose (50 mg/kg b.w.); 2nd group (chronic treatment) — over a period of 4 months one group of animals were injected subcutaneously, twice a week, with 0.10 mg/kg b.w. morphine: the animals were sacrificed 72 hours after the last injection; 3rd group — control rats. Thyroid glands were fixed in Bouin's solution. Paraffin sections, stained with haematoxylin-eosin, were used for morphometric measurements — height of thyrocytes and percentage ratio of the thyroid components: epithelium-follicular lumen - connective tissue [1]. For transmission electron microscopy (TEM) small tissue pieces, fixed in 2.5% glutaraldehyde and postfixed in 1% OsO_4, were used. The ultrathin durcupan sections were examined on an EM "Opton" — 109.

Results

Thyroid gland of animals from the 1st experimental group — 72 hours after acute morphine administration, demonstrated morphological sings of enhanced evacuation of thyroid hormones: increased height of the thyrocytes with dome-shaped apical, zone clear cytoplasm and vacuolized colloid (Fig.1). The percentage of the thyroid epithelium was lower while the relative amount of the connective tissue (blood vessels and connective tissue components included) was significantly higher. By electron microscopy: on the apical surface numerous microvilli, differing in shape and size, were observed — a feature of active colloid resorption (Fig. 2). A great number of lysosomes in apical zone of thyrocytes were present. Some of them were with irregular outlines, localized between dilated cytoplasmic reticulum.

In the thyroid gland of rats of chronically treatment the colloid in the follicle lumena was significantly reduced, certain zones of resorption yet presented, but the

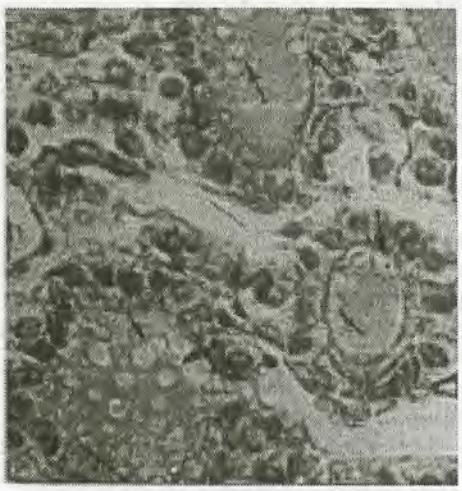

Fig. 1. Thyroid gland of rats 72 h after acute morphine treatment (50 mg/kg b.w.). Histological section, stained by haematoxylin-eosin. Morphological signs of an active evacuation of colloid (I) were presented (× 400)

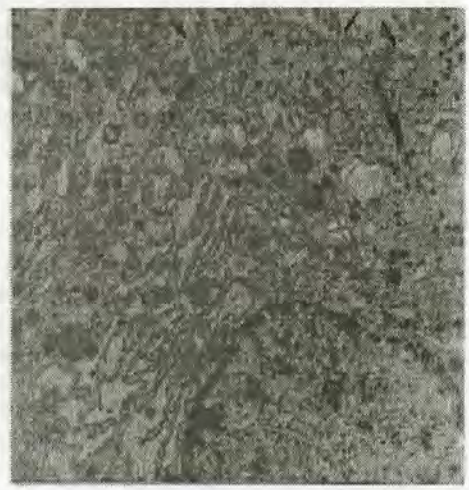

Fig. 2. Thyroid gland of rats 72 h after acute morphine treatment (50 mg/kg b.w.). Electronogram. In apical zone of thyrocyte an abundance of microvilli (I) was observed — (× 7300)

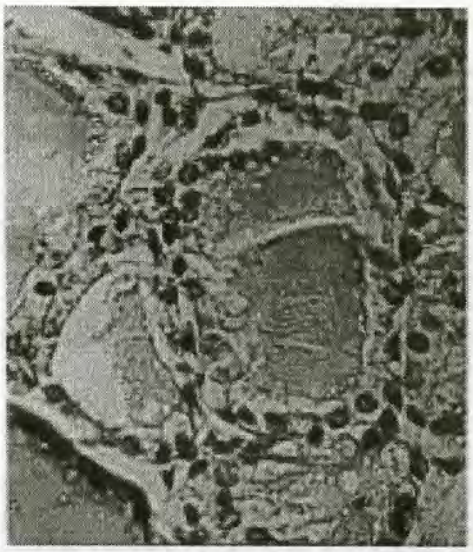

Fig. 3. Thyroid gland of rats after chronically morphine application (0.10 mg/kg b.w. twice a week during 4 months). Histological sections, stained by haematoxylin-eosin. The reduced amount of colloid and signs of functional exhaustion of the gland were observed (× 400)

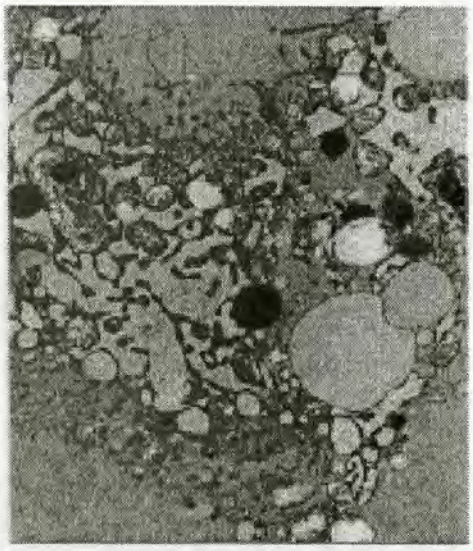

Fig. 4. Thyroid gland of rats after chronically morphine application (0.10 mg/kg b.w. twice a week during 4 months). Electronogram. Considerable changes in the ultrastructure of thyrocytes were observed (reduction of the endoplasmic reticulum and lysis of mitochondria) (× 7 300)

places of destruction, resulting of a total excitation of functional activity, were also visualized. The follicular wall was damaged in certain sites, causing a disorganization of the thyroid cytoarchitectonic (Fig. 3). There was a considerable augmentation of the connective tissue due to an increased vascularization. The nuclei of some thyrocytes were shown to be picnotic. Considerable changes in the ultrastructure of the thyrocytes were observed. Massive dilation and fragmentation of the endoplasmic reticulum was found and many mitochondria were shown to be destructed (Fig. 4).

Discussion

Different explanation of morphine effect of the thyroid function have been proposed. The biochemical investigations showed the decreased TSH levels after morphine application [5,7]. The morphological observations in present study demonstrate that single dose of morphine given to rats stimulate thyroid hormones evacuation and probably hormone secretion. Our results are in accordance with reports of T a i l et al. [12] who found increase of T_4 and T_3 concentrations after morphine application. The fact that morphine suppressed the TSH level and, at the same time increased T_4 and T_3 secretion may indicate that morphine has a short-term direct effect on the thyroid gland [12].

In case of hypothyroidism provoked by propilthiouracil (PTU) treatment or by thyroidectomy, morphine does not decrease serum TSH levels [8]. Thyroxine (T_4) replacement caused a dose-dependent decrease in serum TSH [2]. The authors suggested that morphine may exert its inhibitory effect on TSH by increasing the negative feedback sensitivity to thyroid hormones.

It has been demonstrated that the chronic morphine application significantly decreased the basal and cold-stimulated TSH secretion [6, 10]. Our morphological studies after chronic morphine treatment of rats are in good agreement with those biochemical data. The long-term administration (4 months) of morphine leads to functional exhaustion of the organ and significant destructive damages in the thyroid structure. The data presented here confirm the hypothesis of Tal et al. [12] and suggest that morphine may exert a biphasic effect: a short-term stimulatory effect on the thyroid gland function (in case of acute application) together with an inhibitory action on the hypothalamo-pituitary TSH system (during the chronic treatment).

Identification of morphological (cellular and tissue) changes and biochemical investigation of hormonal status (levels), as well as, the role of intercellular opioid receptors are challenging questions for future research into the influence of opiates upon the thyroid gland.

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