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Potential Effect of Carbimazole on Parotid Acini of Albino Rats

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ABSTRACT

Purpose: This study aimed to study the effect of carbimazole on parotid acini. **Materials and Methods:** 20 adult albino rats were selected and divided into two groups: control group (GI) consisted of 10 rats received distilled water by intra-gastric intubation for 6 weeks and carbimazole group (GII) in which 10 rats received carbimazole dissolved in distilled water with a dose (1.35mg/kg bodyweight/once/day) by intra-gastric intubation for 6 weeks. **Results:** GI illustrated normal histological features of acini. Serous acini were apparently normal in size with pyramidal shaped cells with pyramidal shaped cells of apparently normal height surrounding narrow lumen with basally located nucleus and basophilic cytoplasm. Carbimazole group showed marked destruction in acini. Most of the acini were shrunken with consequent separation between the acini in some areas. Some acini showed apparent loss of cell height and apparent widening of their lumina. **Statistical Results:** GI showed higher mean area % of acini, compared to GII. The difference was statistically significant. **Conclusion:** carbimazole has destructive effect on parotid acini.

KEYWORDS

Parotid; acini; Carbimazole.

INTRODUCTION

Parotid Gland is considered the largest salivary gland (SG).It is a purely serous gland. This gland produces 30% of the total salivary content. Thus, it contributes greatly in facilitation of lubrication, mastication, swallowing and digestion [(1)].

- Paper extracted from Master thesis titled "The potential effect of bone marrow-derived mesenchymal stem cells on parotid salivary glands of carbimazole-treated albino rats (Histological and *Ultrastructural* study)"

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Parotid gland consists of two main elements: parenchyma or epithelial elements (acini, ducts and myoepithelial cells) and supporting connective tissue (C.T) stroma. It is surrounded by dense irregular C.T capsule. From the capsule, septa arise to divide the gland into lobes and lobules[2].

Hyperthyroidism is defined as the clinical syndrome of hyper-metabolism resulting from increased free T4 and/or free T3 serum levels[4]. Antithyroid drugs include wide range of therapeutics for example thiourea derivatives such aspropylthiouracil (PTU) and thionamide derivatives that contain a sulfhydryl group such as methimazole (MMI) and the most recently used carbimazole[5]. Carbimazole is one of several thionamide drugs utilized for the treatment of different diseases causing hyperthyroidism in adults and children. Carbimazole is converted into the active form MMI after its ingestion.[6]

Many studies recorded the adverse reactions of carbimazole in different tissue. Minor side effects of carbimazole were recorded such as itching, rash, urticaria, joint pain, swelling, abnormal sense of taste or smell, nausea, or vomiting. These symptoms are not life-threatening and do not require discontinuation of carbimazole [7]. Many studies reported that carbimazole has major side effects. Impaired taste, impaired olfaction, hearing loss, and tinnitus have been reported in humans administered this drug. Moreover, histopathological evaluation of nasal cavities from rats treated by carbimazole revealed olfactory mucosal damage [8]. A previous study [9] reported that carbimazole administration during pregnancy and lactation resulted into alteration of the thyroid microstructure in the new born rats. Another study [10]reported that prostate glands of rats treated by carbimazole showed gradual decrease in the polysaccharide, and protein contents, beside degenerated prostatic acini and congested blood vessels (BVs).

MATERIAL AND METHODS

1. Animals

Twenty male albino rats weighing from (200-250gm) were used. The rats were housed in separate cages, maximum four rats per cage. Animal handling followed the rules and regulations of the animal experimental studies that were approved by ethical committee including their facilities, diet and method of scarification. The study was performed according to the guidelines of faculty of dental medicine's Animal Ethics Committee (REC18-081). The twenty rats were randomly divided into two equal groups (10 rats each): GI (control): in which 10 rats received distilled water once daily by intra-gastric intubation for 6 weeks. GII (carbimazole group): in which 10 rats received carbimazole dissolved in distilled water with a dose (1.35mg/kg bodyweight/ once/day) by intra-gastric intubation for 6 weeks [11].

Carbimazole was obtained from local drug store under trade name (Neomercazole® 5mg) produced by Amdipharm company, Australia.

2. Specimen collection

At the end of the 6th week, all the animals were euthanized by ketamine over dose and parotid salivary glands were dissected out.

3. Specimen preparation

The specimens were fixed in 10% neutral buffered formalin solution for 48 hours. The specimens were then dehydrated in ascending grades of alcohol, cleared in xylene, and embedded in paraffin blocks. Paraffin cross sections of 4 μm thickness were obtained and mounted on a clean glass slides. The parotid sections were deparaffinized and rehydrated then stained using H&E solutions and examined by light microscope.

Histomorphometric assessment:

Histomorphometric analysis was performed using imageJ software to assess area % of acini.

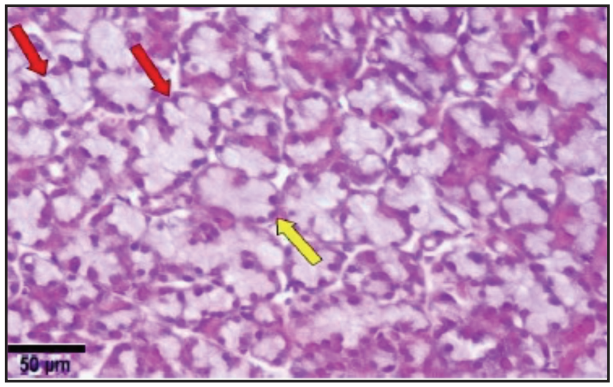
Five fields were analyzed for each specimen at 400x magnification.

Statistical analysis

The obtained data from histomorphometric analysis were statistically analyzed using Independent-samples t-test was used for comparison between studied groups.

RESULTS

Examination of histological sections of GI revealed normal architecture of parotid acini. The serous acini were apparently normal in size with pyramidal shaped cells of apparently normal height surrounding narrow lumen with basally located nucleus and basophilic cytoplasm. (Fig 1)



Figure(1) A photomicrograph of GI showing: normal serous acini with normal pyramidal cells (red arrows).hav basal basophilic nucleus (yellow arrow). and basophilic cytoplasm. (H&E, original magnification x 400).

Histological Examination of GII revealed loss of normal glandular architecture. Most of the acini were shrunken with consequent separation between the acini in some areas. Some acini showed apparent loss of cell height and apparent widening of their lumina. The cells showed large circumscribed cytoplasmic vacuolations. Pyknotic and karyolitic nuclei. Inflammatory cells infiltration as well as extravasated RBCs were detected between the acini. Congested and dilated BVs engorged with RBCs were noticed. (Fig 2)

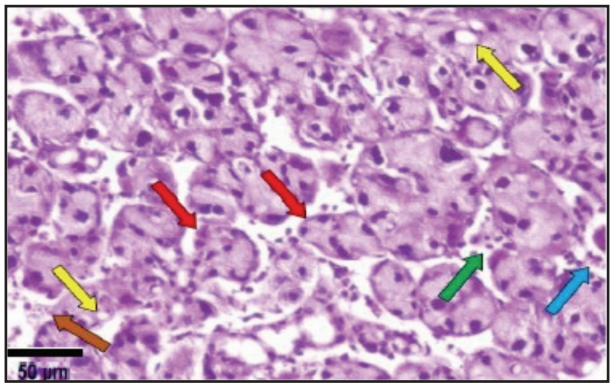


Figure (2) Photomicrograph of GII showing: serous acini with signs of degeneration, apparent. Shrinkage in size (red arrows). Cytoplasmic vacuolations and absence of cytoplasmic basophilia (yellow arrow). Chronic inflammatory cells infiltration (green arrow), extravasated RBCs (blue arrow), Congested and dilated BVs engorged with RBCs (brown arrow). (H&E, original magnification x400).

Statistical results

GI showed higher mean area % of acini, compared to GII. The difference was statistically significant **(table 1&Fig. 3)**.

Table (1): *Showing mean ±SD values, the range values, results of Independent-samples t-test for comparison between GI and GII regarding acini area%.*

Acini area%	Group I	Group II	ANOVA	p-value
Mean±SD	98.19±0.09	63.29±0.09	36.478	<0.001**
Range	98.1-98.3	63.2-63.4		

** *highly significant at p-value <0.001*

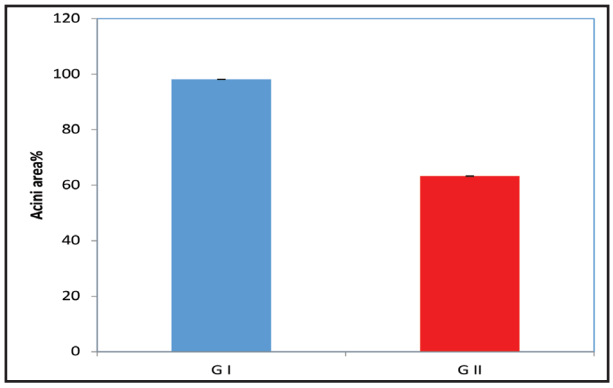


Figure (3) Bar chart representing mean and SD values of acini area% in studied groups.

DISCUSSION

The present study aimed to discover the possible effect of carbimazole on parotid gland acini, since carbimazole is the most commonly used anti- thyroid drug [12].

Histological examination of GI and statistical analysis of acini area % for this group revealed normal acini and acini area% respectively revealed normal acinar. This finding is consistent with previous studies [13].

Histological examination of parotid gland in GII and statistical analysis of acini area % for this group in current research showed that carbimazole caused damage to acinar cells and decrease in acini area%. Similar degenerative results were observed by authors in rat's liver treated with carbimazole [15]. This might be attributed to the oxidative stresses resulting from carbimazole administration. This assumption coincides several studies reported evidence for the induction of dose- and time-dependent oxidative stress by carbimazole [14]. **M**ethimazole the active ingredient of carbimazole caused pknotic nuclei and cytoplasmic vacuoles in hepatic cells caused by an increase of ROS, lipid peroxidation and reduction of catalase activity which lead to oxidative stress production, destruction of DNA, alterations of cellular proteins and enhancement of inflammatory processes that end up by cell death [7].

CONCLUSION

From the previously mentioned results, it could be concluded that carbimazole is able to induce destructive changes on acini of parotid.

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