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Histological Study of the Effect of Salbutamol on Rat Parotid Salivary Gland

[1]A. Esfandiari, [2]A.R. Yousofi and [3]S.M. Naghib
[1]Department of Anatomical Sciences, School of Veterinary Medicine,
Islamic Azad University, Kazeroun Branch, P.O. Box 73135-168, Kazeroun, Iran
[2]Department of Pathological Sciences, School of Veterinary Medicine,
Islamic Azad University, Abadeh Branch, Abadeh, Iran
[3]Young Researchers Club, Islamic Azad University, Kazeroun branch, Kazeroun, Iran

Abstract: Salbutamol is a sympathomimetic agent that has been used for treatment of respiratory diseases such as asthma in human and animals. Salbutamol stimulates β-adrenergic receptors in secretory units of parotid salivary glands and causes increasing of salivation and histological changes. Fifteen adult male rats were used as control and treatment groups. Chronic treatment of salbutamol with dosage of 4 mg kg^{-1} for 15 days revealed remarkable changes on weight of the parotid salivary glands. The weight of rats of treatment group had decreased, but this difference was not significant between control and treatment groups. Hypertrophy of secretory units in the parotid gland were detectable.

Key words: Salbutamol, parotid salivary gland, rat, hypertrophy

INTRODUCTION

The parotid salivary gland is a purely serous gland in rodent that is classified as a compound acinar gland (Banks, 1993). Various histological studies were undertaken on parotid salivary gland in different domestic animals at both light and electron microscopic level.

Morphological and functional study of the effect of isoproterenol on salivary gland cells (Sheetz and Menaker, 1979). Studies of composition of saliva were also reported in mammalia by Young and Schneyer (1981). Extensive studies were done on rat as a laboratory model (Henriksson, 1982; Suzuki and Ohshika, 1985; Schneyer and Humpfreys-Beher, 1987; Ryberg and Johansson, 1995; Mansouri and Motamed, 1996). The effect of isoproterenole on the salivary glands was also studied in hamster by Mehansho *et al.* (1987), in rabbit by Mansouri and Mohammadpour (1999), in dog by Mohammadpour and Jamshidi (2005).

However, no histological evaluation of parotid salivary gland under the effect of salbutamol was seen in male rat. Therefore, present study, describes the effects of salbutamol on the parotid salivary gland of rat at light microscopic level.

MATERIALS AND METHODS

Fifteen adult male Wistar rats weighing between 260-300 g were injected daily for 15 days 4 mg kg^{-1} salbutamol. Treated and untreated rats were anesthetized deeply with ether and parotid salivary glands were excised and after the weighting the glands and minced into 1 mm cubes and fixed in cold 4% phosphate buffered glutaraldehyde for 4 h. The tissues rinsed in buffer and dehydrated through graded ethyl alcohol and cleaned in propylene oxide and embedded in TAAB resin.

Semithin sections of thickness 0.5 μm were obtained using ultra microtome (Reichert-jung, ultra cut Austria equipped with glass knives), stained with toluidine blue and examined by light microscopy. Also, the parotid salivary glands minced into 1 cm cubes, they were placed in 10% buffered formalin as fixative for 24 h, followed by alcohol dehydration and embedding in paraffin sections of glands were stained with haematoxylin-eosin and for histological changes studied. All studies were performed in accordance with National Institues of Health Guide for the care and use of laboratory animals.

RESULTS

Following chronic salbutamol treatment, the enlargement of parotid salivary glands was so pronounced (Fig. 1). There was marked variation in the degree of their enlargement as the parotid salivary gland exhibited about 2-fold increase in wet weight as compared with the glands of untreated controls. The wet weight range of the control glands was 355-415 mg, as compared with 725-845 mg after salbutamol treatment. Using one-

Corresponding Author: A. Esfandiari, Department of Anatomical Sciences, School of Veterinary Medicine,
Islamic Azad University, Kazeroun Branch, P.O. Box 73135-168, Kazeroun, Iran

way ANOVA analysis, the wet weight changes were significant ($p<0.05$). On the other hand, 15 days after treatment showed that the changes in gland are reversible and returns to its normal state.

The parotid salivary gland is a compound acinar gland. It consists of three major components: acini, intercalated ducts and striated ducts (Fig. 2). The acinar cells are all of the serous type in rat (Fig. 2). In untreated glands, the secretory acinar cells contained secretion granules mostly in the apical cytoplasm and their large nuclei were located basally (Fig. 3).

Light microscopic observations revealed that the glandular enlargement was almost entirely due to hypertrophy of the serous secretory units (Fig. 4). Following salbutamol treatment, the cytoplasm of the hypertrophied acinar cells was packed with many large blue-staining secretion granules and the nuclei were compressed towards the base of the cell (Fig. 5).

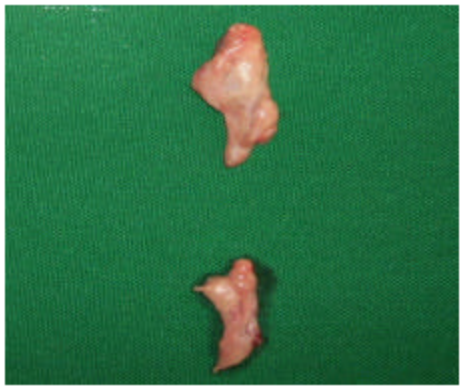

Fig. 1: Greatly enlarged parotid salivary gland of salbutamol (up)treated rat in comparison with parotid salivary gland of untreated control (down)

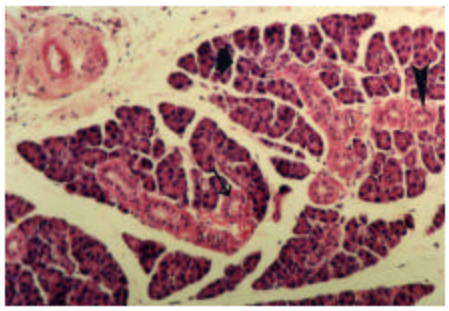

Fig. 2: Light micrograph of untreated control rat parotid salivary gland, showing serous secretory units. The space is between of the secretory units (thick arrow). Intercalated duct (arrowhead) and striated duct (thin arrow) also be seen between the secretory unit. H and E. ×180

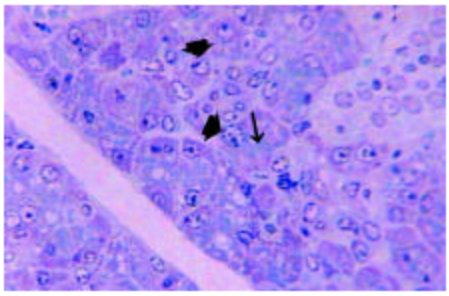

Fig. 3: Light micrograph of a semi-thin section of rat parotid salivary gland in untreated control group. The cells contain a large nucleus (thick arrow) which is basally located some granules are mainly in the apical cytoplasm (thin arrow). Toluidine blue × 720

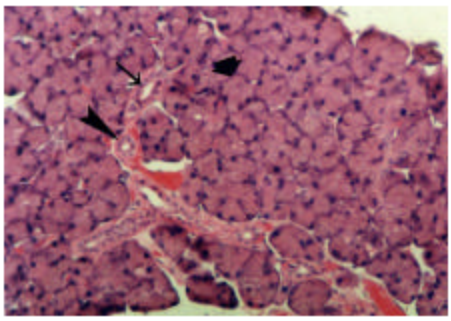

Fig. 4: Light micrograph of rat parotid salivary gland after salbutamol treatment. The space of between the hypertrophied secretory units was decreased (thick arrow). Intercalated duct (arrowhead) and striated duct (thin arrow) without change can also be seen between the secretory unit. H and E. ×180

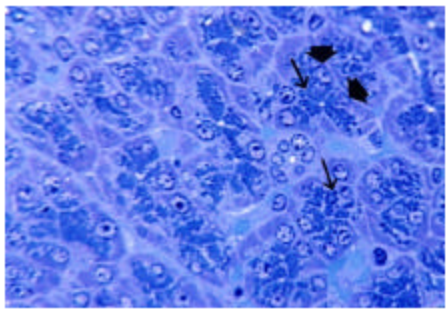

Fig. 5: Light micrograph of a semi-thin section of rat parotid salivary gland after salbutamol treatment. The cytoplasm of the hypertrophied acinar cells is packed with many large blue-staining secretion granules (thin arrows). The acinar cell nuclei are compressed toward the bases of the cells (thick arrows). Toluidine blue. ×720

No morphological changes were noticed in ductual cells after salbutamol treatment (Fig. 2 and 3).

DISCUSSION

The effects of isoprenaline on salivary glands have been extensively studied in rodents. In rats after one injection of isoprenaline, 96-98% of parotid salivary gland amylase in secreted and after daily injections with isoprenaline result in the enlargement is due to hyperplasia and hypertrophy of acinar cells (Byrt, 1966; Lillie and Han, 1973).

The enlarged acinar cells were completely occupied by secretion granules (Robinovitch *et al*., 1977; Simson *et al*., 1978).

This is followed by gradual resynthesis of stores of exportable proteins which is completed between 12-24 h after injection when the cell structure returns to that of the resting stage. After treatment the changes in gland are reversible and the gland apparently returns to its normal state (Fernandez-Sorenson and Carlson, 1974). These findings were essentially in agreement with our finding.

In our study the parotid salivary glands showed 2-fold increase in wet weight. The evidence has indicated that the effects produced by salbutamol treatment in parotid salivary gland are initiated by stimulation of β-adrenergic receptors with subsequent activation of adenylase cyclase and cAMP production. These cellular events usually lead to DNA synthesis in acinar cells. After chronic treatment and stimulation, hypertrophy of the acinar cells accompanied by accumulation of enlarged secretory granules (Robinovitch *et al*., 1977; Suzuki and Ohshika, 1985; Mansouri and Mohammadpour, 2001).

CONCLUSION

The results of this study showed that the following chronic salbutamol treatment, the weight of salivary glands increased and this result was significant between control and treatment groups. Also, the appetite had reduced and the weight had decreased in treatment group.

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