Localization of the atrial natriuretic factor i human inferior turbinates. An immunohistoch study

Localizzazione del fattore natriuretico atriale nei turbinati infer Studio immunoistochimico

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Key words

Turbinates • Atrial natriuretic factor

Parole chiave

Turbinati • Fattore natriuretico atriale

Summary

In man, the architecture of the turbinates is able to modify some of the physiochemical characteristics of the air inhaled. These modifications depend on the nervous system and on the action of neurotransmitters such as vasoactive intestinal peptide, Substance P, calcitonin gene-related peptide and other neuropeptides. As atrial natriuretic factor has been detected in the trachea and lung, the present immunohistochemical study was carried out to establish the presence and localisation of the atrial natriuretic factor on the inferior turbinates of the human being. The findings show atrial natriuretic factor to be present in the serous epithelial cells and in some cells of the *tonaca propria* near the sinusoids and the arteriovenous shunts and the acinar cells of the glands. Atrial natriuretic factor, therefore, could play a part in the stratification of mucus on the luminal surface and also regulate the blood flow of the capillaries, modifying, in this way, the physiochemical features of the air inhaled.

Riassunto

L'architettura dei turbinati dell'uomo è ido cune caratteristiche fisico-chimiche dell'ar dificazioni dipendono dal sistema nervoso e rotrasmettitori come il peptide intestinale stance P, il calcitonin gene-related peptide di. Dal momento che il fattore natriuretic scontrato nella trachea e nel polmone, abb condurre uno studio immunoistochimico su umani per stabilire la presenza e la locali natriuretico atriale. I risultati mostrano che tico atriale è presente nelle cellule epitelia ne cellule della tonaca propria vicino a shunts arterio-venosi e nelle cellule acina Pensiamo che il fattore natriuretico atrial un ruolo nella stratificazione del muco sull le e regolare anche il flusso sanguigno dei c dificare le caratteristiche fisico-chimiche a

Introduction

Chronic diseases of the inferior turbinates may cause obstruction of the nasal airways, but rhinologists have yet to agree as to whether pharmacological or surgical treatment should be carried out in these cases. This disagreement is due to lack of knowledge concerning how many neurotransmitters, which are distributed in the *tonaca propria* and involved in the activity of the nasal mucosa and blood vessels, are involved in the response of the immune system [1] modifying the tissue environment. Recent research has, in fact, demonstrated that neurotransmitters, such as NPT (neuropeptide Y) and somatostatin, in cooperation with adrenaline, exert a vasconstrictor effect, while VIP (vasoactive intestinal peptide) and HIP (histidine-isoleucine peptide), together with acetylcholine, exert a dilating effect and increase glandular secretion. In the basal lamina of the epithelium, furthermore, various neuroend cells have been found which, upon st ternal agents, are thought to release stances; these substances, via reflex the nerve endings, are believed to r microenvironment. The modificati important mechanisms: humidific moregulation. These mechanisms de gioarchitecture of the turbinates turbinates are endowed with an exter promotes contact between the air inh cosa; a *tonaca propria* presenting nu cous glands, the excretory ducts o seen in a deep portion near the ac cuboidal cells, and a distal portion th with the luminal epithelium [2]; and bl ated in the subepithelial, intermedia ers [3].

Table I. ANF: biological actions.

- Natriuresis
- Diuresis
- Vasodilatation
- Myorelaxation

The subepithelial layer presents a capillary network that is deeply anastomosed with the venous sinusoid network, exerting a capacitance function in which dry air causes repletion, while damp air causes depletion. The arteriovenous shunts lying in the deep layer of the *tonaca propria* modulate the exchange of heat at the air/mucosa interface, which is regulated by the blood flow; in fact, the shunts that serve a resistive function are opened by cold air, while they are closed by hot air [4]. These phenomena are regulated by the action of numerous peptides [5], such as VIP [6 7], calcitonin gene related peptide (CGRP) [8], and Sub P [9 10], which act upon the blood vessels. Among the neuropeptides investigated, no attention has been focused on the atrial natriuretic factor (ANF) which, due to its particular properties (Table I), could play a role in the modification of the nasal microenvironment, while numerous studies have explored the role of ANF in the bronchial and alveolar epithelium [11 12].
ANF is known to be a peptide composed of 28 aminoacids, with natriuretic, diuretic and vasodilator actions. In particular, ANF, binding with specific receptors situated in the smooth musculature of the vessels, increases the production of cGMP, determining vasodilatation, resulting in a variation in the blood flow [13 14].
Yue [15] has evaluated the concentration of ANF in the nasal secretion of patients in different pathological conditions, comparing it to haematic ANF concentration; the results indicated that in polyposis and atrophic rhinitis, nasal secretion ANF was lower than the haematic levels, while in simple rhinitis, nasal secretion ANF was greater than that in blood. These data led to the conclusion that ANF production, in nasal secretion, was independent of haematic production. Further studies, for therapeutic purposes, concentrated on the effects of intranasal administration of ANF, at varying dilutions, in various pathological conditions [16].
Although several Authors have shown an interest in ANF in pathological conditions, the nasal mucosa cytotypes involved in its production have not yet been identified.
Aim of this study was to establish, using immunohistochemical methods in normal inferior human turbinates, which ANF-secreting cytotypes could play a part, together with the other neurotransmitters, in the regulation of blood flow and of nasal mucus.

Materials and Methods

Sample fragments of normal inferior taken from ten young patients not acute or chronic rhinopathies. Speci by immersion in Bouin solution, an paraffin embedding. The sections stained for histological study eith toxylin-eosin or with the Mallory-A munostaining for ANF was carried the endogenous peroxidase by incub hydrogen peroxide in phosphate (PBS), pH 7.4, for 5 minutes at ro After blocking the non-specific si goat serum, the sections were treate polyclonal antibody (rabbit, Ser99-T Pharmaceutical, Belmont, CA, USA lutions (1/500, 1/600, 1/800) in a T droxymethyl]aminomethane-HCl) pH 7.2, for 12 hours at 4°C; the se washed in Tris-HCl buffer (three tim The detectors used were the avidin- aminoethylcarbazol method. Contro out in parallel both by omission of th or by using normal rabbit serum a tions.

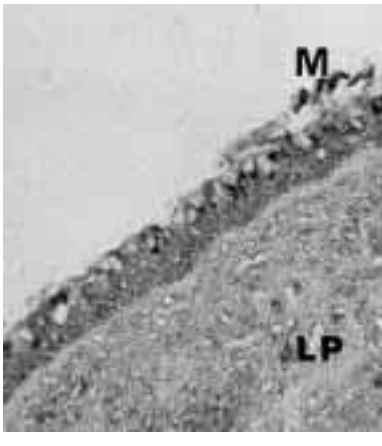

Fig. 1. Human inferior turbinates. Mu and mucus (M) are immunopositive for rests on basal lamina (BL) and ANF-imm and sanguiferous vessels are present i (LP). (10x). Abbreviations: see text.

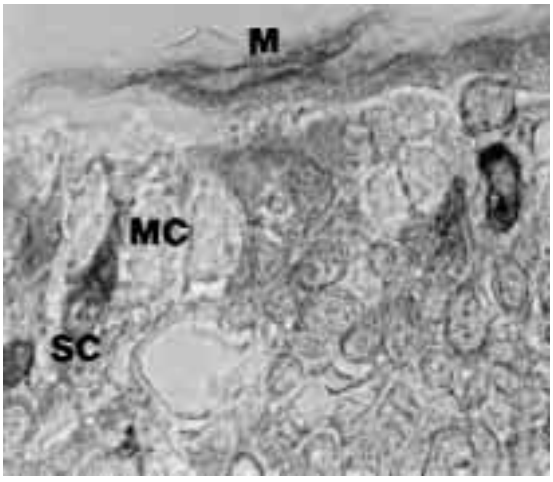

Fig. 2. Human inferior turbinates. ANF-immunopositive serous epithelial cells (SC); ANF-immunopositive mucus (M); ANF-immunonegative mucous cells (MC). (40x). Abbreviations: see text.

Results

Observation under a light microscope of sections of human inferior turbinates from subjects not presenting acute or chronic rhinopathy reveals a *tonaca mucosa* with a pseudostratified epithelium coating comprised of ciliated, serous, basal and globose cells and

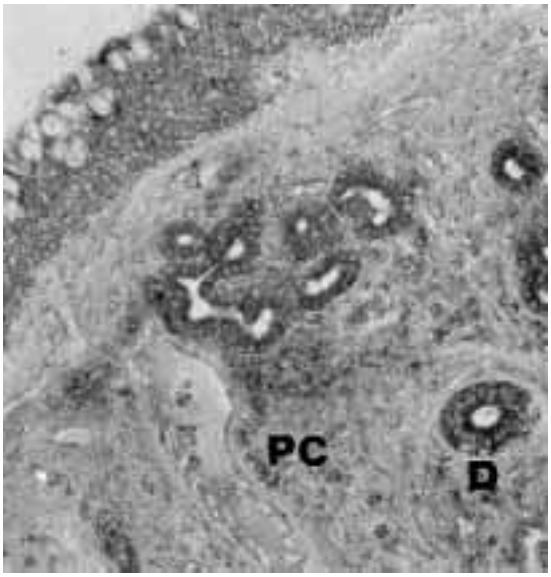

Fig. 3. Human inferior turbinates. Lamina propria: ANF-immunopositive perivascular cells (PC); ANF-immunopositive glandular excretory ducts (D). (25x). Abbreviations: see text.

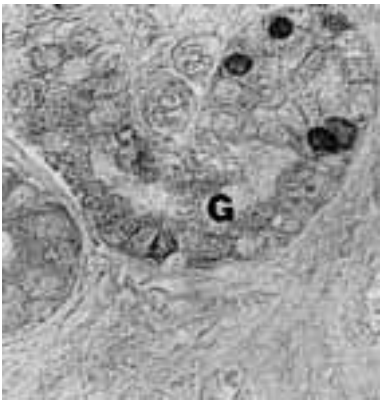

Fig. 4. Human inferior turbinates. ANF gland (G). (25x). Abbreviations: see text

with a thick *tonaca propria* in whic sels and glands are present. In the se tained for ANF, immunopositive cells may be found (Fig. 1), and th uted along the luminal surface, is (Fig. 2). No immunopositivity can basal membrane. Immunopositive ce the *tonaca propria* close to the cap and the serous acinar cells in the munopositive (Fig. 4).

Discussion

The nose, besides being a sense org respiratory system and carries out f modify some of the physiochemical air inhaled. These modifications tak before it is conveyed to the lower mucociliary system, the glands, the b the neurotransmitters. In the presen tions of preparations obtained aft chemical reactions for ANF showed ity in the serous epithelial cells and i would appear to suggest that the AN mucus is synthesised in the serous Mucus is known to be subdivided deep and superficial, respectively so responsible for transporting electro could determine the passage of wa stratum to the sol stratum of the mu creasing the fluidity of the sol laye the beating of the cilia. We, furtherm ANF secreted by the serous epitheli fect the ciliated cells through a parac thus increasing, as reported by G amount of intracellular cGMP that de iary beat rate [17].

As experiments with rat salivary glands have shown [18], the serous cells of the turbinate seromucous glands also present intense ANF immunopositivity.
Studies on the rabbit parotid gland have demonstrated the presence of ANF in the intra- and extralobular excretory ducts, which is believed to regulate salivary fluidity by means of a paracrine mechanism [2]. As the secreted substance accumulates in the deep portion of the excretory duct in human turbinate glands, we think that the ANF secreted by the acinar serous cells may act on the cuboidal cells of the deepest ductal portion to modify the composition and viscosity of the mucus, just as it does in the parotid gland of the rabbit, before being expelled onto the luminal surface.
The presence of immunopositive cells in the *tonaca propria* near the capillaries and venules is, in all probability, related to the paracine action of ANF on blood vessels. In the smooth muscle
endowed with ANF receptor sites, th
induce vasodilatation and, consequer
capacitance of these vessels. Furt
smooth muscle cells of the subendo
of numerous arteriovenous shunts, t
with its receptors, would reduce the
variation in the blood flow.
In conclusion, ANF is thought to regu
tion of the mucus layers by promotin
and, together with the other neurotra
regulate the resistance and capacitar
vessels, thus effecting a thermoregula
This neuropeptide found in the nas
with other peptides could, therefore
vasomotor rhinopathies and in neu
pendent diseases.

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