MEDIATORS OF THE BRONCHIAL MUCOSAL INFLAMMATION

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Abstract: *Establishing a correct diagnosis in acute respiratory infections is essential for their treatment. Within this context, it is important to know the mediators of bronchial mucosa inflammation. There are numerous inflammatory cells which are located along the segments of the respiratory system. The most important mediators of bronchial mucosa inflammation are: histamine, cytokines, prostaglandins, and platelet activating factor (PAF).*

Keywords: *inflammation, bronchial mucosa, mediators.*

Rezumat: *Stabilirea unui diagnostic corect în infecţiile respiratorii acute, este esenţială pentru tratamentul acestora. În acest context, este importantă cunoaşterea mediatorilor inflamaţiei mucoasei bronşice. Există numeroase celule inflamatorii, localizate de-a lungul segmentelor sistemului respirator. Cei mai importanţi mediatori ai inflamaţiei mucoasei bronşice sunt histamina, citokinele, prostaglandinele, leucotrienele şi factorul activator plachetar (PAF).*

Cuvinte cheie: *inflamaţie, mucoasă bronşică, mediatori.*

The bronchial mucosa is made up of epithelium, basement membrane and corion. This is characterized by a ciliated cylindrical and mucipaorus epithelium pseudostratificated, which is separated from the corionic structures represented by a conjunctive tissue, elastic, muscular lamina and nerves, by a basement membrane (4).

The bronchial epithelium is made up of eight types of cells. Out of these, the ciliate cells are the most numerous; five ciliate cells form a mucous cell. They may be found at the level of tracheae up to the terminal bronchioles (5). The apical pole is provided with almost 50 cilia, each of them being made up of an anatomic and functional substratum consisting in an undermembrane basal body, fibrillary roots fixed in cytoplasm and microtubules. Another cellular type encountered at the level of the bronchial epithelium is represented by the mucous cells showing mucigenous secretion granules, at the apical level. At the same time, this cellular type is rich in rugose endoplasmic reticle. It is considered that the number of these cells decreases progressively up to the level of lobular bronchioles, where they normally do not exist any more. It is considered that the secreted mucous is a sulphate protein (6). The other types of cells of the bronchial epithelium are represented by basal, intermediary, serous cells, brush border cells, neuroendocrine cells and Clara cells at the level of the distal bronchioles.

The innervation of the upper respiratory tract has its origin in the vagus nerve and comes from the sympathetic fibres which bring about the five thoracic sympathetic nerves.

It is appreciated that there are four types of nervous fibres at bronchial level (5).

The adrenergic dominant sympathetic fibres are placed in the neighbourhood of the submucous glands and bronchial vessels. It was proved that these fibres inhibit the cholinergic bronchoconstriction though their action at the level of the parasympathetic ganglions. The action of the catecholamines is made through two receptors, adrenergic alpha and beta, which could be found at the level of submucous glands; they change the viscosity and the elastic properties of the mucous.

The cholinergic parasympathetic fibres play an important part in regulating the smooth muscle tonus and that of the bronchial secretion. They are placed within the structure of the bronchial wall. Through their stimulation, the rapid and irreversible bronchoconstriction is accomplished due to the smooth bronchi muscle contraction. Hypersecretion of submucous glands is also determined.

The sensitive fibres are made up of fibres which are sensitive to irritating agents, stretch sensitive fibres and C fibres. These lead the sensitive information towards the central nervous structures. The fibres which are sensitive to the irritating agents are provided with receptors at the level of the bronchial epithelium, which are also sensitive to chemical and physical factors and to inflammation mediators as well, such as histamine and prostaglandins. Through stimulation, these fibres cause cough and reflex bronchoconstriction (3). The C fibres represent a network which is placed at epithelial and submucous level. These are stimulated by different irritating agents, such as kinines.

Through stimulation, the non-adrenergic and non-cholinergic intraepithelial nervous terminations produce different effects, according to the secreted neuropeptidic mediators. The latter include neuropeptidic

Y, cholecystokinin, tachykinins, calcitonin gene-related peptid, vasoactive intestinal polypeptide, histidine-metionine peptide and the histidine-izoleucine peptide.

Describing the action of the neuropeptidic mediators on the bronchial mucosa, it seems that the neuoropeptid Y is counter-transported along with the noradrenalin at the level of the sympathetic fibres, where it may inhibit the cholinergic transmission. Cholecystokinin is known as having bronchoconstrictor effect. Tachykinins include the substance P and the neurokinine A, molecules with proinflammatory action determining vasodilatation, bronchoconstriction, stimulation of the mucous secretion and adherence of polynuclears to the vascular wall. Vasoactive intestinal polypeptide, the histidine-metionine peptide and histidine-izoleucine peptide stimulate the mucous secretion and have vasodilatator effect and strong bronchodilatator effect.

At the level of the upper respiratory tract, numerous cells with inflammatory effect may be attracted, such as: neutrophils, eosinophils, monocytes, mastocytes or macrophages. All these types of cells interact and become active under the action of numerous mediators (1). Approximately fifty mediators of the inflammatory reaction are known, out of which the most important are: cytokines, histamines, metabolites of the arahydonic acid and the platelete activating factor.

Cytokines intervene at the moment when the inflammation occurs at intercellular level (2). They include polypeptides or glycoproteins, influencing the occurrence of the bronchial mucosa inflammation, which is specifically linked to the receptors of the cell they belong to or to the neighbour cell, either though endocrine action or away from their secretion place.

Histamine is stored in the interior of the cells, for example the basophiles or the mastocytes. Although it is considered the first known mediator of the bronchial mucosa inflammation, its role is still unelucidated from the clinical point of view (3). It seems to produce complex effects by the help of two types of membranary receptors, H1 and H2. Histamine influences the stimulation of the mucous secretion, has bronchoconstrictor action and chemotactical properties for eosinophils.

The metabolites of the arahydonic acid are synthesized by the activated cells membrane, being involved in the regulation of the cellular metabolism. The arahydonic acid is synthesized starting from the membranary phospholipids through the action of the phospholipases A2. Its metabolites are the leukotrienes which result from the action of lipoxygenases and prostaglandins, which at their turn result from the cyclooxygenases- action.

The platelet activating factor comes from the membranary phospholipids, being a strong aggregating agent for platelets, neutrophils and monocytes.

It plays a part in the stimulation of the platelet factor 4 release, of the thromboxanes A2 and of the platelet serotonin. It plays also a chemotactic part for eosinophils. It determines changes at the pulmonary structures level, with smooth muscular hyperplasia and inflammatory infiltration. It also determines the bronchoconstrictor effect and through the secretory cells activation or through the proinflammatory action, it may favour the mucous production (1).

It is considered that the origin of the cytokines is multicellular, involving interleukin 1, 3, 4, 5 6 and 8, cachectin and GM-CSF (2). Interleukin 1 is also secreted by macrophages at the contact with an antigen with lymphocytes. The other categories of interleukin are secreted mainly by the lymphocytes T and have a specific role in the inflammation of the bronchial asthma. Cachectin has a stimulation effect for the secretion of prostaglandins with the generation of the cytotoxic free radicals. By this role, the cytotoxic direct effect is appreciated (6). At the same time, it had an important pyrogenic action through the increase of the prostaglandin E2 synthesis at the level of hypothalamus. It is also considered an important proinflammatory mediator, though the activating action of the adhesion molecule, engaging the secondary secretion of interleukin 6.

The derivates of the arahydonic acid are represented by prostaglandin and thromboxanes, through cyclooxygenases.

As bronchodilatators, they have different effects, such as PGE2 or PGD2, PGF2 and TxB2 as bronchoconstrictors. It is considered that PGD2 is involved in the increase of the vascular permeability, which is almost thirty times bigger than that where histamine is involved (2).

Prostaglandins are secreted by cells such as eosinophils, macrophages, mastocytes and are involved in the increase of the mucous alteration through the mucosal and submucosal cellular infiltration

Lipoxygenases is considered the most involved in the regulation and dysfunctionalities within the mucous production at bronchial level (6). It was proved that the inhibition of the arahydonic acid though glucocorticoids determines the reduction of the mucous secretion, while cyclooxygenases, through non-steroidian anti-inflammatories determines the increase of the mucous secretion.

Through lipoxygenases, leukotrienes derive from arahydonic acid. These have bronchoconstrictor effect, increasing the vascular permeability and the synthesis of the platelet-activating factor. They have also a chemotactical effect for neutrophils and eosinophils. They are considered strongly involved in mucous secretion at bronchial level (6). These substances are secreted within neutrophils, eosinophils, and mastocytes.

In conclusion, mucous hypersecretion at bronchial level may occur as a result of the secretory cells stimulation or due to their increase in number. The mediators of this phenomenon come from the inflammatory cells of the autonomous nervous system and from the noradrenergic and noncholinergic intraepithelial nervous terminations. The inflammation may occur as a common stage of different tracts and may be exacerbated by the infection of the respiratory tract, increasing the mucous hyper

secretion at this level, which could be found in the diversity of the bronchopulmonary pathology.

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