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## **EFFECT OF MUCOSAL VACCINES ON THE CYTOKINE SPECTRUM OF THE OROPHARYNGEAL SECRETION IN PATIENTS SUFFERING FROM CHRONIC TONSILLITIS AND THOSE AFTER TONSILLECTOMY**

**Abstract.** *Investigations to determine the character of changes of the immunological parameters in the oropharynx before and after administration of mucosal vaccines of a systemic (OM-85) and local (Respibron) action have been performed. The levels of  $\gamma$ - and  $\alpha$ -interferon, anti-inflammatory cytokines and leukemia inhibitory factor (LIF) were determined by means of immune-enzyme method in patients suffering from chronic tonsillitis at the remission stage, those after tonsillectomy (TE) (1-5 years after surgery) and practically healthy donors. The results of the study are indicative of the fact that administration of mucosal vaccines promotes normalization of interferon and other cytokines parameters, that is, "normalization" vector was similar in both preparations, although delayed hypersensitivity (DHS) signs in case of chronic tonsillitis decreased only after administration of OM-85. Therefore, administration of both mucosal vaccines is an effective means to improve local immunity and decrease the level of local manifestation of sensitization in case of chronic tonsillitis (ChT) (for OM-85).*

**Key words:** *chronic tonsillitis, tonsillectomy, cytokines, oropharyngeal secretion, mucosal vaccines.*

**Introduction.** In recent decades immune prevention with administration of preparations on the basis of bacteria and fungi, so-called mucosal vaccines (MV) or bacterial immune modulators inhabiting on the mucous membranes, has been indicated to be an effective method to reduce sickness rate of infectious-inflammatory diseases of the upper respiratory tract [2,7,8].

Certain reports concerning intensification of systemic humoral and cellular immunity after preventive administration of MV are available [2,6]. The information about the character of immunological fluctuations in the oropharynx and nasal cavity after MV administration are inadequate to form an idea concerning the spectrum of changes of the local immunity in the upper respiratory tract. Due to this fact investigations to determine cytokines level in the oropharyngeal secretion (OPS) appeared to be important, since changes of their content determine the character and vector of development of local immune and allergic reactions. Considering the data concerning the effect of the clinical state of the lymphatic-pharyngeal structures on the local immunity [5], the levels of Th-1 and Th2 cytokine derivatives were examined in patients with chronic tonsillitis and those after tonsillectomy, who underwent immunological prevention with MV administration of a systemic action - type OM-85 (Bronchovaxom) and local action - Respibron.

**Objective:** to determine the efficacy of administration of mucosal vaccines in patients

with different conditions of the lymphatic-pharyngeal ring.

**Materials and methods.** The study included 52 patients at the age from 14 to 35. The control group included 12 practically healthy individuals without pathology of the upper respiratory tract. 21 patients with chronic tonsillitis were included in the group of patients at the remission stage. 19 patients were in the group of those after tonsillectomy (1-5 years after surgery) and did not complain of at the moment of the study. The object of the investigation was non-stimulated oropharyngeal secretion collected before and after MV and treated for immune-enzyme and cytological examinations according to methodological recommendations of the Institute of Otorhinolaryngology, National Academy of Medical Sciences, Ukraine [6]. The preparations OM-85 and Respibron were used according to the instruction during 3 months, and 10 days after the last intake oropharyngeal secretion was collected.

In the liquid phase of oropharyngeal secretion by means of immune-enzyme analysis (reader Lab line, Austria) according to the recommendations [4,5,6] the content of the following cytokines was determined: tumour necrosis factor (TNF- $\alpha$ ), interleukin-1 $\beta$  (IL-1  $\beta$ ), antiviral cytokines  $\alpha$ - and  $\gamma$ -interferon (reagents produced by Ltd Cytokine, RF). Moreover, in the liquid phase of OPS lymphokine content was determined reflecting the presence of delayed hypersensitivity (DHS) – leukemia inhibitory factor (LIF) applying capillary method [7]. The results were statistically

processed by means of non-parametric criterion «U» (Wilcoxon-Mann-Whitney) [1].

**Results and discussion.** The study conducted and analysis of the data obtained have determined that in OPS of patients with chronic tonsillitis and those after tonsillectomy an increased content of anti-inflammatory cytokines was detected compared with healthy individuals, mainly TNF- $\alpha$  in patients after tonsillectomy. According to the studies available and interpretation of the data concerning cytokines level [2,3] it can be indicative of prolongation of the mucous membrane inflammation or its "ability" to exacerbation of inflammatory process. After administration of mucosal vaccines the levels of anti-inflammatory cytokines was characterized by a reliable tendency to decrease ( $0,1 < p < 0,05$ )\* (Fig.1).

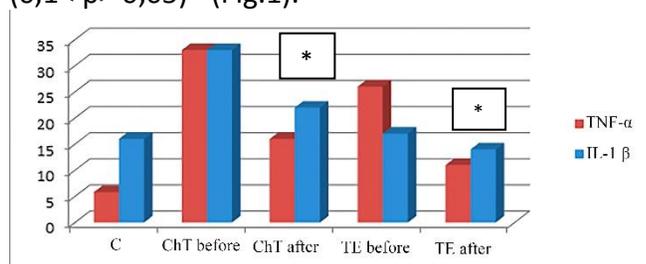


Fig.1. The content of anti-inflammatory cytokines in OPS of patients with chronic tonsillitis and after tonsillectomy before and after administration of MV.

The interferon content in OPS of the examined individuals showed that the lowest levels ( $p < 0,05$ ) concerning  $\alpha$ -interferon were found in those after tonsillectomy, while changes in  $\gamma$ -interferon content were not reliable between the examined groups in spite of considerable fluctuations. The preparations OM-85 and Respibron promoted strengthening of protective properties in OPS both in patients with chronic tonsillitis and those after tonsillectomy, which was manifested in increased interferon concentration in OPS. At the same time, differences in individual values were minimal and therefore the results presented on the figures are in a summarized form (Fig.2).

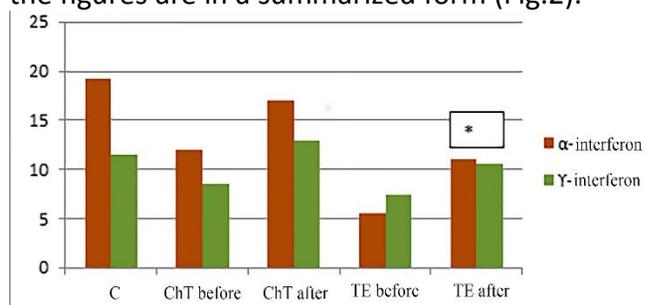


Fig.2. Interferon content in OPS after Respibron and Bronchovaxom administration in the examined groups; \*- reliable ( $p < 0,05$ ) considering the initial level.

The highest functional activity of LIF lymphokine was found in the liquid phase of patients with chronic tonsillitis, which can be indicative of DHS in OPS of patients, that corresponds to the data suggested by a number of authors [5,6]. Intensity of leukemia inhibitory factor from healthy individuals at the liquid phase of OPS after administration of MV decreased only after administration of OM-85 (Fig.3).

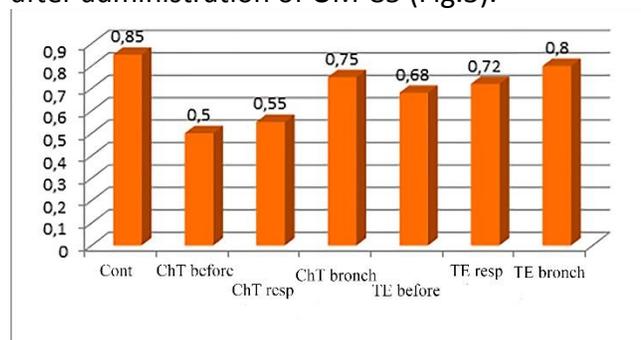


Fig.3. Lymphokine activity - LIF by the index of retardation of leukocyte migration by OPS supernatant in the examined groups after Respibron and Bronchovaxom administration; \*-reliable concerning the group «before» ( $p < 0,05$ ).

**Conclusions.** Therefore, the investigations conducted are indicative of the fact that certain deviations are found in the cytokine spectrum of patients with chronic tonsillitis and those after tonsillectomy, which can suggest the reduction of immunological potential of the oropharynx and increased level of DHS manifestations in case of chronic tonsillitis. Administration of mucosal vaccines of both local and systemic action promotes the normalization of interferon parameters and other cytokines, that is, the vector of "normalization" was similar for both preparations, although DHS signs in case of chronic tonsillitis decreased only after administration of OM-85. The data obtained enable to recommend both preparations increase mucosal immunity, especially for chronic tonsillitis.

**Prospect of further studies.** The obtained results enable to determine peculiarities of immune diagnostics and compare the efficacy of administration of mucosal vaccines of both local and systemic action in patients with different condition of the lymphatic-pharyngeal ring.

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