QUESTIONS OF FORMATION OF OXYGEN DEBT IN THE CONDITIONS OF LARYNGEAL OR HYPOPHARYNGEAL CANCER (LITERATURE REVIEW)

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ABSTRACT — This article provides a detailed literature review with the analysis of the impact of comorbid pathology on the course and prognosis of the primary tumor process. The illuminated factors that influence oxygen delivery to the tissues and the reasons for the rise of oxygen and substrates demand in terms of growth of laryngeal or hypopharyngeal cancer. The oxygen debt is formed, which affects results of the treatment.

KEYWORDS — laryngeal or hypopharyngeal cancer, comorbidity, airway obstruction, mucociliary insufficiency, hypoxemia.

Modest results of treatment [1, 2, 3] and survival [4] of patients with laryngeal or hypopharyngeal cancer are accounted with both a delay in seeking treatment and the combination of main diseases with different pathological processes (up to 77,9% [5]). This very combination of the main and comorbid pathology created a condition for disproportion in oxygen delivery and its need. This disproportion slows down restoring processes and enhanced the so called "hidden" background pathology, which accounts for progress and outcome of postoperative period and the illness in whole. However, in the specialized community there is no adequate evaluation of the impact of concomitant processes on reduction of oxygen delivery in tissues and in the same time increased demand of oxygen and substrates in patients with this pathology.

In one source [6] hypoxia, which is formed at heavy forms of tumors of the larynx/hypopharynx is recognized as one of the factors of unfavorable outcome. The marker of hypoxic changes, tumor necrosis factor of ((TNF)) has multiply exceeded the control data. Variable Illnesses, accompanying the main hypopharyngeal tumor process, were admitted as a key prognostic variable, which should be treated as a major compound at prognosis of treatment outcome. [7].

At a certain degree the importance of such approach is confirmed by existing dependence of the influence of disorder of trophic status on the outcome of oncological process. [8]. Works on efficiency of nutritional therapy in such patients [9] also confirm the importance of correcion of forming oxygen (=trophic) debt.

In patient with laryngeal or hypopharyngeal cancer despite importance of such risk factors as delay in seeking treatment and a high degree of invasion, the comorbidity degree is more decisive for outcome. Expressed comorbidity (48,3%) with high parameters of the Charlson comorbidity index was reported in the study [10]. In another work [11] the authors regard cardiological illnesses as a primary comorbid pathology in this patients. Thus, in 16,3% patients with surgery of tumors in head or neck various cardiologic problems were reported. It should be mentioned that the age of respondents was above 70 years.

Nevertheless, most of researches consider syndrome of bronchial obstruction and obstructive lung disease (OPD) as most frequent comorbid pathologies [1, 12, 13, 14].

Progressive obstructive changes during hypopharyngeal cancer process are displayed with manifested respiratory failure (RF). Studying the impact of methods of anesthesia on development of respiratory failure at surgical removal of larynx/hypopharynx

tumors revealed initial lung-bronchial pathology in all the patients, ventilation failure in 75–80% (in ⅔ of patients as an obstruction). However, speed parameters of ventilation were reduced in 25–55% irrespective of anesthesia methods. And restrictive changes were kept in 100% cases, whereas cases of bronchitis in postoperative period were observed in one third of all the patients. This study [15] found development of different chronic lung diseases in postoperative period in more than in half of the patients. The conclusions of the work indicated that the presence of obstructive and drainage bronchial disorders before the surgery, promotes the development of complications in the bronchial-respiratory system in postoperative period. It is important that manifested disorders in speed indicators of air stream in distal department of the respiratory tree are still preserved after removal of obstruction in proximal department (after surgical removal of the tumors).

The limitation of speed of air stream, being a main pathophysiological criterion of the bronchial obstruction, interrupts the mechanics of aspiration, ventilation/perfusion conditions, regulation of the ventilation [16, 17, 18]. Therefore, COPD manifestations under developing of proximal obstruction of the airways are difficult for clinical assessment. Expiratory limitations in patients with stenosing tumors of larynx/hypopharynx in combination with alterations in the speed of inspiration airway cause changes in aspiration volumes and proportions, which leads to worsening of alveolar ventilation and reduction of blood oxygenation.

The first system experiencing the most strain in the condition of proximal and distal stenosis of the airways is the system of mucociliary clearance. Changes in ventilation parameters leads to overload and dysfunction of the apparatus of mucociliary clearance, which is a characteristic process in the pathogenesis of bronchopulmonary diseases [19, 20]. Proximal obstruction under a tumor process with inflammatory conditions of tracheobronchial tree [21, 22], distal bronchial obstruction independently or in combination put a strain on work of the mucociliary apparatus up to the degree of failure (Mucociliary Transport Failure). The severity of MTF depends directly upon the degree of bronchial obstruction and correlates with the manifestation of endoscopic features of the inflammation and hyperactivity of the bronchi [23]. The degree of MTF is determined not only by the severity of morphological changes [24, 25], the activity of inflammation process in mucosa of bronchi, manifestation of the disorders in structure and functions of cilium apparatus[26], but also by deterioration of viscosity properties of bronchial secretion [27, 28].

Deterioration of speed parameters of gas stream, MTF, bacterial access provide a provocative influence on the immunity, reaction of inflammation in the respiratory system and the course of comorbid diseases. Significant increase in the level of anti-inflammatory cytokines under cancer pathogenesis in organs of respiration are reported by the authors [29, 30]. As a result of the described processes there is manifestation of bronchial obstructions leading to hypoxemia.

Depression of the immune system under tumor progressing is responsible not only for inflammation response but also for the strain in the systems of antibacterial and antiblastoma protection [31, 32]. The strain in anti-inflammatory cellular immunity and antibacterial protection increases demand for oxygen in cells and organs. It was not the purpose of our literature review to provide a detailed study of systems of antiblastoma and antibacterial protection. Nevertheless, the very fact of the strain in these systems and therefore the increase in energy need of the cells has gained importance for development of oxygen imbalance. Summing up, increase in parameters of the right part of oxygen equation (supply = consumption) disrupts the equation and in conditions of reduced oxygen supply leads to oxygen debt in tumor patients.

The problems of dividing function of larynx/hypopharynx. At before-surgical stage dividing function of larynx/hypopharynx plays less importance in forming mucociliary insufficiency than changes in speed characteristics of airways and inflammation. However, they display in involuntary swallow movements, difficulties in swallow, swallowing in small quantities, throat-clearing [33], which leads to microaspiration and exhaustion in mechanism of mucociliary clearance.

A constant effort during an act of breathing accompanied by increase in proximal obstruction of the airways results inevitably in functional exhaustion and less productivity of the muscles involved in the act of breathing. The exhaustion processes of these function of aspiration muscles in patients with larynx/hypopharynx tumors can be described as muscular insufficiency (MI). As a response to resistive strain there is an increase in inspiratory activity of the muscles of larynx/hypopharynx [34], increasing oropharyngeal space and preventing upper respiratory tract from occlusion under forced inhalation. Discoordination in the work of respiratory muscles weakens them, causes changes in biomechanics of a breathing act and disrupts the pattern of ventilation to hyperventilation and hypoxia. There is a hypothesis that the subject to exhaustion is diaphragm and additional muscles (intercostal and pharyngeal muscles) in various degrees. Electromiagraphycal examination [35] of different

groups of respiratory muscles under a forced load showed that decrease of summed functional reserve on the respiratory system is determined by deterioration of functional less in a diaphragm and more in thoracic and other auxiliary respiratory muscles. Diaphragm seemed to be more resistant to strain. [36, 37, 38, 39].

Thus, the progression of tumor creates conditions for reduction of speed of gas flow on proximal level, strain in work of respiratory muscles with narrowing of oropharyngeal airway space and impairment of mucociliary transport, changes in respiratory volumes, development and/or provocation of distal obstruction with poor secretion drainage. The general pathophysiological mode of formation of oxygen debt explains a mutual burden of laryngeal tumors and bronchial obstruction. The result of above mentioned processes is the formation of «hypoxia of delivery».

From the other side a high oxygen demand is connected with the processes of secondary bacterial infection on the background of cancerous intoxication with the strain of systems of antiblastoma and antibacterial protection as well as muscle exhaustion. In the total increased oxygen consumption there is also a role of the energy consumptive postoperative period after tumor removal.

Our own experience of the frame of our clinic confirms the proposed strategies for combined treatment in patients with laryngeal or hypopharyngeal cancer. One-stage radical surgery enables to reduce intoxication and to correct oxygen imbalance – "hypoxia of consumption".

In conclusion, it should be mentioned that unsatisfied oxygen needs lead to manifestation of either latently or openly developing processes, which may display in exacerbation of comorbid and background pathology and complications of the course of postoperative period. This gives evidence to clinical importance of the record of trophic status (formed cases of dysoxia) on all stages of operative treatment in patients with laryngeal or hypopharyngeal cancer.

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