ANTIMICROBIAL PHOTODYNAMIC THERAPY IN VOICE REHABILITATION OF PATIENTS AFTER LARYNGECTOMY

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Abstract

The article is devoted to the problem of voice rehabilitation of patients after laryngectomy. Modern possibilities of repairing laryngeal vocal function, methods for extending the lifetime of voice prostheses are considered. The author's method of prevention of infection of vocal prostheses using the antimicrobial photodynamic therapy (PDT) with chlorin-type photosensitizer Radagel is presented. Performing antimicrobial PDT of vocal prostheses increased the average operating time to 11.9 months compared to the control group (6.8 months), where a monthly dose of 150 mg of fluconazole was used for prevention. The method developed by the authors makes it possible to significantly extend the lifetime of vocal prostheses, is devoid of adverse events, is well tolerated by patients.

Keywords: laryngeal cancer, laryngectomy, vocal rehabilitation, voice prosthesis, photodynamic therapy.

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АНТИМИКРОБНАЯ ФОТОДИНАМИЧЕСКАЯ ТЕРАПИЯ В ГОЛОСОВОЙ РЕАБИЛИТАЦИИ ПАЦИЕНТОВ ПОСЛЕ ЛАРИНГЭКТОМИИ

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Резюме

Статья посвящена проблеме голосовой реабилитации пациентов после ларингэктомии. Рассмотрены современные возможности восстановления голосовой функции после ларингэктомии, способы увеличения срока эксплуатации голосовых протезов, представлен авторский метод профилактики инфекции голосовых протезов с помощью антимикробной фотодинамической терапии (ФДТ) с фотосенсибилизатором хлоринового ряда. Проведение антимикробной ФДТ голосовых протезов позволило увеличить средний срок эксплуатации до 11,9 мес по сравнению с контрольной группой (6,8 мес), где для профилактики использовали ежемесячный прием 150 мг флуконазола. Антимикробная ФДТ позволяет существенно продлить срок эксплуатации голосовых протезов, не имеет побочных явлений, хорошо переносится больными.

Ключевые слова: рак гортани, ларингэктомия, голосовая реабилитация, голосовой протез, фотодинамическая терапия.

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Introduction

Laryngeal cancer is the most common malignant neoplasm of the upper respiratory tract [1]. The characteristic features of laryngeal cancer are its late detection, the ratio of men and women affected being 16:1, with the predominance of men aged over 50, and the morphological uniformity of the tumor [2].

The modern treatment approach suggests that laryngectomy is indicated for most patients with a locally advanced tumor process at T3-4N0-2 stage [3]. Total laryngectomy inevitably leads to the loss of voice function, which causes significant psychological trauma, forcing some patients to refuse to undergo the crippling surgery. Therefore, the most important task after the removal of the larynx is to restore voice function. There are three well-known methods of voice rehabilitation after laryngectomy: esophageal voice, voice-forming devices, and tracheoesophageal bypass surgery with the installation of a voice prosthesis.

The speech therapy method of forming the esophageal voice requires long-term training. Successful mastery of esophageal voice is achieved in 24-83% of patients [4–6]. Voice-forming devices («electrolarynx») are used by no more than 10% of patients who have undergone laryngectomy, since the emerging voice has an unpleasant metallic timbre [7].

The most popular method of voice rehabilitation after laryngectomy at the present stage is tracheo-esophageal bypass surgery with the implantation of a special device, which is a voice prosthesis, into the lumen of the bypass [8]. The first voice prosthesis was developed by the American scientist Singer-Bloom in 1980. The first Russian voice prostheses were developed by V. O. Olshansky and L. G. Kozhanov in 1989 [9]. The voice prosthesis is a valve made of special silicone that provides unidirectional air flow from the trachea to the esophagus and prevents the contents of the esophagus from entering the respiratory tract (Fig. 1). The use of a voice prosthesis makes it possible to achieve speech restoration in more than 90% of patients [10].

The main disadvantage of the tracheo-esophageal bypass technique with voice prosthetics is the need for periodic replacement of the voice prosthesis. Prostheses implanted in the tracheo-esophageal fistula are in non-sterile conditions, which leads to their microbial contamination, perifocal inflammation and leakage of fluid from the esophagus into the lumen of the trachea. Due to the microbiological features of the oral and pharyngeal flora in cancer patients receiving long-term therapy that causes immunosuppression, the development of mucosal candidiasis is a common phenomenon [11]. Potentially pathogenic bacterial and fungal flora destroys the material of the voice prosthesis, and the valve cannot function properly (Fig. 2).

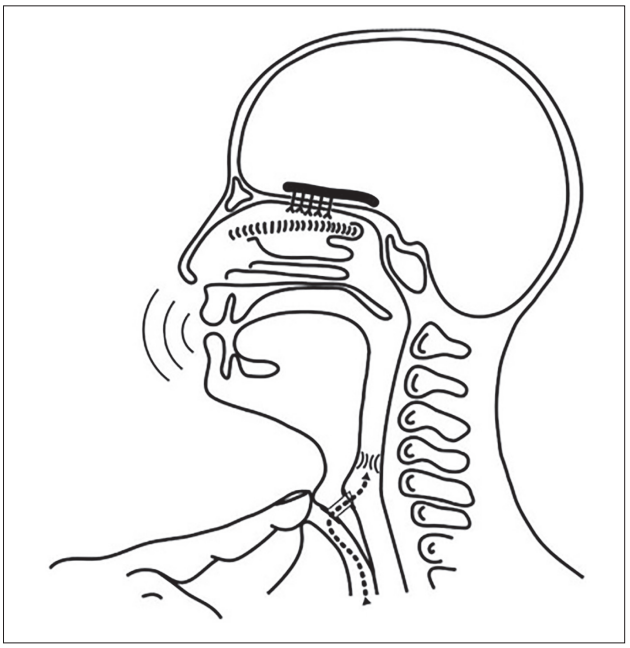

Рис. 1. Механизм образования голоса при трахео-пищеводном шунтировании с голосовым протезированием
Fig. 1. Mechanism of voice formation in tracheo-esophageal shunting with vocal prosthetics

Рис. 2. Микробная контаминация голосового протеза с образованием вегетаций на клапане и пищеводном фланце (стрелка)
Fig. 2. Microbial contamination of the vocal prosthesis with the formation of vegetations on the valve and esophageal flange (arrow)

During the bacteriological study of swabs from voice prostheses during their replacement, various types of fungi and opportunistic bacteria were identified (Staphylococcus aureus, Pseudomonas aeruginosa, Enterococcus faecalis, etc.) [12]. The average service life of a voice prostheses is from 6 to 12 months [13].

Various methods have been developed in clinical practice for preventing the development of infection around the voice prosthesis. These include local treatment with antiseptic and antifungal solutions (3% solution of hydrogen peroxide, 3% solution of Clotrimazole (Candide), 0.01% solution of Miramistin), daily cleaning of the voice prosthesis with a special brush, certain hygienic and dietary recommendations, oral and topical use of probiotics containing lactobacilli, treatment of gastro-esophageal reflux disease, systemic use of antifungal drugs (Fluconazole, Amphotericin, Nystatin, Irunin) [4,7]. Manufacturers have designed voice prostheses with the inclusion of silver threads, which increases the service life of the device [11]. However, the variety of the methods used to solve the problem of voice prosthesis microbial contamination shows that no single effective method of prevention is available. Systemic administration of antifungal drugs is associated with the risk of side effects, the development of microorganisms resistant to antifunginal drugs. This means there is an urgent need to find new approaches to solving the problem of preventing infectious lesions of voice prostheses in patients after laryngectomy.

The progress of medicine has led to the emergence of a fundamentally new method of biological objects treatment: photodynamic therapy (PDT), associated with the interaction of laser radiation and a new class of pharmacological drugs: photosensitizers (PS). Antimicrobial PDT consists in selective oxidative destruction of pathogenic microorganisms by the combined action of PS and optical radiation of the corresponding spectrum, which leads to the development of a photodynamic reaction. In recent years, there have been many reports of successful eradication of various microorganisms with the use of antimicrobial PDT, including data on the effective inactivation of antibiotic-resistant biofilms [14, 15]. Antimicrobial PDT targets viruses, bacteria, fungi and protozoa [16]. Antimicrobial PDT is an effective method for the treatment of purulent and inflammatory diseases of the ENT organs, soft tissues, and periodontal disease [17–23].

The goal of our study was to develop an effective method for preventing microbial damage of voice prostheses in patients after laryngectomy, which would extend the service life of the device. The technical result is the prevention of fungal and bacterial infections development in the area of the voice prosthesis in patients after laryngectomy and the increase of the service life of the device by the use of antimicrobial PDT.

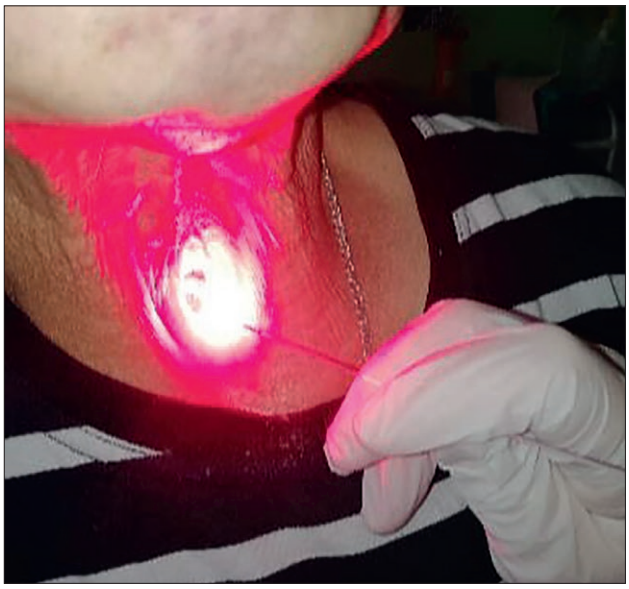

Рис. 3. Сеанс антимикробной фотодинамической терапии голосового протеза
Fig. 3. Session of antimicrobial photodynamic therapy of vocal prosthesis

Materials and methods

We have developed an original method for preventing infection of voice prostheses by the use of antimicrobial PDT with Radagel® chlorin-based PS, 0.5% gel (OOO «RADA-PHARMA», Russia). To do this, a pharmaceutical is injected into the lumen of the voice prosthesis; the drug used is PS (radachlorin or an analog) in gel form, in the quantity of 1-2 ml. The exposure to the PS is for at least 15 minutes. The introduction of the drug into the lumen of the voice prosthesis makes it possible to treat the most affected parts: the valve and the esophageal flange. Then the excess gel is removed by blowing through the voice prosthesis with a 20 ml syringe, and the area is irradiated from the inside with a laser with a wavelength of 662 nm for 5 minutes, at the output power of 400 MW (Fig. 3).

The dose density of the laser radiation necessary and sufficient for the inactivation of microorganisms is 50 J/cm^2. As a source of optical radiation, we use a diode laser with a wavelength of 662 nm, which corresponds to the absorption peak of the PS of the chlorine group. It is recommended to administer laser irradiation using a cylindrical diffuser with a 2 cm long scattering part. The diffuser is inserted into the lumen of the voice prosthesis, which allows treatment of the tracheal and esophageal flanges, the lumen and the valve of the voice prosthesis. Antimicrobial PDT sessions are administered once a month. The total number of sessions is unlimited (until the voice prosthesis fails and has to be replaced). The treatment is absolutely painless. We did not observe any side effects, allergic reactions, or complications during the antimicrobial PDT of voice prostheses.

Таблица
Параметры пациентов групп сравнения
Table
Comparison of patient groups parameters

	Пол Sex		Средний возраст, лет Average age, years	Стадия заболевания Tumor stage		Вид противоопухолевого лечения Type of antitumor treatment			Индекс массы тела / Body mass index
	М	Ж		III	IVA	Хирургическое / Surgical	Комбинированное / Combined	Комплексное / Comprehensive	
I группа (без ФДТ) Group I (without PDT)	10	–	56	6	4	1	6	3	26
II группа (с ФДТ) Group II (with PDT)	10	–	58	7	3	0	7	3	28

In order to evaluate the effectiveness of the developed method, a study was conducted involving 20 patients who underwent laryngectomy with delayed tracheo-esophageal bypass surgery and voice prosthetics. All patients were fitted with Provox prostheses. The patients were divided into two groups of 10 people in each of them.

In the first group of patients (control group), infection prevention was carried out by daily cleaning of the prosthesis with a special brush moistened with a 3% solution of hydrogen peroxide; after each meal, the patients drank a few sips of water. Once a month, patients in the first group took 150 mg of fluconazole per os.

Patients of the second group also followed the recommendations concerning hygienic treatment of the voice prosthesis and nutrition, but were not administered antifungal agents. To prevent the development of infection of the voice prosthesis, they were given antimicrobial PDT sessions once a month based on the method described above.

Both groups of patients were comparable in terms of their age, gender, the stage of the disease, previous therapy type, and nutritional status at the time of inclusion in the study (Table).

In each of the groups, the prosthesis was installed for the first time in 5 patients, and in 5 patients, a replacement prosthesis was installed due to the failure of the previous one. The service life of a prosthesis before the inclusion in the study was from 3 to 18 months (6.4 months on average).

The processing of the clinical data and the results obtained was performed with nonparametric statistical methods. The average values were compared with the Mann-Whitney U test.

Results

The average service life of voice prostheses in patients of the first group, who received 150 mg of fluconazole monthly as a prevention measure, was 6.8 months. In the group of patients who received monthly sessions of antimicrobial PDT, the voice prostheses functioned for an average of 11.9 months. The differences are statistically significant.

Conclusion

Thus, the use of PDT resulted in a 75% increase in the service life of the voice prostheses. The proposed method of infection prevention allows for antiseptic treatment without removing the prosthesis from the patient's body. The antecedence of the authors is confirmed by the pat-

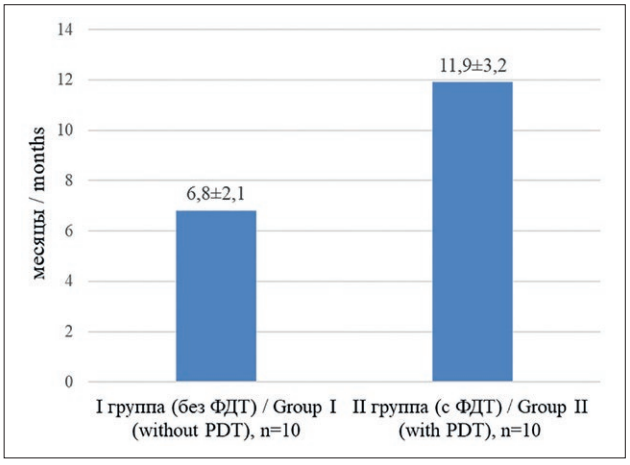

Рис. 4. Время функционирования голосовых протезов в группах сравнения (мес.)
Fig. 4. Operating time of voice prostheses in the compared groups (months)

ent of the Russian Federation for invention No. 2731312 «A Method for the Prevention of Infectious Damage of Voice Prostheses in Laryngectomees», registration date: 01.09.2020.

It should be emphasized that the greatest increase in the service life of voice prostheses due to antimicrobial PDT was recorded in patients who previously needed replacement of the prosthesis more often than once every 6 months. This category of patients should be considered as a priority for antimicrobial PDT. The developed method significantly extends the service life of voice prostheses, which are expensive rehabilitation devices; the method has no side effects and is well tolerated by patients.

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