ORIGINAL ARTICLES

COMPARISON OF PHOTODYNAMIC THERAPY EFFICIENCY USING RADIATION SOURCES WITH DIFFERENT WAVELENGTHS IN THE TREATMENT OF SINUSITIS

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Abstract

Inflammatory diseases of the sinuses – one of the most common nosologies in the practice of otorhinolaryngologist; its pathogenesis is well studied, and treatment recommendations are detailed. Following them, however, cannot completely prevent chronic disease or recurrence. Antimicrobial photodynamic therapy is a promising method of treating sinusitis, which has proved its effectiveness, but has not yet been widely used. This work describes our experience in photodynamic therapy with chlorin e_6 of chronic sinusitis using a new laser diode-based irradiation source. For patients who had previous sinus surgery an adapter for penetration into the sinus through anastomosis was developed and tested. First group of the patients underwent photodynamic therapy (PDT) according to the conventional scheme, using a laser with a wavelength of 662 nm; while the second one underwent PDT using a 405 nm laser. With daily washing of the nasal sinus, the period of inflammation relief (evaluated by the absence of pathological discharge during washing) amounted to 3.8 full days on average in the first group of patients, compared to 5.4 days on average for the second group. We carried out the comparative analysis of the treatment results based on clinical assessment and radiological evaluation (CT) at the time of discharge from the hospital and 1 month later.

Keywords: chronic sinusitis, antibacterial photodynamic therapy, diode laser.

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СРАВНЕНИЕ ЭФФЕКТИВНОСТИ ФОТОДИНАМИЧЕСКОЙ ТЕРАПИИ ПРИ ИСПОЛЬЗОВАНИИ ИСТОЧНИКОВ ИЗЛУЧЕНИЯ С РАЗЛИЧНЫМИ ДЛИНАМИ ВОЛН В ЛЕЧЕНИИ СИНУСИТОВ

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Резюме

Воспалительные заболевания пазух носа – одна из самых распространенных нозологий с хорошо изученным патогенезом в практике оториноларинголога. Для ее лечения разработаны подробные рекомендации, следование которым, однако, не всегда позволяет полностью предотвратить переход заболевания в хроническую форму или возникновение рецидивов. Антимикробная фотодинамическая терапия (ФДТ) – перспективный метод лечения синуситов, уже доказавший свою эффективность, но еще не получивший широкого распространения в клинической практике. В работе описан опыт применения нового источника облучения на основе лазерных диодов, предназначенного для проведения ФДТ хронических синуситов с препаратами хлорина e_6. Для ранее прооперированных пациентов разработана и апробирована насадка для проникновения в пазуху через соустье. I-ой группе пациентов ФДТ проводили по общепринятой схеме с использованием лазера с длиной волны 662 нм, для облучения II-ой группы применяли источник облучения с длиной волны 405 нм. При ежедневном промывании носовой пазухи сроки купирования воспаления (оценивали по отсутствию патологического отделяемого при промывании) для пациентов I-ой группы составили в среднем 3,8 сут, а у пациентов II-ой группы – в среднем 5,4 сут. Проведен сравнительный анализ результатов лечения, которые оценивали клинически и рентгенологически на момент выписки и через 1 мес.

Ключевые слова: хронический синусит, антимикробная фотодинамическая терапия, диодный лазер.

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Introduction

Antimicrobial photodynamic therapy (APDT) is a successfully used method of treating inflammatory diseases based on the inactivation of pathogens caused by the interaction between a drug – a photosensitizer (PS) – and light with certain properties. The development of new types of photosensitizers and radiation sources contributes to the widespread use of APDT in various medical disciplines. For example, antimicrobial photodynamic therapy is used in otorhinolaryngology to treat acute and chronic sinusitis, chronic tonsillitis, chronic otitis, purulent diseases of the larynx [1, 2].

It has been proven that both bacteria and fungi, main pathogens causing the inflammation of mucous membranes of paranasal sinuses, form so-called biofilms [3, 4]. Their occurrence is a kind of defense mechanism that protects bacteria from the effects of the body's immune system and antibiotics. It has been shown that bacteria living in biofilms are more virulent than free-floating forms [5]. In recent decades, there were a lot of reports on the efficiency of the eradication of various microorganisms using APDT, including data on the efficient treatment of gram-negative and gram-positive antibiotic-resistant biofilms [6].

Chronic sinusitis is a polyetiological disease developing due to a combination of causes including congenital anomalies of the immune system, a disruption in the normal anatomy of the nasal cavity and environmental factors such as inflammatory and irritating agents. Common treatment algorithms are not always fully efficient, and the disease exacerbation rate does not decrease in a number of patients after the surgery for the restoration of the normal sinus drainage and aeration [7]. According to national and international standards, the exacerbation should be managed with systemic antibiotics therapy, which, if regularly repeated, cannot but increase the likelihood for antibiotic resistance [8]. In our opinion, PDT can play a preventive role here and serve as a method of treatment allowing to achieve a good effect in case of existing antibiotic resistance and having the potential to prevent and limit the increase in antibiotic resistance in a specific person and the whole population.

Photodynamic therapy of inflammatory chronic sinusitis is mainly intrasinus: the sinus of not operated patients is accessed by means of endonasal maxillary sinus dissection, while the sinus of operated patients is accessed through the dilated junction of the maxillary sinus.

A laser with a wavelength of 662 nm is usually used as an radiation source for PDT with chlorine e6 [9, 10]. However, there is an increasing amount of data on the use of other laser or LED sources but the clinical experience in application of such techniques is still limited [11]. The chlorine based PS has an absorption peak at around 405 nm, and the pilot study of LED irradiation with this wavelength gave a positive result [12], therefore we decided to conduct an in-depth study of its efficiency.

Materials and methods

22 patients (13 men and 9 women) with chronic purulent sinusitis in the exacerbation phase were treated in the ENT department of the Clinical Hospital No. 122 named after L. G. Sokolov of the FMBA of Russia from 2015 to 2017.

The eligibility criterion for patient enrollment in the study of PDT was the chronic maxillary sinusitis in the exacerbation phase confirmed by previous epicrises, findings of computed tomography of paranasal sinuses (the presence of pathological contents in maxillary sinuses) and endoscopic examination (the presence of edema, hyperemia of the nasal mucosa, purulent discharge in nasal meatuses). All patients had undergone surgical treatment for chronic sinusitis, after which the natural junction of the maxillary sinus in the middle nasal meatus or the artificial junction in the inferior nasal meatus remained dilated. Patients with chronic somatic diseases in the exacerbation or decompensation phase were excluded from the study. Exclusion criteria also included intake of antibiotics during the study for this sinusitis exacerbation episode or for any other reason and an advanced polipous process, which would fill the maxillary sinus.

Fotoditazin (VETA-GRAND LLC, Russia, registration licence No. LS 001246 of 18.05.2012) in the form of a concentrate for a solution for infusion of 5 mg/ml was used as a photosensitizer for PDT. On average, 7-9 ml of the PS solution were administered into each sinus, wherein the concentration of the solution for intrasinus administration corresponded to the average concentration for intravenous administration indicated in the package insert. The sinus was rinsed under topical anesthesia using a cannula, then it was blown out with air to release it completely from the liquid. After that, the prepared photosensitizer solution was administered. To prevent the solution leakage, the middle or common nasal meatus was plugged with a cotton tampon moistened with a fotoditazin solution in patients that had undergone infundibulotomy and maxillotomy, respectively. Topical anesthesia was not associated with rinsing itself but was used to ensure comfortable plugging.

ALCOM-MEDICA LLC (Russia) developed and manufactured a low-power unit with replaceable emitters, the "SHUTLE-COMBI IR+" complex based on diode lasers and LED light sources (Fig. 1). The complex allows simultaneous work with different types of low-energy sources. For this study we used laser emitters with working wavelengths of 662 nm and 405 nm. A special curved tip was attached to them to get into the artificial junction of the maxillary sinus (Fig. 2).

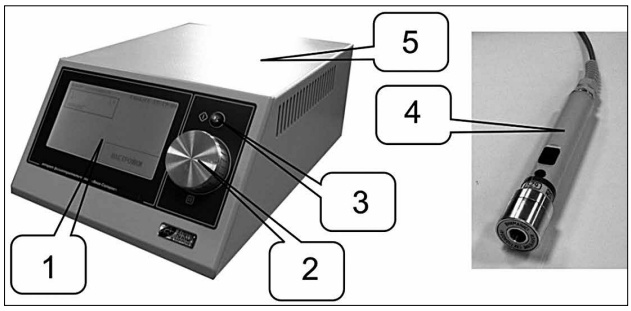

Рис. 1. Комплекс на основе диодных лазеров и светодиодных излучателей «ШАТЛ-Комби ИК+»:
1. графический дисплей с пультом управления
2. ручка регулировки
3. кнопка старт/стоп
4. излучатель
5. блок управления

Fig. 1. Complex based on diode lasers and LED emitters "SHUTLE-COMBI IR+":
1. graphic display with control panel
2. adjustment knob
3. start / stop button
4. emitter
5. control unit

Рис. 2. Насадка для верхнечелюстной пазухи
Fig. 2. Nozzle for maxillary sinus

The patients were divided into two groups. The sinuses of the first group of patients (9 people) were irradiated with a laser with a wavelength of 662 nm and an output power of 50 mW for 20 minutes. 13 patients of the second group were irradiated with a laser with a wavelength of 405 nm and an output power of 100 mW for 20 minutes.

The chosen PDT efficiency assessment criteria were the duration of management of inflammatory process exacerbation based on the presence and amount of purulent discharge from the sinuses, the length of patient's hospital stay and the findings of the X-ray inspection conducted at the end of treatment and repeated 1 month after release.

Results and discussion

Phototoxicity and allergic reactions were not observed in any patients during the study. The emitter was easy to use. The rigid tip allows applying this technique on previously operated patients with a wide junction of the maxillary sinus. Performance of this treatment using a fiber optic light cable would be difficult since the bending angle of the tip for sinus rinsing was large enough and led to the damage of the light cable. The results of inflammation management are shown in the table.

The length of patient's hospital stay corresponds to the daily duration of maxillary sinus rinsing.

The X-ray findings (according to helical computed tomography of the paranasal sinuses) at the end of the treatment and 1 month after it showed improvement in both groups of patients.

Thus, the results of PDT using a laser emitter with a wavelength of 662 nm are comparable with the literature data and confirm the efficiency of this method

Таблица
Сроки купирования воспалительного процесса (появление чистых промывных вод) после сеанса фотодинамической терапии
Table
Terms of the inflammatory process relief (the appearance of clean washing water) after a session of photodynamic therapy

Количество суток до появления чистых промывных вод Days before the appearance of clean washing water	Число пациентов с полностью купированным воспалительным процессом The number of patients with fully arrested inflammatory process			
	I группа (n=9) Group I (n=9)		II группа (n=13) Group II (n=13)	
	Абс Abs	%	Абс Abs	%
3	4	44,5		
4	4	44,5	2	15,5
5			5	38,4
6	1	11	5	38,4
7			1	7,7

in the treatment of sinusitis [10]. The use of an emitter with a wavelength of 405 nm during PDT showed good clinical outcomes: the inflammation was managed but over a longer period than at 662 nm. It should be noted that the work with this type of emitters shows better patient compliance since the majority of the population is familiar with a blue light lamp and its bactericidal activity, which makes it easier to explain the mechanism of action. The nature of discharge in all patients changed on the first day although they did not complete the course. We consider it as an opportunity to study the efficiency of irradiation with a source with a wavelength of 405 nm in bacterial cultures. It would also be interesting to study the efficiency of the light effect on biofilms at this wavelength. The depth of light penetration in tissues at a wavelength of 405 nm is small, so the use of violet light is reasonable when the abnormal focus is located at the surface. Since chlorine e6 based photosensitizers have an intense absorption peak in this spectral band, this significantly reduces the emitter power requirements making this type of irradiation advantageous for the use in the antimicrobial photodynamic therapy of sinusitis.

Conclusion

The described experience of clinical use shows that the laser irradiation at 405 nm is efficient as part of photodynamic therapy of chronic sinusitis and, along with laser irradiation at 662 nm, can be an alternative to the conventional management of sinusitis in the exacerbation phase. To obtain reliable statistical data, more patients should be enrolled, especially to study the efficiency of a 405 nm laser light source.

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