

DOI: 10.18481/2077-7566-2023-19-1-57-63
УДК 616.31-002.157.2:616.34-08

СРАВНЕНИЕ ЭФФЕКТИВНОСТИ ДИОДНЫХ ЛАЗЕРОВ И АППЛИКАЦИОННЫХ СРЕДСТВ В КОМПЛЕКСЕ МЕСТНОГО ЛЕЧЕНИЯ РЕЦИДИВИРУЮЩЕГО АФТОЗНОГО СТОМАТИТА НА ФОНЕ ПРОЯВЛЕНИЙ ВОСПАЛИТЕЛЬНЫХ ЗАБОЛЕВАНИЙ КИШЕЧНИКА И ХРОНИЧЕСКОГО ПАНКРЕАТИТА С СИМПТОМАМИ ГАСТРОЭЗОФАГЕАЛЬНОЙ РЕФЛЮКСНОЙ БОЛЕЗНИ

Усманова И. Н.¹, Лакман И. А.², Ишмухаметова А. Н.¹, Акопян А. П.¹, Аль Мохамед М. А.¹, Юнусова Р. Д.^{1,3}, Шангареева А. И.^{1,4}

¹ Башкирский государственный медицинский университет, г. Уфа, Россия

² Уфимский университет науки и технологий, г. Уфа, Россия

³ Стоматологическая клиника «Премьера», г. Уфа, Россия

⁴ ООО «Стоматологическая клиника «Кремль Дент»»

Аннотация

Цель. В данной работе представлен сравнительный анализ влияния различных диодных лазеров в комплексе местного лечения пациентов с рецидивирующими афтами полости рта на фоне воспалительных заболеваний пищеварительного тракта. **Материалы и методы.** Проведено обследование и комплекс местного лечения, а также динамическое наблюдение 58 пациентов в возрасте от 25 до 45 лет с наличием афтозных высыпаний на слизистой оболочке предверья и собственно полости рта. Пациенты разделены на 2 группы. Для снятия воспаления использованы диодные лазеры с различной мощностью и длиной волны, а также аппликации различных средств, обладающих противовоспалительными, противомикробными, повышающими эпителизацию и регенерацию слизистой оболочки в области афтозного высыпания свойствами. Оценку интенсивности уровня ноцицептивной боли проводили на основании данных визуальной аналоговой шкалы боли (ВАШ). **Результаты и обсуждение.** На протяжении клинического наблюдения в 1–5–7 дней влияние диодного лазера, вне зависимости от длины волны и интенсивности излучения, способствовало снижению интенсивности воспаления, повышению скорости эпителизации слизистой и нивелиации интенсивности уровня боли к $3,0 \pm 0,8$ и $3,5 \pm 0,5$ дням, полная эпителизация афтозных элементов и нивелирование всех жалоб наблюдалась к $4,9 \pm 0,4$ и $4,7 \pm 0,4$ дням местного лечения. **Выводы.** Включение в схему местного лечения хронического рецидивирующего стоматита различных типов диодных лазеров в комплексе с аппликациями способствует не только качественному снятию боли, воспаления, но и ускорению эпителизации и регенерации слизистой оболочки у пациентов с патологией ЖКТ с ГЭРБ и ХВЗК. **Заключение.** Влияние диодных лазеров различной волны и интенсивности в комплексе с аппликациями порошкообразной формы тромбоцитарной аутологичной плазмы, бензадамина и лиофилизата гиалуронидазы 64 МЕ и самоадгезивного пластира Ora-Aid обладает высокой клинической эффективностью в комплексе местного лечения рецидивирующего афтозного стоматита на фоне заболеваний желудочно-кишечного тракта с симптомами гастроэзофагеальной рефлюксной болезни и хроническими воспалительными заболеваниями кишечника.

Ключевые слова: афты, классические и опосредованные заболевания ЖКТ с ГЭРБ, болезнь Крона, хронический неспецифический язвенный колит, диодный лазер, ноцицептивная боль, самоадгезивный пластирь Ora-Aid, хлоргексидин, порошкообразная форма тромбоцитарной аутологичной плазмы, хлоргексидин

Авторы заявили об отсутствии конфликта интересов.

Ирина Николаевна УСМАНОВА ORCID ID 0000-0002-1781-0291
д.м.н., профессор кафедры терапевтической стоматологии с курсом ИДПО, Башкирский государственный медицинский университет, г. Уфа, Россия
irinausma@mail.ru

Ирина Александровна ЛАКМАН ORCID ID 0000-0001-9876-9202
к.т.н., доцент кафедры биомедицинской инженерии, заведующая научной лабораторией исследования социально-экономических проблем регионов, Уфимский университет науки и технологий, г. Уфа, Россия
Lackmania@mail.ru

Амина Насимовна ИШМУХАМЕТОВА ORCID ID 0000-0003-0892-0058
к.м.н., доцент кафедры внутренних болезней, Башкирский государственный медицинский университет, г. Уфа, Россия
amina.ishmukhametova@mail.ru

Анаит Погосян АКОПЯН ORCID ID 0000-0001-8436-58610
к.м.н., доцент кафедры неврологии ИДПО, Башкирский государственный медицинский университет, г. Уфа, Россия
ano-akopian@yandex.ru

Аль Мохамед МОХАМЕД АБДУЛКАРИМ ORCID ID 0000-0000-0933-5865
аспирант кафедры терапевтической стоматологии с курсом ИДПО, Башкирский государственный медицинский университет, г. Уфа, Россия
mohamadhlil@hotmail.com

Рита Дамировна ЮНУСОВА ORCID ID 0000-0003-4556-0864
аспирант кафедры терапевтической стоматологии с курсом ИДПО, Башкирский государственный медицинский университет; врач-стоматолог-терапевт, Стоматологическая клиника «Премьера», г. Уфа, Россия
rita-a-a1990@ya.ru

Алия Ирековна ШАНГАРЕЕВА ORCID ID 0000-0002-9673-1654
ассистент кафедры терапевтической стоматологии с курсом ИДПО, Башкирский государственный медицинский университет; врач-стоматолог-пародонтолог, ООО «Стоматологическая клиника «Кремль Дента», г. Уфа, Россия
180780 lena@mail.ru

Адрес для переписки: Ирина Николаевна УСМАНОВА
г. Уфа, 45008, ул. Ленина, 3
+7 (917) 3497793
irinausma@mail.ru

Образец цитирования:
Усманова И. Н., Лакман И. А., Ишмухаметова А. Н., Акопян А. П., Аль Мохамед М. А., Юнусова Р. Д., Шангареева А. И. СРАВНЕНИЕ ЭФФЕКТИВНОСТИ ДИОДНЫХ ЛАЗЕРОВ И АППЛИКАЦИОННЫХ СРЕДСТВ В КОМПЛЕКСЕ МЕСТНОГО ЛЕЧЕНИЯ РЕЦИДИВИРУЮЩЕГО АФТОЗНОГО СТОМАТИТА НА ФОНЕ ПРОЯВЛЕНИЙ ВОСПАЛИТЕЛЬНЫХ ЗАБОЛЕВАНИЙ КИШЕЧНИКА И ХРОНИЧЕСКОГО ПАНКРЕАТИТА С СИМПТОМАМИ ГАСТРОЭЗОФАГЕАЛЬНОЙ РЕФЛЮКСНОЙ БОЛЕЗНИ. Проблемы стоматологии. 2023; 1: 57-63.

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DOI: 10.18481/2077-7566-2023-19-1-57-63

Поступила 13.04.2023. Принята к печати 05.05.2023

DOI: 10.18481/2077-7566-2023-19-1-57-63

COMPARISON OF DIODE LASERS EFFICIENCY AND APPLICATIVE AGENTS IN THE COMPLEX OF LOCAL TREATMENT OF RECURRENT APHTHOUS STOMATITIS AGAINST THE BACKGROUND OF INFLAMMATORY DISEASES OF THE DIGESTIVE TRACT WITH SYMPTOMS OF GASTROESOPHAGEAL REFLUX DISEASE AND CHRONIC INFLAMMATORY BOWEL DISEASES

Usmanova I.N.¹, Lakman I.A.², Ishmukhametova A.N.¹, Akopyan A.P.¹, Al Mohamed M.A.¹, Yunusova R.D.^{1,3}, Shangareeva A.I.^{1,3}

¹ Bashkir State Medical University, Ufa, Russia
² Ufa University of Science and Technology, Ufa, Russia
³ Premier Dental Clinic LLC, Ufa, Russia
⁴ Kremlin-Dent Clinic LLC, Ufa, Russia

Annotation

Objective. This paper presents a comparative analysis of the effect of various diode lasers in the complex of local treatment of patients with recurrent oral aphthae on the background of inflammatory diseases of the digestive tract. **Materials and methods.** An examination and a complex of local treatment were carried out, as well as dynamic observation of 58 patients aged 25 to 45 years with the presence of aphthous rashes on the mucous membrane of the vestibulum and the oral cavity itself. The patients participating in the study were divided into 2 study groups. To relieve inflammation, diode lasers with different power and wavelength were used, as well as applications of various means with anti-inflammatory, antimicrobial, increasing epithelialization and regeneration of the mucous membrane in the area of the aphthous element. The estimation of the level of intensity of nociceptive pain level was assessed based on the data of the visual analog pain scale (VAS). **Results and discussion.** During the clinical observation of 1–5–7 days, the effect of a diode laser, regardless of the wavelength and intensity of radiation, contributed to a decrease in the intensity of inflammation, an increase in the rate of mucosal epithelialization and a leveling of the intensity of the pain level. A decrease in the intensity of pain was observed on average by 3.0 ± 0.8 and 3.5 ± 0.5 days, complete epithelialization of aphthous elements and leveling of all complaints was observed by 4.9 ± 0.4 and 4.7 ± 0.4 days of local treatment. **Conclusions.** The inclusion of various types of diode lasers in the scheme of local treatment of aphthous stomatitis in combination with applications are highly effective methods and contributes not only to the qualitative relief of pain, inflammation, but also contributes to the acceleration of epithelialization and regeneration of the mucous membrane in this group of patients. **Summary.** The effect of diode lasers and applications of powdered platelet autologous plasma, benzylamine hydrochloride and hyaluronidase 64 MU lyophilizate and Ora-Aid self-adhesive patch have high clinical efficacy in the complex of local treatment of recurrent ulcerative stomatitis against the background of inflammatory diseases of the digestive tract with symptoms of gastroesophageal reflux disease and chronic inflammatory bowel diseases.

Keywords: aphthae, diseases of the digestive tract with symptoms of gastroesophageal reflux disease, Crohn's disease, chronic ulcerative colitis, diode laser, nociceptive pain, self-adhesive patch Ora-Aid, lidase, powdered form of platelet autologous plasma, chlorhexidine

The authors declare no conflict of interest.

Irina. N. USMANOVA ORCID ID 0000-0002-1781-0291

Grand PhD in Medical Sciences, Professor, Department of Therapeutic Dentistry with a Course of Institute of Additional Professional Education, Bashkir State Medical University, Ufa, Russia
+7 (917) 3497793
irinausma@mail.ru

Irina A. LAKMAN ORCID ID 0000-0001-9876-9202

PhD in Technical Sciences, Leading Researcher of the Central Research Laboratory, Bashkir State Medical University; Head of the Scientific Laboratory for the Study of Social and Economic Problems, Ufa University of Science and Technology, Ufa, Russia
Lackmania@mail.ru

Amina N. ISHMUKHAMEDOVA ORCID ID 0000-0003-0892-0058

PhD in Medical Sciences, Associate Professor of the Department of Therapeutic Dentistry with the Course of Institute of Additional Professional Education, Bashkir State Medical University, Ufa, Russia
amina.ishmukhametova@mail.ru

Anait P. AKOPYAN ORCID ID 0000-0001-8436-5610

PhD in Medical Sciences, Associate Professor of the Department of Neurology, Bashkir State Medical University, Ufa, Russia
ano-akopian@yandex.ru

Al M. MOHAMED ABDULCARIM ORCID ID 0000-0000-0933-5865

Post-graduate Student of the Department of Therapeutic Dentistry with a Course of Institute of Additional Professional Education, Bashkir State Medical University, Ufa, Russia
mohamadhilal@hotmail.com

Rita D. YUNUSOVA ORCID ID 0000-0003-4556-0864

Post-graduate Student of the Department of Therapeutic Dentistry with a Course of Institute of Additional Professional Education, Bashkir State Medical University; Dentist-Therapist, Premier Dental Clinic LLC, Ufa, Republic of Bashkortostan, Russia
puma-a-a1990@ya.ru

Aliya I. SHANGAREEVA ORCID ID 0000-0002-9673-1654

Assistant of the Department of Therapeutic Dentistry with a Course of Institute of Additional Professional Education, Bashkir State Medical University; Dentist-Periodontist, Kremlin-Dent Clinic LLC, Ufa, Russia
180780 lena@mail.ru

Correspondence address: Irina. N. USMANOVA

Ufa, 450008, st. Lenin, 3
+7 (917) 3497793
irinausma@mail.ru

For citation:

Usmanova I.N., Lakman I.A., Ishmukhametova A.N., Akopyan A.P., Al Mohamed M.A., Yunusova R.D., Shangareeva A.I. COMPARISON OF DIODE LASERS EFFICIENCY AND APPLICATIVE AGENTS IN THE COMPLEX OF LOCAL TREATMENT OF RECURRENT APHTHOUS STOMATITIS AGAINST THE BACKGROUND OF INFLAMMATORY DISEASES OF THE DIGESTIVE TRACT WITH SYMPTOMS OF GASTROESOPHAGEAL REFLUX DISEASE AND CHRONIC INFLAMMATORY BOWEL DISEASES. Actual problems in dentistry. 2023; 1: 57-63. (In Russ.)

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DOL: 10.18481/2077-7566-2023-19-1-57-63

Received 13.04.2023. Accepted 05.05.2023

Modern scientific studies conducted in Russia and abroad provide data on risk factors and features of manifestations of pathology of the oral mucosa in the form of recurrent ulcerative stomatitis (recurrent aphthous oral cavity ICD – K12.0) in patients of various ages. Recently, the prevalence of this pathology has been observed against the background of inflammatory diseases of the gastrointestinal tract with symptoms of gastroesophageal reflux disease, chronic inflammatory bowel diseases (Crohn's disease and chronic ulcerative colitis), which contributes to the development of complex methods of local treatment [1, 5, 6, 16, 17, 3].

The complex of local treatment of recurrent ulcerative stomatitis includes high-quality therapeutic and preventive measures to reduce acute alterative inflammation, the intensity of the level of nociceptive pain, increase epithelialization and regeneration of the mucous membrane epithelium of the mouth. For the successful implementation of these moments, many different methods and means are used, including the use of light therapy, low-intensity laser radiation, diode lasers [4, 8–10, 12, 15, 18, 19].

The mechanism of action and biological effects of laser biostimulation consists in the depth of penetration of the beam up to 6 mm, which contributes to increased cell proliferation, a decrease in the level of inflammatory mediators, growth factors, as well as stimulation of microcirculation and an increase in tissue oxygenation [2, 7, 13, 20, 21].

Taking into account the etiology, pathogenesis, clinical manifestations of chronic recurrent stomatitis, it is advisable to use diode lasers and agents with pronounced anti-inflammatory, epithelializing and regenerating properties in a complex of local treatment, as well as contributing to a decrease in the level of nociceptive pain, which determined the relevance and purpose of our study.

The aim of the study was a comparative study of the effect of diode lasers and applicative agents in the complex of local treatment of recurrent ulcerative stomatitis, manifested against the background of inflammatory diseases of the digestive tract.

Material and methods of research

Based on an open, prospective study, a sample of 57 (33.53% of the initial set of subjects) patients with recurrent ulcerative stomatitis on the mucous membrane of the oral cavity was conducted and 2 clinical groups were formed: the I clinical group included 29 patients with aphthous rashes on the background of inflammatory diseases of the digestive tract with symptoms of gastroesophageal reflux disease and chronic inflammatory bowel diseases – chronic gastritis and duodenitis (HCG and D), (n = 15) and chronic secondary biliary-dependent pancreatitis (CKD), (n = 14); the II clinical group consisted of 28 patients with recurrent aphthae against the

background of clinical manifestations of chronic inflammatory bowel diseases – Crohn's disease (CD), (n = 17) and chronic nonspecific ulcerative colitis (UC) (n = 11).

The dental examination included an assessment of complaints and symptoms, the clinical condition of the oral mucosa, the intensity of the level of nociceptive pain on the VAS scale (visual analog scale) [11].

Local treatment of recurrent oral aphthae localized on the mucous membrane of the vestibule and the oral cavity itself was carried out by a dentist, general treatment of inflammatory diseases of the digestive tract was carried out by a gastroenterologist, a general practitioner according to standard protocols for the clinical management of these diseases.

The administration of systemic drugs (immunocorrecting drugs, antihistamines, sedatives, vitamin complexes) in all observed individuals was carried out according to individual indications.

In patients of the first study group, the complex of local treatment of recurrent aphthous stomatitis consisted of a single treatment of the aphthae surface with 0.06% chlorhexidine solution, a single non-contact treatment of the hyperemia zone, the surface of the aphthous element covered with fibrinous plaque, a zone without hyperemia with a diode laser «RISASSO Lite» (wavelength 650–670 nm., laser radiation power 0.8 W, constant mode), closure of the treated surface of the aphtha with a powdered form of platelet autologous plasma. At home, applications of powdered platelet autologous plasma with a multiplicity of 2 times a day for 4 days are recommended [14].

In the second study group, the complex of local treatment of ulcerative stomatitis included alternate treatment of the aphthal surface with solutions of benzadamine and hyaluronidase 64 MU lyophilizate lasting 5 minutes, exposure with a Doctor Smil D5 diode laser (therapeutic mode, wavelength 810 ± 10 nm, laser radiation power was 1.0 W, continuous mode, distance from the surface of the aphthous element 3 mm), closure of the surface of the aphthous element with a self-adhesive patch Ora-Aid until its complete dissolution. At home, the patient performed a two-time treatment of the aphthal surface with a benzadamine solution lasting 5 minutes and a two-time closure of the aphthal surface with an Ora-Aid self-adhesive patch until it was completely dissolved.

To compare pain scores between clinical subgroups before and after the local treatment complex, the non-parametric Wald-Wolfowitz criterion was used for independent samples, and the Wilcoxon signed rank test was used for intra-group comparison as a test capable of reliably detecting differences in dependent samples. The null hypothesis in both criteria was the assumption that there were no differences in the indicator in the samples. It was believed that there were significant differences if the p-level did not exceed 0.05. Statistical calculations were performed using the R environment (the Desktools and dplyr libraries).

Results and discussion

Mainly in patients with inflammatory diseases of the gastrointestinal tract (GI tract) with symptoms of gastroesophageal reflux disease (GERD) and chronic inflammatory bowel diseases (CIBD), complaints of heartburn, acid belching, pain in the sternum, nausea, discomfort after eating, flatulence, unstable pain syndrome in the right and left sides prevailed. Left iliac region.

During the dental examination, patients complained of a feeling of sharp pain, tingling, burning and tension of the oral mucosa in the area of aphthous rash located on the oral mucosa.

During an objective examination, single or multiple aphthous elements of irregular polygonal shape, of various sizes, covered with a yellowish coating were observed on the mucous membrane of the vestibule and the mucous membrane epithelium of the mouth itself. The number of aphthous eruptions varied from one to five.

In patients with the presence of classical and mediated gastrointestinal diseases with symptoms of gastroesophageal reflux disease, the number of relapses 1 time per year prevailed in 15 (100%) patients with chronic gastritis and duodenitis, 2 times a year in 14 (100%), in patients with CIBD, the frequency of relapses varied from 2 to 3 times a year, respectively, in 29.41% and 70.59% of cases, from 1 to 2 times a year in 36.36% and 63.64% of cases (Table 1).

The ongoing complex of local treatment included the use of diode lasers of various sizes (650–670 nm and 810 nm) and intensities (0.8–1.0 W), as well as various applications (powdered form of platelet autologous plasma, self-adhesive patch Ora-Aid), which are highly effective in treating patients with aphthous stomatitis manifested against the background of inflammatory diseases of the gastrointestinal tract with GERD and CIBD. These methods of local treatment have pronounced anti-inflammatory properties and stimulate the process of epithelialization and regeneration of the oral mucosa.

Before local treatment was carried out, in all cases, observed patients with gastrointestinal tract with GERD and CIBD and the presence of aphthous elements on the oral mucosa, complaints about the presence of different levels of nociceptive pain intensity on the VAS scale prevailed (Table 2.3).

In the Ia and Ib clinical subgroups, the intensity level of nociceptive pain before treatment averaged 5.3 ± 0.7 and 5.8 ± 0.4 points ($p > 0.4$), in IIa and IIb 6.5 ± 0.5 and 6.2 ± 0.6 points ($p > 0.5$), which corresponded to the level of significant pain on the VAS scale (Table 2.3).

The results of the assessment of the level of nociceptive pain on the VAS scale showed that on the 3rd day, from the start of local treatment, there was a decrease in the intensity of pain syndrome in the Ia and Ib study subgroups by 1.5 ($p < 0.1$) and 1.7 ($p < 0.05$) times, respectively, in the IIa and IIb study subgroups in 1.6 ($p < 0.001$) and 1.8 ($p < 0.1$) times from the initial data, the level of pain in the groups corresponds to moderate (Table 2, 3).

In the II study group, the effectiveness of reducing the level of pain intensity is more significant compared to study group I (especially in subgroup IIa: by the third day, differences are achieved at the level of $p < 0.01$ for all types of pain).

This may be due to the ability of patients to more fully isolate the mucosa in the area of aphthous rash due to the use of a self-adhesive patch Ora-Aid, which has a keratoplastic effect, contributed to the protection of the mucosa during meals, as well as during conversation and individual hygiene. A similar effect is associated with patients of the first study group, since the powdered form of platelet autologous plasma in its composition contains platelets, due to which the synthesis of inflammatory cytokines occurs and the production of intercellular matrix proteins increases, fibroblast stimulation (Table 2, 3).

Table 1

Prevalence of recurrent oral aphthae and number of recurrences per year in the study groups and subgroups

Таблица 1. Распространенность рецидивирующих афт полости рта и количество рецидивов в год в исследуемых группах и подгруппах

Clinical groups / pathology of the oral mucosa	Study group I with inflammatory diseases of the gastrointestinal tract with GERD (n = 29)				Study group II with chronic inflammatory bowel disease (n = 28)			
	Ia study subgroup with chronic gastritis and duodenitis (CG D with GERD) (n = 15)		Ib study subgroup with chronic secondary biliary pancreatitis on the background of hyperacidic gastric secretion (n = 14)		IIa study subgroup with Crohn's disease (n = 17)		IIb study subgroup with chronic nonspecific ulcerative colitis (n = 11)	
	total	%	total	%	total	%	total	%
Recurrent oral aphthae	15	100	14	100	17	100	11	100
ICD 10–12.0	15	100					4	36,36
Aphthae Relapses 1 Time Per Year			14	100	5	29,41	7	63,64
Aphthae Relapses 2 Times Per Year					12	70,59		

Table 2

Dynamics of changes of level of intensity of nociceptive pain in study group 1

Таблица 2. Динамика изменения уровня интенсивности ноцицептивной боли в I исследуемой группе

Complaints before and after treatment	A complex of local treatment I study group (n = 29)					
	Ia study subgroup - chronic gastritis and duodenitis with GERD symptoms (n = 15)		Ib study subgroup - chronic secondary biliary pancreatitis with GERD symptoms (n = 14)			
	Before treatment	The 3 rd day of treatment	After treatment (day 5)	Before treatment	The 3 rd day of treatment	After treatment (day 5)
The level of pain intensity on the VAS scale in points						
Pain during taking a meal	5,4 ± 0,5	3,9 ± 0,1** $p_1 = 0,008$	0*** $p_1 < 0,001$	6,2 ± 0,7 $p_0 = 0,215$	4,2 ± 0,8 $p_1 = 0,112$ $p_2 = 0,667$	0*** $p_1 < 0,001$ $p_2 = 1,0$
Pain during a conversation	5,3 ± 0,7	3,3 ± 0,5 $p_1 = 0,078$	0*** $p_1 < 0,001$	5,5 ± 0,4 $p_0 = 0,588$	3,1 ± 0,9* $p_1 = 0,050$ $p_2 = 0,702$	0*** $p_1 < 0,001$ $p_2 = 1,0$
Pain during individual oral hygiene	5,2 ± 0,8	3,6 ± 0,3 $p_1 = 0,208$	0*** $p_1 < 0,001$	5,8 ± 0,2 $p_0 = 0,451$	3,1 ± 0,93** $p_1 = 0,005$ $p_2 = 0,588$	0*** $p_1 < 0,001$ $p_2 = 1,0$
The average amount of points	5,3 ± 0,7	3,6 ± 0,3 $p_1 = 0,059$	0*** $p_1 < 0,001$	5,8 ± 0,4 $p_0 = 0,433$	3,5 ± 0,6* $p_1 = 0,013$ $p_2 = 0,921$	0*** $p_1 < 0,001$ $p_2 = 1,0$

$p0$ – p-level when assessing differences between subgroups before treatment (Wald-Wolfowitz criterion), $p1$ – p-level when assessing differences within a subgroup before and after treatment (Wilcoxon criterion), $p2$ – p-level when assessing differences between subgroups after treatment (Wald-Wolfowitz criterion)

*, **, *** – differences before and after treatment are significant at $p < 0,05$, $p < 0,01$, $p < 0,001$, respectively

Table 3

Dynamics of changes of level of intensity of nociceptive pain in study group II

Таблица 3. Динамика изменения уровня интенсивности ноцицептивной боли в II исследуемой группе

Complaints before and after treatment	A complex of local treatment Study group II (n = 28)					
	IIa study subgroup – Crohn's disease, (n = 17)			IIb study subgroup – chronic nonspecific ulcerative colitis (n = 11)		
	before treatment	The 3 rd day of treatment	After treatment (day 7)	Before treatment	The 3 rd day of treatment	After treatment (day 7)
The level of pain intensity on the VAS scale in points						
Pain during taking a meal	7,0 ± 0,1	4,6 ± 0,4*** $p_1 < 0,001$	0*** $p_1 < 0,001$	6,5 ± 0,4 $p_0 = 0,215$	4,1 ± 0,9* $p_1 = 0,050$ $p_2 = 0,322$	0*** $p_1 < 0,001$ $p_2 = 1,0$
Pain during a conversation	6,2 ± 0,8	3,7 ± 0,2** $p_1 = 0,003$	0*** $p_1 < 0,001$	6,1 ± 0,9 $p_0 = 0,934$	3,3 ± 0,7 $p_1 = 0,084$ $p_2 = 0,457$	0*** $p_1 < 0,001$ $p_2 = 1,0$
Pain during individual oral hygiene	6,3 ± 0,7	3,6 ± 0,2*** $p_1 = 0,001$	0*** $p_1 < 0,001$	5,9 ± 0,6 $p_0 = 0,415$	3,1 ± 0,9 $p_1 = 0,075$ $p_2 = 0,410$	0*** $p_1 < 0,001$ $p_2 = 1,0$
The average amount of points	6,5 ± 0,5	4,0 ± 0,3*** $p_1 < 0,001$	0*** $p_1 < 0,001$	6,2 ± 0,6 $p_0 = 0,567$	3,5 ± 0,8 $p_1 = 0,065$ $p_2 = 0,399$	0*** $p_1 < 0,001$ $p_2 = 1,0$

$p0$ – p-level when assessing differences between subgroups before treatment (Wald-Wolfowitz criterion), $p1$ – p-level when assessing differences within a subgroup before and after treatment (Wilcoxon criterion), $p2$ – p-level when assessing differences between subgroups after treatment (Wald-Wolfowitz criterion)

*, **, *** – differences before and after treatment are significant at $p < 0,05$, $p < 0,01$, $p < 0,001$, respectively

Table 4

Duration of aphthous epithelialization (in days) in the dynamics of local treatment in study group I

Таблица 4. Длительность эпителизации афт (в днях) в динамике проводимого местного лечения в I исследуемой группе

Epithelization time in days	Local treatment complex I study group (n = 29)		
	Ia study subgroup - chronic gastritis and duodenitis with GERD symptoms (n = 15)	Ib study subgroup - chronic secondary biliary pancreatitis with GERD symptoms (n = 14)	p-level
The beginning of epithelization 3 day of treatment	3,0 ± 0,9	3,1 ± 0,9	0,897
Final epithelization day 5	4,9 ± 0,1	4,7 ± 0,3	0,632

Table 5

Duration of aphthae epithelialization (in days) in the dynamics of local treatment in study group II

Таблица 5. Длительность эпителизации афт (в днях) в динамике проводимого местного лечения во II исследуемой группе

Epithelization time in days	A complex of local treatment Study group II (n = 28)		
	IIa study subgroup - Crohn's disease, (n = 17)	IIb study subgroup - chronic nonspecific ulcerative colitis (n = 11)	p-level
The beginning of epithelization 3 day of treatment	4,9 ± 0,1	4,7 ± 0,2	0,148
Final epithelization day 7	6,4 ± 0,5	6,2 ± 0,8	0,621

On the 7th day of clinical follow-up, all patients with pathology of the gastrointestinal tract and CIBD formed groups and subgroups, regardless of the applied complex of local treatment, there was no nociceptive pain in the complaints ($p < 0.001$), which is associated with epithelialization of aphthous rashes, and which consequently led to an improvement in the well-being of patients and an improvement in the quality of life (see Table 2.3).

In all clinical cases, regardless of the complex of local treatment of ulcerative stomatitis, all patients have a leveling of complaints of painful tingling, burning, tension on day 3, their absence with complete epithelialization of aphthous elements by days 5 and 7.

Treatment of the surface of aphthous elements with diode lasers contributed to a decrease in the size of the aft on average by 3 and 5 days of local treatment and the presence of complete epithelialization of the mucosa by 5 and 7 days in 100% of cases of clinical observations (Table 4.5).

For patients with recurrent oral aphthae of the study group I, the time of complete epithelialization was 4.8 ± 0.2 days, for patients of the study group II, on average 6.3 ± 0.6 days, which is 1.3 days longer ($p = 0.043$).

Conclusion

Thus, in the complex of local treatment of chronic recurrent stomatitis, it is advisable to use diode lasers «RISASSO Lite» and «Doctor Smil D5» and various application tools. Improvement of the clinical condition of the mucous membrane of the vestibule and the oral cavity itself, a decrease in the level of intensity of nociceptive pain were observed in all study groups.

However, the results of clinical observations, on the third day prove a more intense effect in reducing the level of nociceptive pain when using the self-adhesive patch Ora-Aid, which has a keratoplastic effect, nevertheless, the rate of epithelialization is 1.3 days faster when using applications of powdered platelet autologous plasma.

A direct dependence of the rate of epithelialization on the presence of the clinical course of inflammatory diseases of the digestive tract with symptoms of gasteroesophageal reflux disease and chronic inflammatory bowel diseases is observed.

In turn, applications with solutions of benzadamine and hyaluronidase 64 MU lyophilizate, self-adhesive patch Ru-Aid have more pronounced anti-inflammatory, analgesic and keratoplastic properties in comparison with applications of powdered platelet autologous plasma. As evidenced by the statistical significance of the differences with a decrease in the the level of intensity of nociceptive pain and the inverse dependence on the rate of epithelialization.

The influence of the diode laser «RISASSO Lite» and «Doctor Smil D5» as well as applications of powdered platelet autologous plasma, benzadamine and hyaluronidase 64 MU lyophilizate and self-adhesive patch Ora-Aid contributed to the leveling of complaints of painful tingling, burning, mucosal tension on average by the 3rd and 5th day of observation in all study groups.

Conclusions

The inclusion of diode lasers in the scheme of local treatment contributed to a more effective relief of local

symptoms and complaints in patients of the study groups with the presence of aphthous rashes on the mucous membrane of the vestibule and the oral cavity itself.

Thus, in patients with clinical manifestations of chronic recurrent aphthous stomatitis (ICD K 12.0) against the background of manifestations of inflammatory diseases of the digestive tract with symptoms of gas-

troesophageal reflux disease and chronic inflammatory bowel diseases, the inclusion of diode lasers «RISASSO Lite» and «Doctor Smil D5» and applications of powdered platelet autologous plasma, benzadamine and Hyaluronidase 64 IU lyophilizate and Ora-Aid self-adhesive patch is effective and justified, due to anti-inflammatory, analgesic and epithelializing action.

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