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SURGICAL TREATMENT OF ORAL LEUKOPLAKIA

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Abstract

Background: The effectiveness of care for patients with leukoplakia depends on how timely and accurately the disease was diagnosed and also by the subsequent choice of the optimal method of treatment. In recent decades, surgery is increasingly using methods that are alternative to standard surgical methods. *Purpose*: to justify, develop and evaluate treatment algorithm of verrucous and erosive-ulcerative forms of oral leukoplakia with a SIN2 histological structure. *Materials and Methods*: to achieve this goal, a comprehensive clinical and laboratory examination of 155 patients with oral leukoplakia was performed, which appealed to the Department of Therapeutic Dentistry of the Bogomolets National Medical University in the period from 2011 to 2015. All patients underwent clinical and laboratory tests. *Results*: after removal of the affected area of the mucosa by radiation of an erbium laser, wound healing under fibrinous plaque was observed at 7.0 ± 0.5 days. When excision of the mucous membrane with a scalpel, the healing took place under the iodinine swab through the granulation phase for 14.0 ± 1.5 days. In patients after the operation of excision of the area of verrucous or erosive-ulcerative oral mucosa leukoplakia with laser radiation without antimicrobial and anti-inflammatory therapy on the third day, in 95% of cases there is no pain syndrome and collateral edema in the postoperative area. After traditional treatment, despite the use of antibiotics and non-steroidal anti-inflammatory drugs, 56% of patients complained of pain, and 62% had collateral edema. *Conclusions*: the use of ErrYAG laser laser radiation in the surgical treatment of patients with verrucous and erosive-ulcerative forms of leukoplakia promotes acceleration of healing processes of a postoperative wound twice as fast as in the control group. The use of laser technology reduces the risk of inflammatory purulent complications and helps to prevent the recurrence of the disease.

Keywords: precancerous diseases, leukoplakia, surgical treatment, erbium laser.

Introduction

The problem of treating patients with leukoplakia is an urgent task of therapeutic dentistry. Recently, along with traditional conservative methods of treating this disease, a fundamentally new tactic of timely, adequate treatment using laser systems is being developed [1].

The effectiveness of care for patients with leukoplakia depends on how timely and accurately the disease was diagnosed and also by the subsequent choice of the optimal method of treatment [2]. Conservative methods of treatment are acceptable only for the flat form of leukoplakia. In case of the verrucous and erosive-ulcerative forms of leukoplakia, treatment should be surgical. And even with the traditional surgical treatment of these forms of leukoplakia, recurrences of the disease are possible and, due to the traumatic nature of this method, the disruption of the regeneration process in the postoperative period [1,3]. Therefore, it is necessary to look for methods that allow more careful carving of the affected parts of the oral mucosa (OM) and promote the activation of reparative processes in the postoperative wound.

In recent decades, surgery is increasingly using methods that are alternative to standard surgical methods. Excision of the affected area is effected by exposure to low temperatures, radio-wave coagulator, electrocoagulator, and laser radiation [2,4].

Laser technologies have become widespread in various directions of dentistry, due to intra- and postoperative benefits.

Operations performed with a laser do not contradict the standard procedures that are used in surgical treatment. According to the studies, the use of laser radiation affects the course of surgical operations and further healing of the wound surface. When carrying out operations using a laser, the vessels coagulate with the drying of the operating field, provides a better visualization of the working surface. Laser light guides allow access into hard-to-reach areas of the operating field. The laser beam has a bactericidal effect, reduces swelling, hyperemia and pain in the postoperative area, improves the quality of life of patients in the postoperative period. In addition, the laser beam has an immunomodulatory effect and accelerates the processes of regeneration of the oral mucosa [5].

According to clinical studies, almost all patients report the absence or reduction of pain after laser surgery, compared to patients who underwent surgery with standard surgical instruments. Very often after such an operation it is not necessary to sew a postoperative wound, it is more comfortable for the patient during the operation and to a large extent improves the quality of his life in the postoperative period [6].

To date, high-performance pulsed lasers of a new generation have been developed, that ensure the accessibility and visualization of the operation field, anesthesia, hemostasis, lymphostasis, excision of a large area without subsequent imposition of an iodine-shaped tampon. In the postoperative period, there is a decrease in pain syndrome, a decrease in edema, and an acceleration of tissue regeneration [6].

In this connection, it is of interest to study and introduce into practice dentists the treatment of the verrucous and erosive-ulcerative forms of oral leukoplakia using surgical lasers of the latest generation.

Objective: to justify, develop and evaluate treatment algorithm of verrucous and erosive-ulcerative forms of OM leukoplakia with a SIN2 histological structure.

Methods

To achieve this goal, a comprehensive clinical and laboratory examination of 155 patients with oral leukoplakia was performed, which appealed to the Department of Therapeutic Dentistry of the Bogomolets National Medical University in the period from

2011 to 2015. Among them were 87 (56.1%) men and 68 (43.9%) women. The age of patients ranged from 25 to 70 years and averaged 46.6 ± 2.63 years. They found various forms of leukoplakia: flat, elevated; verrucous and erosive-ulcerative.

All patients underwent clinical and laboratory tests.

Biopsy of the leukoplakia for histological and histochemical examination was carried out as follows: the biopsy specimen was fixed in 10% neutral formalin (pH 7.4). After the meeting on gistoprotsesor embedded in paraffin with a melting point of 54 ° C for histology and immunohistochemistry (IHC). Serial sections 5 μm thick were placed on glass plates coated with poly-L-lysine. Tissue antigens were detected using monoclonal antibodies from mice to K8 (TS1, `Thermoscientific`) and Ki-67 (MM1,` Thermoscientific`). Immune complexes were detected using the UltraVision Quanto Detecton System HRP (" Thermoscientific ") detection system, the sections were stained with Mayer's hematoxylin.

During the histological examination, the control specimen was the unchanged epithelium, which was taken from the adjacent mucosal areas of the leukoplakia. The histological evaluation of the test material was established according to the WHO classification (2005).

Statistical processing of the obtained data was carried out using the software Statistica 10.0. Given the abnormal distribution of the extracted statistical indicators, a comparison of two independent groups performed with nonparametric method using the Mann-Whitney U test. Shall be deemed authentic differences in the average at the level of statistical significance of $p < 0,01$.

Treatment: the main group - 25 patients with verrucous and erosive-ulcerative forms of oral leukoplakia with the SIN2 histological structure; control group - 15 patients with verrucous and erosive-ulcerative forms of oral leukoplakia, who were treated according to treatment protocols (2004).

All patients with different forms of leukoplakia were recommended and conducted:

• Professional oral hygiene with mandatory training and hygiene control throughout the treatment, interdental hygiene;

• replacement of old and amalgam fillings, removal of teeth that cannot be treated, grinding of sharp edges of teeth, and rational prosthetics using homogeneous metals;

• elimination of bad habits;

• functional, selective teeth grinding;

• diet therapy (restriction in taking spicy, hot, salty, sour food)

• consultation of doctors of other specialties with subsequent treatment if necessary;

• biopsy for histological and immunohistochemical studies.

Treatment and prevention measures (TPM) of verrucous and erosive-ulcerous forms of oral leukoplakia with SIN2 histological structure was as follows.

1. Antiseptic treatment of the oral cavity.

2. Surgical treatment using erbium laser radiation: under infiltration anesthesia with a 4% solution of Ubistesin 0.5-1.0 ml, the oral mucosa was removed by a focused beam of an erbium laser with a wavelength of 2940 nm in ablation mode at a distance of 0.5 mm from the wound surface to light contact with a sapphire fiber cloth (light guide), with a power of 4 W, a pulse duration of 700 μs in the "long" mode, with an energy of 300 mJ, a frequency of 20 Hz, an exposure time of 15 s per 1 cm with an air-water spray .

Recommendations for the patient (homecare):

1. Local treatment: 1-2 times a day application to the area of the operating wound of the therapeutic gel "Vivax Dent" with a peptide complex, "Neovitin" ® and aloe vera gel, rinsing with "Vivax Dent" balm with a peptide complex, "Neovitin" ® And aloe vera gel. Individual oral hygiene (IOH): toothpaste "Vivax Dent" with a peptide complex and

betulavit and a toothbrush - "Medium".

2. General treatment: intramuscular administration of the drug "Erbisol®Extra" – 2 ml twice a day for 10 days; multivitamin complex "Pikovit Forte" – one tablet twice a day.

Erbisol ® Extra is a hydrolysate of cell membranes of embryonic tissue and its main active ingredients include low molecular weight peptides and glycopeptides [4]. He belongs to the new generation of the class of endogenous regenerative biological immunomodulating mediators. This drug is characterized by a mild therapeutic effect, thanks to which the harmonized systemic interaction of immunomodulating and anti-inflammatory effects against the background of pronounced membrane-stabilizing and antioxidant effect is realized by normalization of the reparative-regenerative potential of damaged organs and tissues.

Results

In a complex clinical-laboratory study, 155 patients with a clinical diagnosis of leukoplakia of the oral mucosa in 52 (33.55%) were flat, 28 (18.06%) were elevated, 48 (30.97%) verrucous and 27 17,42%) erosive-ulcerative form of leukoplakia.

The histological evaluation of the material was carried out in accordance with the WHO classification of leukoplakia (2005).

A biopsy analysis of patients with leukoplakia showed that leukoplakia without atypia is more often histologically observed in patients with flat leukoplakia in 28 patients (53.85%), 15 patients (28.84%) had SIN1 and nine patients (17, 31 %) - SIN2. In patients with the elevated form of leukoplakia, histologically it occurs in two (7.14%) leukoplakia without atypia, in seven (25.0%) - SIN1 and in nineteen (67.86%) - SIN2. In patients with verrucous leukoplakia histologically observed in 11 (22.95%) - SIN1 leukoplakia, in 24 (50.0%) - SIN2, in 10 (20.83%) - SIN3. In this case, in the clinical picture of verrucous leukoplakia, histologically, in three patients, we detected cancer of oral mucosa. In patients with erosive-ulcerative leukoplakia histologically, 11 (40.74%) had SIN2 leukoplakia and 16 (59.26%) had SIN3.

We have developed differentiated protocols for the treatment of oral mucosa leukoplakia, depending on the morphological and immunohistochemical parameters of the affected mucosa.

The effectiveness of therapy was evaluated in all patients on the basis of clinical picture changes, duration of remission and frequency of relapses and laboratory (cytological) data.

The clinical efficacy of the treatment was evaluated at the end of the course of therapy. The dynamics of clinical manifestations of the disease in the treatment process was analyzed in each group of patients according to the terms of complete or partial disappearance of objective and subjective signs of the disease.

Complex therapy of patients with another group of observations with oral mucosa leukoplakia with the use of TPM had a positive effect on clinical and laboratory indicators.

For example, in the first days after surgery, no pain syndrome was noted in 17 (68.0%) patients of the main group, and only nine (60.0%) of the control group until the third day after the operation. Moreover, in the main these complaints were preserved in patients with localization of elements in the region of the movable part of oral cavity vestibule mucous membrane with the spread to the transitional fold. Despite the fact that all patients in the postoperative period were advised to avoid receiving irritating and solid foods, this fact was most often the cause of the intense pain syndrome (Figure 1).

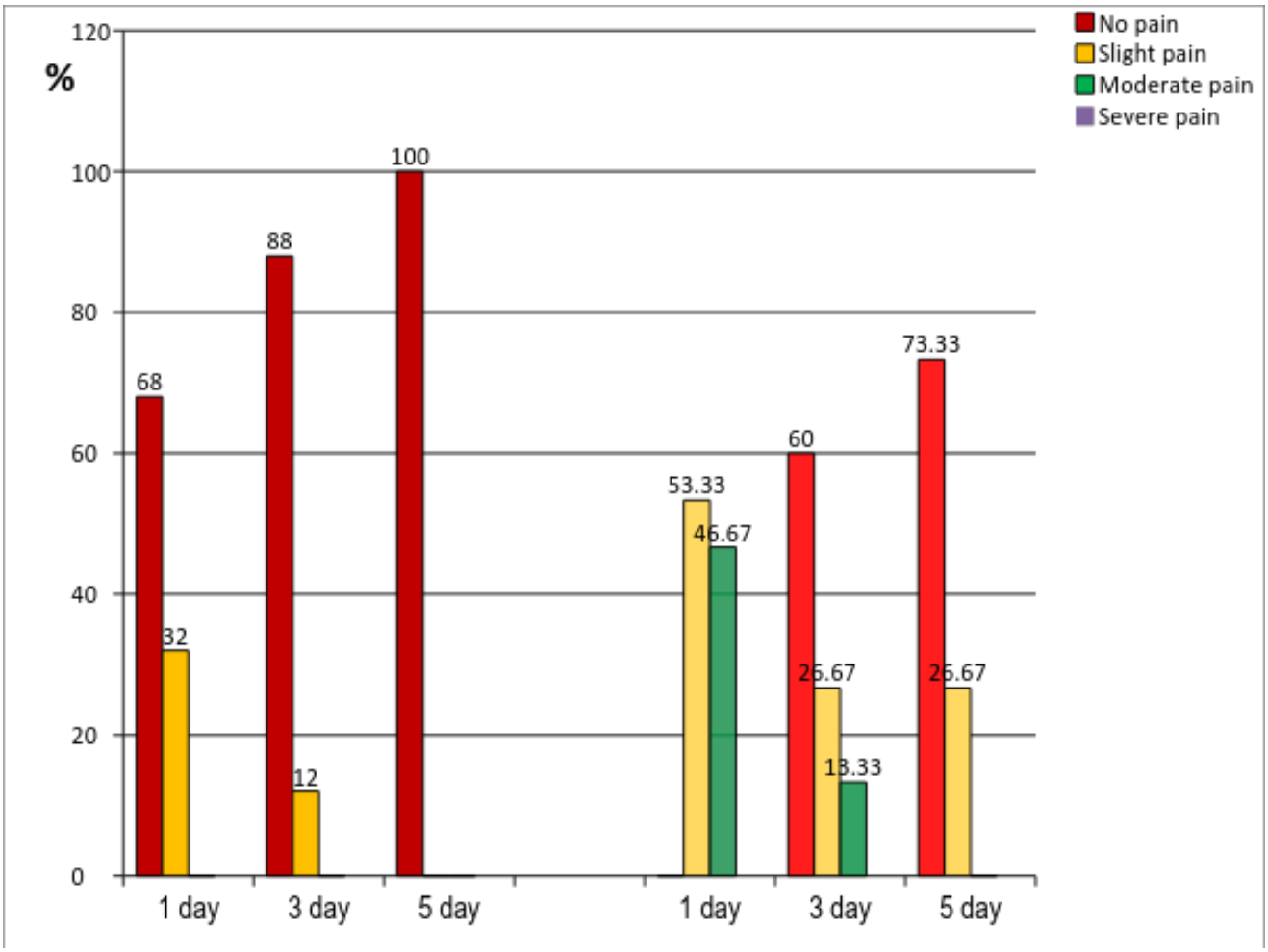

Fig. 1. Distribution of patients of the third observation group depending on the severity of the pain syndrome

In 22 (88.0%) patients of the main group, only mild hyperemia was observed on the third day in the surgical intervention zone, and only one (6.67%) in the control group. And on the fifth day in 21 (84.0%) patients of the main group, the mucous membrane in the surgical intervention zone acquired the habitual coloration, and in the control group only in three (20.0%) patients (Table 1).

Table 1. The distribution of patients of the third group depending on the observation state of mucosa in surgery zone

Group	Time range (days)	Oral mucosa state in operation area									
		Normal colour		Slight hyperemia		Moderate hyperemia		Intense hyperemia		Cyanose	
		absolute value	%	absolute value	%	absolute value	%	absolute value	%	absolute value	%
Main	1	-	-	1	4.0	21	84,0	3	12,0	-	-
	3	2	8,0	22	88,0	1	4,0	-	-	-	-
	5	21	84,0	4	16,0	-	-	-	-	-	-
Control	1	-	-	-	-	3	20,0	12	80,0	-	-
	3	-	-	1	6,67	9	60,0	5	33,33	-	-
	5	3	20,0	9	60,0	3	20,0	-	-	-	-

Twelve (80.0%) patients of the control group had a significant amount of fibrinous plaque on the surface of the wound on the third day after the operation, and a small amount of fibrinous plaque was observed in 24 (96.0%) patients of the main group at the same time. On the fifth day, epithelization took place in all patients of the main group (Fig. 2).

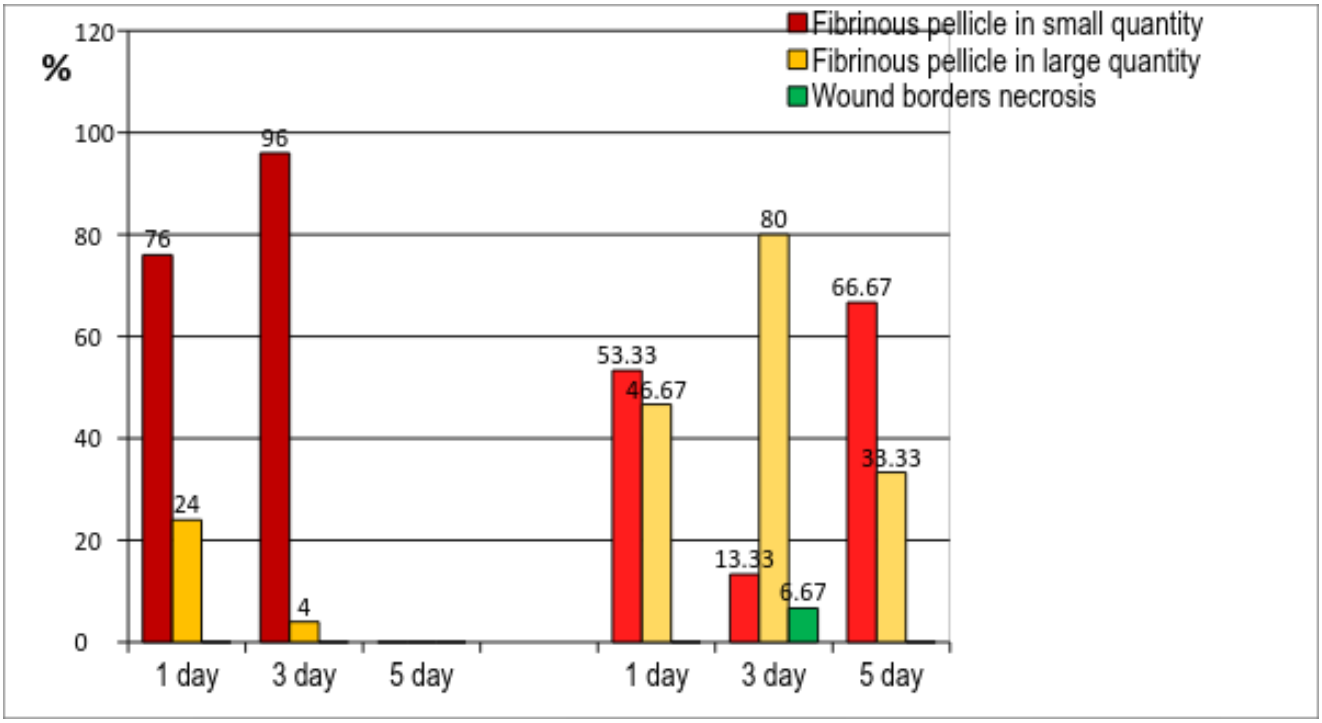

Fig. 2. Distribution of patients of the observation group depending on the state of the wound surface.

Slightly pronounced collateral edema on the first day after the operation of excision of OM by erbium laser radiation was observed in 20 (80.0%) patients. In the control group,

seven (46.67%) patients had it. On the third day, poorly pronounced collateral edema persisted only in four (16%) patients in the main group, and in 21 (84%) patients it completely disappeared. On the fifth day, 24 (96%) patients of the main group had no collateral edema phenomena, and only one (6.67%) had a collateral edema in the control group (Table 2).

Table 2. The distribution of patients of the third group depending on the observations of collateral surrounding soft tissue swelling

Group	Time range (days)	Surrounding tissues oedema							
		None		Slight		Intense		Intense oedema with skin hyperemia	
		absolute value	%	absolute value	%	absolute value	%	absolute value	%
Main group	1-й	-	-	20	80,0	5	20,0	-	-
	3-й	21	84,0	4	16,0	-	-	-	-
	5-й	24	96,0	1	4,0	-	-	-	-
Control	1-й	-	-	7	46,67	8	53,33	-	-
	3-й	-	-	8	53,33	7	46,67	-	-
	5-й	1	6,67	12	80,0	2	13,33	-	-

Discussion

Thus, after the TPM, postoperative period proceeded without complications, more comfortable for operated patients with insignificant severity of pain syndrome and collateral edema.

The surface area of the wound in the patients of the main group decreased by 1.6 times on the third day, and by 3.3 times on the fifth day in comparison with the baseline level, in patients of the control group - 0.8 and 2.2 times, respectively. The release of the wound from the burned scab and complete epithelization in the patients of the main group were observed at 4.5 ± 0.5 day. The end result of the healing of wounds after exposure to laser was the formation of gentle scar with little fibrosis.

At the same time, in patients with oral mucosa leukoplakia, a positive dynamic of cytogenetic indices, proliferation and destruction indices of the nucleus was recorded in the TPM, while in the control group it was not so significant.

Thus, the frequency of cells with micronucleus in patients of the main group after treatment decreased by 2.3 times, and in the control group by 1.58 times. The frequency of cells with protrusions in the main group after treatment decreased 4.71 times, and in the control group - 2.58 times. The frequency of detection of protrusions of the "broken egg" type in patients of the main group decreased by 4.56 times. According to the results of our study, after the treatment, the cumulative disturbances of the cytogenetic disorders (the sum of cells from the micronucleus and protrusions) in the cells of buccal epithelium were 1.16 ± 0.36 in the patients of the main group, and 2.17 ± 0.22 in the control group, respectively, The differences are statistically significant. There was a positive dynamics of decrease in the indices of the violation of the proliferation of buccal epithelial cells in patients of both groups after the treatment. Thus, the frequency of cells with two nuclei in patients of the main group decreased after treatment by 3.5 times, and in the control group - by 2.29 times, respectively. There was also a significant positive dynamics of decrease in apoptosis indices

in the cells of the buccal epithelium of the main group after the TPM.

Analysis of the index of labeled antibodies to the Ki-67 protein of epithelial cell nuclei revealed a pronounced tendency to normalize proliferative activity in patients receiving TPM. So, against the background of the therapy, the proliferation index for Ki-67 decreased significantly. The amount of distribution of Ki-67 positive cells in the layers of the epithelium also changed. The number of proliferating cells decreased in its own mucosa. Thus, the TPM in complex therapy of patients with oral mucosa leukoplakia leads to an expressive decrease in the morphological signs of the lesion of the oral mucosa and a decrease in the proliferative activity of the epithelium of the affected areas.

Later, all patients were observed at the Department of Therapeutic Dentistry of the Bogomolets National Medical University for 1.5 years. It should be noted that in the basic group in one patient after 12 months of disease relapse. The analysis showed that this was due to the aggravation of his disease of the gastrointestinal tract. In the control group after six months, there was one case of recurrence, and another three patients at 12 months.

The results suggest that TPM is highly effective in the treatment of oral mucosa leukoplakia, which makes a promising further implementation of TPM in the dental practice.

Conclusions.

1. After removal of the affected area of the mucosa by radiation of an erbium laser, wound healing under fibrinous plaque was observed at 7.0 ± 0.5 days. When excision of the mucous membrane with a scalpel, the healing took place under the iodinine swab through the granulation phase for 14.0 ± 1.5 days.

2. In patients after the operation of excision of the area of verrucous or erosive-ulcerative oral mucosa leukoplakia with laser radiation without antimicrobial and anti-inflammatory therapy on the third day, in 95% of cases there is no pain syndrome and collateral edema in the postoperative area. After traditional treatment, despite the use of antibiotics and non-steroidal anti-inflammatory drugs, 56% of patients complained of pain, and 62% had collateral edema.

3. The use of ErrYAG laser laser radiation in the surgical treatment of patients with verrucous and erosive-ulcerative forms of leukoplakia promotes acceleration of healing processes of a postoperative wound twice as fast as in the control group. The use of laser technology reduces the risk of inflammatory purulent complications and helps to prevent the recurrence of the disease.

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