ORIGINAL ARTICLES

THE EFFECT OF PHOTODYNAMIC THERAPY ON THE WOUND PROCESS DYNAMICS IN PATIENTS WITH PURULENT HAND DISEASES

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Abstract

Despite the progress in modern surgery, the number of patients with purulent finger and hand diseases keeps growing these days in the clinical practice of surgeons. In recent years, there has been a tendency to develop more severe forms of panaritium and phlegmon in an increasingly young contingent of patients. Increasingly, doctors refuse to use the classical method of managing a postoperative wound of the hand involving the installation of drainage tubes. This phenomenon is polygenic and calls for special attention due to the frequent deplorable consequences of a treatment failure. The high urgency of this issue in Moscow Hospital No. 4 has become a rationale to study the effect of photodynamic therapy (PDT) on the course of the wound process in patients with this pathology.

The purpose of this work is to develop a technique to advance the treatment outcomes for patients with purulent finger and hand diseases in case of open postoperative wound treatment.

This study includes a comparative analysis of the wound process dynamics in 49 (49.5%) patients who underwent a photodynamic therapy session in the postoperative period and in 50 (50.5%) patients who received an open wound treatment after the operation. Photodynamic therapy was performed on the second postsurgical day by a laser apparatus "Atkus-2" (wave length 661 nm) with a gel form of the chlorin-series photosensitizer photoditazin in the form of an application at the rate of 1 g ml per 3–5 cm^2 of the wound surface. The power density was chosen in the range of 0.1–1 W / cm^2, and the time of exposure to the wound varied from 30 to 400 seconds, depending on the area of the wound.

To assess the dynamics of the wound process in the postoperative period, we took measurements of all the patients' wound areas on the 1st and 5th days, monitored the gross impression daily. In the patients who received PDT, we observed an earlier wound cleansing and remitting of the inflammatory process, acceleration of the edge epithelization, and earlier appearance of the granulation tissue by an average of 2 days. In the group of patients who were treated with PDT in the postoperative period, on the 5th day, the wound defect decreased by an average of 1 cm^2, which amounted to 22.4%, in the control group – by 18%. The analysis of cytological and morphological patterns also revealed an accelerated switch from the inflammatory stage of the wound process to the reparative one - the reparative processes in the PDT group began earlier by 2 days. The microbiological analysis of wound exudate showed a downregulation of microflora after a PDT session - only in 6 cases pathogens were identified in the repeated seeding, which amounted to 12.24% of the group compared to 38% of the control group. After a session of photodynamic therapy, patients noted a significant reduction in pain, including during dressings. The pain syndrome immediately after the session decreased by 2–3 points. By the 5th day it became moderate – 4–5 points. In the control group, this indicator on the 2nd day was 8 points, decreasing by the 5th day to 6 points. For all analyzed indicators, the groups had statistically significant differences ($p < 0.001$).

Acceleration of postoperative wounds healing enabled to shorten the inpatient stay by 6 days and bring a vast improvement to the treatment quality for this group of patients, which allows considering photodynamic therapy as a high potential method for postoperative treatment of purulent finger and hand diseases.

Keywords: photodynamic therapy, purulent diseases of the hand, panaritium, phlegmon, wound process, photosensitiser, necroectomy.

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ВЛИЯНИЕ ФОТОДИНАМИЧЕСКОЙ ТЕРАПИИ НА ДИНАМИКУ РАНЕВОГО ПРОЦЕССА У ПАЦИЕНТОВ С ГНОЙНЫМИ ЗАБОЛЕВАНИЯМИ ПАЛЬЦЕВ И КИСТИ

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Резюме

Несмотря на высокий уровень развития современной хирургии, в клинической практике современных хирургов продолжает расти количество пациентов с гнойными заболеваниями пальцев и кисти. В последние годы отмечается тенденция к развитию более тяжелых форм панарициев и флегмон у всё более молодого контингента больных. Все чаще врачи отказываются от использования классического метода ведения послеоперационной раны кисти с установкой дренажных трубок. Это явление полиэтиологично и требует особого внимания в связи с нередкими печальными последствиями неудачного лечениях. Высокая актуальность данной проблемы в ГБУЗ ГКБ № 4 г. Москвы стала основанием для проведения исследования влияния фотодинамической терапии (ФДТ) на течение раневого процесса у пациентов с данной патологией.

Целью данной работы является разработка методики с использованием ФДТ для улучшения результатов лечения пациентов с гнойными заболеваниями кисти при открытом ведении послеоперационных ран.

В данном исследовании проведен сравнительный анализ динамики раневого процесса у 99 больных, из них 49 (49,5%) пациентам в послеоперационном периоде выполняли курс ФДТ, 50 (50,5%) послеоперационную рану вели открытым способом. ФДТ выполняли на 2–е сутки после операции. Для ФДТ использовали гелевую форму фотодитазина (фотосенсибилизатор хлоринового ряда) в виде аппликации из расчета 1 мл геля на 3–5 см^2 раневой поверхности. Сеанс облучения проводили с использованием лазерного аппарата «Аткус–2» (длина волны 661 нм). Плотность мощности составляла 0,1–1 Вт/см^2, время воздействия на рану варьировали от 30 до 400 сек в зависимости от площади раны.

Для оценки динамики раневого процесса в послеоперационном периоде всем пациентам выполняли измерение площади раневого дефекта на 1–е и 5–е сутки, ежедневный контроль макроскопической картины. У пациентов после выполнения ФДТ отмечено более раннее очищение раны и купирование воспалительного процесса, ускорение краевой эпителизации и более раннее появление грануляционной ткани в среднем на двое суток в сравнении с контрольной группой. В этой группе на 5–е сутки площадь раневого дефекта уменьшилась в среднем на 22,4% (1 см^2), в контрольной группе – на 18%. При анализе цитологической и морфологической картин выявлено ускорение перехода от воспалительной стадии раневого процесса к репаративной: репаративные процессы в группе с ФДТ начинались раньше в среднем на двое суток, в сравнении с контрольной группой. При микробиологическом анализе раневого экссудата отмечалось снижение количества микрофлоры после курса ФДТ, лишь в 6 случаях (12,2%) в повторном посеве выявлены возбудители, в контрольной группе данный показатель составил 38%. После курса ФДТ больные отмечали существенное снижение болевого синдрома, в том числе и при перевязках. Болевой синдром сразу после курса ФДТ снижался на 2–3 балла, к 5–м суткам становился умеренным: 4–5 балла. В контрольной группе данный показатель на 2–е сутки составлял 8 баллов, снижаясь к 5–м суткам до 6 баллов. По всем анализируемым показателям группы имели статистически значимые различия ($p<0,001$).

Ускорение заживления послеоперационных ран позволило сократить сроки стационарного пребывания на 6 суток и существенно улучшить качество лечения данной группы пациентов, что позволяет считать ФДТ высокоперспективным методом послеоперационного лечения гнойных заболеваний пальцев и кисти.

Ключевые слова: фотодинамическая терапия, гнойные заболевания кисти, панариций, флегмона, раневой процесс, фотосенсибилизатор, некрэктомия.

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Introduction

Over the past decades, certain successes have been achieved in developing an integrated approach to the treatment of purulent pathology of the hand [1]. However, many doctors note a tendency to increase the number of deep forms of panaritium and severe forms of phlegmon, rapid progression of inflammation of the superficial forms of panaritium, which is associated with a decrease in the immune system resistance to infections, insufficient level of medical care at the outpatient stage, the neglect of microtrauma by patients, a tendency to self-medication, and the appearance of antibiotic-resistant strains of microorganisms. At the same time, the contingent of patients has become significantly younger [2].

Purulent pathology of the hand requires special attention due to the fact that unsuccessful treatment frequently has sad consequences, and surgery does not prevent disability [2, 3, 4].

Currently, the main method of treating this pathology is surgery. The application of primary sutures after the most radical necroectomy and drainage is the best option for completing the surgical intervention. However, despite the progress in modern pharmacology and the emergence of new drugs with a wide range of antibacterial effects, many surgeons still choose open wound management in many cases. The time of wound healing with this tactic is significantly longer than with the installation of drainage and irrigation systems. In addition, bandages with this method are very painful, and the probability of secondary infection of the post-surgical wound with the development of mixed infections with nosocomial flora increases significantly [5, 6]. Often, the cause of open wound management can also be an extensive tissue defect after necroectomy and the impossibility to simultaneously reduce the edges of the wound without significant tension. Quite often, there are cases of widespread diffuse purulent lesions, in which it is impossible to perform a single-stage radical necroectomy. Pronounced tissue edema, extensive skin damage up to necrosis of all its layers require the use of open wound management. The use of open wound management makes it possible to achieve good results, but requires a balanced and energetic approach of the attending physician.

Doctors increasingly use photodynamic therapy (PDT) in the treatment of purulent diseases [7, 8]. The evolutionary development of this method of treatment, a large selection of photosensitizers (PS) and laser devices [9], the absence of severe adverse reactions makes PDT one of the advanced methods for the treatment of purulent wounds. A good anti-inflammatory effect, bacteriostatic effect, and a positive effect on the course of the wound process [10-12] gives grounds for studying the use of PDT in purulent hand surgery as well.

In the literature sources available for study, there is no data on the use of PDT in the treatment of purulent pathology of the hand, which was the reason for this study.

Materials and methods

From June 2018 to March 2020, the results of treatment of 99 patients aged from 18 to 90 with purulent diseases of fingers and hand were studied at the Purulent Surgery and Clinical Diagnostics Department of the State Medical Institution City Clinical Hospital No. 4 of the Healthcare Department of Moscow.

Depending on the method of wound management, the patients were divided into 2 groups: in the control group (n=50), patients underwent classic surgical treatment followed by open wound management; patients of the study group (n=49) did not have their wound sutured either, but on the 2nd day after surgical treatment, a course of PDT was administered.

All patients were given a detailed written (in the form of patient brochure) and oral explanation about the method used, after which they were offered to sign a voluntary informed consent. The criteria for inclusion in the trial were the patient's written voluntary consent, age over 18, the presence of purulent hand disease, extensive wound defect after surgery or contraindications to suturing the wound (bitten, crushed wounds), questionable viability of the wound tissues. Patients who refused to participate in the study or refused further observation and hospital stay were excluded from the study.

A random sample was taken from the studied population, with randomization based on random numbers method. The control and study groups were equal in number and composition.

According to the results of the study, men of working professions suffer most often from purulent diseases of the hand (27.3%), there is a high incidence among pensioners (30.3%), while elderly women suffer from purulent diseases of the hand more often than men: 16% vs. 14.1%. This may be explained by the tendency of older women to self-medication and more frequent concomitant diseases that significantly aggravate the course of purulent pathology (polyarthritis, diabetes mellitus); in addition, women of this category do more household chores than men. High numbers of cases among the unemployed (36%) are due to domestic injuries.

We analyzed the causes of purulent diseases of the hand, from which it follows that the most common cause of this pathology is microtrauma (24%), as well as wounds of various etiologies (19%); often patients (13.6%) do not remember or deny the fact of injury.

The most frequently detected pathology in the study was deep forms of panaritium (40.9%), whereas surface forms of panaritium were significantly less common. This is due to the fact that in the absence of adequate therapy, the latter very quickly develop into more severe forms, transforming into deep forms within a few days. In addition, about a third (35%) of patients were hospitalized for a hand phlegmon.

The first stage of treatment in all patients was surgical treatment, performed urgently in the first hours after the patient's admission to the hospital. The volume and nature of the surgical intervention were determined taking into account the prevalence and localization of the purulent focus; they differed depending on the nosological form. Purulent foci were accessed with classic incisions described in traditional methods. If possible, efforts we made to avoid cuts on the working surfaces of the fingers and hand. Incisions should be optimal in localization and size to ensure the necessary wound revision and a comprehensive necroectomy. Only the skin was dissected with a scalpel; all the underlying tissues were pushed apart with hooks and clamps to maximize the integrity of important anatomical structures (neurovascular bundles, tendons). In the presence of long-term non-healing purulent wounds, a gentle excision of the turned-in or callous edges of the wound was performed. After the removal of pus, a radical necroectomy was performed, with a careful treatment of tissues that were inflamed but viable. Then local treatment of postoperative wounds was performed: daily dressings with antiseptic solutions, antibacterial therapy with cephalosporin-type drugs and fluoroquinolones (with medication adjustment according to the results of bacteriological research), infusion, and detoxification therapy. Analgesic therapy was administered if necessary (at the request of the patient) with standard non-steroidal anti-inflammatory drugs. In the presence of concomitant pathology, adequate symptomatic therapy was administered after consultation with corresponding specialists. The purpose of all therapeutic measures was to eliminate the purulent focus and create optimal conditions for the fastest possible healing of purulent wounds with good functional and cosmetic results.

The first dressing with full-fledged wound rehabilitation was performed on day 2 after the operation (on the first day only the upper layers of the bandage were removed, the condition and viability of the skin of the surrounding tissues were evaluated, and the underlying layers of the bandage were left intact for fear of bleeding and severe pain). Subsequently, debridement of wounds was performed daily.

The PDT course involved the use of photoditazine e6 of chlorin type as PS (OOO «Veta-Grand») in the form of a gel in applications at the rate of 1 ml of gel per 3-5 cm^2 of the wound surface. The irradiation was provided with Atkus–2 laser device (ZAO «Poluprovodnikovyie Pribory», St. Petersburg), with the wavelength of 661 nm. The exposure of the wound to drug was according to the manufacturer's instructions: 15-20 minutes in lightless conditions. The irradiation time during external light supply with the use of light guides with a polished end or microlens was calculated according to a standard formula depending on the power density.

$$T\ (sec) = D\ (J/cm^2)/Ps(W/cm^2),\ \text{where}$$

T is the irradiation time,
D is the required light dose (energy density),
Ps is the power density.

The energy density applied to the wound should be on average 30-40 J/cm^2. At an energy density of less than 30 J/cm^2, a weak effect was observed, the wound microflora was not destroyed completely, and at an energy density of more than 40 J/cm^2 and necrotization of healthy wound tissues was observed. The power density of the light emitted by the semiconductor laser was selected in the range of 0.1-1 W/cm^2, the time of exposure to the wound varied from 30 seconds to 10 minutes, depending on the area of the wound. The power density was chosen depending on the size of the light spot. For the convenience of conducting PDT courses, the power density values for the most commonly used laser output power values and light spot sizes were presented in the power density table for different spot sizes and laser power [7].

The PDT course was performed in a dressing ward. The distance from the end of the light guide to the wound surface was 1.5-2 cm (Fig. 1).

A macroscopic assessment of the dynamics of the wound process was carried out on a daily basis, with the recording of the condition of the edges, walls and bottom of the wound (color, number of necrosis areas, fibrinous pellicle), the condition of the surrounding tissues (the degree of hyperemia, edema, infiltration), the nature of the wound discharge (purulent, serous, sanioserous), the amount of exudate (abundant, moderate, scanty), its smell and color, the dynamics of granulation tissue development (timing, color, shine, granularity, bleeding), the dynamics of epithelization at various stages of the wound process.

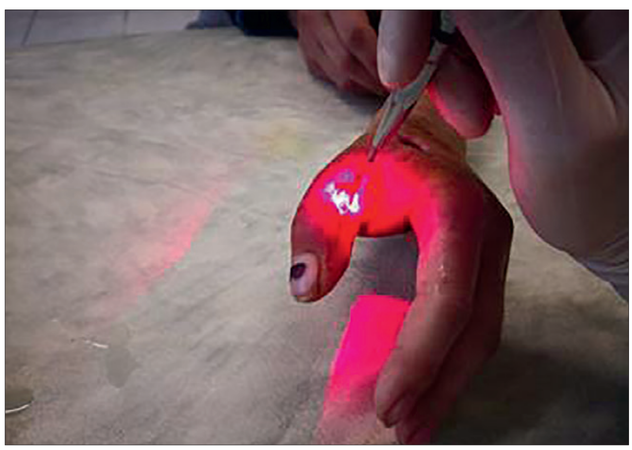

Рис. 1. Сеанс ФДТ
Fig. 1. Session of PDT

The dynamics of the wound process was assessed in the study based on M. I. Kusin's classification (1977) [14]:

1. Inflammation phase (wound cleansing, vascular changes).
2. Regeneration phase (formation and maturation of granulation tissue).
3. Epithelialization phase.

To assess the healing time of purulent wounds, the area of the wound surface was measured immediately after the surgery and on the day 5 with the determination of the healing acceleration rate.

The area of an irregular wound was calculated by the formula (Khotinyan V. F., 1983) [15]:

$$S = 0.25Lk - C, \text{ where}$$

S is the area of the wound;
L is the perimeter of the wound;
k is the regression coefficient (for wounds close to a square in shape: 1.013; for wounds with irregular contours: 0.62);
C is a constant, equal to 1.29 and 84.34, respectively.

Wound healing V (%) was estimated by the formula:

$$V=(S_1-S_2)/(t^* S_1) *100, \text{ where}$$

S_1 is the area of the wound determined during the previous measurement;
S_2 is the area of the wound at the moment;
t is the number of days between measurements.

During the normal course of healing, the daily decrease in the wound area is 4%.

In both groups, intraoperatively and on day 5, microbiological material was taken for culture seeding to determine the wound microflora. The bacteriological material was collected with a cotton swab and placed in a sterile test tube with a medium, after which it was seeded in culture medium in Petri dishes.

To study the effect of the treatment on the course of the wound process, a cytological study was used by the method of taking smears/prints of the wound surface. During each period of the study, two smear prints were taken from one area of the wound surface. Smears/prints were obtained during dressing after preliminary removal of liquid exudate from the wound surface during the surgery, on days 2 and 4 after the start of treatment. The study took into account the dynamics of cellular elements: unchanged neutrophilic leukocytes, altered neutrophils, immature mononuclear elements, macrophages, young and mature fibroblasts and fibrocytes. The cytogram was calculated with oil immersion method. 400 cells in each case were considered in the study.

Morphological examination of tissues from the purulent wound area in all patients was performed at the beginning of treatment, on the days 3, 5 and 7 days after the start of treatment.

To assess the subjective pain syndrome in the postoperative period, the patient was asked to assess the degree of pain syndrome in points according to the standard visual analog scale [16] daily during dressing.

Statistical processing of the obtained data of our own observations was carried out with Microsoft Office 2017 applications package (Word, Excel). The calculations were performed in MedCalc Statistical Software version 17.0.4 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2017). The work uses the methods of descriptive statistics. The parameters are specified with the use of the median of the standard square deviation. The medians of the minimum and maximum values were used for the nonparametric distribution of the studied indicators.

When comparing the data, an analysis of variance (the Kruskal-Wallis test) was applied, and for repeated changes, an analysis of variance of repeated measurements was used.

The average values were compared with the determination of the measurement error and the reliability of the parameter differences between the studied groups. The significance level (p) is assumed to be less than 0.05.

Results

During irradiation, patients did not notice discomfort or pain; some patients (n = 21) noticed paresthesia of «light tingling» type in the area of exposure to the beam. No hyperthermia and no local inflammatory reaction were observed during the PDT course and after it.

Due to the abundant innervation of the hand area, all patients experienced a high level of pain syndrome at admission, with the average evaluation of 9 (8-10) points. Initially, there were no significant differences in the severity of pain syndrome between the groups (p=0.23). In the traditional treatment group, the severity of the pain syndrome averaged 8 (7-10) points. On day 5, the patients noted that a high level of pain syndrome remained, with average severity level of 6 (4-8) points. On day 9, the severity of the pain syndrome averaged 5 (3-9) points.

In the PDT group, patients also noted severe pain on the day after surgery, but after performing the PDT course, there was a significant decrease in pain syndrome to 6 (4-8) points, including during wound dressing. The pain syndrome became moderate by day 5, at an average of 4.5 (3-7) points, and then decreased to an acceptable level. On day 9, the severity of the pain syndrome was 4 (2-6) points (Fig. 2).

In the group of patients who underwent PDT, the dynamics of the wound process was significantly better: perifocal inflammatory phenomena subsided faster, and the wound defect was cleared of purulent detritus, the appearance of granulation tissue and marginal epithelization began earlier (Table 1).

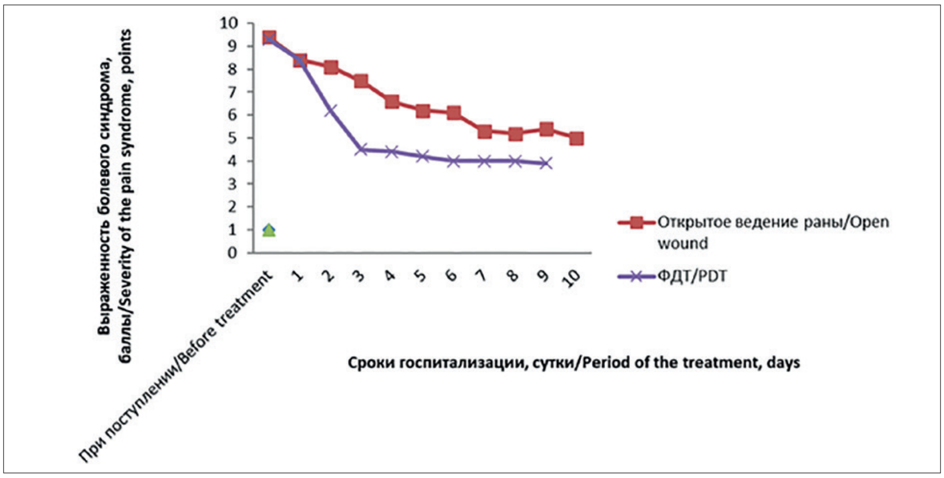

Рис. 2. Динамика выраженности болевого синдрома в группах
Fig. 2. Dynamic of the pain syndrome in groups

Таблица 1
Динамика клинической картины раневого процесса в основной и контрольной группах
Table 1
Dynamic of clinical pattern of the wound process in the control and experimental groups

Группы Group	Стихание перифокального воспаления, сутки Reduction of perifocal inflammation, day	Очищение ран, сутки Purification of wounds, day	Появление грануляций, сутки Appearance of granulations, day	Начало эпителизации, сутки Beginning of epithelialization, day
Без ФДТ Without PDT (n=50)	7 (5–11)	8 (5–12)	8 (4–10)	8 (6–10)
ФДТ PDT (n=49)	5 (2–10)	5 (2–8)	5 (3–12)	6 (3–13)
p	<0,0001	<0,0001	<0,0001	<0,0001

Таблица 2
Изменение размеров ран в основной и контрольной группах
Table 2
Changing the size in groups of the open wounds in the control and experimental groups

Группы Group	Площадь раны интраоперационно, см² Wound area after surgery, cm²	Площадь раны, 5-е сутки, см² Wound area 5th day, cm²	Изменение размера, 5-е сутки, % Changing of the sizes 5th day, %
Без ФДТ Without PDT (n=50)	4,3 (0,9–146,2)	3,4 (0,9–126,9)	18,8 (10,7–22,9)
ФДТ Without PDT (n=49)	4,4 (0,6–134)	3,4 (0,5–105,1)	22,4 (15,0–41,7)
p	0,99	0,77	<0,001

The area of wounds in patients immediately after the surgical stage of treatment ranged from 0.63 cm² to 146 cm², depending on the nosological form of the disease. In the group with the traditional method of postoperative wound management, the surface area of the wound defect decreased by an average of 0.9 cm² over 5 days, amounting to 18.8% of the initial size of the postoperative wound, which indicates a sluggish wound process. In the group of patients who underwent PDT in the postoperative period, on the day 5, the wound defect decreased by an average of 1 cm² (22.4%) (Table 2).

The analysis of the results of cytological examination of wound prints allows us to evaluate the nature of the wound process and the effectiveness of the treatment.

The cytological picture in the materials obtained from surgical wounds on the day of surgery was characterized by a pronounced inflammatory reaction standard for the purulent process, the presence of purulent-necrotic exudate in the area of the wound bottom, a large number of dystrophically altered neutrophil leukocytes are found in smears/prints from the wound surface, and the free-lying microflora is observed (Table 3).

In traditional surgical treatment with open management of purulent wounds, the cytological picture is that of a delayed course of the wound process with a prolonged period of purification of wounds from pathogenic microorganisms and foreign particles, with a longer phagocytosis process, the prolonged presence of dystro-

Таблица 3
Динамика цитологических показателей гнойных ран в основной и контрольной группах, %
Table 3
Dynamic of the cytological indicators of purulent wounds in the control and experimental groups, %

Элементы цитограммы Cytogram elements	Интраоперационно во всех группах Upon the surgery in all groups	Группа / Group			
		Без ФДТ Without PDT		ФДТ With PDT	
		На 2-е сутки 2nd day	На 4-е сутки 4th day	На 2-е сутки 2nd day	На 4-е сутки 4th day
Нейтрофилы, из них: **Neutrophils incluing:**	97,9±2,1	96,5±2,3	93,2±2,3	93,8±2,2	76,7±2,3
Неизмененные Unchanged	12,5±1,1	20,3±2,3	40,1±4,8	65,3±2,2	56,5±1,1
Дистрофически измененные Dystrophic altered	85,4 ±3,5	76,2±3,	53,1±3,6	28.5±2,2	20,2±2,2
Мононуклеарные фагоциты, из них: **Mononuclear phagocytes including:**	1,9±0,3	2,8±0,3	5,6±0,4	4,5±0,2	13,5±0,4
Моноцитарные Monocytic	1,7±0,1	1,9±0,1	4,0±0,4	3,3±0,2	8,4±0,4
Зрелые макрофаги Mature macrophages	0,2±0,1	0,9±0,1	1,6±0,3	1,2±0,1	4,1±0,2
Фибробласты: Fibroblasts:	Отс. abs.	0,7±0,1	1,2±0,1	1,6±0,1	5,9±0,1
Юные Young	Отс. abs.	0,7±0,1	1,2±0,1	1,3±0,1	4,8±0,1
Зрелые Mature	Отс. abs.	Отс. abs.	Отс. abs.	0,3±0,1	1,1±0,1
Фиброциты Fibrocytes	Отс. abs.	Отс. abs.	Отс. abs.	Отс. abs.	2,0±0,1
Эпителий Epithelium	Отс. abs.	Отс. abs.	Отс. abs.	Отс. abs.	1,9±0,1
Детрит / Detritus*	+++	+++	++	+/-	Отс. abs.
Фибрин Fibrin*	+++	+++	+++	+	+/-
Микрофлора Microflora*	+++	+++	++	+/-	Отс. abs.
Незавершенный фагоцитоз Incomplete phagocytosis*	+++	+++	++	+/-	Отс. abs.

* Степень выраженности гисто-химической реакции
* The rate of the histochemical reaction

phically altered neutrophils, as well as with the preservation of a pronounced amount of both microflora, fibrin and necrotic detritus. A low content of macrophages indicates a sluggish inflammatory process in the exudation stage. The delayed appearance of a small number of cellular elements of the fibroblastic series indicates a delayed onset of the proliferative stage of inflammation.

Changes in the studied cytological patterns after PDT showed an accelerated transition from the inflammatory type cytogram: previously, there was a progressive decrease in the number of neutrophil leukocytes, an increase in the number of monocytic and mature macrophage elements. Fibrous structures of connective tissue appeared earlier, and the number of fibroblasts increased, mainly due to juvenile forms. There were no phenomena of incomplete phagocytosis or free-lying microflora; the amount of fibrin progressively decreased. The cells of the squamous epithelium also appeared faster.

The obtained results of the analysis of the cytological picture indicate a positive effect of PDT on the healing process of postoperative wounds due to the acceleration of the processes of cellular differentiation of the fibroblastic series, and the early onset of epithelialization.

In terms of microbiological picture, monoculture was detected in 79 cases (79.8%) in cultures seeded intraoperatively, whereas associations of pathogens were found in 20 patients (20.2%). Among all pathogenic organisms, Staphylococcus aureus was most

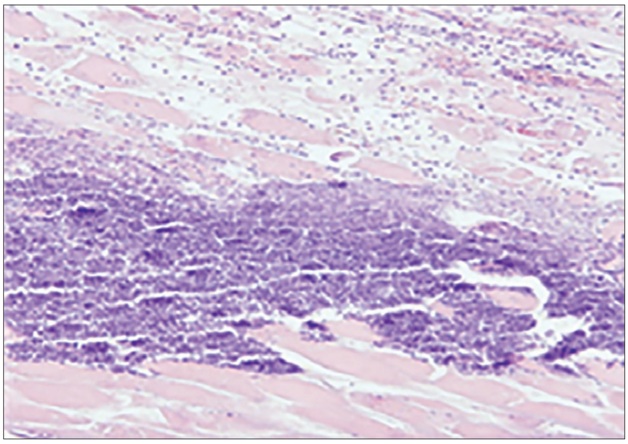

Рис. 3. Гистологическое исследование биоптата из тканей раны во время операции. Нейтрофильная инфильтрация, отек тканей. Некроз мышечных волокон. Окраска гематоксилином и эозином. Увеличение х120.
Fig. 3. Biopsy from wound tissue during surgery. Neutrophilic infiltration, tissue edema. Muscle fiber necrosis. Hematoxylin and eosin staining. Magnification x120.

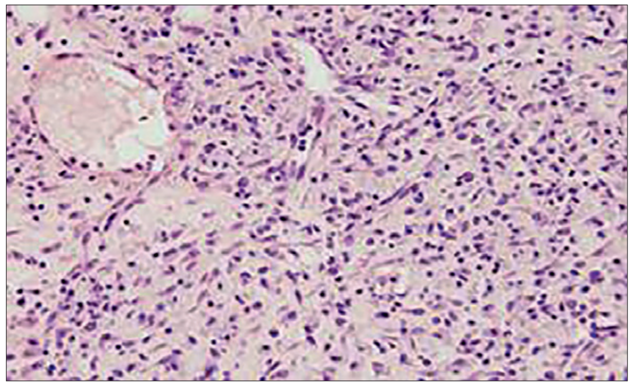

Рис. 4. Гистологическое исследование биоптата из тканей раны пациента контрольной группы на 3-и сутки после операции. Лейкоцитарная инфильтрация (определяются нейтрофилы), полнокровные сосуды, со стазами и плазматическим пропитыванием стенок. Окраска гематоксилином и эозином. Увеличение х200.
Fig. 4. Biopsy from the tissue of the wound of control group on the 3rd day after surgery. Leukocyte infiltration (neutrophils are present), congested vessels, with stasis and plasma impregnation of the walls. Hematoxylin and eosin staining. Magnification x200.

often found in cultures, in 35 cases (35.6%), Escherichia coli was detected in 11 patients (11.1%), epidermal staphylococcus in 7 (7.1%), pyogenic streptococcus in 5 (5.05%) and group B streptococcus (Str. agalacticae) in 6 (6.06%). Much less often (1-2%), Pasteurella, Actinomycetes, Klebsiella, Enterobacter, as well as Aspergillus mold fungi were found in the culture. In 25 cases (25.8%), sterile cultures were obtained, and the analysis of the data revealed that all patients with this result were operated on an outpatient basis or received antibacterial therapy.

In associations, the most common microorganisms were E. coli (2%), *Streptococcus agalactiae* (2%) and *Candida fungus* (2%). The less common ones were Enterobacter (1.52%), *Klebsiella aerogenes* (0.51%), *Streptococcus viridans* (0.51%), and *Proteus* (1%). It is noteworthy that *Klebsiella*, *Proteus* and *Candida* fungi were not detected as a monoculture, forming an association with *Staphylococcus aureus* in all cases.

In the study group, immediately after the PDT course on day 2, new cultures were seeded. In all cases, the results were sterile.

Then, cultures were seeded from patients of both groups on day 5 of inpatient treatment. The results of the analysis of microbiological findings differed significantly depending on the treatment method. In the control group, repeated microbiological examination revealed initial microflora in 19 cases (38%), despite daily dressings with antiseptics and antibacterial therapy received. In the group that underwent PDT, pathogens were detected in 6 cases in repeated cultures, which was 12.24%. Thus, the results of the microbiological study demonstrate a positive effect of PDT on the contamination of the wound surface.

All patients underwent intraoperative histological examination, with the condition similar in both groups: during surgical treatment, pronounced alterative/exudative changes were detected. Necrotically altered tissues with massive infiltration by leukocytes with a polymorphic nuclear structure were found in the bottom of the wound and its walls. The necrosis zone was separated from intact tissues by a torus demarcationis of leukocytes with full-blooded vessels, the permeability of the walls of which was increased; the impregnation with plasma proteins and blood corpuscles was determined, with pronounced stasis and multiple focal perivascular hemorrhages against the background of fibrinoid necrosis of the vascular wall of the microcirculatory bed, which indicated a significant disorder of microcirculation (Fig. 3).

In the group with traditional treatment, on day 3 after surgery, the bottom and edges of the wound are covered with a scab consisting of necrotic tissues and fibrinous exudate. Deeper than this layer is a layer of fibrin fibers with leukocyte infiltration and focal hemorrhages; the neutrophils of this layer are dystrophically altered. The vessels in this zone are characterized by pronounced fullness with microthrombs of various nature, and the phenomena of lymphostasis are determined (Fig. 4).

On day 5, a fibrino-purulent plaque with signs of fragmentation was detected on the wound surface. In various areas of the wound surface, the initial signs of granulation formation appear: chaotically located capillaries with multiple macrophages and rare undirected fibroblasts are formed at various stages of development. Well-expressed perivascular and focal neutrophil infiltrates persist. In the deep layers of the wound edge, the content of neutrophilic leukocytes decreases, and the number of undirected fibroblasts increases, but macrophages prevail in quantity.

On day 7 (Fig. 5) of the postoperative period, there is a decrease in the number of fibrinous overlays and necrotic tissues, the degree of neutrophil infiltration in the surface zone decreases, microthrombs and sludge syndrome phenomena in the vascular lumen are less often detected, the phenomena of tissue edema and perivascular diapedesis hemorrhages disappear. The number of microcirculation disorders decreases. In the perivascular areas, when stained with toluidine blue, rare granule cell with degranulation phenomena are detected. In the area bordering on intact tissues, small foci of granulation tissue appear with small vessels forming, macrophage cells with signs of proliferation, fibroblasts and numerous polymorphonuclear leukocytes.

In patients who underwent PDT, on day 3 after the session (day 5 of the postoperative period), the wound surface is covered with a narrow necrotic scab with fibrinous inclusions, but the thickness of fibrinous deposits is significantly less, there is an intensive cleansing of the surface from necrotic scab elements. Foci of granulation tissue begin to form under the scab, with newly formed capillaries and cellular elements of the macrophage and fibroblastic series. At the border with the underlying healthy tissues, a zone of hemo– and microcirculation disorders is determined, with moderate intravascular fullness and stasis, and an insignificant number of circulatory diapedetic hemorrhages is detected. Edema and neutrophil infiltration are significantly less pronounced, but the number of macrophages and undirected fibroblasts is much higher (Fig. 6).

The functional activity of the macrophage component increases significantly after a course of PDT, which is confirmed by the PAS-positive foamy cytoplasm in cells. The Brachet reaction determines the pyroninophilia of the cytoplasm and nucleoli of fibroblasts and young endotheliocytes, which indicates a pronounced RNA activity (Fig. 7).

By day 5 after PDT (day 7 of the postoperative period), the wound surface is completely cleared of necrotic elements and fibrin, granulation tissue is actively formed in all areas with newly formed vertically oriented capillaries and fibroblasts between them, and pronounced fibrillogenesis (Fig. 8).

The morphological studies conducted indicate that the use of PDT in the treatment of purulent wounds significantly accelerates the wound process and improves the purification of wounds from fibrinous/purulent exudate and scab elements, which is associated with both reparative processes stimulation due to activation the transport of oxygen and nutrients in the forming granulation tissue, and the creation of conditions conducive to earlier and active formation of granulation tissue and faster healing of a purulent wound.

During irradiation, patients did not notice discomfort or pain; some patients (n=21) noticed a slight tingling in the area of exposure to the beam.

The use of PDT made it possible to stop the inflammatory process faster, accelerate the development of the regenerative phase, which was noticed in the shorter duration of treatment. The patients of the control group were in the hospital for an average of 14 (7-29) days, after which they received outpatient medical care for 7 (4-10) days. Wound healing in the group was slowed down by an average of 22 (13-36) days. In the group where patients received PDT, the terms of inpatient treatment averaged 8 (4-21) days, with the outpatient stage averaging 7 (5-9) days; wounds healed completely by day 14 (10-27) ($p<0.0001$).

In the traditional open management of postoperative wounds, repeated amputation in the early postoperative period was performed in 21 patients (42.0%), and amputation was required in 2 patients with pandactylite of the first and second fingers during repeated surgery, 1 patient with anaerobic phlegmon of the hand and forearm had surgery five times. Patients who underwent a course of PDT required repeated surgical treatment in 4 cases (8.2%), while 1 patient with anaerobic phlegmon of the hand and forearm underwent repeated necroectomy 4 times.

There were no complications or allergic reactions during PDT. No hyperthermia and no local inflammatory reaction were observed during the PDT course and after it.

None of the patients who participated in the study applied again with the development of recurrent purulent inflammation. It should be noted that patients from the group with classical treatment more often noted a restriction of the function of the finger or hand due to the development of a dense scar fused with the underlying tissues. Patients whose wounds were exposed to laser radiation, on the contrary, noted the formation of soft scars that did not fuse to the surrounding tissues, did not limit the function and visually seemed neat.

We provide a clinical example illustrating the successful use of PDT.

Patient B., 58 years old, was undergoing inpatient treatment in the department of purulent surgery for pandactylite of the first finger of the left hand.

4 days before admission to the hospital, he was operated on an outpatient basis for subcutaneous panaritium. He receives conservative therapy for type 2 diabetes. Upon admission, the patient's condition was of moderate severity. On examination, a transverse postsurgical wound of a linear shape with abundant purulent discharge was noted. The edges of the wound are severely edematous, with areas of necrosis. A distinct

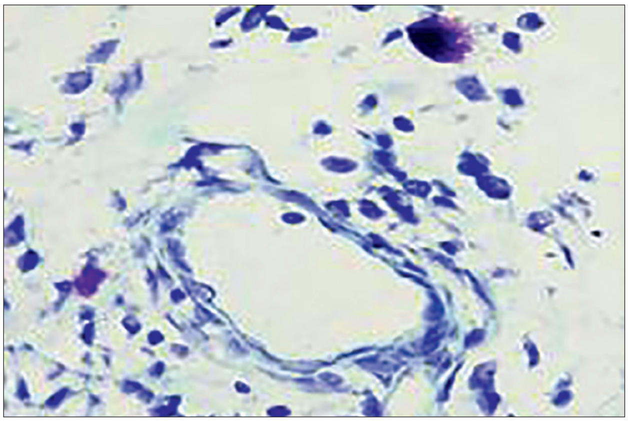

Рис. 5. Гистологическое исследование биоптата из тканей раны пациента контрольной группы на 7–е сутки после операции. Метахроматичные тучные клетки в периваскулярной области. Окраска толуидиновым синим. Увеличение х900.
Fig. 5. Biopsy from the tissue of the wound of control group on 7th day. Metachromatic mast cells in the perivascular region. Toluidine blue staining. Magnification x900.

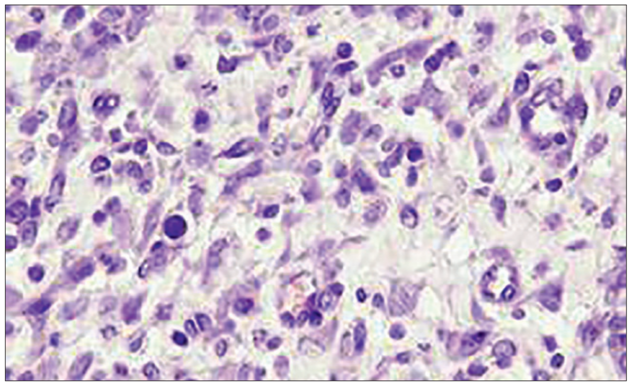

Рис. 6. Гистологическое исследование биоптата из тканей раны пациента исследуемой группы на 5-е сутки послеоперационного периода. Сосудистые элементы с макрофагальными клетками и отдельные неориентированные фибробласты. Окраска гематоксилином и эозином. Увеличение х900.
Fig. 6. Biopsy from the tissue of the wound of experimental group on 5th day of postoperative period. Vascular elements with macrophage cells and some non-oriented fibroblasts. Hematoxylin and eosin staining. Magnification x900.

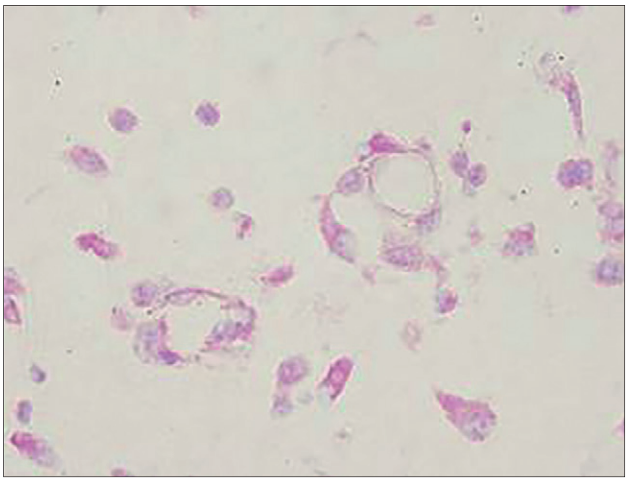

Рис. 7. Гистологическое исследование биоптата из тканей раны после ФДТ на 5-е сутки послеоперационного периода. Пиронинофилия цитоплазмы и ядрышек эндотелиоцитов и фибробластов. Окраска на РНК по Браше. Увеличение х900.
Fig. 7. Biopsy from the tissue of the wound of experimental group on 5th day of postoperative period. Pyroninophilia of the cytoplasm and nucleoli of endotheliocytes and fibroblasts. RNA staining according to Brachet. Magnification x900.

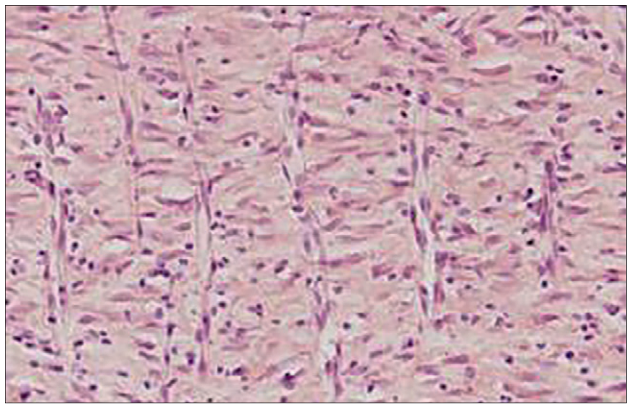

Рис. 8. Гистологическое исследование биоптата из тканей раны на 7–е сутки лечения после операции. Созревание грануляционной ткани с вертикальными сосудами, горизонтально ориентированными фибробластами и выраженным фибриллогенезом. Окраска гематоксилином и эозином. Увеличение х400.
Fig. 8. Biopsy from the tissue of the wound of experimental group on 7th day of treatment after surgery. Maturation of granulation tissue with vertical vessels, horizontally oriented fibroblasts and pronounced fibrillogenesis. Hematoxylin and eosin staining. Magnification x400.

crepitation was detected in the interphalangeal joint. The X-ray showed destruction in the area of the interphalangeal joint. The glucose level at admission was 15.8 mmol/l. Surgical treatment, necrosequestrectomy was performed urgently; due to the pronounced swelling of the wound edges, it was not possible to suture the wound defect. On day 2, examination (Fig. 9) found tissue swelling, pronounced perifocal inflammation, cloudy discharge, and persisting multiple necrosis. A course of PDT with photoditazine was performed (application of 3.5 ml of gel, exposure of 10 minutes, power density of 1 W/cm^2).

In intraoperative culture, *St. pyogenes* was isolated, sensitive to vancomycin, amoxiclav, ciprofloxacin, levofloxacin, erythromycin. On day 2 after the course, a dry black scab was noted in the wound (Fig. 10a), perifocal inflammatory phenomena decreased, the amount of discharge decreased.

Further, the inflammatory phenomena gradually subsided (Fig. 10 b, c). When the new culture was seeded, microflora from the wound was not detected, after

Рис. 9. Пандактилит первого пальца левой кисти на 2–е сутки после операции, экспозиция фотосенсибилизатора.
Fig. 9. Pandactylitis of the 1st finger of the left hand on the 2nd day after surgery, exposure of the photosensitizer.

a b c

Рис. 10. Пандактилит первого пальца левой кисти:
a – на 2–е сутки;
b – на 4–е сутки;
c – на 5–е сутки после ФДТ.
Fig. 10. Pandactylitis of the 1st finger of the left hand:
a –2nd day;
b – 4th day;
c – 5th day after PDT

which secondary stitches were applied to the wound. The patient was discharged on day 9 after surgery, with sutures removed on day 6 after the third surgery. The wound completely healed on day 14. During the control examination: an irregular scar on the lateral surface of the finger without signs of inflammation, soft, not fused to the underlying tissues, pinkish in color. The finger is somewhat shortened after joint resection (Fig. 11), its function is partially limited.

Discussion

This study is part of a previously conducted scientific work [17, 18] aimed at studying the effect of laser radiation on the results of treatment of patients with purulent pathology of the hand.

Currently, there is a wide range of different methods to improve treatment outcomes for this pathology. Foreign scientists widely use open management of postoperative wounds with various auxiliary techniques (plasma

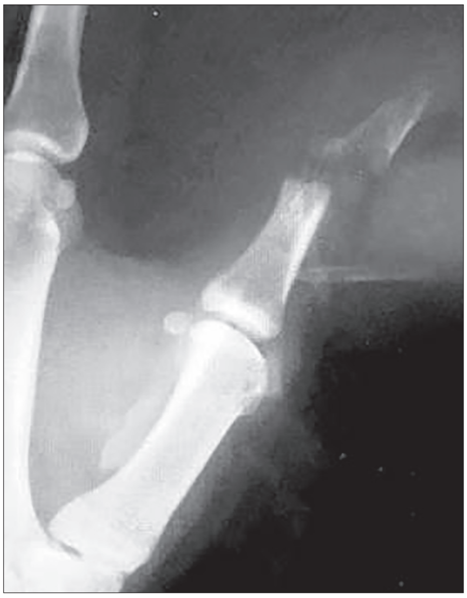

Рис. 11. Рентгенограмма сустава после резекции.
Fig. 11. X-ray of the joint after resection.

therapy, wound management in a liquid environment, cryotherapy, vacuum therapy, etc.). Active use of physical factors in practice, such as ultrasound irradiation, hyperbaric oxygenation, direct current, contributed to improving the effectiveness of treatment of patients with purulent pathology.

Russian and foreign doctors increasingly use plasma flows in the treatment of deep forms of panaritium; the effect of argon plasma intensifies the development of granulation tissue. In recent years, the physical and biostimulating activity in relation to the wounds of the NO-containing plasmodynamic gas flow has been actively studied. One of the new methods used in the treatment of both acute and chronic wounds is the local use of vacuum dressings: the Vacuum–assisted closure (VAC-therapy) method, the principle of ToFig.al negative pressure (TNP). However, the high cost of consumables and the anatomical features of the hand currently create limitations that do not allow for the wide use of this technique in hand surgery.

To date, in the treatment of purulent wounds, an arsenal of technical means is used that have a particular physical effect on the wound, for example, the treatment of wounds with a pulse jet. The technique of using low- and medium-frequency ultrasound in the treatment of purulent wounds has proven itself well. Due to the fact that ultrasound propagates differently in living and devitalized tissues and is reflected at the interface between them, it accelerates the processes of necrotic tissues rejection. At the same time, many authors point to the damaging effect of ultrasound on healthy tissues, which limits its use in hand surgery due to the concentration of important functional structures in a small volume of tissues. Lasers have also achieved great popularity, having become widely used in surgery. The convenience of high-energy lasers, diode laser scalpels in surgical treatment, as well as their high efficiency, allows us to consider their use as a promising technique. Due to the flexibility and elasticity of the light guide and the contact method of diode laser scalpel use, surgery can be performed in hard-to-reach parts of the operated area, which is its significant advantage over other laser systems. In the application of a carbon dioxide laser, a significant factor is its non-contact use and the fact that no consumables are required.

Among the conservative methods in recent years, enzymatic debriming, methods of influencing the wound process with gas flows in the NO therapy mode and low-intensity laser radiation have been widely used to prepare wounds for plastic surgery. However, the use of high-energy lasers and plasma streams in hand surgery requires the development of a technique to exclude damage to delicate anatomical structures that determine the functioning of the entire hand.

All of the above methods require a balanced approach due to the impact on the surrounding tissues, which is critical due to the small volume of tissues in the hand area, and due to the fact that the equipment and consumables used for the treatment are expensive, and the repairs of the equipment are also difficult.

In addition to having a positive effect, the use of PDT is also a relatively safe method. PDT produces a pronounced anti-inflammatory effect, stimulates phagocytosis and accelerates granulation formation due to the absorption of laser energy by tissues; it has a positive effect on microcirculation, which activates the repair process. PDT is characterized by selectivity of exposure, which is due to the absorption of PS by tissues with high proliferative activity, enhanced metabolism and bacterial agents. The specifics of the application of this technique is the absence of pronounced destructive lesions of the wound tissues, the relative painlessness of the procedure, and the possibility of treating deep tissues. The bactericidal effect is limited to the zone of laser irradiation of sensitized tissues, which helps to avoid the side effect observed when using antibiotics and antiseptics for the treatment of surgical infection with local PDT. After a course of PDT, there is a decrease in bleeding during wound dressing.

PDT has a fairly narrow range of contraindications (the presence of severe, non-correctable pathology in patients: hypersensitivity to the drug; severe renal or hepatic failure; decompensated phase cardiovascular diseases; pregnancy and lactation; childhood; the threat of bleeding due to blood clotting disorders), so the treatment can be administered to the absolute majority of patients.

The introduction of PDT into a wide clinical practice will not only improve the results of treatment, but also make it possible to abandon the use of systemic antibacterial drugs and create opportunities for a rapid tranfer of inpatients to outpatient treatment [19, 20].

Conclusions

According to the findings of the study, it can be concluded that PDT has a beneficial effect on the course of the wound process, contributing to the normalization of microcirculation, early cleansing of wounds from detritus, the appearance of granulation tissue and marginal epithelization. In the absence of the possibility of wound suturing, PDT significantly accelerates healing, and, therefore, reduces the duration of hospital stay, which allows us to consider this method highly promising and justified for use in clinical practice.

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