

Abstract

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**LONG-TERM CONSEQUENCES OF THE USE OF  
AUTOLOGOUS PLATELET-RICH PLASMA IN  
THE TREATMENT OF PATIENTS WITH DIABETIC ULCERS,  
AND MEDICAL AND SOCIAL ADAPTATION OF SUCH  
PATIENTS**

**Relevance of the problem.** According to the International Diabetes Federation (IDF), the number of patients with diabetes in the world reached 463 million people in 2019. One of the most severe local complications of diabetes is diabetic foot syndrome manifested through the development of diabetic ulcers on the lower extremities, which leads to poor quality of life and disability.

**Objective.** To evaluate the long-term outcomes after the use of autologous platelet-rich plasma in the treatment of patients with trophic ulcers secondary to type 2 diabetes mellitus and to study the peculiarities of medical and social adaptation of the patients who underwent such treatment vs. traditional methods.

**Materials and methods.** Study subjects were divided into two groups. The main group included 55 patients; the comparison group included 50 patients. Patients in the comparison group were treated according to the standard scheme in accordance with the recommendations of the International Working Group on the Diabetic Foot (IWGDF 2015). Treatment of patients in the main group was based on the above recommendations and corrected local treatment scheme according to our proposed method using autologous platelet-rich plasma. When studying the effectiveness of treatment, we used adapted EuroQol EQ-5D-5L questionnaire.

Statistical data were processed using the Student's t-test. The difference in average values at  $p < 0.05$  was taken as statistical significance.

**Conclusions.** It was found that the recurrence of ulceration in the main group of subjects occurred less frequently, as compared with patients in the comparison group ( $p < 0.05$ ).

Long-term follow-up period showed that 34 (72.3%) subjects in the main group had no mobility problems vs. 21 (46.7%) subjects in the comparison group. In the main group, 44 (95.7%) subjects did not require assistance in daily living activities vs. 35 (77.8%) subjects in the comparison group. In the main group, 33 (70.2%) subjects could participate in normal daily activities vs. 17 (37.8%) subjects in the comparison group.

37 (78.7%) patients in the main group were not prone to depression and in the comparison group, only 18 (40%) subjects were not depression-prone, which is 1.9 times less ( $p > 0.05$ ).

**Keywords:** social adaptation, autologous plasma, trophic ulcer, diabetes mellitus.

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## Резюме

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## ВІДДАЛЕНІ НАСЛІДКИ ВИКОРИСТАННЯ АУТОЛОГІЧНОЇ ПЛАЗМИ, ЗБАГАЧЕНОЇ ТРОМБОЦИТАМИ ПРИ ЛІКУВАННІ ХВОРИХ НА ДІАБЕТИЧНІ ВИРАЗКИ ТА ЇХНЯ МЕДИКО-СОЦІАЛЬНА АДАПТАЦІЯ

**Актуальність проблеми.** За Міжнародної Діабетичної Федерації (IDF) численність хворих на ЦД у світі на 2019 рік становила 463 мільйонів осіб. Одним із тяжких місцевих ускладнень ЦД є синдром діабетичної стопи, проявом якого є розвиток діабетичних виразок нижніх кінцівок, що веде до зниження якості життя та втрати працездатності.

**Мета роботи.** Оцінити віддалені результати після використання аутологічної плазми, збагаченої тромбоцитами, при лікуванні хворих на трофічні виразки на тлі цукрового діабету II типу та вивчити особливості медико-соціальної адаптації хворих, які піддалися такому лікуванню у порівнянні з традиційними методиками.

**Матеріали і методи.** Досліджені були розподілені на дві групи. В основну групу увійшло 55 хворих, у групу порівняння – 50. Хворим групи порівняння проводили лікування за стандартною схемою згідно з рекомендаціями міжнародної робочої групи по діабетичній стопі (IWGDF 2015). Лікування хворих основної групи базувалося на наведених вище рекомендаціях та корекцією місцевого лікування за запропонованою нами методикою з використанням аутогенної плазми, збагаченої тромбоцитами. При вивченні ефективності лікування був застосований адаптований нами опитувальник EuroQol EQ-5D-5L.

Статистичну обробку результатів проводили з використанням t-критерію Ст'юдента. За достовірність результату приймалася різниця середніх значень при  $p < 0,05$ .

**Висновки.** Виявлено, що рецидив виразкування у основній групі досліджених був менш часто, у порівнянні з хворими групи порівняння ( $p < 0,05$ ).

У віддалений період після лікування поміж реципієнтів основної групи не було проблем з пересуванням у 34 (72,3 %) осіб, у групі порівняння – 21 (46,7 %).

Анкетовані основної групи не потребували допомоги у обслуговуванні у 44 (95,7 %) осіб, а у групі порівняння – у 35 (77,8 %). Можливість брати участь у звичайній повсякденній діяльності анкетовані основної групи мали у 33(70,2%) досліджених, а у групі порівняння – у 17 (37,8%).

Загальна якість життя та психоемоційний стан анкетованих основної групи, хворі які не піддавались депресії був у 37 (78,7%) досліджених, а у групі порівняння –у 18 (40 %) анкетованих, що менше у 1,9 разу ( $p > 0,05$ ).

**Ключові слова:** соціальна адаптація, аутогенна плазма, трофічна виразка, цукровий діабет.

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## Introduction

According to WHO and the International Diabetes Federation (IDF), the number of patients with diabetes in the world reached 425 million people in 2017. 727 billion US dollars were spent on the treatment of diabetes mellitus and its complications worldwide [1]. Despite high financial costs, the disease is usually accompanied by a substantial number of general and local complications, which lead to disability and mortality [8].

One of the local severe complications of DM is diabetic foot syndrome. 16-18% of patients with diabetes develop ulcerative defects of the lower extremities, and the treatment requires significant effort, time, and economic costs. In 28% of such patients, complications lead to various types of amputations, which affects the quality of life and social status [2]. Recently, autologous platelet-rich plasma (APRP) has been tested for the treatment of trophic ulcers. Platelets are thought to initiate wound healing by releasing local growth factors that activate reparative processes in tissues [3, 4].

One of the main directions of national medicine is the restoration of the patients' quality of life. The state of health is usually assessed not only in terms of pathological process severity but also from the point of view of the impact that the disease has on self-care, household, and social activity of patients. In order to assess the quality of life of patients, various questionnaires are used which take into account both physical and psycho-emotional indicators. One of them is the EuroQol EQ-5D-5L questionnaire, which makes it possible to assess the quality of life and medical and social adaptation of patients [5, 7].

### Relevance of the problem

The ever-increasing incidence of diabetes and the growing number of complications that accompany the disease challenge scientists and practitioners to improve the effectiveness of treatment of such complications since this cannot be achieved using traditional methods. The latter affecting the social adaptation of patients determines the relevance of the problem.

**Objective:** to evaluate the long-term outcomes after the use of autologous platelet-rich plasma in the treatment of patients with trophic ulcers secondary to type 2 diabetes mellitus and to study the peculiarities of medical and social adaptation of the patients who underwent such treatment vs. traditional methods.

### Materials and methods

The study was conducted at the Department of Vascular Surgery and Burn Department of the Sumy Regional Clinical Hospital (SRCH) in 2013–2019. One hundred five patients with neuropathic ulcers secondary to type II diabetes were studied. The inclusion criteria were limited to neuropathic trophic ulcers in the form of diabetic foot syndrome (DFS) secondary to type II diabetes mellitus. Patients were selected based on PEDIS classification. This classification included such functional and anatomical characteristics as perfusion, extent, depth, infection, sensation. The main group and the comparison group included patients with trophic foot ulcers of 5 to 10 cm<sup>2</sup> lasting for as long as four weeks and more. At the same time, the study included patients with soft tissue involvement with no affection for bones and joints.

The exclusion criteria were severe concomitant oncological diseases, decompensated coronary heart disease, lesions of the musculoskeletal system in the ulcer area, the ischemic form of the diabetic foot, chronic diseases of internal organs, and systems in the acute phase.

Study subjects were divided into two groups. The main group included 55 patients; the comparison group included 50 patients. Patients in the comparison group were treated according to the standard scheme in accordance with the recommendations of the International Working Group on the Diabetic Foot (IWGDF 2015). Treatment of patients in the main group was based on the above recommendations and corrected local treatment scheme according to our proposed method using autologous platelet-rich plasma [6]. When studying the effectiveness of treatment, we used an adapted questionnaire, which included five questions and five answers

to each of them, depending on the severity of complaints. These questions were: level of patient's mobility, peculiarities of self-care, attitude to daily activities, pain in the wound area, the presence of anxiety (depression).

Mobility was assessed using the following options: The patient has no problems walking; the patient has minor complaints – comfortable walking for up to 200 meters; the patient has moderate complaints – comfortable walking for up to 100 meters; the patient has serious problems walking; the patient is not able to walk.

Self-care causes no problems for a patient when washing and dressing independently; self-care causes minor problems when washing or dressing independently; self-care causes moderate problems when washing and dressing independently; self-care causes serious problems so that the patient can only partially take care of oneself or cannot take care of oneself at all.

The attitude to daily activities includes work, study, participation in family affairs and leisure at this level: No problems, minor problems, moderate problems, serious problems, and extremely serious problems. Given the presence of neuropathic ulcers, most patients did not experience pain; only a few of them noted hyperesthesia in the foot area. Therefore, pain syndrome was not considered as an indicator of social adaptation. The state of anxiety or depression was qualified as follows: The patient does not experience anxiety or depression; the patient experiences minor anxiety; the patient experiences moderate anxiety or depression; the patient experiences intense depression; the patient experiences extremely severe depression, inhibited thinking, constant anxiety.

In addition, according to this questionnaire, a scale was developed that characterized the general health status of patients with a score from 0 to 100. A score of 0 corresponds to the worst state of health, and 100 corresponds to the best state of health. Patients were asked to independently mark their health status on the given scale. The survey of patients in both groups was conducted in 12–15 months after discharge from the hospital. In the main group, the feedback was positive in 47 patients, and in the comparison group – in 45 patients. The obtained results are grouped and presented in Table 1.

Statistical data were processed using the Student's t-test. The difference in average values at  $p < 0.05$  was taken as statistical significance.

### Results and discussion

According to obtained responses, relapse of ulcers in patients of the main group occurred in 2 (4.2%) patients vs. 8 (17.8%) subjects in the comparison group, which is 3.4 times higher ( $p < 0.05$ ).

34 (72.3%) recipients in the main group did not have any mobility problems, and in the comparison group, 21 (46.7%) respondents had walking difficulties, which is 1.5 times worse ( $p < 0.05$ ). In the main group, there were 11 (23.4%) patients and 1 (2.1%) patient, respectively, who complained of minor problems (comfortable walking for up to 200 meters) and moderate problems (comfortable walking for up to 100 meters); among patients in the comparison group, similar answers were given by 17 (37.8%) and 3 (6.7%) subjects, respectively. 1 (2.1%) recipient in the main group had serious mobility problems, and in the comparison group, there were 3 (6.7%) individuals with similar problems. The survey in the comparison group showed extremely severe mobility problems in 1 (2.2%) recipient (almost unable to move). There were no similar consequences among the subjects of the main group.

When identifying problems with self-care, it was found that 44 (95.7%) recipients in the main group did not have any self-care difficulties. Among patients in the comparison group, this indicator was lower; namely, 35 (77.8%) individuals had no difficulties regarding self-care. Moderate problems were found only in 3 (6.4%) recipients in the main group vs. 8 (17.8%) subjects in the comparison group, which is 2.8 times higher ( $p < 0.05$ ). 1 (2.2%) patient in the comparison group had serious problems with self-care, while no such problems were identified in the main group. 1 (2.2%) person in the comparison group was not able to take care of himself. There were no similar consequences among the subjects of the main group.

The next criterion evaluated in the questionnaire was the level of typical daily activities, namely: the ability to perform minor housework, to study, to participate in family affairs and leisure. Among the patients in the main group, 33 (70.2%) of the studied

**Table 1 – Survey results demonstrating medical and social consequences in patients with trophic ulcers secondary to type 2 diabetes mellitus who underwent treatment with autologous platelet-rich plasma vs. traditional methods**

Severity of complaints	Social adaptation indicators							
	Mobility		Self-care		Normal daily activities		Anxiety (depression)	
	Main group (n 47)	Comparison group (n 45)	Main group (n 47)	Comparison group (n 45)	Main group (n 47)	Comparison group (n 45)	Main group (n 47)	Comparison group (n 45)
<b>No complaints</b>	34 (72.3%)	21 (46.7%)	44 (95.7%)	35 (77.8%)	33 (70.2%)	17 (37.8%)	37 (78.7%)	18 (40%)
<b>Minor complaints</b>	11 (23.4%)	17 (37.8%)	–	–	11 (23.4%)	17 (37.8%)	7 (14.9%)	10 (22.2%)
<b>Moderate complaints</b>	1 (2.1%)	3 (6.7%)	3 (6.4%)	8 (17.8%)	2 (4.2%)	7 (15.5%)	2 (4.2%)	12 (26.7%)
<b>Serious complaints (problems)</b>	1 (2.1%)	3 (6.7%)	–	1 (2.2%)	1 (2.1%)	3 (6.7%)	1 (2.1%)	3 (6.7%)
<b>Extremely severe pain (problems)</b>	–	1 (2.2%)	–	1(2.2%)	–	1(2.2%)	–	2 (4.4%)

individuals had no problems with the above activities vs. 17 (37.8%) individuals in the comparison group. Among the patients of the main group, there were 11 (23.4%) and 2 (4.2%) subjects complaining of minor and moderate problems with normal daily activities, respectively, vs. 17 (37.8%) and 7 (15.5%) subjects in the comparison groups, respectively. Serious problems with normal daily activities were experienced by 1 (2.1%) patient in the main group vs. 3 (6.7%) subjects in the comparison group. At the same time, among the individuals in the comparison group, 1 (2.2%) person had very serious problems with normal daily activities. There were no similar consequences among the subjects of the main group.

Another important indicator in the survey was a psycho-emotional state of patients, which included anxiety or depression. 37 (78.7%) patients in the main group did not report such complaints vs. 18 (40%) in the comparison group, which is 1.9 times less ( $p < 0.05$ ). Minor and moderate manifestations of anxiety or

depression were reported in 7 (14.9%) and 2 (4.2%) patients in the main group, respectively, vs. 10 (22.2%) and 12 (26.7%) subjects in the comparison group, respectively. There was 1 (2.1%) patient with severe symptoms of anxiety or depression in the main group, and 3 (6.7%) subjects with similar conditions in the comparison group. Extremely severe depression was observed in 2 (4.4%) recipients in the comparison group, while in the main group, there were no similar manifestations.

According to the scale that characterized the overall state of health, patients in the main group assessed the overall state of their body significantly better than patients in the comparison group. On a digital scale from 1 to 100, patients of the main group rated their health status at 82.9 points, and patients of the comparison group – at 62.4, which is 1.3 times less ( $p > 0.05$ ).

Given the above, the use of APRP in the treatment of patients with neuropathic ulcers can be considered a priority.



## Conclusions

1) Recurrence of ulceration in the main group occurred less often than in the comparison group ( $p < 0.05$ ).

2) Long-term follow-up period showed that 34 (72.3%) subjects in the main group had no mobility problems vs. 21 (46.7%) subjects in the comparison group, which is 1.5 times less ( $p < 0.05$ ). In the main group, 44 (95.7%) subjects did not require assistance in daily living activi-

ties vs. 35 (77.8%) subjects in the comparison group, which is 1.2 times less ( $p > 0.05$ ). In the main group, 33 (70.2%) subjects could participate in normal daily activities vs. 17 (37.8%) subjects in the comparison group, which is 1.9 times less ( $p < 0.05$ ).

3) 37 (78.7%) patients in the main group were not prone to depression and in the comparison group, only 18 (40%) subjects were not depression-prone, which is 1.9 times less ( $p > 0.05$ ).

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## Conflict of interest

The authors declare no conflict of interest.

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