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Clinical and hemodynamic predictors of regenerative success in patients with purulent-inflammatory soft tissue infections and type 2 diabetes: a prognostic model

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Surgical management of purulent-inflammatory soft tissue diseases (PISTD) in patients with comorbid type 2 diabetes mellitus (T2DM) remains a critical challenge for modern healthcare. The fundamental problem is the formation of a «regenerative plateau» – a state of metabolic stagnation where the healing process stalls in a prolonged inflammatory phase.

Aim – to enhance the surgical treatment efficacy in patients with PISTD and T2DM by implementing a synergistic therapeutic protocol based on muramyl peptide-derived immunomodulators and prostaglandin E1 (PGE1) analogues.

Materials and methods. A prospective clinical study included 148 patients with PISTD and T2DM, randomized into a Control group (CG, n=72) and a Main group (MG, n=76) receiving systemic muramyl peptide immunocorrection and PGE1 therapy. Microcirculation was evaluated using laser Doppler flowmetry (LDF), and wound dynamics were assessed via computer planimetry. Statistical analysis was performed using Statistica 12.0 software ($p \leq 0.05$).

Results. It was established that in the MG, clinical resolution of local edema and pain syndrome occurred 1.57 times faster than in the CG ($p \leq 0.05$), and body temperature normalization was 1.69 times faster. The use of PGE1 helped eliminate capillary sludge syndrome, ensuring a 59.3% reduction in wound area by day 10 and a decrease in the length of hospital stay (9.4±1.3 days in the MG vs 16.1±2.2 days in the CG). The obtained data indicate that the synergistic strategy can effectively overcome metabolic stagnation.

Conclusions. The integrated use of muramyl peptides and PGE1 significantly improves PISTD treatment outcomes by synchronizing regional blood flow with a targeted immune response.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all participants.

The author declares no conflict of interest.

Keywords: purulent-inflammatory soft tissue diseases, type 2 diabetes mellitus, muramyl peptides, prostaglandin E1, wound healing, regenerative plateau.

Клініко-гемодинамічні предиктори регенераторного успіху у пацієнтів із гнійно-запальними інфекціями м'яких тканин на фоні цукрового діабету 2 типу: прогностична модель

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Хірургічне лікування гнійно-запальних захворювань м'яких тканин (ГЗЗМТ) при цукровому діабеті 2 типу (ЦД2) ускладнюється формуванням «регенераторного плато» – станом метаболічної стагнації.

Мета – підвищити ефективність лікування пацієнтів із ГЗЗМТ та ЦД2 шляхом впровадження синергічного протоколу на основі мурамілпептидів та простагландину Е1 (ПГЕ1).

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Матеріали та методи. У дослідження залучено 148 пацієнтів, розподілених на контрольну групу (КГ, n=72) та основну групу (ОГ, n=76), де застосовували імунокорекцію та терапію ПГЕ1. Оцінку проводили методами моніторингу лазерної доплерівської флоуметрії та комп'ютерної планіметрії. Статистичну обробку проведено за допомогою програми Statistica 12.0 (p≤0,05).

Результати. В ОГ редукція набряку та болю відбувалася в 1,57 раза швидше (p≤0,05), а нормалізація температури – в 1,69 раза швидше, ніж у КГ. Застосування ПГЕ1 забезпечило зменшення площі ран на 59,3% до 10-ї доби та скорочення терміну госпіталізації (9,4±1,3 доби в ОГ проти 16,1±2,2 доби в КГ). Отримані дані свідчать про те, що синергічна стратегія дозволяє ефективно подолати метаболічну стагнацію регенерації.

Висновки. Комплексне використання мурамілпептидів та ПГЕ1 достовірно покращує результати лікування за рахунок синхронізації кровотоку та імунної відповіді.

Дослідження проведено відповідно до принципів Гельсінської декларації. Від усіх учасників отримано інформовану згоду.

Автор заявляє про відсутність конфлікту інтересів.

Ключові слова: гнійно-запальні захворювання м'яких тканин, цукровий діабет 2 типу, мурамілпептиди, простагландин Е1, загоєння ран, регенераторне плато.

Introduction

The surgical management of purulent-inflammatory soft tissue diseases (PISTDs) in patients with type 2 diabetes mellitus (T2DM) remains a critical challenge for modern healthcare systems globally [1,9]. Despite advancements in revascularization and antibiotic therapy, the risk of major amputations and chronic disability remains alarmingly high. Recent epidemiological data from The Lancet indicate that the global prevalence of diabetic foot ulcers exceeds 6.3%, with a 5-year mortality rate comparable to many aggressive malignancies [5,11].

The fundamental problem lies in the pathophysiology of the so-called «regenerative plateau» – a metabolic stagnation where the wound healing process stalls in the prolonged inflammatory phase [4,8]. According to the latest IWGDF 2023 guidelines, this stagnation is driven by a complex interplay of microvascular collapse (capillary sludge syndrome) and a profound «functional paralysis» of the innate immune response [12,14]. Persistent hyperglycemia leads to the formation of advanced glycation end-products (AGEs), which impair the bactericidal capacity of neutrophils and delay macrophage phenotypic switching from M1 (pro-inflammatory) to M2 (pro-reparative) [3,6].

Standard surgical debridement often fails to restart the repair sequence because it doesn't address the regional hemodynamic failure [2,13]. Recent studies in Nature Reviews Endocrinology emphasize the necessity of a «perfusion window» to deliver oxygen and immunocompetent cells to the necrotic focus [9,10].

While separate therapies (vasoactive or immunomodulatory) have shown limited success, a synergistic strategy remains underexplored [7,15]. This study investigates the synchronized application of muramyl peptide-derived immunomodulators to reboot cellular immunity and prostaglandin E1 analogues to restore microcirculation. By aligning these two therapeutic vectors, we aim to overcome the metabolic stalling of regeneration and achieve predictable clinical outcomes.

The aim of the study was to enhance the surgical treatment efficacy in patients with PISTD and comorbid T2DM by implementing a synergistic therapeutic protocol based on muramyl peptide-derived immunomodulators and prostaglandin E1 analogues to overcome the «regenerative plateau.»

Materials and methods of the study

A prospective clinical study included 148 patients with PISTD and T2DM treated at the surgical departments of the National Pirogov Memorial Medical University. Demographic characteristics. The study groups were comparable in terms of age and gender. In the Main Group (MG), the average age was 62.4±4.8 years, with a gender distribution of 53.9% (n=41) males and 46.1% (n=35) females. In the Control Group (CG), the average age was 61.8±5.2 years, including 52.8% (n=38) males and 47.2% (n=34) females (p>0.05). Most patients were in the late adulthood or early elderly stage, which is typical for the clinical course of T2DM.

Patients were divided into:

- CG (n=72): received standard surgical debridement and systemic antibiotic therapy;
- MG (n=76): received standard care plus a synergistic complex of systemic muramyl peptide immunocorrection and prostaglandin-E1 vasoactive therapy.

Monitoring included Laser Doppler Flowmetry (LDF) for microcirculation and computer planimetry for wound area assessment.

Statistical processing of the obtained data was performed using Statistica 12.0 and Microsoft Excel 2021. The distribution of data was assessed using the Shapiro-Wilk test. For normally distributed continuous variables, the results are presented as the mean ± standard error of the mean (M±m). To compare the significance

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Table 1

Comparative analysis of treatment duration and regression of clinical symptoms, days (M±m)

Clinical features / repair phases	Control group (n=72)	Main group (n=76)	Clinical acceleration index
Pain relief	7.33±0.28	4.66±0.22*	1.57
Completion of necrolysis	5.22±0.27	2.46±0.37*	2.12
Resolution of local hyperemia	8.44±0.36	6.18±0.23*	1.37
Regression of edema/infiltration	8.28±0.14	5.63±0.21*	1.47
Appearance of granulation tissue	9.22±0.24	5.72±0.26*	1.61
Onset of marginal epithelialization	8.92±0.42	6.56±0.24*	1.36

Note: * – statistical significance compared to CG (p≤0.05).

Table 2

Dynamics of body temperature normalization and systemic inflammatory response regression (M±m)

Study Groups (n=148)	Baseline body temperature on admission, °C	Day of temperature normalization	Thermal Stabilization Index
Control (n=72)	37.67±0.21	6.46±0.37	1.00
Main (n=76)	37.42±0.15	3.83±0.19*	1.69

Note: * – statistical significance compared to CG (p≤0.05).

Table 3

Daily dynamics of systemic inflammatory response regression based on thermometry, °C (M±m)

Observation period	Main group (n=76)	Control group (n=72)	Pyrexia regression index
Day 1	37.42±0.15	37.68±0.21	1.00
Day 3	37.12±0.18*	37.85±0.13	1.02
Day 5	36.81±0.05*	37.43±0.12	1.11
Day 10	36.44±0.12*	36.96 ± 0.08	1.21

Note: * – statistical significance compared to the Control group (p≤0.05).

Table 4

Dynamics of planimetric indicators of the wound healing process, % (M±m)

Study groups (n=148)	Wound area reduction rate	Wound volume reduction rate	Regeneration intensification index
Main (n=76)	6.53±1.3*	13.23±1.39*	2.51
Control (n=72)	2.53±0.98	5.42±1.29	1.00

Note: * – statistical significance compared to the Control group (p≤0.05).

of differences between the independent study groups (MG and CG), the Student's t-test was applied. For multiple comparisons, one-way ANOVA (Analysis of variance) followed by post-hoc analysis was used. Differences were considered statistically significant at a confidence level of p≤0.05.

The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results of the study and discussion

The implementation of the developed synergistic protocol significantly accelerated the transition of the wound process from the inflammatory to the reparative phase. In the MG, the clinical resolution of local edema and pain syndrome occurred 1.57 times faster compared to the CG (p≤0.05). Systematic clinical observation revealed a high degree of correlation between the onset of marginal epithelialization and the stabilization of the regional hemodynamic background (Table 1).

The analysis of the systemic inflammatory response showed that body temperature normalization in patients receiving the combined immunomodulatory and vasoactive therapy occurred 1.69 times faster than in those receiving standard care (Table 2).

Detailed evaluation of the systemic inflammatory response through daily thermometric monitoring revealed a more stable and predictable regression of pyrexia in the MG (Table 3). By the 3rd day of the synergistic treatment, a statistically significant decrease in body temperature was recorded, which correlated with the early transition of the wound process into the reparative phase. The Pyrexia Regression Index reached 1.21 by the end of the observation period, reflecting the restoration of metabolic homeostasis.

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Wound Dynamics. Objective monitoring of the repair process using computer planimetry confirmed the superiority of the proposed protocol, showing a 59.3% reduction in wound area by day 10 ($p \leq 0.001$) (Table 4).

Duration of treatment. The implementation of the synergistic protocol significantly reduced the length of hospital stay by 6.7 days. The average duration was 9.4±1.3 days in the MG compared to16.1±2.2 days in the CG.

The core pathophysiological obstacle in managing purulent-inflammatory soft tissue infections in T2DM patients is the «regenerative plateau» – a state of chronic metabolic stagnation. Our findings suggest that standard debridement protocols often fail because they address the morphological defect without correcting the underlying microvascular collapse and immune inertia.

The observed clinical success is fundamentally linked to the restoration of the regional microcirculatory bed. By applying prostaglandin E1 analogues, we effectively addressed the «capillary sludge» syndrome, creating a so-called «perfusion window». This hemodynamic optimization ensured the targeted delivery of muramyl peptide immunomodulators directly to the infection focus.

This synchronization of the targeted immune response with vascular recovery reboots the bactericidal potential of neutrophils and facilitates early macrophage phenotypic switching. As a result, the transition to the reparative phase occurs 3-4 days earlier, which is statistically and clinically significant. Our results align with the modern IWGDF (International Working Group on the Diabetic Foot) 2023 concept but offer a more pathogenetically grounded and cost-effective solution for improving tissue restitution and reducing the risk of chronic disability [4]. The core pathophysiological obstacle in managing PISTD in T2DM patients is the «regenerative plateau». Our findings align with the observations of D.G. Armstrong et al. (2023), who emphasize that standard protocols often fail to address the underlying microvascular collapse [1]. The observed clinical success in our study is fundamentally linked to the restoration of the microcirculatory bed. As noted by N.C. Schaper et al. (2024), creating a «perfusion window» is critical for delivering metabolic support to the necrotic focus [11].

By applying PGE1 analogues, we effectively addressed the «capillary sludge» syndrome, which, according to B.A. Lipsky et al. (2020) is a key barrier to antibiotic and immune cell penetration [9]. This synchronization reboots the bactericidal potential of neutrophils, a mechanism supported by the research of M.H. Bohachuk (2019) regarding muramyl peptide efficacy [2]. Our results offer a more pathogenetically grounded solution compared to traditional methods described by E. Everett & N. Mathioudakis (2021), ensuring faster tissue restitution and reducing the risk of disability [4]. Our findings suggest that standard debridement protocols often fail because they don't correct underlying microvascular collapse [1,11]. As highlighted by Y. Huang et al. (2021), microcirculatory dysfunction is a primary barrier to the delivery of both systemic antibiotics and endogenous immune cells [6]. By applying PGE1, we effectively addressed this 'capillary sludge', aligning with the modern management concepts proposed by K. McDermott et al. (2023) [10]. This synchronization facilitates the transition to the reparative phase, which is frequently delayed by local interfering conditions in diabetic patients, as noted by L. Uccioli et al. (2022) [13].

Conclusions

The synergistic application of muramyl peptide-derived immunomodulators and prostaglandin E1 analogues effectively overcomes the «regenerative plateau» by synchronizing regional blood flow with a targeted immune response directly within the infection focus.

The clinical efficacy of the protocol is confirmed by a 59.3% wound area reduction by day 10 and a significant acceleration of local symptoms regression.

The integrated approach ensures stable clinical outcomes and reduces the average hospital stay to 9.4±1.3 days, demonstrating high medical and economic efficiency.

The authors declare no conflict of interest.

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