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Synergistic effect of muramyl peptide immunocorrection and prostaglandin-based vasoactive therapy in the treatment of purulent-inflammatory soft tissue diseases

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Abstract

The treatment of purulent-inflammatory soft tissue diseases (PISTD) in type 2 diabetes mellitus (T2DM) patients remains a challenge due to the "regenerative plateau" phenomenon.

The Purpose of the Study is to improve surgical treatment efficiency in PISTD and T2DM patients by implementing a synergistic strategy based on muramyl peptide-derived immunomodulators and prostaglandin E1 analogues to restore microcirculation and activate the macrophage-neutrophil link.

Methods. A clinical study involved 148 patients (control group n=72, standard care; main group n=76, muramyl peptides + prostaglandin E1). Morphometric and immunocytochemical analyses were performed.

Results. The proposed therapy eliminated capillary sludge within 2–3 days. Myeloperoxidase (MPO) activity recovered to 72.0±6.1%. Computer planimetry showed a 59.3% wound area reduction by day 10. The average hospital stay was shortened to 9.4±1.3 days ($p \leq 0.05$). **Conclusions.** The combined approach effectively reboots tissue regeneration by synchronizing immune response and regional blood flow.

Key words: purulent-inflammatory soft tissue diseases; type 2 diabetes mellitus; immunomodulation; muramyl peptides; microcirculation; prostaglandin E1; regenerative plateau.

Background. The management of purulent-inflammatory soft tissue diseases (PISTD) in patients with type 2 diabetes mellitus (T2DM) remains one of the most formidable challenges in modern septic surgery. Despite significant advancements in antibiotic therapy and surgical debridement techniques, the global burden of diabetic foot ulcers and soft tissue infections continues to rise, with high recurrence rates exceeding 40% within the first year [1, 6]. Recent international guidelines, including the IWGDF 2023 updates, emphasize that the complexity of these infections stems from a multi-layered pathogenetic failure, where chronic hyperglycemia acts as a catalyst for both microvascular collapse and profound immune dysfunction [2, 5].

The clinical hallmark of PISTD in diabetic patients is the formation of a "regenerative plateau" - a state of metabolic and immunological stagnation where the wound bed preparation (TIME concept) fails to progress into the reparative phase despite adequate sanitation [10, 14]. Current research suggests that this "stalling" is driven by a synergistic failure of regional microcirculation, often manifesting as capillary sludge syndrome, and the "functional paralysis" of the macrophage-neutrophil link [3, 7]. The inability of immunocompetent cells to reach the necrotic focus due to impaired perfusion leads to persistent bacterial colonization and suboptimal tissue restitution [12, 15].

The Aim of the Study. To enhance the surgical treatment of soft tissue infections in type 2 diabetic patients by implementing a synergistic protocol of muramyl peptide immunocorrection and prostaglandin-based vasoactive therapy to overcome the "regenerative plateau" and restore regional microcirculation.

Materials and Methods

Study Design. A prospective clinical study was conducted at the National Pirogov Memorial Medical University. The cohort included 148 patients with PISTD and comorbid T2DM. **Groups.** Patients were randomized into: 1.**Control group (n=72):** Received standard surgical debridement and systemic antibiotics. 2. **Main group (n=76):** Received standard care plus the developed complex: systemic muramyl peptide-derived immunomodulators (2 mg intramuscularly) and prostaglandin E1 analogues (20 mcg intravenously). **Diagnostics.** Evaluation included NBT-test (nitroblue tetrazolium reduction), myeloperoxidase (MPO) activity, laser Doppler flowmetry (LDF), and computer planimetry for wound area monitoring.

Results and Discussion. Microcirculation Recovery. In the main group, the elimination of capillary sludge syndrome and stabilization of regional perfusion were recorded on days 2–3 (Table 1). This created a "perfusion window" for the delivery of immunocompetent cells to the infection site.

Table 1

Dynamics of regional microcirculation in study groups *(M±m)*

Study Groups	Center of Inflammation (Point 1)		Border of Inflammation (Point 2)		Beyond the Border (Point 3)		Symmetrical Area (Control Point)	
	Before treatment	Day 11 of	Before treatment	Day 11 of	Before treatment	Day 11 of	Before treatment	Day 11 of
Main Group	24.45± 4.371 ***	15.35± 1.488 **	14.92± 1.661	15.8± 1.001**	12.56± 1.635*	17.5± 1.722**	12.13± 1.38	17.6± I.6523**
Control Group	23.565± 5.328	12.8± 1.1046	17.5± 2.0659	13.4± 1.1442	I2.21± 2.2579*	13.0± 1.1025’	I2.57± 2.1447	13.1± 1.3124*

Note:* — $p \leq 0.05$ compared to the initial level (before treatment); ** — $p \leq 0.1$ compared to the control group at the corresponding stage of treatment; *** — $p \leq 0.001$ compared to the symmetrical control area (healthy tissue).

Immunomorphological Dynamics. A significant recovery of the bactericidal potential of neutrophils was observed. The stimulation index of the NBT-test increased

significantly. and MPO activity reached **72.0±6.1%** (Table 2) in the main group compared to persistent inertness in the control. Morphological analysis revealed that the transition from the inflammatory to the reparative phase occurred **3–4 days earlier** in the main group. Cytological imprints confirmed the active transformation of polyblasts into macrophages (**7.2±0.5%**).

Table 2

Comparative dynamics of non-specific cellular resistance indicators (M±m)

Indicators	Study Group	Normal values	observation period			
			Before surgery	Day 3	Day 7	Day 10
Phagocytic activity, %	Main	50 – 80	37,49± 0,742	46,30± 0,461*	52,22± 0,743 *	54,19± 0,574
	Control		38,35± 0,862	44,83± 0,57	44,58± 1,12	46,07± 0,668*
Phagocytic index, units	Main	5 – 9	3,89±0,244	6,17±0,34	7,75±0,33	7,67±0,36
	Control		4,05±0,191	5,58±0,29	8,08±0,36	6,58±0,34
Spontaneous NBT-test, %	Main	5 – 12	14,08±0,47	11,83±0,3	10,17±0,36	10,58±0,38
	Control		13,92±0,47	11,50±0,31	9,08±0,48	10,83±0,69
Stimulated NBT-test, %	Main	20 – 40	30,17±0,60	35,50±0,56	36,42±0,48	40,17±0,50
	Control		32,58±1,28	37,33±1,16	39,00±1,14	37,42±1,12
Stimulation index	Main	3 – 5	2,10±0,06	2,92±0,11*	3,61±0,13*	3,83±0,13
	Control		2,38±0,13	3,29±0,16	4,86±0,18	3,54±0,19*

Note: * *— statistical significance $p \leq 0.05$ compared to the initial level.*

Clinical Outcomes. Computer planimetry demonstrated a highly significant reduction in wound area. By day 10. the regression reached 59.3% (Table 3) in the main group (vs. 26.4% in the control; $p \leq 0.05$). The average rate of healing was 7.6% per day. The implementation of the synergistic protocol allowed for the reduction of the inpatient stay by 6.7 bed-days. The average duration was 9.4±1.3 days for the main group versus 16.1±2.2 days for the control ($p \leq 0.05$).

Table 3

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

Indicator / Observation stages	Admission	Day 3	Day 5	Day 7	Day 10
Wound Area (S),					
Main group (n=76)	64.8±3.2	61.4±2.2	39.7±1.9∗	31.2±0.8∗	26.4±1.8∗
Control group (n=72)	66.2±3.5	65.2±1.8	54.1±0.8	49.1±0.7	41.3±2.4
Area Reduction. %					
Main group (n=76)	-	5.2%	38.7%	51.9%*	59.3%*
Control group (n=72)	-	1.5%	18.3%	25.8%	37.6%
Healing Rate (V). %/day					
Main group (n=76)	-	2.6%	17.6%*	10.7%*	5.1%
Control group (n=72)	-	0.7%	8.5%	4.6%	5.3%

Note: —$p \leq 0.001$ statistical significance compared to the control group.*

Morphological and Histological Changes. Histological analysis of biopsy specimens from the main group on day 5 demonstrated a significant synchronization of repair processes. In patients receiving muramyl peptide immunocorrection to the analogues. the transition reparative phase was observed 3–4 days earlier. combined with prostaglandin E1.

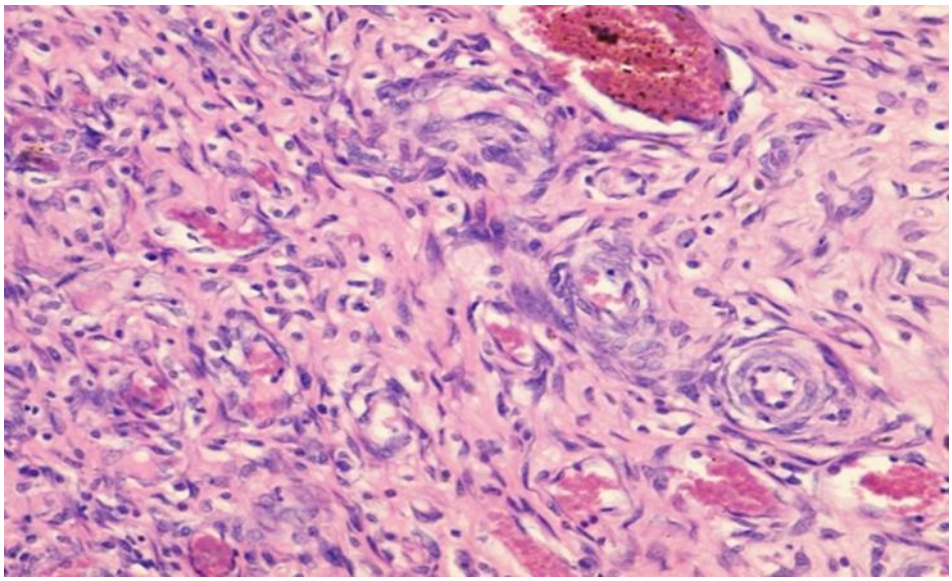

Fig. 1. Wound bed of the main group (Day 5). Active neoangiogenesis and stabilization of the microcirculatory bed. H&E stain. x200.

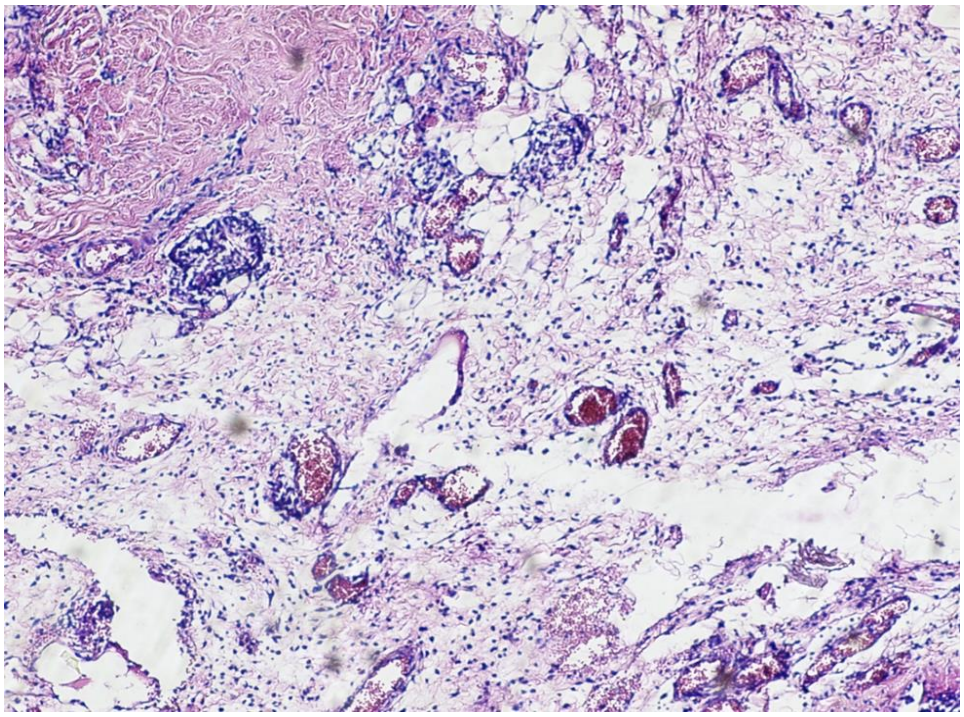

Fig. 2. Reparative phase in the main group (Day 7). Proliferation of fibroblasts and active macrophage transformation. H&E stain. x400.

Discussion. The core problem in T2DM is the premature cessation of repair. defined as the "regenerative plateau". Our study demonstrates that this is caused by microvascular dysfunction and immunometabolic paralysis. The systemic use of Alprostadil ensured the delivery of cells by stabilizing microcirculation within 2–3 days. This "perfusion window" allowed muramyl peptides to activate the bactericidal systems (MPO 72.0±6.1%). Unlike the control. the main group showed an active transition to the reparative phase. achieving a 59.3% wound area reduction and shortening hospital stay to 9.4±1.3 days.

Conclusions. The present study demonstrates that the conventional surgical approach to purulent-inflammatory soft tissue diseases in patients with type 2 diabetes often fails due to a profound synchronization deficit between the microcirculatory bed and the innate immune response. Our findings align with global clinical trends [1. 2. 5]. confirming that chronic hyperglycemia creates a persistent "regenerative plateau" characterized by capillary sludge syndrome and phagocytic inertia.

The clinical and morphofunctional data obtained in this research provide a pathogenetic basis for a shifting paradigm in diabetic wound management: from passive wound bed preparation to active. targeted synchronization of tissue repair. By integrating muramyl peptide-derived immunomodulators with prostaglandin E1 analogues. we achieved a

"perfusion window" that effectively reboots the structural restitution of tissues. The synergy of these pharmacological agents not only addresses the local necrotic focus but also mitigates the systemic immunometabolic stalling of regeneration.

1. The clinical course of purulent-inflammatory soft tissue diseases in patients with type 2 diabetes mellitus is characterized by the formation of a "regenerative plateau". driven by a dual pathogenetic mechanism: systemic microangiopathy (capillary sludge syndrome) and functional paralysis of the macrophage-neutrophil link. evidenced by reduced myeloperoxidase activity and a deficit of small CD4+ lymphocytes.

2. The synergistic application of muramyl peptide-derived immunomodulators and prostaglandin E1 analogues effectively reboots the reparative process by synchronizing immune response and regional blood flow. The elimination of capillary sludge within the first 2–3 days creates a crucial "perfusion window." enabling the targeted delivery of immunocompetent cells to the necrotic focus and restoring their bactericidal potential (recovery of *MPO* activity to 72.0±6.1%).

3. Morphological and cytological analysis confirms that the proposed therapeutic strategy accelerates neoangiogenesis and fibroblast proliferation. ensuring the transition from the inflammatory to the reparative phase 3–4 days earlier than with standard surgical protocols.

4. The practical implementation of this combined approach provides significant clinical and economic benefits. achieving a 59.3% reduction in wound area by the 10th day of treatment and shortening the average inpatient stay by 6.7 days (to a total of 9.4±1.3 days).

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