UDC 617.55-089.843-092:616.8-009.7-085.851
DOI https://doi.org/10.32782/2226-2008-2025-5-8

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APPLICATION OF PERINEURAL ADMINISTRATION OF FIBROBLASTS AND PRP IN TOURNIQUET SYNDROME: A SURGEON'S PERSPECTIVE

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Introduction. Tourniquet syndrome causes compression-ischemic neuropathy and remains a significant challenge in combat-related limb injuries. Regenerative therapies using platelet-rich plasma (PRP) and fibroblasts may enhance neural recovery through trophic, angiogenic, and anti-inflammatory mechanisms.

Objective. To evaluate the clinical efficacy of perineural administration of PRP and autologous dermal fibroblasts in patients with tourniquet-induced neuropathy.

Materials and methods. A prospective study was conducted at the Military Medical Clinical Center of the Southern Region (Odesa, 2023–2024). Thirty-two patients with lower-limb injuries complicated by tourniquet application were examined. Group I (n = 17) received multimodal pharmacotherapy plus perineural PRP injections (3 sessions of 4 mL under ultrasound guidance) followed two weeks later by autologous fibroblast transplantation (30 million cells). Group II (n = 15) received pharmacotherapy only. Outcomes included pain intensity (VAS), motor and sensory function recovery, hospital stay duration, and complications.

Results. Group I demonstrated significantly faster reduction of neuropathic pain (VAS decreased from 8.9 to 3.6 at one month vs. 9.1 to 4.9 in controls, $p < 0.05$), earlier return of active distal motor function (10–14 days vs. > 4 weeks), and quicker recovery of tactile and pain sensitivity (7–10 days vs. approximately 4 weeks). Length of hospital stay was reduced by 10–17 days (35.8 ± 4.2 vs. 57.3 ± 5.1 days). Analgesic demand decreased by 50% after 2 weeks and by 75% at one month. No infectious complications occurred; local pain and transient edema were the most common mild adverse effects. No amputations were required.

Conclusions. Perineural PRP and fibroblast therapy accelerates functional recovery, decreases analgesic load, and shortens rehabilitation period in tourniquet neuropathy. The approach appears safe and feasible in military hospital practice but requires multicenter randomized trials to standardize dosing, timing, and protocols.

Keywords: military surgery, limb vasculature, tourniquet syndrome, regenerative medicine, rehabilitation.

УДК 617.55-089.843-092:616.8-009.7-085.851

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ЗАСТОСУВАННЯ ПЕРИНЕВРАЛЬНОГО ВВЕДЕННЯ ФІБРОБЛАСТІВ І PRP ПРИ ТУРНІКЕТНОМУ СИНДРОМІ: ПОГЛЯД ХІРУРГА

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У статті представлено клінічне дослідження ефективності периневрального введення збагаченої тромбоцитами плазми (PRP) та фібробластів у лікуванні компресійно-ішемічної нейропатії, спричиненої тривалим накладанням турнікета. PRP-терапія, яка використовує аутологічний концентрат тромбоцитів, показала здатність активізувати регенеративні процеси, зменшувати запалення та стимулювати ангіогенез і ремієлінізацію. Отримані результати засвідчили значно швидше зниження больового синдрому, поліпшення моторної функції, відновлення чутливості та скорочення тривалості перебування в стаціонарі у пацієнтів першої групи. Також спостерігалося зменшення потреби в анальгетиках.

Автори підкреслюють необхідність подальших багатоцентрових досліджень для стандартизації протоколів застосування PRP у нейрореабілітації.

Ключові слова: військова хірургія, судини кінцівок, турнікетний синдром, регенеративна медицина, реабілітація.

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Стаття поширюється на умовах ліцензії

Introduction

Platelet-rich plasma (PRP) therapy is based on the use of an autologous patient-derived material – a concentrate of platelets rich in growth factors (PDGF, TGF-β, VEGF, etc.) that promote activation of tissue regeneration processes [1, 2]. In the context of neuropathy arising after prolonged compression of the neurovascular bundle by a tourniquet (particularly under extreme combat conditions) [3], PRP may stimulate the recovery of intra- and extraneural structures [1, 4]. Growth factors released by platelets enhance angiogenesis and myelination and activate macrophage-mediated clearance of damaged areas, thereby creating a favorable environment for axonal regrowth [4, 5].

Moreover, mechanical administration of PRP directly into the perineural zone provides a local concentration of regenerative signals and reduces local inflammation [5]. Experimental models of peripheral nerve injury demonstrate accelerated regeneration of damaged nerves and increased nerve conduction velocity compared with controls [6, 7]. It is also important to note that PRP therapy is highly compatible with other neurorehabilitation methods. The synergistic effect of a combined approach contributes to improved motor reinnervation and reduced neuropathic pain [8, 9].

In addition, current regenerative medicine protocols increasingly use combined therapy with autologous mesenchymal stromal/stem cells (MSCs) derived from bone marrow, adipose tissue, or peripheral blood. MSCs are capable of modulating immune responses, secreting numerous biologically active factors (including exosomes), stimulating endogenous tissue regeneration, and supporting anti-apoptotic processes within the injury zone [1–3].

Combination therapy with PRP + MSC enhances the efficiency of structural repair, prolongs the regenerative stimulus due to the sustained paracrine effect of MSCs, potentiates angiogenesis and neuroprotection, and reduces fibrotic changes. Such therapeutic strategies are being investigated in the context of treatment for neurodegenerative diseases (including ALS within clinical protocols), muscle atrophy, contractures, chronic pain, recovery after complex limb trauma, and in orthopedic and sports medicine [1, 2]. In neuropathy caused by prolonged (> 1.5 hours) tourniquet-induced compression of the neurovascular bundle (especially in combat settings) [3], PRP may stimulate recovery of intra- and extraneural structures [1, 4, 10]. Importantly, both PRP and MSC therapy integrate well with other neurorehabilitation modalities, with a synergistic effect contributing to improved motor reinnervation and reduction of neuropathic pain [11–14].

Aim of the study is to assess the effectiveness of fibroblast and PRP administration in patients with compression-ischemic neuropathy caused by prolonged tourniquet application to a limb (over 1.5 hours).

Materials and Methods

The study was conducted at the Military Medical Center of the Southern Region in 2023–2024. A total of 32 patients were examined. Group I consisted of 17 patients who, in addition to analgesic medications (pregabalin, carbamazepine, quetiapine, clomipramine, amitriptyline), received perineural PRP injections under ultrasound guidance three times every two days, each injection consisting of 4 mL of concentrate over the course of one week, followed by perineural administration of fibroblast culture obtained from autologous skin (dose: 30 million) two weeks later. All injections were administered at the sites where tourniquets had been applied and under visual control.

Group II consisted of 15 patients who received only pharmacological therapy. The presence of neuropathy was confirmed clinically.

The mean age of the examined patients was 34.6 ± 1.2 years. The study included patients with lower-limb injuries: lower-leg injuries (64.7% in Group I and 60.0% in Group II), foot injuries (35.3% in Group I and 40.0% in Group II). In Group I, major vascular injury was present in 52.9%; in Group II, in 53.3% of the wounded (tibial vessels were ligated; popliteal artery injuries were reconstructed with an autovenous graft in 2 wounded patients in Group I and 1 patient in Group II). The average number of tourniquets applied was 1.4 ± 0.6 in both groups. Tourniquet application sites: upper third of the thigh – 23.5% in Group I and 20% in Group II; middle third of the thigh – 58.8% in Group I and 60.0% in Group II; lower third of the thigh – 17.6% in Group I and 20.0% in Group II. The duration of tourniquet application to the limb also did not differ: in Group I, the tourniquet remained on the limb for 1.5–2.5 hours in 9 (52.9%) patients; in Group II – in 8 (53.3%) patients; all other patients had a duration over 2.5 hours. All patients underwent staged surgical wound management as needed.

The main manifestations of tourniquet syndrome were: tissue edema (100.0%), sensory disturbances – pain (100.0%), numbness (93.7%), paresthesia (87.5%), tingling (78.1%), muscle weakness or paresis (71.9%), muscle rigidity and tenderness on palpation (56.2%), signs of reperfusion syndrome (46.9%) – weakness, tachycardia, acidosis, darkened urine. Fasciotomy was performed in 13 (76.4%) patients of Group I and 10 (66.7%) of Group II ($\chi^2 = 0.38$, $p > 0.05$).

Preparation of PRP and fibroblast cultures was performed according to standard protocols [14]. Perineural administration was carried out under ultrasonographic guidance. In ultrasound imaging of the sciatic nerve *(n. ischiadicus)* in areas designated for perineural injection, the nerve appears as an oval or triangular hyperechoic structure with a homogeneous internal granular pattern characteristic of fascicular organization, surrounded by a thin hypoechoic epineurium. In the transverse view, it appears as a "honeycomb-like" structure, whereas in the longitudinal view it presents as parallel echogenic lines corresponding to fascicles and connective-tissue septa. In the subgluteal region, the nerve is located beneath the gluteus maximus muscle, between the *m. gluteus maximus* and *m. quadratus femoris*, lateral to the ischial tuberosity and medial to the greater trochanter. In the mid-thigh, it is visualized beneath the *m. biceps femoris* and above the surface of the *m. adductor magnus* as a hyperechoic cord 5–7 mm in diameter, without intraneural blood flow on Doppler imaging, which allows clear differentiation from adjacent vascular structures.

During perineural injections, the needle is introduced in-plane with the ultrasound beam via a lateral or medial approach, with the needle tip positioned 1–2 mm from the epineurium. After the introduction of a small amount of fluid, uniform spread of the solution around the nerve is observed as a hypoechoic halo gradually separating the nerve from surrounding tissues. This pattern indicates correct perineural placement of the solution and confirms the absence of intraneural injection. The injection volume depends on the purpose of the procedure: 5–10 mL is typically used for diagnostic blocks, and up to 20 mL for complete sensory or therapeutic blocks.

After injection, displacement of the nerve is observed without deformation of its fascicular pattern, which is a safety criterion for the procedure. In contrast, intraneural injection is characterized by localized increased echogenicity and disruption of the fascicular structure, requiring immediate cessation of the procedure. Successful blockade is indicated by visualization of complete circumferential filling of the space around the nerve, whereas lack of uniform surrounding spread indicates inadequate needle positioning.

Ultrasound guidance for perineural administration of pharmacological agents in the sciatic nerve region enables precise identification of anatomical variability, determination of nerve depth, and avoidance of injury to adjacent vessels. This is particularly important when applying neuroprotective therapy, PRP, or regenerative injections in the treatment of neuropathies, neuropathic pain, or compression syndromes. Ultrasound guidance provides a high level of positioning accuracy (95–98%), reduces the risk of intraneural injury, and enables control of the actual volume and direction of active agent distribution.

The study was conducted in compliance with current bioethical standards [15]. All patients provided informed consent to participate. The study protocol was approved by the Local Ethics Committee of the Center for Reconstructive and Regenerative Medicine on 10 September 2023. Statistical analysis was performed using partial analysis methods with the χ^2 test [16].

Research results and their discussion

The mean duration of treatment in Group I was 35.8 ± 4.2 days, whereas in Group II it was 57.3 ± 5.1 days ($p < 0.05$).

Acute kidney injury that developed in 4 patients of Group I and 3 patients of Group II against the background of rhabdomyolysis was resolved in both groups after 3–5 dialysis sessions.

The intensity of pain syndrome in Group I was lower than in Group II (Table 1), with the greatest difference observed at later follow-up points.

The need for analgesic medication in patients of Group I was significantly lower. After 2 weeks, the doses were reduced by half, and after one month – by 75%, while in Group II the reduction in the need for neuropathic pain medications was minimal.

Perineural administration of fibroblasts and platelet-rich plasma (PRP) in compression-ischemic neuropathy caused by prolonged tourniquet application has several important advantages compared with traditional treatments. First, pain in the affected area decreases much faster – noticeable relief of neuropathic pain is observed within 5–7 days, whereas in standard therapy improvement occurs at 2–3 weeks. Muscle strength recovery was also faster: active movements in distal segments appeared at approximately 10–14 days, whereas with the conventional approach this required more than 4 weeks. Sensory recovery – including tactile and pain sensitivity – occurred on average within 7–10 days during PRP therapy, which is a substantially better outcome compared to the typical 4-week partial recovery under standard treatment. Static-dynamic functions (balance, coordination, weight-bearing) also improved earlier – usually by week 2–3, compared with week 4–6 under medication-only therapy. Due to this accelerated recovery, patients receiving bioactive therapy stayed in the hospital 10–17 days less on average compared with patients who did not receive bioactive treatment.

Among complications occurring during treatment with fibroblasts and PRP, the most common were local pain and discomfort at the injection site (82.4% of patients), which resolved within 30 minutes; tissue swelling and hyperemia (23.5% of patients); and shooting pain or paresthesia (11.8% of patients) in the nerve's innervation zone during the first 1–2 days after the procedure. No infectious complications were observed, which we attribute to strict adherence to aseptic protocols. In 2 patients, technical difficulties occurred due to soft-tissue damage in the injection area. In all cases, limb amputation was avoided.

Conclusions

Perineural administration of PRP and fibroblasts significantly reduces neuropathic pain manifestations in patients with tourniquet-induced neuropathy and decreases medication load by 25–75%.

It shortens treatment and rehabilitation duration by more than 10–14 days, reduces hospital stay, lowers the risk of disability, and facilitates faster return of wounded personnel to active duty.

The therapy is safe, well tolerated, and can be combined with other treatment methods, making it suitable for use in hospital settings and at the outpatient rehabilitation stage.

Despite encouraging preclinical results and early clinical case series, widespread implementation of PRP and MSC-based therapy for neuropathies caused by tourniquets

Table 1

Pain intensity in clinical groups (VAS, points)

Group	Baseline	After 7 days	After 14 days	After one month
Group I (n = 17)	8.9 ± 0.2	6.5 ± 0.3	5.1 ± 0.2	3.6 ± 0.2
Group II (n = 15)	9.1 ± 0.3	6.9 ± 0.4	5.8 ± 0.3*	4.9 ± 0.4*

Note. * – differences between groups are statistically significant.

or other injuries requires randomized multicenter studies to determine optimal concentrations of active components, injection frequency, and timing in both acute and chronic phases of injury. This will allow the development of standardized protocols ensuring maximal benefit for patients within comprehensive neurorehabilitation.

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Надійшла до редакція 14.09.2025
Прийнята до друку 02.12.2025
Електронна адреса для листування samarskiyigor2702@gmail.com