



PLATELET-RICH PLASMA (PRP) FOR THE TREATMENT OF PROBLEMATIC SKIN WOUNDS

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ABSTRACT

OBJECTIVE: To show platelet-rich plasma (PRP) application of problematic skin wounds and to evaluate the results from the treatment.

MATERIAL AND METHODS: A total of 31 patients with problematic skin wounds had been treated at the clinic for a period of five years (from May 2010 to September 2015) with the following patient sex ratio: male patients– 13 and female patients– 18. Average age– 46,5 (22-82). Patients with Type 2 Diabetes– 10, with decubitus ulcers– 2, traumatic– 29, with infection– 12, acute– 15, chronic– 16. Based on a scheme developed by us, all cases were treated by administering platelet-rich plasma, derived by PRGF Endoret system. Follow-up period was within 4 – 6 months (4,5 on average). We used platelet rich plasma derived by PRGF Endoret system, applied on the wound bed on a weekly basis.

RESULTS: The results have been evaluated based on the following functional scoring systems - Total wound score, Total anatomic score and Total score (20). The baseline values at the very beginning of the follow-up period were as follows: Total wound score – 10 p.; Total anatomic score – 8 p., Total score – 15 p. By the end of the treatment period the score was 0 p., which means excellent results, i.e. complete healing of the wounds.

CONCLUSION: We believe that the application of PRP may become optimal therapy in the treatment of difficult to heal wounds around joints, bone, subject tendons, plantar surface of the foot, etc., as it opens new perspectives in the field of human tissue regeneration.

Keywords: problematic skin wounds, platelet rich plasma, functional scoring scales

Since ancient times skin wounds treatment included a number of locally applied remedies. Contemporary treatment procedures on the other hand involve a variety of recovery approaches: conservative (non-operative) and operative methods, which result in different application modes. Several etiological factors are associated to the development of this condition, such as: chronic venous disease, peripheral arterial disease, neuropathy, arterial hypertension, physical trauma, hematologic disorders, skin infection, inflammatory diseases, neoplasia, nutritional and iatrogenic alterations [1]. Due to population aging and the

increase of risk factors for atherosclerosis, such as smoking, obesity and diabetes, there is a clear trend to the increase of these values [2].

Skin wounds that do not heal in at least 6 weeks and were caused by high energy trauma are called *problematic skin wounds*. Therapeutic treatment of such wounds is significantly challenging in the following cases: prominence of bones, ligaments or metal, in patients with another underlying disease or when reconstructive surgery is impossible. Major types of problematic skin wounds are *acute*, *hard-to-heal* and *chronic wounds*. Acute wounds heal in a particular biological sequence that could be slowed down by the presence of skin defects, patient's old age and underlying diseases. Skin wounds which do not recover in a 4-week standard method treatment for the particular pathology are called *hard-to-heal wounds*. The wounds that cannot heal for more than three months on the other hand are the so called *chronic skin wounds* [2].

Wound healing occurs during a fixed sequence of complex biological processes – hemostasis, inflammation, granulation tissue formation, epithelialization, neovascularization, collagen synthesis, and wound contraction. It involves a sequence of events that begin at the moment of injury and continue for several subsequent months and can be divided into three stages: inflammation, proliferation and remodeling [3, 4]. A number of clinical studies demonstrate insufficiency of growth factors in chronic wounds that could be explained with the reduction of their production and release, sequestration, prominent degradation or a combination of these mechanisms [5]. Analysis of chronic wounds tissue material shows that growth factor production is significantly reduced in comparison to acute wounds. The bacterial or cellular protease present in the wound leads to fast metabolism of growth factors [6]. This fact has contributed to the improvement of contemporary treatment approaches with the application of additional biological stimulation of wound defect. This new treatment concept involves the application of platelet-rich plasma into the wound because it carries the most important growth factors for tissue recovery and thus becomes a valuable alternative to complex surgical methods [7]. The term PRP can be defined as the volume fraction of blood plasma, which has an increased concentration of platelets, from a baseline serum level. PRP is mainly a platelet concentrate in plasma, in which white blood cells

and other blood components also are present in minor proportions [8]. The mechanism of action for PRP gel is thought to be the molecular and cellular induction of normal wound healing response similar to that seen with platelet activation [2, 9]. PRP accelerate all phases of wound healing (most prominent in angiogenesis) [2, 9].

MATERIAL AND METHODS:

A total of 31 patients with problematic skin wounds had been treated at the clinic for a period of five years (from May 2010 to September 2015) with the following patient sex ratio: male patients– 13 and female patients– 18. Average age– 46,5 (22-82). Patients with Type 2 Diabetes– 10, with decubitus ulcers– 2, traumatic– 29, with infection– 12, acute– 15, chronic– 16. The distribution of the patients is shown in Table 1 and Table 2 respectively. All cases were treated in a procedure developed by us, which includes

platelet rich plasma obtained by PRGF Endoret system. The treatment algorithm we used is as follows: first there is surgical treatment and debridement of the wound. The first PRP application is on the second postoperative day. It is derived as follows: the necessary amount of blood is drawn in blood collection tubes containing sodium citrate. Tubes are centrifuged with speed of 1800 rev./min. for 8 minutes. Using pipettes the plasma is drawn off and 10% CaCl₂ activator is added to it at a ratio of 1 ml. plasma to 50 microliters of activator. The resulting mixture is active in 5 min. Fibrin clot is formed after approximately 40 minutes. Activated plasma is used to infiltrate the wound edges and the fibrin clot is used to fill the wound itself. A sterile dressing soaked with physiological saline is applied. The procedure is repeated on a weekly basis until the wound problem is resolved in full. No antibiotic treatment is administered to those patients.

Table 1. Distribution of the patients with acute wounds, according to the specified data

sex	m	m	m	m	m	m	m	m	m	f	f	f	f	f	f	f
open fracture	+	+												+		
operative wound with dehiscence					+	+	+			+	+	+	+		+	
traumatic arthrotomy			+													
conquassation				+					+							+
type 2 diabetes	+				+					+				+		
size cm ²	30	6	18	25	10	12	10	8	6	3	7	8	10	12	18	
depth	I	I	II	I	III	IV	V	III	II	III	I	II	I	III	II	
anatomical region	1	1	4	5	7	7	8	9	2	3	7	7	4	7	6	
infection	*		*			*		*		x			x			

Legend: Depth of the wound - I bone, II tendon, III muscle, IV fascia, V fat (subcutaneous tissue) Anatomical region - 1 ankle, 2 Achilles, 3 Tendon, 4 med. malleolus, 4 front. surface of the ankle, 5 foot, 6-calcaneus, 7 lateral. malleolus, 8 calf , 9 patella; Infection - S.aureus - *, E. Coli – x

Table 2. Distribution of the patients with chronic wounds, according to the specified data

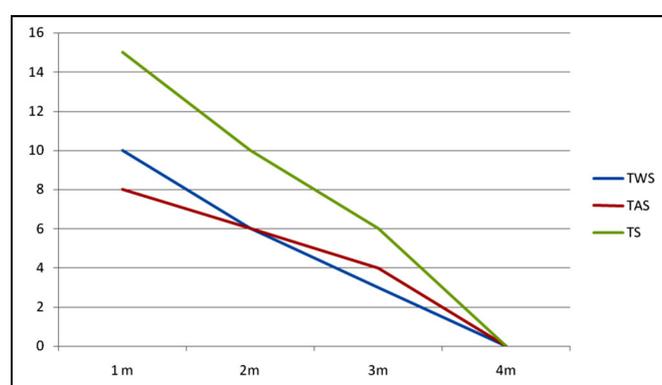
sex	m	m	m	m	m	f	f	f	f	f	f	f	f	f	f	f
decubitus wound						+	+									
traumaticwound			+	+						+	+		+			
type 2 diabetes		+				+	+	+	+			+				
operative wound with skin necrosis without metal osteosynthesis		+			+				+			+		+	+	
operative wound whit skin necrosis with metal osteosynthesis	+							+								+
size cm ²	5	8	4	5	4	8	7	6	12	4	5	16	6	4	10	12
depth	I	II	I	III	I	IV	III	I	V	I	III	IV	IV	IV	I	II
anatomical region	6	2	6	5	7	2	5	6	7	8	5	7	9	7	7	7
infection		*		*			*		x			*				x
M. Parkinson							+									
paraplegy			+													

Legend: Table 2-Depth of the wound - I bone, II tendon, III muscle, IV fascia, V fat (subcutaneous tissue) Anatomical region - 1 ankle, 2 Achilles, 3 Tendon, 4 med. malleolus, 4 front. surface of the ankle, 5 foot, 6-calcaneus, 7 lateral. malleolus, 8 calf , 9 patella; Infection - S.aureus - *, E. Coli – x, MO- metal osteosynthesis

RESULTS:

Follow-up period was 4-6 months (average 4.5). The results were evaluated using the following functional scoring systems, offered by Cancela et al. - Total wound score, Total anatomic score and Total score [2]. Baseline of monitored our wounds, according to these evaluation systems were: Total wound score – 10 p., Total anatomic score – 8 p. and Total score – 15 p. At the end of the treatment period, the items were respectively - 0 p., which means excellent results, i.e., complete healing of the wounds in all of our patients, regardless of the type of the treated wound. (Fig. 1) The differences are only in the number of PRP applications, i.e., duration of treatment, the average term for skin and tissue recovery was 3 months.

Fig. 1. The change in the number of points according to the criteria for wound-healing.



DISCUSSION:

The most important conclusion from this study is that the use of the PRP in treating problematic skin wounds resulted in complete healing of all cases, regardless of the etiology of the wound or the accompanying diseases of the patient. Chronic skin wounds are relatively common and sometimes continuous treatment is required because of the loss of growth factors necessary for the healing process. Chronic skin wounds can also develop complications from a super infection [10]. The standard therapy consisting of bandages, wound debridement and also skin plastic, cannot provide proper healing because it does not produce enough growth factors to support the healing process [11]. Diabetes and its complications are the third main cause of death in the USA and about 60 % of all non-traumatic amputations are performed in diabetics. The complication of diabetic foot is the most common reason for hospital admission of diabetic patients, frequently evolving to amputation. Amputation is a high cost procedure, besides the social and emotional

components, leading young patients in a productive age to disability. Amputation of the lower extremity costs an average of US\$40,000 per wound. It has been demonstrated that the longer a wound is present, the greater chance it has to result in an amputation [2, 5, 12]. In a retrospective group study of neuropathic ulcers in diabetic feet Margolis and others reported a more pronounced efficacy with better effects in more severe wounds as a result of the use of PRP than the standard use of treatment methods [13]. In a study reported by El-Sharkawy et al. it was found that PRP made visible changes in monocyte-mediated release of proinflammatory cytokines / chemokines and is observed to increase the level of lipoxin A4 - limiting the inflammation process and the development of infection [14]. Very interesting data reported in an article by Bielecki et al. shows inhibited growth of *S. aureus* caused by PRP and its activity against *Escherichia coli* [4]. Anitua et al. examined 14 patients in an open and randomized study to evaluate the effect of PRP in chronic ulcers. They report better effect in healing in 80% of cases after 8 weeks of treatment, while in the control group healing was observed in 20%. Lack of leukocytes is reported in tested products and according to the authors this is due to the high concentration of growth factors [5].

In our study we review the implementation of PRP in patients with acute and chronic skin wounds (types of problematic skin wounds). We can conclude that out of 31 patients treated with PRP, the acute cases healed faster, with fewer applications (6-8) and a median time to full wound-healing of two months. In the chronic wounds' treatment a larger number of applications (10-16) were applied and healing took longer than 4 months. In our series of patients we did not find any side effects and complications probably due to the autologous qualities of PRP. A particular advantage of PRP is its application as an added biological material into a wound which accelerates the phases of wound healing and leads to an impressively high rate of complete healing - 100% in all our patients. This method may be applied in ambulatory care and is an alternative to a large number of complex, expensive and not always successful therapeutic surgical procedures.

CONCLUSION

We believe that the application of PRP has its place in the treatment of problematic skin wounds because it improves and accelerates wound healing. Furthermore, PRP is used in regenerative medicine because it provides growth factors and scaffolds. PRP also has antimicrobial properties that can help prevent infection [15].

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