



## CLINICAL RESULTS FROM THE TREATMENT OF CHRONIC SKIN WOUNDS WITH PLATELET RICH PLASMA (PRP).

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### ABSTRACT

**PURPOSE:** To show platelet rich plasma (PRP) application of chronic skin wounds and to evaluate the results from the treatment.

**MATERIAL AND METHODS:** A total of 14 patients with problematic skin wounds had been treated at the clinic for a period of five years (from May 2009 to December 2014) with the following patient sex ratio: male patients - 5 and female patients - 9. Average age - 48,5 (30-76). Patients with Type 2 Diabetes - 4, with decubitus ulcers - 6, traumatic - 8, with infection - 5. 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).

**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 - 12 p.; Total anatomic score - 10 p., Total score - 17 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:** chronic skin wounds, functional scoring systems, platelet rich plasma,

### INTRODUCTION

Skin ulcers are defined by the loss of tissue that includes the epidermis and the dermis, at times affecting the adipose tissue and the muscle fascia. There is not spontaneous recovery and the tissue lesion many times results in a fibrous scar [1]. Skin ulceration is a clinical problem, with an incidence of 0.78 %. The financial cost of treatment of such wounds is enormous [2]. 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. 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 [1].

The healing process is dynamic and involves complex events that include 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]. Several experimental clinical studies have demonstrated the reduction of growth factors of chronic wounds. Platelet aggregation has the leading role in the process of skin healing since it is responsible for releasing growth factors, adhesion molecules and lipids, which regulate migration, proliferation and function of keratinocytes, fibroblasts and endothelial cells [4, 5].

The analysis of supernatant of chronic wounds compared to acute wounds revealed a considerable decrease of the growth factors in the former, observing a quick metabolization of the growth factors due to proteases found in the wound, of bacterial or cellular source. On the other hand, in diabetic ulcers and due to venous insufficiency, the decrease of the growth factors occurs due to a mechanism of sequestrum by fibrin around the capillaries [6]. Therefore, biological stimulation of the wound with platelet rich plasma (PRP) (which drives the most important factors for skin and tissue repair) has been recently introduced as a possible alternative to complex surgical methods.

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 [7]. A concentration of 1,407,640 cells/ $\mu$ l (with a standard deviation of 320,100) has been suggested as ideal for the definition of PRP [8]. This number corresponds to a platelet count about 4-5 times higher than that contained in the blood, it usually ranges from 150,000 for the 350.000/ $\mu$ l (approximately an average value around 200.000/ $\mu$ l) [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].

**MATERIALS AND METHODS**

For a period of five years (May 2009 to December 2014) in the clinic were treated 14 patients with chronic skin wounds divided by sex as follows: 5 men and 9 women. Average age was 48.5 years (30-76). 4 patients were with type 2 diabetes, 6 with decubitus, 8 with traumatic, 5 with infection. The distribution of the patients is shown in Table 1. All cases were treated in a procedure developed by us, which includes platelet rich plasma obtained by PRGF Endoret system.

**Table 1.** 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
decubitus wound						+	+							
atrophic wound			+								+		+	
diabetes		+				+	+	+	+			+		
bite wound										+				
Skin necrosis without metal osteosynthesis		+			+				+			+	+	+
Skin necrosis with metal osteosynthesis	+							+						
puncture wound				+										
size cm <sup>2</sup>	5	8	4	5	4	8	7	6	12	4	5	16	6	4
depth	I	II	I	III	I	IV	III	I	V	I	III	IV	IV	IV
anatomical region	6	2	6	5	7	2	5	6	7	8	5	7	9	7
infection		*		*			*		x			*		
M. Parkinson							+							
paraplegia			+											

**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, MO - metal osteosynthesis.

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 3,8% sodium citrate. Tubes are centrifuged with speed of 1800 rev./min. for 8 minutes. Using pipettes the plasma is drawn off and 10% CaCl<sub>2</sub> 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. Sterile dressing 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.

**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 [10]. Baseline

of monitored our wounds, according to these evaluation systems were: Total wound score - 12 p., Total anatomic score - 10 p. and Total score - 17 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. The differences are only in the number of PRP applications, i.e., duration of treatment, the average term for skin and tissue recovery was 5 months. One patient had a complication - hyperkeratosis.

**DISCUSSION**

A wound is considered chronic when it does not heal after a period of three months [2]. Chronic cutaneous wounds are a frequent problem and are often difficult to heal because they lack the growth factors necessary for the healing process, and are frequently complicated by superinfection [11]. Conventional therapies such as dressings, surgical debridement, and even skin graft cannot provide satisfactory healing since these treatments are not able to provide enough necessary growth factors to modulate

the healing process [11]. Patients with chronic ulcers frequently have to undergo long-term dressing regimens and repetitive debridement without a definitive outcome. Some commercial recombinant growth factor products, like becaplermin, but its time-release delivery is a significant problem because it is liquid and quickly disappears once it has been applied to the wound. Additionally, the product is expensive and most patients cannot afford such high cost [11].

Liu H et al. found that PRP makes significant changes in monocyte-mediated release of proinflammatory cytokines/chemokines and increases the level of lipoxin A 4, thus limiting inflammation and infection [12]. Bielecki et al reported that PRP gel inhibits the growth of *S. aureus* and is active against *Escherichia coli* [13]. Anitua et al. developed an open, randomized pilot study with controlled assistance standard in order to evaluate the effects of rich plasma in growth factors when treating chronic ulcers in 14 patients. The detection of high concentration of platelets and release of growth factors demonstrated an average healing superficial area of 80 % of the treated group, against 20 % of the superficial healing observed in the control group, after eight weeks [14, 15].

Crovetti et al. followed the evolution of chronic skin wounds of 24 patients with autologous or homologous

platelet gel (PG), depending on the case, having observed complete healing of nine patients after an average of 10 applications and a decrease of pain in all cases [1].

The review of our material of 14 patients found that in chronic wounds were applied on average between 12 and 20 applications and was recorded average period of 5 months of healing. In our series of patients not seen any side effects and complications, which is most likely due to the fact that PRP is autologous substance. In its application to a biological material is added in wounds is accelerated phase of wound healing, leading to extraordinary high rate of complete healing - 100% in our contingent of patients.

## CONCLUSIONS

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. PRP not only stimulates the wound, but also possess antimicrobial properties, which may contribute to the prevention of infections. This method can be performed ambulatory and is an alternative to the plurality of complex, expensive and not always successful therapeutic medical procedures.

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### Acknowledgments:

No institutional finding or grants as well as technical assistance or contributions of this research has been obtained by the author.

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*Please cite this article as:* Kosev P, Sokolov T. Clinical results from the treatment of chronic skin wounds with platelet rich plasma (PRP). *J of IMAB.* 2015 Apr-Jun;21(2):797-800. DOI: <http://dx.doi.org/10.5272/jimab.2015212.797>

Received: 07/04/2015; Published online: 26/06/2015



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