The use of autologous PRP gel as an aid in the management of acute trauma wounds

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SUMMARY

Autologous platelet-rich plasma (PRP) gel is increasingly used in the treatment of a variety of soft and bony tissue defects, such as accelerating bone formation and in the management of chronic non-healing wounds. We performed this study to assess the benefits of using autologous PRP gel in the treatment of acute limb soft tissue wounds. 59 patients with acute wounds (open fractures, closed fractures with skin necrosis and friction burns) were randomised into two groups. Group A (32 patients) were treated with conventional dressings and Group B (27 patients) were managed with local application of PRP gel. Gustillo grade IIIb or IIIc open fractures were not included in this study, as these injuries required coverage with flap. The clinical endpoints were the healing rate and/or the time required to bring about adequate tissue regeneration in order to undergo reconstructive plastic surgery. The rate of wound healing rate was significantly faster in Group B at week 1, 2 and 3 ($p = 0.003$, $p < 0.001$ and $p < 0.001$, respectively). The mean time to plastic reconstruction in Group B was 21.26 days, S.D. = 1.35 vs 40.6 days in Group A, S.D. = 5.27 ($p < 0.001$). This study has shown that PRP gel treatment can be a valuable and effective aid in the management of acute trauma wounds.

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Introduction

Autologous platelet-rich plasma (PRP) gel is increasingly used in almost all fields of surgery for the treatment of a variety of soft and hard tissue defects, most notably in accelerating bone formation and in the management of chronic non-healing wounds.[2,14,16,17,28] Over the past 2 decades, extensive cellular and molecular details have been elucidated regarding the regulation of cutaneous wound healing.[18] It is now clear that no single exogenous agent can effectively mediate all aspects of a wound healing response. Platelets (PLT)[4] are a rich source of the complex group of growth factors essential to natural wound healing.

Degranulation of platelets by proteins such as thrombin causes them to release these factors. Platelet granules contain a variety of physiologically active substances, such as catecholamines, serotonin, adenosine triphosphate (ATP), albumin, fibrinogen, osteonectin, osteocalcin, calcium ions, various clotting factors and locally active growth factors, such as platelet-derived growth factor (PDGF), transforming growth factor-α (TGF-α), transforming growth factor-β (TGF-β), insulin-like growth factor (IGF), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF) and epidermal growth factor (EGF).[1,3,26,27] The extraction of platelet concentrates through plasmapheresis is a process by which platelet-rich plasma (PRP) is taken from the patient, at a concentration of 300% of normal blood levels.[22]

In this study we used autologous PRP gel to treat soft tissue acute wounds. Our aim was to assess if treating acute wounds with PRP gel would significantly enhance (1) the healing rate and (2) the time required to achieve adequate tissue regeneration in order to undergo reconstructive plastic surgery.

Materials and methods

Preparation of platelet-rich plasma gel

There is a variety of systems for extraction and preparation of PRP gel. In our unit we use the PRP Fast system (Bioteck). This system consists of disposable PRP Fast tubes that were used together with a bench-top centrifuge. The appropriate amount of patient's blood and ACD-A (anticoagulant citrate dextrose solution) injected into the PRP Fast disposable units and centrifuged for 20 min at 3200 rpm. Following centrifugation, the blood sample is separated in different blood fractions. After further separation, the extracted PRP is collected in a syringe. For sufficient clot formation, the PRP is used with autologous thrombin solution at a ratio 10:1.[15]

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Table 1
Description of the type of wounds in both groups

Type of the wounds	Group A (no. of patients)	Group B (no. of patients)
Open fracture of the tibia	21	16
Close fracture of the tibia with skin necrosis	5	4
Wide friction burns in the femur	6	5
Acute injury of the Achilles tendon	0	1
Open bimalleolar fracture	0	1

Table 2
The mean time required to bring about adequate tissue regeneration in order to undergo reconstructive plastic surgery

	Group B	Group A	p
Mean (days ± S.D.)	21.26 ± 1.35	40.6 ± 5.27	<0.001

p-Values below 0.05 were considered significant.

Patient groups

Following appropriate approval by the local ethics committee 59 consecutive patients with acute traumatic wounds were recruited for the study. The types of wounds are summarised in Table 1. Patients with Gustilo grade IIIb or IIIc open fractures were not included in this study, as these injuries required coverage with a flap. Using computer-generated random numbers the patients were randomised into two groups (control Group A and PRP Group B). The clinical endpoint was the time required to bring about adequate tissue regeneration in order to undergo reconstructive plastic surgery.

The control Group A included 32 patients with acute trauma wounds which were treated with conventional methods. Conventional treatment consisted of topical washing and cleaning of the wounds, removal of the necrotic tissues as appropriate, and dressing with Vaseline gauze every 2 days. There were 20 men with a mean age of 38 years (range 19–52) and 12 women with a mean age of 31 years (range 22–49). 21 patients had an open tibial fracture. Ten patients had type II and eleven had type IIIa fracture, according to Gustillo classification.[8] Five patients had high energy closed tibial fractures with extensive skin necrosis on the anterolateral aspect of the tibia (Table 1). In all patients with open tibial fractures after surgical debridement of the wounds, an external fixation system was applied. All patients underwent antibiotic therapy as required.

The PRP Group B included 27 patients with acute trauma wounds which were treated with local application of PRP gel. We had 14 men with a mean age of 36 years (range 20–56) and 13 women with a mean age of 32 years (range 23–47). 16 patients had open tibial fracture. According to Gustilo classification,[8] nine patients had a type II and the rest had a type IIIa fracture. Four patients had high energy closed fractures of the tibia with accompanying extensive skin necrosis at the anterolateral aspect of the tibia. Five patients had wide friction burns in the femur with skin necrosis, one patient had a skin defect and a split of the paratendon after acute injury in the area of the Achilles tendon, and one patient had an open bimalleolar fracture (Table 1). The patients with open fractures of the tibia were treated with an external fixation system, after appropriate surgical debridement. 48–72 h later, following exclusion of infection, the first PRP gel was applied at the wound. The patient with the open bimalleolar fracture was treated with a plate-screws internal fixation system and the first PRP gel was then applied to the wound. In the remaining patients, the PRP gel was applied immediately after the surgical debridement of the wounds. All the patients were then treated as outpatients and the PRP gel was applied once weekly in a small aseptic room in the outpatient clinic. Before the placement of PRP, the wounds were washed and cleaned, and after the placement of PRP the wounds were covered with gauze sponges. No anaesthesia was required for the application of PRP. All patients underwent antibiotic therapy as required.

Measurements

The day of the first surgical therapeutic procedure in Group A patients and the day of the first application of PRP in Group B patients were defined as day 0. Thereafter, measurement of the wound's surface and estimation of the pain were performed every 7 days. The pain was measured with the visual analogue scale (VAS scale).[21] We decided to use the VAS because it is easy to use, provides reproducible results, is applicable to a variety of practice settings and it is also sensitive to treatment effects.[25]

The quotient initial surface (cm^2)/surface at the end of every week (cm^2) was used to define a constant variable, in order to estimate the healing rate. The quotient represents a modification of the surface area, measured in cm^2 and named MS_{number}, where number is the time-point. For example, MS_1 was defined the modified surface at the end of the first week and MS_2 the modified surface at the end of the second week. This way, the surfaces of the wounds among the patients were comparable.
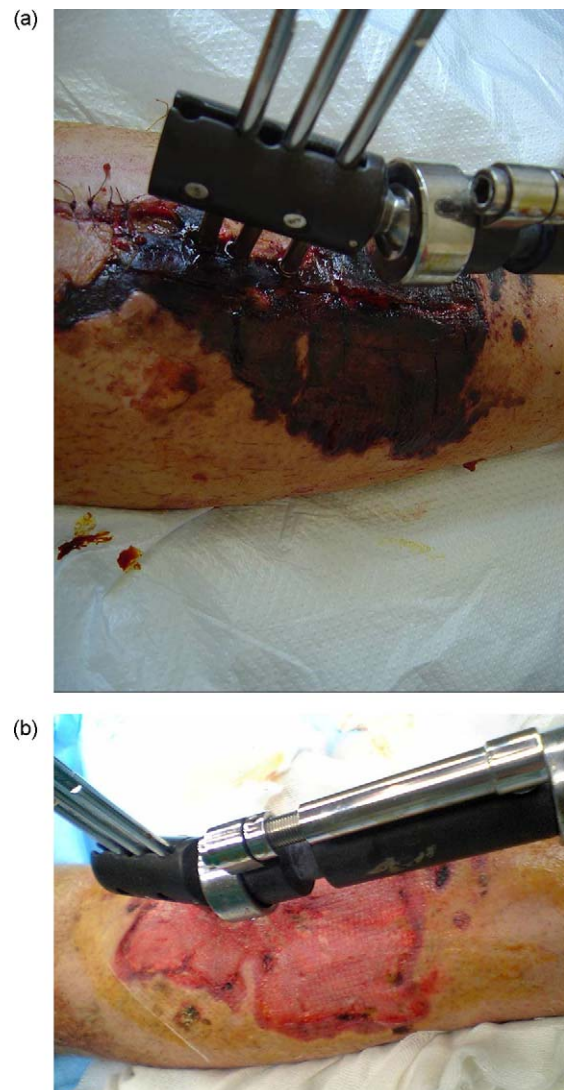

Figure 1. (a) A 38 years old male patient with a fracture of the right tibia and extensive skin necrosis (b) Healing process after 2 applications of PRP.

The mean time needed for the preparation and application of the PRP gel, the duration of hospitalisation, the healing of the fractures, and the side effects of the PRP were also recorded.

Statistics

The sample size to perform this prospective randomised clinical trial, was determined using the software Epi Info6, Version 3.3.2. The statistical program STATISTICA for Windows 5.0 (StatSoft, Inc., Tulsa, USA) and specifically the non-parametric Mann–Whitney U test was used to analyse data. Statistical significance was defined at $p < 0.05$.

Results

The mean duration of follow up was 6 months (range 2.5–21 months). The mean time needed for the preparation and the application of the PRP gel was 52 min (range 42–62 min). All the fractures united except one patient with an open IIIa fracture of tibia who developed non-union, due to inadequate stabilisation of the fracture. The external fixation device was replaced with an intramedullary nail and the fracture united. Neither local or systemic side effects nor signs of infection were recorded.

In Group B, the time required to bring about adequate tissue regeneration in order to undergo reconstructive plastic surgery

Figure 2. (a) A 32 years old female patient with an open bimalleolar fracture, treated with plate and screws internal fixation system (b) Healing process after 2 applications of PRP (c) Final result after plastic reconstruction.

Table 3
The modified surface at the end of the first (MS$_1$), the second (MS$_2$) and the third (MS$_3$) week

MS	Group B	Group A	p
Mean MS$_1$ (cm^2 ± S.D.)	1.14 ± 0.07	1.09 ± 0.04	0.003
Mean MS$_2$ (cm^2 ± S.D.)	1.32 ± 0.13	1.19 ± 0.05	<0.001
Mean MS$_3$ (cm^2 ± S.D.)	1.57 ± 0.18	1.30 ± 0.07	<0.001

p-Values below 0.05 were considered significant.

Table 4
Pain estimation at the various time-points

Time-point	Group B	Group A	p
Day 0 (mean ± S.D.)	85.19 ± 14.21	82.66 ± 16.57	0.532
Day 7 (mean ± S.D.)	78.26 ± 14.21	79.31 ± 16.54	0.787
Day 14 (mean ± S.D.)	66.3 ± 18.67	80.94 ± 16.47	0.002
Day 21 (mean ± S.D.)	57.59 ± 17.73	79.81 ± 17.21	<0.001

p-Values below 0.05 were considered significant.

Figure 3. The healing rate of the wounds during the 3-week treatment period in Group B and Group A patients.

was in all patients 3 weeks, except one patient who needed 4 weeks (mean 21.26 days). After this period of time, patients underwent plastic surgery (Figs. 1a and b and 2a–c). The patient with the injury in the area of the Achilles tendon had excellent outcome with complete coverage of the tendon, so she did not need any plastic reconstruction. In Group A patients, the mean time required to bring about adequate tissue regeneration was 40.59 days. In patients treated with PRP gel, the time required to have surgery was significantly shorter ($p < 0.001$) (Table 2). Split skin grafts were used in all plastic procedures.

At the end of the first week, the mean MS$_1$ of Group B patients was 1.14 and the mean MS$_1$ of Group A patients was 1.09. There was a significant difference between the two groups ($p = 0.003$) (Table 4). Significant differences were also recorded at the end of the second and at the end of the third week ($p < 0.001$) (Table 3). The mean MS$_2$ for Group B was 1.32 and for Group A was 1.19. The mean MS$_3$ for Group B and Group A patients was 1.57 and 1.30, respectively (Table 3).

There was no significant difference between Group B and Group A in the pain scores reported at day 0 and at the end of the first week, but Group A had significantly higher pain scores at the end of the second and at the end of the third week (Table 4).

Discussion

Platelet concentrates function as a tissue sealant and a drug-delivery system that contains a host of powerful mitogenic and chemotactic growth factors. Haemostasis is achieved through the formation of a fibrin clot that is initiated by the activation and aggregation of platelets. Beyond maintaining haemostasis, the fibrin clot then provides a matrix for the migration of tissue-forming cells and endothelial cells involved in angiogenesis and the remodelling of the clot into repair tissue. Several in vitro and in vivo models show that all kinds of cells involved in tissue regeneration are sensitive to Growth Factors. Fibroblasts are strongly reactive to bFGF, PDGFa and PDGFb, IGF and EGF.[12] Endothelial cells are sensitive to bFGF and VEGF.[20] Human mesenchymal cells, which are recruitable during tissue regeneration process, are up-regulated by PDGFs as well.[13] Angiogenesis is particularly stimulated by VEGF, PDGF and bFGF.[6] Angioneogenesis is also helped by pericytes, which are in turn dependent on PDGF and VEGF availability.[11] Chondrocytes, osteoblasts and periosteal cell growth is up-regulated by platelet-derived factors such as PDGF and bFGF.[7,10,19]

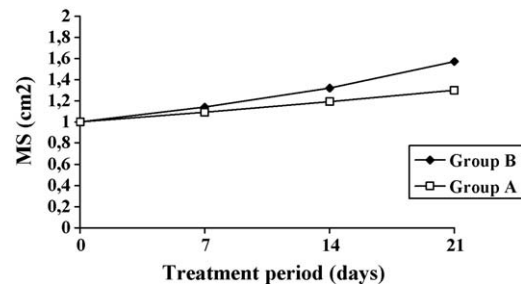PRP gel has been described to be effective in combined soft and bony tissue reconstruction in facial plastic surgery as well in oral and maxillofacial surgery.[2,16,28] On the other hand, several authors reported the effectiveness of PRP gel in the treatment of non-healing chronic wounds,[5,9,14,17,23,24] but to the best of our knowledge there are no previous studies looking at the use of PRP in acute wounds.

In this study we have demonstrated the benefits of topical PRP gel in the management of acute soft tissue wounds. We have shown that patients treated with PRP gel achieved faster healing rates and adequate tissue regeneration in order to undergo plastic reconstruction in nearly half the time. A rapidly healing rate increase was recorded in Group B patients during the 3-weeks treatment period (Fig. 3). The area needed coverage by the use of split skin grafts was reduced to the 35.65% (range 23–49%) of the initial measurement of the wound in the period of 21.26 days. Neither adverse reactions nor signs of infection were observed when treating patients with PRP gel, probably due to the autologous origin of PRP. In addition, Group B patients reported less pain than Group A patients.

Conclusions

This study showed that the PRP gel is very useful for the treatment not only of chronic or non-healing wounds, but also can be very effective even in acute trauma wounds. This system may be of particular relevance in hospitals which do not have an on-site team of plastic surgeons and patients are treated exclusively under the care of orthopaedic surgeons. PRP provides a less costly alternative to other previously described augmentation techniques and also presents a patient-friendly and operator-safe alternative. These results encourage the further clinical study of the method to achieve earlier wound healing in acute injuries.

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