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The effects of platelet rich plasma on healing of full thickness burns in swine

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ABSTRACT

Introduction: Platelet rich plasma (PRP) is rich in growth factors and has been shown to improve healing in a variety of wounds. We determined the effects of PRP on healing and scarring in full thickness porcine burns with and without tangential excision and grafting (TEG).

Methods: Standardized full thickness 5 cm by 5 cm burns were created on each of the backs and flanks of 10 anesthetized female pigs (25 kg) using a validated model. The burns were created with a heating device that emits heat at a temperature of 400 °C for a period of 30 s. The burns were randomized to one of six treatments: no TEG or PRP, no TEG+PRP, early (day 2) TEG and no PRP, early TEG+PRP, late (day 14) TEG and no PRP, and late TEG+PRP. Tangential excision was performed down to viable tissue and autografts were 0.2 mm thick. When used, a thin layer of autologous PRP was applied below the graft. All wounds were then treated with a topical antibiotic ointment 3 times weekly for 42 days. Digital images and full thickness biopsies were taken at 9, 11, 14, 18, 21, 28, 35 and 42 days after injury to determine percentage reepithelialization, scar depth, and scar contraction. Tissue sections were stained with H&E and viewed by a dermatopathologist masked to treatment assignment.

Results: There was no reduction in platelet and white blood cell concentrations in PRP and blood samples for the first 14 days after-full thickness burns. A total of 120 burns were created on 10 animals evenly distributed between the six treatment groups. Burns undergoing early TEG reepithelialized fastest and with the thinnest scars followed by late TEG. Burns that did not undergo TEG had the slowest reepithelialization and greatest amount of scarring. Application of PRP had no additional effects on reepithelialization, scar depth, or scar contraction in any of the treatment groups.

Conclusions: Addition of PRP had similar effects on reepithelialization and scarring of full thickness porcine burns as standard topical antibiotic ointment regardless of whether the burns underwent excision or grafting or the timing of excision and grafting.

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1. Introduction

Platelet-rich plasma (PRP) is the plasma fraction of autologous blood in which the platelet concentration is considerably higher than in whole blood due to processing and concentration [1]. Activated platelets release key wound healing factors including platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), and epidermal growth factor [1,2]. By delivering supra-physiological concentrations of a variety of growth factors and cytokines these preparations are used to enhance wound healing in bone and soft tissue injuries. Unfortunately, studies regarding the potential benefits of PRP in both animals and humans with burns are contradictory and inconclusive [3–11].

While superficial burns generally heal within 2 weeks with minimal if any scarring, deeper burns generally take greater than 3 weeks to heal and result in significant scarring unless excised and grafted with a split thickness autologous skin graft [12–14]. As a result, excision and grafting of full thickness burns has become the standard of care.

The goals of the current study were twofold. First, to compare the healing of full thickness burns treated with or without autologous PRP in a swine model. Second, to determine whether addition of PRP to early and delayed excision and grafting of full thickness burns improves healing and reduces scarring in a porcine model.

2. Methods

2.1. Study design

We performed a prospective, randomized animal experiment. The study was approved by the Institutional Animal Care and Use Committee and was conducted in the institutional division of laboratory and animal research in accordance with national guidelines [15].

2.2. Animals

In this study we used 10 female domestic pigs weighing approximately 20–25 kg. Pigs were chosen for this in vivo experiment because it has been demonstrated that of all animals, pig skin most closely resembles that of the human [16]. Animals were given a standard diet ad lib several days prior to the investigation and were fasted overnight before any procedures.

2.3. Experimental protocol

2.3.1. Animal preparation and sedation

We used a previously validated porcine model of full thickness burns that were tangentially excised and grafted with a split thickness autologous skin graft [17]. Animals were sedated with a combination of acepromazine 0.1 mg/kg, atropine 0.02 mg/kg, ketamine 20 mg/kg, and xylazine 2 mg/kg by intramuscular injection. The pigs were then intubated endotracheally and maintained under a surgical plane of anesthesia with isoflurane 1–3% in O_2 USP. The hair on the backs and flanks of each pig was clipped.

2.3.2. Burn creation

While under general anesthesia, twelve 5 cm by 5 cm burns were created on each pig's back and flanks using a specialized radiant heating device. The burns were spaced at least 2 cm from each other. We used a heating coil heated to 400° C, which emits infra-red/visible light radiation that heats the skin surface. The burn infliction device was placed in direct contact with the animal's skin for a period of 30 s thus creating full thickness burns on the back and flanks of the animal. In each of the ten animals we created three rows of four burns each (Fig. 1).

2.3.3. Treatment allocation

The burns were then randomized to one of the following six treatment groups, equally distributed between the animals, using a computerized random number allocator:

1. A negative control group that did not receive any excision and grafting or PRP.
2. A control group that was treated with topical PRP two days after burn injury with no additional excision and grafting.
3. A treatment group that was excised and grafted two days (early) after burn injury without PRP.
4. A treatment group that was excised and grafted two days (early) after burn injury with PRP applied topically beneath the graft.
5. A treatment group that was excised and grafted 14 days (late) after burn injury without PRP.
6. A treatment group that was excised and grafted 14 days (late) after injury with PRP applied topically beneath the graft.

Each animal had an equal number of each treatment group randomly assigned to the different anatomical locations (i.e., 12 burns, 6 treatment groups, 2 of each treatment group per pig). The allocation of treatment groups to various anatomical locations (i.e., cranial or caudal) was balanced to account for any anatomical variation in healing.

2.3.4. Preparation of autologous PRP

Immediately prior to the application of PRP to the burn wounds, anticoagulated whole blood was drawn from the pigs' ear veins in three 60 ml sterile syringes, with each 60 ml blood comprising of 52 ml whole blood and 8 ml anticoagulant citrate dextrose formula A (ACD-A; Arteriocyte Medical Systems, Hopkinton, MA). Thus, PRP was prepared freshly, from blood collected immidiately prior to the application. The blood was then processed by a commercially available device (Magellan®, Arteriocyte, Hopkinton, MA) for 15 min to yield 7 ml of PRP from each 60 ml batch. The PRP was mixed with a combination of Ca+/thrombin in a ratio of 10:1 forming a gel in sterile 5 cm by 5 cm molds and transferred to the wounds using a sterile spatula. Approximately 1.5 ml of PRP+ calcified thrombin was applied to cover each wound.

Hematology analysis was performed for each whole blood and PRP sample prepared at each designated time point to quantify the concentrations of platelets and white blood cells.

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