Platelet Rich Fibrin Matrix for Improvement of Deep Nasolabial Folds

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ABSTRACT

Objective: To evaluate the efficacy of a single injection of platelet rich fibrin matrix for the correction of deep nasolabial folds.

Methods: Whole blood was obtained from subjects, and a proprietary system (Sepragen®, Cascade Medical Enterprises, Inc., Wayne, NJ) was used to produce an activated autologous platelet rich fibrin matrix (PRFM). PRFM was injected subdermally or intradermally below the nasolabial folds. Subjects were photographed before and immediately after treatment; nasolabial folds were rated by the treating physician before and after treatment using the Wrinkle Assessment Scale (WAS). Patients were then seen at 1, 2, 6 and 12 weeks after treatment, and WAS scores were assigned to the nasolabial folds and photographs taken.

Results: All patients were treated to full correction, with a mean reduction in WAS score of 2.40. At 1 week after treatment, this difference decreased to 1.10, but rose to 1.55, 1.45 and 1.75 at 2, 6, and 12 weeks after treatment, respectively. No patient noted any fibrosis, irregularity, hardness, restricted movement or lumpiness.

Conclusions: PRFM can provide significant long-term diminution of deep nasolabial folds without the use of foreign materials. PRFM holds significant potential for autologous dermal augmentation.

RESULTS

All subjects completed the study. All subjects noted mild bruising which resolved completely within a week of treatment. Results were analyzed by depth of injection (subdermal vs. intradermal), but no significant differences were noted and the results were then analyzed noted complete PRFM immediately after treatment, but slightly less than optimal results thereafter. The least improvement was noted at the one week visit, although still improved compared to prior treatment. Compared to before treatment, subjects on average had a 2.40 point improvement in WAS scores immediately after treatment (p<0.001), which decreased to 1.10 points at the 1 week visit (p<0.001). The improvement gradually increased through the 12 week visit, at which time there was no statistically significant difference compared to the improvement noted immediately after treatment.

DISCUSSION

Platelet alpha granules contain a number of growth factors which are released upon platelet activation. These GFs are released in specific ratios which vary over time. Most autologous platelet gel systems commercially available today deliver low concentrations of fibrinogen but high concentrations of platelets, which are activated with exogenous thrombin and calcium; this generally leads to an immediate, massive and unsustained release of GFs. Some prior studies have shown early but transient histologic and clinical effects associated with such systems, while others have failed to demonstrate any substantial improvement. However, a more comprehensive and sustained effect may require a more physiologic stimulus.

Platelets in a natural setting will release GFs upon activation in specific concentrations and ratios and continue to synthesize and secrete these factors for up to a week. We believe an amplification of the natural wound response mediated by concentrated platelets and their growth factors may produce the most efficacious method of focused autologous collagen expansion when injected into and below the dermis. We investigated the use of a simple, FDA-approved device to produce a platelet rich fibrin matrix to stimulate dermal cells in vivo. The PRFM stays in suspension for approximately 10 minutes after activation, during which time it can be injected easily through a 30 gauge needle. The polymerization of fibrin begins slowly, but accelerates at the higher temperature of the body once injected. 

Azzarelli et al. and Cervelli and Gentile reported on a single case of a depressed scar and 22 cases of Romberg-Parry disease, respectively, treated with autologous fat mixed with PRFM. PRFM is produced by a proprietary method using a thixotropic gel to produce a fibrinogen and platelet rich plasma by low speed centrifugation. These platelet have been show to be highly viable (55% at 7 days after harvesting) and show sustained release of PDGF-BB, VEGF-A and TGF-β over 4.5 million non-surgical procedures were performed in the U.S. in 2008 for skin rejuvenation. While neurotoxins and energy based skin treatments are commonly used to improve minor rhytids, volume deficiency in areas of deeper folds, such as the nasolabial folds, typically is treated with injectable or implantable dermal fillers. Disadvantages typically include the need for incisions to place synthetic implants, transient effects of temporary, resorbable fillers and foreign body reactions such as encapsulation, granuloma formation and chronic or delayed infections, in the case of injectable permanent fillers. While some injectable soft tissue fillers currently available (e.g., poly-L-lactic acid) rely on a host tissue fibrotic response to produce volume enhancement, they still rely on synthetic, non-biologic implantable materials. An autologous source for promotion of soft tissue deposition in areas of depletion is desirable.

Human growth factors have been extensively investigated, and there are now clinical applications of individual growth factors: keratinocyte growth factor (Kepivance®; Biovittum AB, Stockholm, Sweden) for oral mucositis and platelet derived growth factor (Regranex®; Sygen/Loss Management, Inc., London, England) for the treatment of pressure sores. In vitro studies have shown increased endothelial cell proliferation. A third generation of platelet rich products has been developed which has shown to enhance early healing, in both animal and human models, in a transient way. We have utilized a novel system which produces an autologous, platelet rich fibrin matrix (PRFM), which delivers a more sustained and physiologic platelet growth factor response to augment deep nasolabial folds (NLFs) in humans. We believe this approach can provide a safe and effective correction of deep NLFs and may be applicable in other areas of the face.

METHODS AND MATERIALS

Five healthy adult subjects with moderate to severe NLFs were enrolled in the study. Approximately 16 cc of blood was collected via standard venipuncture using a 21 gauge butterfly needle and 2 proprietary collection tubes (Fibrinet, Cascade Medical Enterprises, Wayne, NJ) containing a thixotropic separator gel. The tubes were then centrifuged at 1100 PRF for 6 minutes, after which the platelets were resuspended in the supranatant fibrin rich plasma, and then transferred to a second tube containing a solution of calcium chloride. This activated suspension was then injected intradermally or subdermally below the NLFs through 30 and 27 gauge needles, respectively, within 10 minutes of activation. All NLFs were treated to full correction. The subjects and the treating physician completed assessments (before and immediately after treatment, and at each follow up visit), which included a rating of the NLF severity using the Wrinkle Assessment Score (WAS). Follow up visits were scheduled at 1, 2, 6 and 12 weeks after treatment. Digital photographs were obtained before and immediately after treatment and at each follow up visit.

CONCLUSIONS

Single treatment with PRFM can produce a moderate correction of deep nasolabial folds, without development of excessive fibrosis or the use of a foreign substance. Unlike other dermal stimulators (e.g., poly-L-lactic acid), PRFM produces its effect rapidly. We are currently expanding our clinical trials, treating more subjects in both dermal and subdermal planes as needed. Further study is needed to clarify the specific biological and clinical effects of PRFM.