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Research Article

The Comparison of Platelet-Rich Plasma Versus Injectable Platelet Rich Fibrin in Facial Skin Rejuvenation

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Background/Objective. Platelet-rich plasma (PRP) has a widespread use in various indications including dermatological conditions. Injectable platelet-rich fibrin on the other hand is prepared without anticoagulants and seems to have a sustained action. This study aimed to compare PRP and PRF injection treatments for facial skin rejuvenation in terms of efficacy, patient satisfaction, and side effects. *Patients and Methods*. Patients who received facial intradermal injections of PRP or PRF for skin rejuvenation were included in this study. Patients received three injections one month apart and evaluated at follow-up visits for cosmetic results using a high-resolution UVA-light video camera and a surface evaluation software at three regions (frontal, nasolabial, and canthal) as well as for patient satisfaction and side effects. *Results*. A significant marginal superiority of PRF over PRP was only evident for some canthal cosmetic parameters (canthal smoothness and wrinkles); however, the two groups did not differ in terms of other cosmetic regional parameters. For canthal smoothness, the difference was significant at three months. The two groups did not differ in terms of side effects, pain, and patient satisfaction. *Conclusion*. This study obtained slightly better outcomes with PRF injections when compared to PRP for facial rejuvenation only at canthal region and only at three months, which disappeared later during the treatment. PRF may represent a viable alternative to PRP for that indication owing to its easier preparation, absence of anticoagulants, and possibly its sustained effect. Further large studies are warranted.

1. Introduction

Skin aging is a natural process affected by environmental factors (for example, sun exposure, smoking, air pollution, alcohol consumption, and nutritional problems), as well as genetic factors; and it results in cosmetic alterations with negative impacts on self-image and social acceptance [1]. Such an impact should be particularly prominent for facial skin, one of the most recognizable parts of the body. Periorbital area is prone to changes such as hyperpigmentation, skin laxity, and development of wrinkles.

Facial skin rejuvenation aims to reverse aging process to restore younger cosmetic appearance, either with surgical or nonsurgical cosmetic procedures, latter being more demanded recently [1]. Among nonsurgical approaches, injection of platelet-rich plasma (PRP), a platelet concentrate obtained from autologous plasma, has recently gained popularity for facial skin rejuvenation, as well as for other dermatological conditions [1–5]. PRP contains a wide range of proteins/growth factors including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor beta (TGFβ); thus, has the potential to rejuvenate the skin through improvement of angiogenesis, tissue remodeling, stem cell stimulation, cellular proliferation/regeneration, and hyaluronic acid production [3].

Several studies mention the use of anticoagulants and rapid release of growth factors as potential/theoretical drawbacks of PRP [6–8]; however, disadvantages of these properties have not been evaluated directly in terms of

efficacy or safety. Such potential concerns led to the development of second-generation platelet concentrates where blood was drawn without anticoagulant and centrifuged immediately [9]. The second-generation platelet-rich fibrin (PRF) has platelets and leukocytes entrapped in the fibrin clot; and growth factors are released slowly over a sustained period [10]. In addition, PRF does not require activation. Lower overall platelet count on the other hand may be considered a potential drawback of PRF. Injectable PRF prepared with slow speed centrifugation is a very recent concept [11]. There are only few studies on the use of PRF in facial skin rejuvenation or related indications [6, 12–15], and no study, so far, has compared PRF and PRP in a dermatological setting.

This study aimed to compare PRP and PRF injection treatments for facial skin rejuvenation in terms of efficacy (cosmetic results as assessed by a quantitative system evaluating skin topography), patient satisfaction, and side effects.

2. Patients and Methods

2.1. Patients. Adult subjects who were admitted to our clinic for facial skin rejuvenation due to cosmetic reasons who received facial intradermal injections were included in this prospective cohort study. Patients were allocated into the following two groups based on patients' preferences after informing each patient on each of the two study treatments: PRP or PRF group. The study protocol was approved by the local ethics committee, and the study was conducted in accordance with the Declaration of Helsinki. All subjects provided informed consent prior to study entry.

2.2. Interventions

2.2.1. Preparation of PRP and PRF for Injection. Depending on the study group, PRP or PRF was prepared for injection using the whole blood of each patient. Eight milliliters of venous blood were drawn from antecubital vein into two self-vacuum T-LAB PRP tubes or two self-vacuum T-LAB PRX tubes for the preparation of platelet-rich plasma (PRP) or platelet-rich fibrin (PRF), respectively. T-LAB kits for PRP and PRF has Class IIb and Class IIa certificate, respectively. T-LAB PRP tubes has anticoagulant sodium citrate at 3.8% concentration, but T-LAB PRX tubes do not have any anticoagulant. Both samples were centrifuged for 2 minutes with T-LAB M415P centrifugation device at 2000 rpm. Approximately 4 to 5 ml supernatant was obtained in total and withdrawn to an injector.

2.2.2. Injections. A topical local anesthetic cream with 2.5% lidocaine and 2.5% prilocaine (EMLA Cream, AstraZeneca LP, Wilmington DE) was applied over the injection sites one hour before the procedures. Injections were done in sitting position on three facial regions (frontal, canthal nasolabial) bilaterally. For each region on either side (right or left), symmetric total injections of 0.5 ml PRP or PRF was done intradermally using a 27–30 gauge needle. Again, for each region, 0.5 ml solution was divided into five equal parts and injected at five different points within the region (each 0.1 ml). To prevent clotting, particularly to prevent the rapid clotting of PRF, all injections were made immediately after preparation. When clotting occurred, a fresh material was prepared again. This application was done at baseline and repeated at 1 month and 2 months.

2.3. Assessments. At baseline and follow-up visits (at 1, 3, and 6 months), the skin was evaluated using Visioscan® VC-20 Courage high-resolution UVA-light video camera and SELS (Surface Evaluation of Living Skin) software (Khazaka Electronic, Cologna, Germany) at three facial regions bilaterally as follows: frontal, lateral canthal, and nasolabial. Three measurements were made on each region at left and right, and the average of six measurements was used for the analyses. Following parameters were evaluated for all regions: skin smoothness (Sesm), skin roughness (Ser), scaliness (Sesc), and wrinkles (Sew). In addition, average spot size, average gradient, and desquamation index were evaluated for frontal region. Treatment was questioned at 6-month visit and subjects self-rated treatment efficacy as follows: 0, not sufficient; 1, sufficient; 2, good; and 3, excellent. Subjects also self-rated pain using 10-point visual analog scale (VAS) following injection. In addition, subjects were questioned for any side effect at each visit.

2.4. Statistical Analysis. Statistical Package for Social Sciences (SPSS) Version 21 was used for the analysis of data. Prior to data collection, Visioscan measurements were made by the same observer in ten subjects at a single region to estimate intraobserver variability defined as the difference in repeated measurements by the same observer. For this estimation, the intraclass correlation coefficient (ICC) including 95% confidence interval was used in a two-way mixed single measures model with absolute agreement. Descriptive data are presented in mean ± standard deviation, median (range), or number (percentage) and were appropriate. Two-way ANOVA for repeated measurements was used to compare the two treatment groups in terms of changes in skin parameters over time. For comparison of the groups in terms of continuous variables, Student's t-test for independent samples or Mann–Whitney U test was used depending on normality. Pearson's Chi-square test or Fisher's exact test was used for the comparison of categorical variables. A p value <0.05 was considered indication of statistical significance.

3. Results

3.1. Patient Characteristics. A total of 55 subjects (PRP group, $n = 23$; PRF group, $n = 32$) were included in the study. The mean age was 36.4 ± 8.9 years (median: 34 y, range: 23–58 y). Most subjects were female ($n = 52$, 94.5%). The two groups did not differ in terms of age ($p = 0.337$) and sex distribution ($p = 0.370$). Intraclass correlation coefficient (ICC) for intraobserver variability estimated prior to data collection at the canthal region for smoothness was 0.846

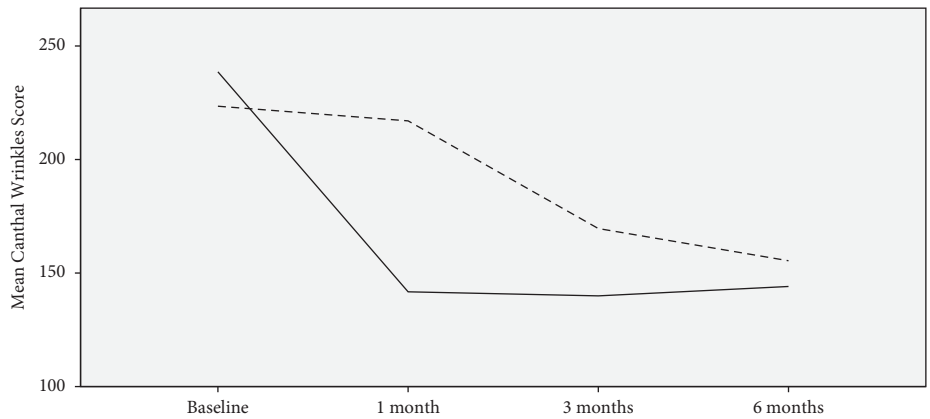

Figure 1: Changes in canthal wrinkles scores over time: dotted line, PRP group; straight line, PRF group.

(95% CI, 0.633–0.966) (Cronbach's alpha: 0.946, p for F test: <0.001).

3.2. Comparison of the Groups for Cosmetic Efficacy Parameters. The two groups (PRP vs. PRF) did not differ in terms of changes in frontal parameters over time ($p > 0.05$ for all). Similarly, the two groups did not differ in terms of changes in nasolabial parameters over time ($p > 0.05$ for all). However, a significant difference was present in terms of canthal smoothness and wrinkle ($p = 0.025$ and $p = 0.028$, respectively) (Figures 1 and 2) with better (lower) scores for PRF group, while no difference was detected in canthal roughness and scaliness ($p > 0.05$ for both). For canthal smoothness, at only 3 months the difference reached statistical significance ($p = 0.048$); for canthal wrinkles, the difference did not reach significance at any of the time points.

3.3. Side Effects. Table 1 shows the comparison of the groups in terms of side effects. The two groups did not differ in terms of the frequencies of individual side effects or frequency of experiencing any side effect.

3.4. Patient Satisfaction and Pain Scores. The two groups did not differ in terms of self-rated treatment efficacy scores PRP group, median: 2, range: 1–3; PRF group, median: 2, range: 1–3, $p = 0.743$. Similarly, the two groups did not differ in terms of VAS scores PRP group, median: 5, range: 0–7; PRF group, median: 5, range: 2–7, $p = 0.860$.

4. Discussion

This study compared two different platelet concentrates (PRP versus injectable PRF) for facial skin rejuvenation and found marginally better cosmetic outcomes with PRF, although the two treatments were similar in terms of side effects, patient satisfaction, and pain. To the best of our knowledge, this is the first study comparing PRP and PRF injections in facial skin rejuvenation.

Since PRP has the potential to activate the synthesis of extracellular matrix elements including collagen [16–18], it has been used for dermatological disease and cosmetic problems including skin rejuvenation for about a decade [1, 3, 5, 19, 20]. An earlier study examined the use of PRP injections for face and neck rejuvenation in 23 patients and found clinical improvement (in terms of nasolabial folds, horizontal neck bands, skin microrelief for snap test, skin homogeneity and texture, skin tonicity, and periocular wrinkles) in addition to patient and physician satisfaction [19]. In the study by Banihashemi et al., PRP was tested for facial rejuvenation and significant improvements was found for periorbital dark circles, for periorbital dark circles and nasolabial folds, and for periorbital dark circles according to patients', treating physician's, and a second dermatologist's evaluation, respectively [1]. In a recent study, Everts et al. examined the use of PRP injections for facial skin rejuvenation, and biometric instrumental evaluations was made in addition to patient-reported outcomes [21]. The treatment resulted in following improvements: decrease in brown spot counts and area, decrease in wrinkle count and volume, improvements in skin redness and firmness, decrease in SLEB thickness, and increase in SLEB density without affecting subcutaneous fat. The treatment was also satisfactory based on patient evaluation. Cameli et al. found significant improvements of skin texture, skin gross elasticity, skin smoothness parameters, skin barrier function, and capacitance after PRP injections for skin rejuvenation [22]. PRP has also been tested for infraorbital dark circles, crow's feet wrinkles, and periorbital hyperpigmentation with success [23–25]. In a recent systematic review of 36 studies and 3172 patients on the use of PRP in facial rejuvenation [2], either as monotherapy or in combination, 29 studies reported significant improvements in certain parameters (facial wrinkles, aging, pigmentation, nasolabial folds, acne scars, and tissue volume); however, the authors emphasized the lack of uniformity in reporting PRP preparations and assessments tools, which complicates drawing robust conclusions. Similarly, in another review on the use of platelet preparations in facial rejuvenation and wound healing, majority of the studies showed significant benefit [15]. Current evidence suggests that PRP injection represent a valuable treatment option for facial rejuvenation with good results and safety.

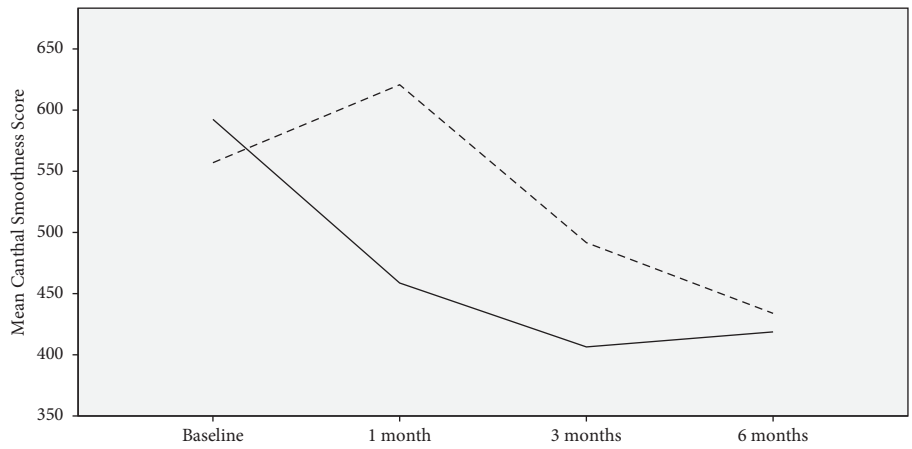

Figure 2: Changes in canthal smoothness scores over time: dotted line, PRP group; straight line, PRF group.

Table 1: Comparison of the groups in terms of side effects.

Side effect	PRP group ($n = 23$)	PRF group ($n = 32$)	p
Redness	13 (56.5%)	25 (78.1%)	0.087
Bruise	4 (17.4%)	2 (6.3%)	0.223
Burning	1 (4.3%)	4 (12.5%)	0.387
Edema	1 (4.3%)	0 (0.0%)	0.418
Any side effect	19 (82.6%)	31 (96.9%)	0.149

So far, few studies examined the use of PRF in facial skin rejuvenation, another platelet concentrate prepared without the use of anticoagulants, thus having a fibrin matrix. In their histological study, Sclafani and McCormick [26] reported activation of fibroblasts and new collagen deposition, development of new blood vessels, intradermal collections of adipocytes, and stimulation of subdermal adipocytes following injection of PRF matrix into the skin. The same author successfully used PRF matrix for facial cosmetic treatments such as for deep nasolabial folds, volume-depleted midface region, superficial rhytids, and acne scars [13, 14, 27]. Liang et al. used the combination of PRF plus nanofat-derived stromal cells for skin rejuvenation with satisfactory results [12]. Moein et al. reported significant improvements in nasolabial folds with PRF matrix [28].

Injectable platelet-rich fibrin (PRF) is a second-generation autologous platelet concentrate slightly different than PRP, both in terms of preparation procedures and structure [6]. Choukroun and Ghanaati first described differential centrifugation concept and introduced injectable PRF [11]. It is prepared with slow speed centrifugation, it is fully autologous and has no added anticoagulants unlike PRP, and thus, it would not arise hypersensitivity concerns. Although platelet-rich fibrin matrix has been used for several indications including dermatological conditions for about a decade [9, 12–14, 26–29], injectable liquid PRF prepared by low-speed centrifugation is a relatively new concept [11]. Injectable PRF has several theoretical advantages over PRP such as no need for external anticoagulants, shorter preparation time, sustained release of growth factors over prolonged time, lesser cellular proliferation, and prolonged retention of morphology [6]. However, studies on the use of this new biomaterial for facial skin rejuvenation are scarce. Shashank and Bhushan reported two cases who received injectable PRF treatments for facial skin with successful results (to rejuvenate under eye area and for temporary correction of facial skin folds) [6].

Several studies have compared PRF and PRP in indications other than facial skin rejuvenation. A 2020 randomized controlled trial (RCT) in dentistry compared the regenerative potential of PRP and PRF scaffolds in immature permanent maxillary central incisors with necrotic pulps and obtained similar outcomes with both treatments, except for higher amount of crown discoloration with PRF [30]. Another controlled but nonrandomized trial compared PRF and PRP injections in sacroiliac joint dysfunction and obtained significantly better clinical results with PRF in the long-term [31]. Although not directly compared, a recent systematic review and meta-analysis of RCTs of 23 studies and 1440 patients examined the results of two treatments (PRP versus PRF) in arthroscopic rotator cuff repair [32]. In summary, when compared to controls, PRP improved retear rate, functional scores (constant score, the University of California Los Angeles score, and the American shoulder and elbow surgeons score), and the visual analog score, whereas PRF resulted only in improved constant score, suggesting better role for PRP in that particular indication. This study found slightly better cosmetic results with PRF, only at the canthal region at three months, which may be attributed to different pharmacokinetics (long lasting effect) and structure of PRF. However, it is of note to mention that the difference disappeared at 6 months; thus, this finding may only indicate an earlier treatment response with PRF, but not necessarily better response in the long-term.

This study has a prospective cohort design without randomization and the patients were allocated to the study groups according to their own decision. This may be a potential source of bias and represents a major limitation of the study; thus, results should be interpreted accordingly. Future studies with more robust design, i.e., randomized controlled studies, are warranted. Another potential limitation of the present study is the lack of data on final solution concentrations and platelet counts prior to injection of the

solutions. Such measurements would allow better cross comparison with other studies and improve reproducibility.

5. Conclusion

The present study compared PRP with injectable PRF in facial skin rejuvenation and found marginal superiority of PRF over PRP, only for the treatments of the canthal region and only at three months. In addition to this finding, easier preparation and absence of hypersensitivity concerns due to anticoagulants may render this biomaterial an alternative to PRP in this indication. Potentially longer duration of action may result in long lasting effects with more satisfactory cosmetic results. Further large-scale studies comparing the two modalities are warranted to draw firm conclusions.

Data Availability

All data used and included in this study are available from the corresponding author upon reasonable request.

Ethical Approval

The study protocol was approved by the local ethics committee (Istanbul Kent University Ethics Committee, no: 2020/03, date: July 7, 2020).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

All authors contributed to the study conception and design. Statistical analysis was designed and performed by Nilhan Atsu. Material preparation and data collection were performed by all authors. The first draft of the manuscript was written by Nilhan Atsu, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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