

Evaluation of the Effect of Platelet-Rich Fibrin Matrix in the Correction of Periorbital Wrinkles: An Experimental Clinical Trial

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ABSTRACT Introduction: Skin rejuvenation techniques have gained substantial popularity due to increased life expectancy over recent years. Platelet-rich fibrin matrix (PRFM) is the new generation of platelet aggregate products that have surfaced in recent years to treat skin aging.

Objectives: We intend to use PRF to correct periorbital wrinkles in 15 volunteers and evaluate its effectiveness in this study.

Methods: To evaluate the efficacy of PRFM intervention, eight men and women over the age of thirty entered our study. Blood samples were taken and were immediately centrifuged at 700rpm for 5 minutes. PRFM was extracted from the plasma and injected at the sub-dermis site in periorbital areas. The initial severity of periorbital wrinkles was determined by Visioface 1000D, and obtained data were delivered to the statistical unit for statistical analysis. Scoring and evaluation were based on tissue volume and depth and were measured before and twelve weeks after injection. Adverse effects were also taken into consideration.

Results: The results demonstrated noticeable improvement in deep, fine, and small wrinkles, periocular hyperpigmentation, and overall skin freshness of the injection site. The subjects had swelling in the injection site for up to one day after the injection, which resolved without complications.

Conclusions: PRFM was observed to have potential in skin rejuvenation, demonstrating promising outcomes in terms of safety and long-term effects in improving skin condition.

Introduction

Throughout the years, concerns regarding skin aging have increased substantially, even affecting the young generations due to increased life expectancy [1]. The dermis, the inner layer of skin, which mainly consists of collagen and elastin, has the role of forming skin structure. The aging process destructs the elasticity of these fibers and reduces the production of hyaluronic acid; thus, skin aging results from a lack of elasticity, collagen bundle fragility, and fragmentation [2, 3]. Alongside intrinsic factors, environmental factors such as chemical exposure, ultraviolet radiation, smoking, and psychological changes also play a noticeable part in the aging process [3, 4]. Some studies have discussed the possible role of reactive oxygen species (ROS) in leading the skin aging process; however, despite the endeavors to discover the underlying mechanism, its pathogenesis is yet to be fully comprehended [5].

Skin aging is categorized into two subgroups, which are intrinsic and extrinsic aging. Intrinsic aging progresses with age and can be described by epidermal thinning and fine wrinkles. However, deep wrinkles, hyperpigmentation, and skin laxity can be observed in extrinsic skin aging, which is greatly impacted by chronic sun exposure. All in all, skin wrinkles are the hallmark of skin aging [4, 6].

In recent years, many exogenous filler materials have been put to the test in the hope of improving skin wrinkles by volume augmentation. The mainstay of filler disadvantages is its absorbable nature, which reduces its effect over time. Among these methods, platelet-rich plasma (PRP) injection has recently attracted significant attention. PRP consists of concentrated platelet and growth factors obtained via venous blood centrifuge [7]. Platelet-rich fibrin matrix (PRFM) is the new PRP generation that is richer in growth factor concentration, enabling it to have a significantly better outcome in stimulating angiogenesis, tissue regeneration, and wound healing. Moreover, PRFM induces mesenchymal stem cell (MSC) migration to the site of injection, which bears imperative regenerative function [2].

Currently, various exogenous fillers are utilized globally, including in Iran. High cost, owing to the exogenous nature of the filler and transient side effects such as edema, erythema, encapsulation, granuloma formation, and even chronic or delayed infection, minimizes its popularity [8]. Conclusively, PRF as a natural autologous filler has the potential to be a safe candidate with long-lasting effects.

Objectives

Several studies have concluded that PRF is an effective route in reducing skin wrinkles with minimal side effects. Its side effects are mainly limited to transient erythema at

the injection site [9]. This study intends to use PRF to correct periorbital wrinkles in 15 volunteers and evaluate its effectiveness.

Methods

Study Design and Participants

In this prospective clinical trial, sixteen adult women and men over the 30-year-old with facial wrinkles who volunteered to participate were included in the study. Participants were excluded in cases younger than 30 years old, significant past medical history, such as connective tissue disorder, myocardial infarction, hypertension, pregnancy, and use of immunomodulatory or anticoagulation (e.g., Aspirin, Warfarin) medication. The purpose of the study and all side effects of the intervention were clearly explained to all participants. They were assured their information would remain confidential, and they were permitted to withdraw from the study if they requested. Subsequently, written informed consent was obtained from all patients. The sample size was estimated based on a study by Sclafani et al [10], based on the mean wrinkles assessment score before and after the intervention, taking into account the first type error of 5%, 80% power, and an effect size of 0.8, calculating to a total of 15 participants.

Intervention

For intervention, after evaluating the patient's medication and drug history, the total depth of wrinkles before injection was measured with the Visophysis device. Decosept and a tourniquet were applied, and a 15cc blood sample was taken with a syringe at a 15-degree angle from the brachial vein, transferred to three 5cc tubes, and immediately centrifuged at 700 rpm for 5 minutes. Then, using a canola, except for 1 cm above the tubes, the rest of the plasma, which had a gel-like consistency, was transferred to a 5-cc sterile syringe. After this, PRF was transferred to 1 cc syringes by sterile connection. Simultaneously with the beginning of the blood collection process, local anesthesia (Xyla P Cream, Tehran Chemie) was used at the injection site. The duration of local anesthesia was at least 30 to 50 minutes, based on the patients' anesthesia capacity. After sterilizing the injection site with betadine, a 3cc PRF solution was injected into the wrinkles around the eyes with a canola number 27 on both sides. The injection was performed at the sub-dermis site and in one session. The patients were advised to visit our clinic in case of delayed alleviation of swelling or adverse effects, such as infection. Also, since the effectiveness of PRF was to be evaluated in our study, the use of creams or other products was not recommended. Participants were also informed that they could also be present at work on the same day of the procedure without any problems.

Outcome Assessment

The initial severity of periorbital wrinkles was determined by Visioface 1000D (CK electronic, manufactured in Germany), and obtained data were delivered to the statistical unit for statistical analysis. Scoring and evaluation were based on tissue volume and depth and were measured before and twelve weeks after injection. Patients were also advised to visit in case of developing any complications.

Data Analysis

Data were entered into SPSS version 21 and subsequently analyzed. An independent sample t-test was used to evaluate the difference in tissue volume among the groups. A P-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Research Ethics Committee of the Shiraz University of Medical Sciences and was conducted in compliance with the relevant guidelines and regulations and the Declaration of Helsinki. Written informed consent was obtained from the patients in our study. The purpose of this research was completely explained to the patients, and they were assured that their information would be kept confidential by the researcher. The present study was approved by the Medical Ethics Committee of the academy (Ethical Code: IR.SUMS.MED.REC.1400.480) and registered in the clinical trials database (Code: IRCT20220218054054N1).

Results

Sixteen patients, consisting of eight males and eight females, were included in our study. Each participant was evaluated based on changes in the left and right side periorbital wrinkles after PRF injection. The subjects had swelling in the

injection site for up to one day after the injection, which resolved without complications. We measured tissue depth with a Visophys device before and twelve weeks after injection. During this period, none of the people had any complications and all were completely satisfied. The tissue volume score of the participants included in our study is demonstrated in Figure 1. Also, Figure 2 demonstrates the cosmetic appearance of the results of our study.

There was no significant difference among the male and female groups regarding tissue volume before injection at both sides. ($P=0.964$ and 0.240 for right and left, respectively). Furthermore, As demonstrated in table 1, the tissue volume size on both sides significantly decreased, both in males and females, after PRF injection (Table 1). However, there was no significant difference among males and females regarding tissue volume after injection ($P=0.784$ and 0.427 , for right and left, respectively) or amount of tissue volume change ($P=0.828$ and 0.0339 , for right and left, respectively)

It should be noted that following PRF injection, in addition to improving deep wrinkles, noticeable improvement was observed in fine and small wrinkles, periocular hyperpigmentation, and overall skin freshness of the injection site. All subjective reports among our participants reported satisfaction and were eager to repeat and recommend this procedure.

Discussion

In recent years, platelet concentrates injection has gained global popularity, which, combined with the increased demand for skin rejuvenation techniques, calls for further clinical assessment of the safety and function of these products. PRF is the new evolutionary face of platelet-rich aggregates [11]. This study puts the effect of PRF under conduction and observed significant improvement in periorbital skin rejuvenation accompanied by significant patient satisfaction.

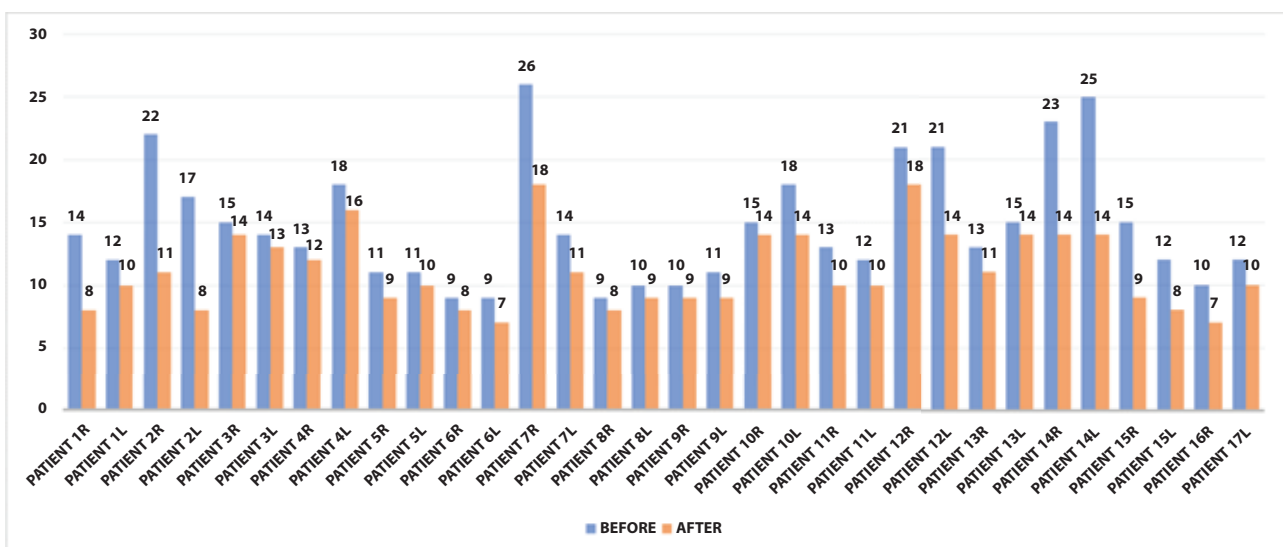


Figure 1. Changes in tissue volume before and after platelet-rich Fibrin injection among females (patients 1 to 8) and males (patients 9 to 16).

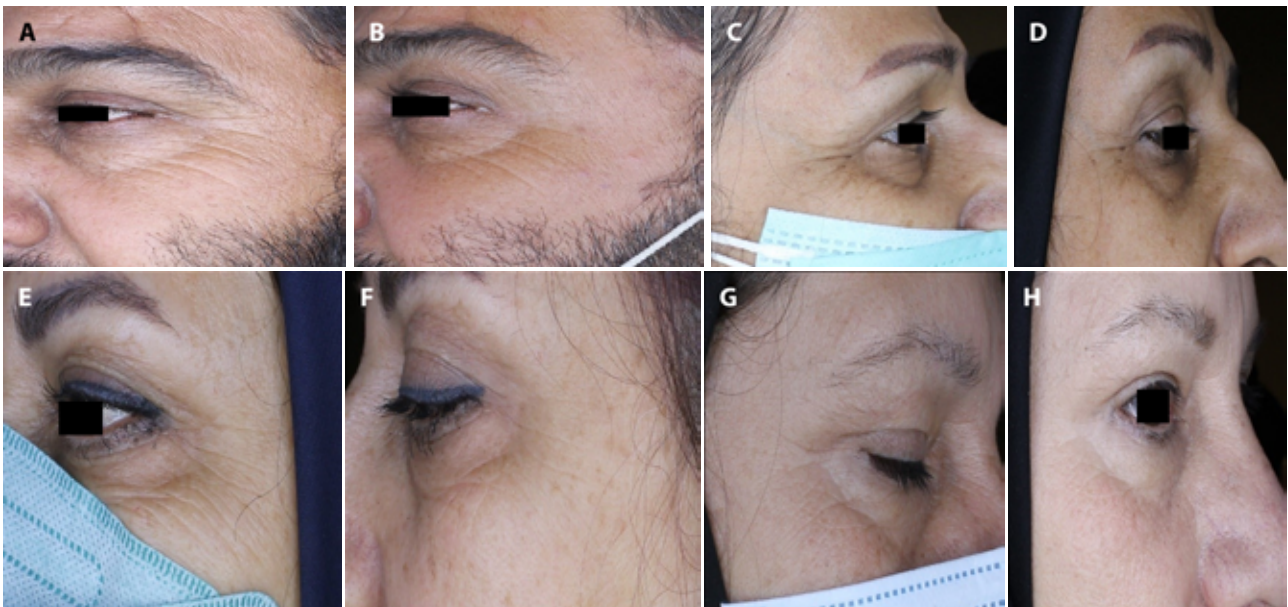


Figure 2. Results of platelet-rich fibrin matrix in the correction of periorbital wrinkles.

Table 1. Tissue volume score and changes based on gender and laterality.

| Gender | Right | | | | Left | | | |
|---------------|--------------|--------------|-------------|----------|--------------|--------------|-------------|----------|
| | Before | After | Change | P-value* | Before | After | Change | P-value* |
| Female; n= 15 | 14.88 ± 6.13 | 11.00 ± 3.59 | 3.88 ± 3.94 | 0.027 | 13.13 ± 3.23 | 10.50 ± 2.88 | 2.63 ± 2.67 | 0.027 |
| Male; n=15 | 15.00 ± 4.75 | 11.50 ± 3.59 | 3.50 ± 2.73 | 0.008 | 15.75 ± 5.12 | 11.63 ± 2.62 | 4.13 ± 3.36 | 0.010 |
| P-value* | 0.964 | 0.784 | 0.828 | - | 0.240 | 0.427 | 0.339 | - |

* Independent sample t-test

PRF, the second generation of platelet concentrates, is superior to PRP in numerous aspects. First of all, PRF preparation consists of only one centrifugation step, making it simpler than PRP preparation [12]. As a result of declined centrifuge speed, PRF has been observed to contain higher volumes of growth factors, leukocytes, fibrin, and platelets than PRP, resulting in a more boosted growth factor-mediated functional aftermath [11]. Secondly, PRF is completely autologous and does not contain any exogenous additives, which supports the natural physiologic polymerization of fibrin. Growth factor binding and platelet capture are facilitated via the three-dimensional fibrin structure of PRF that results in the enhancement of the gradual and long-term release of cytokines and growth factors. Moreover, this fibrin mesh is also responsible for cell proliferation and differentiation and the formation of new blood vessels [11, 12]. Finally, PRF prompts cell proliferation, migration, differentiation, and adhesion accompanied by anti-inflammatory properties that further support its therapeutic aptitude in bone regeneration, wound healing, improving scar appearance, and stimulating hair growth [2, 13].

This study utilized a PRF solution for periorbital wrinkles, and the depth of the wrinkles was assessed via a Visophysis

device. The results revealed significant improvement in deep wrinkles in all candidates. Furthermore, noticeable improvements were also noted in fine and small periorbital wrinkles. This result is also in line with previous studies on the benefits of PRF [11].

Along with the diminishing wrinkles, improvement in skin hyperpigmentation and overall freshness were also of significance. Maisel-Campbell et al. conducted a systematic review of the benefits of PRP injection and observed significant improvement in skin texture through different studies [14]. A Chinese study conducted on the effect of PRP injection also concluded that skin quality was significantly enhanced in participants with a substantial decline in wrinkles, pores, and texture. Furthermore, PRP treatment was detected to inhibit UV-B-induced tyrosinase and metalloproteinase-1 (MMP-1) upregulation, which along with tropoelastin and fibrillin induction, results in photoaging enhancement [15]. The benefits of platelet aggregate products take root from not only its high concentration of growth factors, but also its gelatin constituents. The gelatin part has the potential to bring elasticity and a good support system for wrinkles, cavities, and skin relaxation[16]. In addition, these platelet aggregate products contain cell adhesion proteins

which could help keep the skin tight and smooth [15]. The decline in hyperpigmentation that was observed in our study is consistent with previous studies and is due to the fact that platelet aggregate products increase skin thickness and ameliorate collagen content which results in reduced pigmentation [11, 14, 15].

The patients in the present study had a 12-week follow-up session to evaluate their skin quality post-PRF injection. The periorbital wrinkles, skin hyperpigmentation, and overall freshness were held down, therefore, adding support to the long-term effect of the PRF procedure. Liang et al. did a 6,12,24-month follow-up after nano fat-PRF injection and observed that patient satisfaction was of significant worth even after the 12-month mark [4]. All in all, these findings shed light on the PRF's potential as a long-term and safe skin rejuvenating technique.

Skin aging can substantially impact each individual's quality of life. Youth, health, and activity are three major ideals that are starting to grow in the community's lives. Therefore, skin wrinkles can have psychosocial outcomes in people's lives. A study conducted in Germany concluded that those who underwent cosmetic procedures had higher quality of life [17]. Conclusively, PRF as a potent procedure for skin rejuvenation may, in turn, advance the quality of life in the population.

Throughout our study, adverse effects of PRF were taken into consideration, and the reports were promising as no adverse effects were seen other than the first-day injection site edema. This finding was in line with previous studies [11]. Over the literature, no major adverse reactions were reported, and the side effects are observed to be only limited to slight bruising in the injection site [4, 11, 18].

Some limitations should be addressed. Due to the Covid-19 pandemic, patients were only evaluated after 12 weeks, and frequent visits were not applied, limiting our statistical power for the clinical outcomes assessment, while no objective documentation of their satisfaction was carried out. However, all patients reported satisfaction and were eager to repeat and recommend this procedure. Additional limitations include the relatively limited number of participants and the treated areas.

Conclusion

In summary, this study demonstrated that intradermal PRF injection could be considered as a safe, long-term technique accompanied by favorable objective facial skin rejuvenation and improving patient satisfaction. Along with diminishing wrinkles, improvements in skin hyperpigmentation and overall freshness were also of significance. However, further longitudinal studies need to be carried out to assess the long-term outcomes of PRF injection. Also, studies with

higher sample sizes are warranted to understand the extent of improvement and also possible side effects.

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