International Journal of Dermatology, Venereology and Leprosy Sciences

E-ISSN: 2664-942X
P-ISSN: 2664-9411
www.dermatologypaper.com
Derma 2023; 6(1): 41-45
Received: 30-10-2022
Accepted: 15-12-2022

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Assessment of the efficacy and safety of platelet rich plasma gel injection in facial rejuvenation and wrinkles

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DOI: https://doi.org/10.33545/26649411.2023.v6.i1a.133

Abstract
Background: Changes in the three-dimensional geometry of the underlying structures contribute to the ageing process of the human face, just as the skin's surface textural wrinkling does.
Objective: To evaluate the efficacy and safety of platelet rich plasma gel injection in facial rejuvenation and facial wrinkles.
Methods: This study was carried out on 10 subjects presented by facial wrinkles. Patients were subjected to platelet rich plasma gel injection after taking an informed consent. They were assessed clinically by global assessment scale before treatment and at the end of follow up period.
Results: After administration of plasma gel, all subjects significantly improved clinically immediately. This finding confirmed by significant improvement of global assessment scale.
Conclusions: Plasma gel seem to be safe, effective and well tolerated in treatment of facial wrinkles and rejuvenation.

Keywords: Platelet rich plasma gel, facial rejuvenation, wrinkles

Introduction

Wrinkles and sun damage from ageing skin are cosmetic issues that can have a psychological impact and lead patients to seek therapy guidance. The sun causes epidermis anomalies like lentigines and the breakdown of collagen, which leads to the appearance of wrinkles and telangiectasias due to sun exposure. Sun-damaged epidermis can be revitalised with a number of various treatments [1].

Changing facial features in three dimensions (3D) and the skin's surface granular wrinkling are both contributors to the ageing process. The phenotypic appearance of the face throughout life, soft tissues (subcutaneous fat, muscle, and fascia), and skeletal support (bone and dentition). Gravity, skeletal remodelling, subcutaneous fat redistribution and loss, hormonal instability, prolonged sun exposure, and smoking are the main factors adding to face ageing. Stress, nutrition, lifestyle choices, toxic substances, and illness are all external variables that can impact one's facial look [2].

With the advancement of the age, wrinkles and grooves become more prominent on person's face. Sun injury and the ensuing solar elastosis are major causes of fine lines and wrinkles on the skin's surface. Collagen depletion at the epidermis-dermis interface and a rise in dermal elastin whirls are hallmarks of this condition [3].

Replacing the signs of ageing with a more young appearance is a major goal of facial rejuvenation. The field of face rejuvenation has undergone fast and significant changes as physicians and patients seek more effective and safer treatments [4].

For elimination of facial wrinkles and skin contour defects, injectable substances are widely available. The ideal soft tissue substances should be non-antigenic, non-inflammatory, stable after injection, non-migratory, nontoxic, non-carcinogenic, long lasting but resorbable and easy to apply [5].

PRP, or platelet-rich plasma, is a plasma concentrate made from the patient's own blood. Another form of PRP autologous filler could be obtained from PRP concentrate by thermal treatment and is known as plasma gel. Platelet rich plasma gel including both platelet rich fibrin matrix (PRFM) and a plasma gel new natural dermal fillers that use the patient's own blood as the product [6].

PRP contains significant amounts of growth factors that has been shown to enhance rejuvenation effect. PRP gel injectable filler can be used as one of the modalities for skin rejuvenation [6].

The aim of this work was to evaluate the efficacy and safety of platelet rich plasma gel injection in facial rejuvenation and facial wrinkles.

Patients and Methods

This study was carried out on 10 subjects presenting with facial wrinkles, aged from 35-55 years and were willing to join the study and have realistic expectation who selected from the attending the Outpatient Clinic of Dermatology and Venereology Department of Tanta University Hospitals. Tanta University's Ethical Council gave their approval to the research. Patients gave their signed, written permission after being fully told of all risks and benefits.

Exclusion criteria were pregnancy, lactation, systemic disease, history of keloid formation or foreign body reaction, other previous cosmetic treatments or facial surgery, known allergy or hyper sensitivity to material or to lidocaine, patients using NSAIDs, those with a history of recurring face or labial herpes simplex, and those who are currently suffering from or have a history of any procoagulative or thromphilic condition, systemic corticosteroids, anticoagulant or blood thinners such as aspirin, warfarin, etc. and heavy smokers.

All subjects were subjected to full history taking, thorough general and dermatological examination, routine laboratory investigations for all patients to exclude anemia and bleeding disorders. Detailed dermatological examination of face was done to assess the depth of creases on the face.

Preparation of platelet rich plasma (PRP) gel

According to Hom *et al* technique [6] a 10 ml whole venous blood was obtained from each participant and collected in the sterile tubes. Five vacuum tubes (2 ml) equipped with anticoagulant were used. Each test tube was centrifuged at a speed of 1800 g for 15 min.s. After spinning the blood samples, we got two distinct layers of plasma: the platelet-poor plasma (PPP) on top and the red blood cell-rich plasma (PRP) on the bottom. A 5 ml concentrate of activated PRP was obtained by first carefully aspirating the PPP to prevent it from mixing with the PRP, and then preparing the PRP for activation with calcium gluconate at a ratio of 0.01 millilitre of calcium gluconate to 1 millilitre of PRP. The PRP was separated into five 1 millilitre vials and heated in a hot water pool between 600 C and 1000 C for at least one min. before being chilled in a cold water pool between 8^5 C and 0^5 C for at least one min. After all of this work, PRP will have the consistency of a thick gel [7, 8].

Technique of injection

A topical anesthetic cream (lidocaine 5%) was applied to the face for 15 min.s. Injection points were selected according to patient assessment. Before the procedure began, the topical anaesthetic was washed off and the face was cleansed with local antiseptic solution and then rinsed with regular water. Next, the plasma gel was injected slowly, intradermally, at a depth of 3 to 4 millimetres, at an angle of 30 degrees to the epidermis, using a sterile, single-use 30 G syringe and strict aseptic procedure. Each shot was given with the needle's opening facing upward. All efforts were made to avoid injecting near a vein or artery.

Injection methods differed as follows based on target organ: Both the "linear threading technique" and the "fanning technique" were used to infuse half a millilitre of plasma gel into each side of the face to fix the nasolabial folds. The linear threading technique [9] involves inserting the entire length of the needle into the centre of the nasolabial fold and injecting the gel while gently drawing the needle rearward, resulting in the placement of the gel threads in a longitudinal orientation within the nasolabial fold. For the fanning technique [10], a needle was entered at the cheek's periphery, just as it would be for the linear threading technique; however, after injecting one line, the needle's orientation was altered and additional lines were injected. After inserting the syringe at the outer edge of the marionette line and injecting as with the linear threading technique, we withdrew it and reinserted it 5–10 mm adjacent to the first puncture site and administered 1 millilitre of plasma gel into each side using the "cross-hatching method" [11]. This process was carried out again, this time at 90 degrees to the first set of lines. To help the plasma gel spread and take the shape of the nearby tissues, gentle massage was applied after insertion.

Patients were also instructed to refrain from massaging or applying prolonged pressure to the treated regions for a full week after treatment because prolonged contact to cold could disrupt normal platelet function.

Evaluation of therapy

All subjects were assessed at the baseline before plasma gel treatment session and they asked to follow-up after 2, 4, 12 weeks for assessment of the results as follow:

1) Clinical assessment

All subjects were assessed at initial visit, 2 weeks, 1 month and at the 3-month follow-up, the results are as follows:

Global assessment for degree of clinical improvement according to the three blinded dermatologists [12]

Using a 5-point scale, a digital analysis extrapolated to standardised worldwide photos was performed to calculate the degree of improvement [12] as follow;

- 0= No change
- 1= Slight improvement (1-25%)
- 2= Moderate improvement (26-50%)
- 3= Significant improvement (51-75%)
- 4= Excellent improvement (<75%)

2) Subject satisfaction [13]

At the conclusion of the follow-up phase, subjects in both groups were given a questionnaire to complete grading their level of happiness with the outcomes relative to the pretreatment condition [13];

1=Very dissatisfied
2=Dissatisfied
3= Neutral
4=Satisfied
5=Very satisfied

3) Safety assessment

All subjects were asked to record any injection related side effects noted immediately after treatment or at the end of follow up period. These side effects included any injection-related pain, bleeding from injection site, local swelling, ecchymosis, erythema, infection and other injection related

events.

Statistical analysis

IBM SPSS, version 20.0(14), was used for the data input and analysis (Armonk, NY: IBM Corp). Quantitative and percentage descriptions were used for qualitative information. For this purpose, we used the Kolmogorov-Smirnov test to make sure that the data were normally distributed. Quantitative information was summarised with the help of the lowest and highest values, mean, standard deviation, median, and interquartile range (IQR). The acquired findings were deemed significant at the 5% level.

Results

Assessment the efficacy and safety of the therapeutic procedures

I) Clinical assessment: All subjects were assessed at base line before injection and at the end of follow up period (12 weeks after) as follow:

1. Global assessment for degree of clinical improvement according to the three blinded dermatologists [12]: (Table 1)

PRP gel administration resulted in therapeutic improvements of varying degrees across all participants as follow; 2 subjects (20%) showed significant improvement (grade 3), 6 subjects (60%) showed moderate improvement (grade 2), and 2 subjects (20%) showed slight improvement (grade 1).

2. Subject satisfaction[13]: (Table 2)

All subjects showed various grades of satisfaction after platelet rich plasma gel injection as follow; 5 subjects (50%) were very satisfied (grade 5), 5 subjects (50%) were satisfied (grade 4).

3. Safety assessment: (Table 3)

Mild complications were reported in after injection of plasma gel as follow: Local swelling at the site of injection was reported in 2 subjects (20%). Two subjects (20%) reported lasting for 3 days and Ecchymosis is managed with a topical anti-coagulant and anti-edematous ointment. Two subjects (20%) complained of pain during injection for few mins. only. Erythema was reported in 2 subjects (20%). No subjects reported infection after injection.

Table 1: Global assessment for degree of clinical improvement

Degree of improvement	PRP gel	
	No.	%
4=Excellent improvement (>75%)	0	0.0
3=Significant improvement (51-75%)	2	20.0
2=Moderate improvement (26-50%)	6	60.0
1=Slight improvement (1-25%)	2	20.0
0=No change	0	0.0

Table 2: Assessment according to subject satisfaction

Subject satisfaction	PRP gel	
	No.	%
5=Very satisfied	5	50.0
4=Satisfied	5	50.0
3=Neutral	0	00.0
2=Dissatisfied	0	00.0
1=Very dissatisfied	0	00.0

Table 3: Assessment according to side effects

Side effects	(PRP gel)	
	No.	%
Local swelling	2	20.0
Pain	2	20.0
Ecchymosis	2	20.0
Erythema	2	20.0
Infection	0	0.0

Case (1)

Photo 1: A 42- year- old female with different types of facial wrinkles. (a, b, c) before PRP gel injection (d, e, f) after 3 months with significant improvement

Discussion

When we age, our skin thins and loses extracellular matrix, which causes our skin's tensile resilience and viscoelasticity to degrade. Wrinkle formation begins in one's thirties, peaks in one's forties, and is thought to be on the rise in one's fifties [15].

In current study, all subjects showed immediate improvement after PRP gel injection that maintained till the end of follow up period and confirmed by statistically improvement of wrinkles according to global assessment.

Our findings were in close agreement with those of Doghaim *et al*. (2019) [16], who evaluated the efficacy and safety of platelet-poor plasma gel as an autologous dermal filler for facial rejuvenation in a study involving 52 women who presented with facial ageing and were given two

injection sessions separated by two weeks. All plasma gel-treated subjects demonstrated statistically significant clinical improvement in face wrinkles at the end of the follow-up period, as measured by a decline in the mean value of their WSRS with a P-value 0.05 compared to that before plasma gel treatment sessions. Additionally, 52.9% demonstrated change, and 47.1% indicated considerable improvement, in facial skin texture and homogeneity.

Our results also were in agreement with Neinaa *et al*., 2020[17] who conducted a clinical and dermoscopic comparative study. There was statistically significant clinical improvement (P value < .012) and improvement of the skin texture and homogeneity after plasma gel injection.

Also, many studies found that there was statistically significant gradual improvement in WSRS of nasolabial fold wrinkles over 12 weeks after plasma gel injection [18-20].

Our study showed statistical significance improvement in pigmentation over the period of follow up and this result was in agreement with Neinaa *et al*., 2020 [17[who found that there was improvement in pigmentation by dermoscopic examination.

There have been many hypotheses proposed to describe the mechanism of action of plasma gel. Gelled platelet-rich plasma is a generational platelet product that features a fibrin structure in three dimensions. It has a higher density and greater elasticity at larger scales. Fibrin captures thrombocytes and their accompanying growth factors, allowing them to trickle out to the wound location over time. Studies on the efficacy of PRP gel in promoting wound healing have shown that levels of PDGF, VEGF, bFGF, and TGF are highest on the first day after administration and progressively decline over the following days. (21-23) Traditional PRP injections lack this quality. Angiogenesis, cell motility, cell proliferation, and collagen deposition are all processes that are known to be influenced by PDGF, TGF, IGF, EGFR, HER2, and VEGF [24, 26].

At the end of this study, all subjects showed various grades of satisfaction. 50.0% of subjects were very satisfied, 50.0%were satisfied. These results were in agreement with Neinaa *et al*., 2020, Choi *et al*., 2017 and Doghaim *et al*., 2019 [16-18] reported that all the patients were satisfied after PRP gel injection.

At the end of our study, revealed that there was improvement of wrinkles, photoaging, global assessment of degree of clinical improvement in younger age subjects and those with low wrinkles. Surprisingly, there was improvement of pigmentation clinically over follow up period.

In current study, Adverse effects to plasma gel administration were brief and very mild including minor pain, local swelling at the site of injection, ecchymosis, and erythema. Local reactions were likely procedure-related rather than product-related due to their self-limiting character and brief duration.

Sclafani., 2010, Doghaim *et al*., 2019 and Neinaa *et al*., 2020 [16-19] reported that no subjects complained of any erythema, soreness, fibrosis, irregularity, hardness, or lumpiness at the injection site at any time.

Our study has some limitations, including a limited sample size and a relatively brief time of follow up. Plasma gel may be a hopeful therapeutic choice for aesthetically correcting facial wrinkles and enhancing facial rejuvenation, despite it does not last for a long period.

Conclusions

Plasma gel seems to be a well-tolerated clinically effective therapeutic option as a natural non-surgical facelift. Also, plasma gel has an affordable cost, more safety, more stability and less complications compared to other modalities.

Financial support and sponsorship: Nil

Conflict of Interest: Nil

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How to Cite This Article
Ziada MY, Engi Skaker ESE, Ismael EM, El-Tatawy RA. Assessment of the efficacy and safety of platelet rich plasma gel injection in facial rejuvenation and wrinkles. International Journal of Dermatology, Venereology and Leprosy Sciences. 2023;6(1):41-45.