# Platelet-rich plasma in facial rejuvenation

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**Objective**
This study aimed at evaluating the effect of using a combination of platelet-rich plasma (PRP) and hyaluronic acid (HA) 3.5% using microneedling in facial skin rejuvenation and to estimate the visible skin improvement and patient satisfaction.

**Background**
PRP has attracted attention in the field of dermatology, specifically in the aesthetic field for skin rejuvenation. HA is involved in maintaining skin hydration. PRP along with HA offers a good combination for skin rejuvenation via microneedling for augmentation of collagen content, for increasing moisture, and for offering a rich source of growth factors.

**Materials and methods**
A total of 30 participants were enrolled in study and received facial treatments with PRP and HA through microneedling using dermapen every 2 weeks, and the results were evaluated through the assumed visual assessment scale.

**Results**
The results yielded statistically significant improvement concerning skin texture, dullness, acne, acne scars, wrinkles, wide pores, pallor, and firmness compared with baseline. Moreover, enrolled participants showed marked satisfaction with the results with minimal adverse effects.

**Conclusion**
PRP along with HA represents a potentially effective and safe material for skin rejuvenation through microneedling using dermapen.

**Keywords:**
hyaluronic acid, microneedling, platelet-rich plasma, rejuvenation

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## Introduction

Skin is a multifunctional organ, but alongside every other system, it is subjected to both intrinsic (chronological) and extrinsic (environmental) aging, resulting in a loss of functional capacity. Cutaneous aging manifests as an observable change in the external appearance of the skin [1].

Platelet-rich plasma (PRP) is a highly concentrated autologous solution of plasma prepared from a patient's own blood. PRP contains platelets that are purported to release numerous growth factors that may be valuable in numerous dermatologic applications. PRP is a relatively new treatment modality with studies suggesting its utility in aesthetic dermatology. The combination of PRP with other therapies is particularly interesting. PRP has been used for rapid healing and tissue regeneration in many fields of medicine. PRP application could be considered as an effective procedure for facial skin rejuvenation [2,3].

Hyaluronic acid (HA), one of glycosaminoglycan GAGs, forms proteoglycan aggregates, which are large complexes of HA and HA-binding prostaglandins. Their cross-linking to other matrix proteins such as the collagen network results in the formation of supermolecular structures and functions to increase tissue stiffness. Changes of these molecules are important contributors to skin aging. They can be safely used in combination in patients seeking facial rejuvenation procedures with long-lasting efficacy [4,5].

Microneedling or percutaneous collagen induction is a new modality used for skin rejuvenation, tightening, and scar remodeling. It offers a simple and effective treatment for photoaged skin with minimal disruption of the epidermis, thus limiting adverse effects and minimizing downtime. It has also being used as vehicles to deliver molecules across the skin, in addition to its use in combination treatments with topical agents or light sources. It is a promising minimally invasive treatment option with the advantage of increased collagen production [6,7].

The current study aimed at evaluating the combined treatment of PRP and HA for facial rejuvenation by microneedling concerning acne scars, acne, pallor, texture, dullness, wide pores, firmness, and wrinkles.




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## Materials and methods

This is a clinical trial study performed at Outpatient Clinics of Dermatology, Venereology, and Andrology Department, at Menoufia University Hospitals, in the period from September 2017 to January 2019, after the approval of the Committee of Human Rights in Research in Menoufia University, and a written consent was obtained from eachparticipant. The study included 30 Egyptian participants who were randomly selected and treated with PRP and HA. Their average age is between 20 and 45 years, with mean age of 30.07 years. The average number of sessions is three to six treatments, with a mean of 4.37, with 2-week interval between sessions.

Inclusion criteria were chronological skin aging (wrinkles, loss of elasticity, and skin tightness), skin dullness, pallor, active acne, and acne scars.

Exclusions criteria were severe psychological disorders, any active infection or chronic disease of the skin, bleeding or clotting disorders or any platelets disorders, pregnancy and lactation, history of keloid formation, metabolic disorders such as diabetes mellitus, individuals with a history of syncope during or immediately after venipuncture, patients with hemoglobin less than 12, and patients on anticoagulants such as aspirin and warfarin.

All patients were subjected to full history including age, sex, and occupation, frequency of sun exposure, following diet regimen and unhealthy lifestyle like smoking, addiction, stress, and previous treatment attempts. The loss of healthy skin appearance was classified according to our assumed visual analog scale (VAS) score assessed by both investigators and patients. VAS score ranges from 1 (none) to 4 (severe) concerning skin texture, skin sagging/firmness, skin dullness, wrinkles, active acne, acne scars, and facial pallor. Mild cases had the score of 2, moderate cases had the score of 3, and severe cases with 4 score. Skin type according to Fitzpatrick classification was assessed in all patients. Complete blood picture and coagulation profile were performed to exclude anemia and bleeding disorders. Written informed consent was obtained before the procedure.

To prepare PRP, single-spin method had been used. A volume of 10 ml of each participant's venous blood was drawn manually using a 10 ml sterile syringe. Then, whole blood was instilled to citrated tubes (10% Na citrate) and centrifuged at 3500 rpm for 20 min until all red blood cells separate from plasma and the buffy coat became clearly visible. The lower portion of plasma (platelet rich) and the buffy coat were collected in 5 ml needle. Platelet-poor plasma portion was separately collected and used as an extra coat at the end of session. No activator was used.

In all cases, PRP was mixed with 0.5 ml 3.5% HA gel. To reduce pain, local anesthetic cream and ice were applied before the procedure. The mix of PRP and HA was applied to skin simultaneously with microneedling using Dermapen all over the face; the remaining portion of plasma (platelet-poor plasma) was used as a final coat after microneedling. At the end of the treatment, ice and antibiotic cream were applied locally, and patients were asked to avoid any contact with their face for 3–4 h. Vitamin C (1000 mg/day) and sun protection were recommended.

Digital photography of the face was done before each session and 1 week after last session (frontal and side views). Visual assessment was done at fourth and eighth week from the end of treatment.

All of the treated patients were reached by phone and asked to rate their satisfaction on our assumed scale ranging from 1 to 5 (1 = no improvement, 2 = slight improvement, 3 = moderate improvement, 4 = good improvement, and 5 = worsened), for overall improvement and individual satisfaction with skin texture, skin sagging/firmness, skin pigmentation, wrinkles, acne, acne scars, wide pores, and facial pallor. In addition, using the same rating scale, three independent physicians rated the overall aesthetic improvement by assessing before and after digital photographs on a scale ranging from 1 to 5 (1 = no improvement, 2 = slight improvement, 3 = moderate improvement, 4 = good improvement, and 5 = worsened).

Data were coded and entered using the statistical package SPSS version 25 (IBM Corp., Armonk, NY, USA). Data were summarized using mean, SD, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired *t*-test when comparing two groups and analysis of variance with multiple comparisons post-hoc test when comparing more than two groups. *P* values less than 0.05 were considered as statistically significant [8].

Photographs were captured with a standardized digital camera, and clinical changes of facial skin were documented over time with the same photographer and the same camera settings.

## Results

The study yielded visible improvement in all included items including roughness, dullness, pallor, acne, acne

scars, wide pores, lack of firmness, and wrinkles with varying degrees, as shown in Table 1 and Figs. 1–3.

There was a significant relation between a larger number of sessions and the improvement in acne scars, texture, and wide pores, as shown in Table 2.

There was good acne scar improvement with mean number of sessions of 5.33) ($P$ = 0.002), good texture improvement with mean number of sessions = 5.25 ($P$ < 0.001), and good wide pores improvement with mean number of sessions of 4.00 ($P$ = 0.016).

An interesting finding also was that wide pores revealed better improvement in older patients ($P$ = 0.035). Moreover, patient satisfaction was significantly related with number of sessions ($P$ = 0.001).

## Discussion

PRP has been reported to augment dermal elasticity by stimulating the removal of photo-damaged extracellular matrix components and inducing the synthesis of new collagen by dermal fibroblasts via various molecular mechanisms. It contains seven fundamental growth factors: platelet-derived growth factors (PDGFaa, PDGFbb, and PDGFab), transforming growth factor β (TGFβ1 and TGFβ2), epithelial growth factor, and vascular endothelial growth factor. These growth factors modulate cell proliferation, differentiation, and angiogenesis. Studies have shown that adult

**Figure 1**


A noticed improvement in skin texture, acne, and increased facial glow.

**Table 1 The percentage of overall improvement in all items and patient satisfaction**

| Items | Degree of improvement | Count | % | Items | Degree of improvement | Count | % |
|---|---|---|---|---|---|---|---|
| Acne scar improvement | Mild | 2 | 13.3 | Dullness improvement | Mild | 14 | 51.9 |
| | Moderate | 7 | 46.7 | | Moderate | 7 | 25.9 |
| | Good | 6 | 40.0 | | Good | 6 | 22.2 |
| Texture improvement | Mild | 12 | 40.0 | Wide pores improvement | No | 3 | 12.5 |
| | Moderate | 10 | 33.3 | | mild | 15 | 62.5 |
| | Good | 8 | 26.7 | | Moderate | 5 | 20.8 |
| Firmness improvement | Mild | 17 | 56.7 | | good | 1 | 4.2 |
| | Moderate | 13 | 43.3 | Wrinkles improvement | mild | 9 | 50.0 |
| Acne improvement | No | 3 | 16.7 | | Moderate | 7 | 38.9 |
| | Mild | 6 | 33.3 | | good | 2 | 11.1 |
| | Moderate | 5 | 27.8 | Patient satisfaction | mild | 3 | 10.0 |
| | Good | 4 | 22.2 | | Moderate | 12 | 40.0 |
| Blushing | No | 6 | 20.0 | | good | 15 | 50.0 |
| | Mild | 16 | 53.3 | | | | |
| | Moderate | 6 | 20.0 | | | | |
| | Good | 2 | 6.7 | | | | |

**Table 2 The relation between number of sessions and improvement in texture, acne scars and wide pores**

| Items | Degree of improvement | Number of sessions | | | | |
|---|---|---|---|---|---|---|
| | | Mean | SD | Minimum | Maximum | *P* |
| Acne scar improvement | Mild | 3.00 | 0.00 | 3.00 | 3.00 | 0.002 |
| | Moderate | 3.86 | 0.69 | 3.00 | 5.00 | |
| | Good | 5.33 | 0.82 | 4.00 | 6.00 | |
| Texture improvement | Mild | 3.58 | 0.67 | 3.00 | 5.00 | <0.001 |
| | Moderate | 4.60 | 0.84 | 3.00 | 6.00 | |
| | Good | 5.25 | 0.89 | 4.00 | 6.00 | |
| Wide pores improvement | No | 3.00 | 0.00 | 3.00 | 3.00 | 0.016 |
| | Mild | 4.40 | 0.99 | 3.00 | 6.00 | |
| | Moderate | 5.40 | 0.89 | 4.00 | 6.00 | |
| | Good | 4.00 | - | 4.00 | 4.00 | |

*$P$>0.05 is statistically insignificant.

**Figure 2**


A noticed improvement in skin dullness, wide pores, and texture.

**Figure 3**


A noticed improvement in acne scars and skin texture.

mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells express cell membrane receptors to growth factors in PRP. These transmembrane receptors in turn induce an activation of an endogenous internal signal protein, which causes the expression of (unlocks) a normal gene sequence of the cell such as cellular proliferation, matrix formation, osteoid production, and collagen synthesis, and they act through the stimulation of normal healing, just much faster [9,10].

PRP has anti-inflammatory properties. It decreases the inflammation through inhibitory effects on natural factor κB activity which is the cornerstone in inflammatory process in active acne, which may explain improvement in active acne patients. It has also inhibitory effect on proinflammatory interleukin-6 (IL-6) while increasing tissue inhibitor of matrix metalloproteinases [11,12].

HA is one of the most hydrophilic molecules in nature. HA binds to water giving it a stiff viscous quality. Moreover, HA has been reported to be an appropriate choice to support dermal regeneration in hand with augmentation as many studies showed the efficacy of HA mesotherapy in the prevention and treatment of skin aging, and showed a decrease of proapoptotic matrix metalloprotease-1 and proinflammatory ILs (IL1β and IL6), as well as an increase in collagen-1. So, injections of HA within the intradermal layer create an effect comparable to that of a basin of hydration in the dermis by bringing water into the extracellular matrix [13,14].

So, combining PRP and HA gains the benefit of both of them by increasing collagen induction by PRP and dermal hydration by HA plus the antiapoptotic and anti-inflammatory effect.

Microneedling has been used for a broad range of applications including skin rejuvenation, acne scarring, wrinkles, surgical scars, dyschromia, melasma, enlarged pores, and transdermal drug delivery. This minimally invasive procedure got a specific interest for patients who desire measurable clinical results from treatments with minimal recovery time [15].

We conducted the present clinical study on 30 patients with different signs of unhealthy and aging skin including roughness, dullness, pallor, acne, acne scars, wide pores, lack of firmness, and wrinkles. The present study spent about 15 months to be accomplished, with no serious or persistent adverse effects detected. The treatments were well tolerated, with only minor adverse effects during and after the treatments, including erythema, spotty bleeding, and burning sensation. These resolved within few days without any treatment. This was in agreement with El-Domyati *et al.* [6], who reported erythema and spotty bleeding during the procedure and even after the first session, satisfactory results to the patients were observed, which supports the suggestion that HA and PRP treatments may have additive effects.

The study question was, is a combination of PRP and HA beneficial in face rejuvenation via microneedling?

In our clinical trial study, we collected data through our assumed VAS score assessed by both investigators and patients. VAS score ranges from 1 (none) to 4 (severe) concerning skin texture, skin sagging/firmness, skin dullness, wrinkles, active acne, acne scars, and facial pallor. Mild cases had the score of 2, moderate cases had the score of 3, and severe cases with 4 score. Three independent physicians rated the overall aesthetic improvement by assessing before and after digital photographs on a scale ranging from 1 to 5 (1 = no improvement, 2 = slight improvement, 3 = moderate improvement, 4 = good improvement, and 5 = worsened).

Data were summarized using mean, SD, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables.

There are various PRP preparation methods. Although an optimal platelet concentration is still not known, a platelet concentration of more than 1 million/μl (~4–7 times the mean levels) is generally regarded as the therapeutically effective concentration of PRP [16].

Concerning the activation of platelets, no activator was used because activation agents include $CaCl_2$, thrombin, dry needling (multiple tissue perforations before injections to release thrombin in the local environment), and calcium gluconate, and also collagen is a natural activator of PRP, thus when PRP is used in soft tissue, it does not need to be exogenously activated [17].

We applied platelet-poor plasma part at the end of every session with intention to inject more cells, to further hydrate the skin.

This study revealed that number of sessions has a direct effect on clinical outcome, including acne scars, which showed significant improvement ($P$ = 0.002) with increase in number of sessions, and this agrees with Tantari and Murlistyarini [18].

Moreover, texture showed very significant improvement with increased number of sessions ($P$ < 0.001), which was in agreement with a previous study by Hogan *et al.* [19].

Wide pores improvement also revealed direct relation with number of sessions ($P$ = 0.016).

An interesting finding also was that wide pores revealed better improvement in older patients ($P$ = 0.035), and also patients' satisfaction was significantly related with number of sessions ($P$ = 0.001).

This is in contrary to a previous study by Choi *et al.* [20], which mentioned that there was a direct relation between wrinkle improvement and number of sessions. In our study, there was no significant relation between number of sessions and wrinkles improvement, which is because a larger sample of older participant (only 6.7% with obvious wrinkles in our study) and a larger number of sessions is required to evaluate this relation.

So, further studies with larger samples are required as PRP sessions can be performed many times until the targeted cosmetic results are obtained because growth factors are not mutagenic; they act through normal gene regulation [21].

All included items of unhealthy skin appearance including roughness, dullness, pallor, acne, acne scars, wide pores, lack of firmness, and wrinkles showed noticed improvement with different degrees.

Another previous study by Ulusal [22] revealed that even after the first treatment, this combination therapy with HA and PRP provided satisfactory results for facial rejuvenation, which supports that they may have additive effects, and this agrees with the present study.

According to the present study, we found that application of PRP mixed with HA conducted via microneedling procedures is safe to perform, generating effective facial skin rejuvenation, with high levels of patient satisfaction with no complications or reports of adverse effect.

Hashim *et al.* [23] proved that PRP appears to augment the cosmetic outcomes of microneedling without increasing the risk for adverse events by comparing the results with treatment with microneedling only, and this goes in hand with the present study.

In the present study, we used microneedling instead of injections as a method of PRP and HA delivery and that gained the advantage of avoiding repeated trauma to reticular dermis, which may result in inflammation and fibrosis as revealed in a study by Charles-de-Sá *et al.* [24], who mentioned that in the long term, the presence of inflammation and microangiopathy caused by PRP injection could lead to trophic alteration of the skin and the precocious aging process.

Concerning the relation between age and overall improvement, more large-scale studies are needed to evaluate better results.

However, for the relation between number of sessions and the improvement in firmness, dullness, acne, and wrinkles, more studies including participants in a specific age with a larger number of sessions are needed to evaluate better results.

## Conclusion

Combination of PRP and HA is an efficient and safe method of facial skin rejuvenation by microneedling method.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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