

Efficacy of platelet rich plasma (PRP) on skin rejuvenation: A systematic review

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Background: With the increase in life expectancy, middle aged and elderly people comprise a substantial percentage of the population worldwide. Since aging often manifests itself in the human skin, skin rejuvenation methods have gained a lot of popularity. Current medical modalities such as botulinum toxin injection, fillers, and laser therapy can provide symptomatic relief of skin aging signs without the ability to induce changes at a cellular level. In recent years, Platelet Rich Plasma (PRP) therapy has been emerging as a revolutionary treatment with the ability to induce cell growth in the skin, which results in retarding and reversing the aging process. Therefore, this study was conducted to determine the efficacy of PRP therapy in skin rejuvenation.

Methods: A comprehensive search was conducted using PubMed, Google Scholar, and Cochrane library. Articles published only in English from 2000 to 2015 were included. The keywords used were platelet rich plasma, PRP, skin rejuvenation, skin aging, skin, platelet rich plasma therapy.

Results: A total of ten articles were retrieved and included for analysis. Eight studies showed improvement of the skin wrinkles. The other two studies reported improvements in the nasolabial fold. Clinical assessments were based on patient satisfaction or feedback questionnaire, pre- and post-treatment photography, and skin biopsy. The results showed a significant improvement in the skin appearance, elasticity, texture, and homogeneity.

Conclusion: In conclusion, PRP therapy is an effective and safe treatment for skin rejuvenation with no significant difference in varying techniques of PRP preparation and injection.

Keywords: platelet concentrates; platelet rich plasma; skin rejuvenation

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INTRODUCTION

The global population had experienced an increase in life expectancy since the last five decades leading to intensive and inquisitive search for methods and interventions in order to slow down the signs of aging. Recent scientific and technological advancements have made it possible to reduce the manifestation of aging. According to the statistical reports released by the American Society for Aesthetic Plastic Surgery, there has

been an increase of more than 300% in the total number of skin rejuvenation procedures since 1997 ¹. Surgical and nonsurgical procedures account for 33% and 67% of the procedures used to rejuvenate the skin, respectively ¹. It is evident that there is a higher demand for nonsurgical procedures.

Visible marks of the aged skin include dryness, UV dyschromia, wrinkles, and sagging skin. Histologically, the aged skin is characterized by a flattened dermal-epidermal junction, dermal atrophy, and minimal fibroblasts as the photo-

damaged skin contains unorganized collagen fibrils and undergoes elastic degeneration. To summarize, the primary goals of medical aesthetic treatments are to minimize the facial volume loss and reduce the appearance of wrinkles, as they are among the most obvious changes of the aged skin. Wrinkle formation in the aging skin occurs due to the degeneration of the collagen fibers and deposition of the elastic content of the skin. These changes lead to damage to the dermal extracellular matrix due to the impairment of the structural integrity. The skin resilience is also reduced². Currently, there are a number of methods for skin rejuvenation including laser, light and other energy-based treatments, chemical peeling, and other non-ablative methods. All of these methods result in a more youthful appearance but each has its own advantages and disadvantages. Dermal fillers (DF) and botulinum injections are quick and effective treatments to eliminate the wrinkles. Both present no downtime, but DF injection may result in short-term effects such as necrosis and skin irregularities and botulinum injection may cause undesired muscle paralysis. Laser therapy and chemical peeling are other treatment options which may result in side effects such as skin burning and alteration of the skin color, particularly in patients with a darker skin type. Recently, regenerative dermatologic treatments have been added to the regimen to further enhance the clinical results and minimize the downtime. Studies have shown that application of a mixture of growth factors may stimulate collagen synthesis and epidermal thickening, which improves the skin tone, minimizes the wrinkles, and repairs other signs of facial aging^{3,4}. In this regard, Platelet Rich Plasma (PRP) therapy for skin rejuvenation is performed by injecting the patient's own platelet and fibrin into the skin. It has been reported to activate and stimulate cell proliferation and collagen synthesis, minimize the wrinkles, and improve the overall skin appearance^{5,6}.

PRP is a product of the whole blood that has a high concentration of platelets. It contains a number of different growth factors and other cytokines that are released through degranulation and stimulate healing of hard and soft tissues⁷. Seven growth factors and three adhesion molecules have been shown to have higher concentrations in PRP compared to the whole blood, thus accelerating

cell regeneration at the site of injection as well as during its topical application. Despite the fact that PRP is a widely used terminology and abbreviation, it can be further classified based on harvesting techniques of platelet from the whole blood i.e. pure platelet-rich plasma (P-PRP), leukocyte- and platelet-rich plasma (L-PRP), pure platelet-rich fibrin (P-PRF) (also known as PRFM), and leukocyte- and platelet-rich fibrin (L-PRF). Its classifications are also crucial factors of consideration as they are closely associated with the success rate of platelet therapy⁸. The platelet-rich fibrin matrix (PRFM) is formed by adding a small amount of calcium chloride (CaCl_2) to PRP to initiate fibrinogen cleavage and fibrin polymerization. The PRFM can be injected within 10 to 12 minutes after adding CaCl_2 using a 30-gauge needle. If the mixture is kept for a longer time, polymerization of the fibrin yields a gel or solid fibrin clot.

Even though the efficacy of PRP for skin rejuvenation remains uncertain, it is widely used in medical aesthetics with many physicians making promising claims¹. This calls for thorough evaluation of several possible complications such as the risk of rejection, infection, and allergic reactions. In this regard, this study was conducted to review the clinical evidence in order to determine the efficacy of PRP therapy for skin rejuvenation.

METHODS

A systematic literature review was conducted. Electronic databases such as Cochrane library, PubMed, and Google Scholar were searched for relevant literature. The included keywords were platelet rich plasma, PRP, skin aging, skin rejuvenation, skin lines, skin texture, skin wrinkle, topical PRP, topical platelet rich plasma, platelet rich plasma injection, and platelet rich plasma therapy. Randomized clinical trials (RCT), retrospective studies, case studies, and case reports published in English from 2000 to 2014 were included. Data were extracted from the selected literature using a research table. Details such as the sample size, duration of the study, patient, intervention, comparison, outcomes and study design (PICO) of the reviewed papers were also noted. Pre-procedure and post-procedure cares, assessment methods, outcomes, and complications of the studies were summarized in the tables and analyzed.

RESULTS

The search was initiated from PubMed using the mentioned keywords. The initial results showed several articles on "platelet rich plasma". Then, individual searches were conducted for keywords, such as "aging skin", "skin wrinkles", and "skin rejuvenation". Thereafter, a combination of keywords was used. Two research articles were chosen to be included in this study. No related article was found on Cochrane library. Meanwhile, the use of the keywords individually or in combination to search Google Scholar resulted in 474 articles on platelet rich plasma. a manual search was performed using a combination of keywords. Abstracts of the articles with relevant titles were screened. Research articles were included upon fulfillment of all inclusion criteria. Upon completion of the literature search, ten articles were extracted from PubMed and Google Scholar involving a total of 675 participants. The details of included articles are shown in Table 1. Comparison of the results and side effects of the studies are listed in Table 2. The details of PRP preparation including starting blood, methodology of PRP preparation, and the technique of PRP injection are listed in Table 3. All platelet concentrates were used for skin rejuvenation. Nine studies recruited 653 patients for PRP monotherapy whilst 11 patients received PRP therapy in combination with laser and another 11 patients were controls. Sixty-five patients in two studies received PRFM for skin rejuvenation. All PRP concentrates were injected intradermally with the exception of one study which incorporated topical applications for 22 patients. None of the patients withdrew or refused follow up in all studies. PRP was activated prior to injection in 8 studies with the exception of one study in which PRP was injected for 37 participants without activation. However, the details of PRP preparation and activation were not clearly explained in one study on 30 participants conducted by Banihashemi *et al.*⁹.

DISCUSSION

PRP therapy is widely used for various medical conditions such as repair and regeneration of the bone and cardiac cells. However, variations in the preparation of PRP and treatment methodology

Table 1. Selected studies with details of PICO framework of each study.

Author/Study design	Title	Problem/Population	Intervention	Comparison	Outcome
Banihashemi <i>et al.</i> ⁹ Case Series	Effect of Platelets Rich Plasma on Skin Rejuvenation	Individuals with Glogau score of II and III	Subdermal and intradermal injections of 1 cc PRP in upper zone of face, 1 cc in cheeks and 1cc in lower zone of face	Pre and post treatment	There was inconsistency in self-between assessments by patients and the physician, and a mild to moderate improvement in periorbital wrinkle and dyschromia was reported.
Kapoor ¹⁰ Case Series	Platelet rich plasma a novel treatment for skin rejuvenation	Individuals with Glogau score of II and III (Moderate to advanced wrinkle)	Superficial dermal or deep dermal or subdermal injection of activated PRP	Pre and post treatment	Overall results were found to be satisfactory to good on the graded scale. There was improvement in skin texture and a volatizing effect on the face was noted.
Mehryan <i>et al.</i> ¹¹ Case Series	Assessment of efficacy of platelet-rich plasma (PRP) on infraorbital dark circles and crow's feet wrinkles	Fitzpatrick skin types III and IV, and a history of infraorbital dark circles and/or mild periorcular wrinkles for at least 1 year	Intradermal injections of PRP (0.5 ml and 1.5 ml) into tear trough area and crow's feet wrinkles on each side	Pre and post treatment	The improvement in infraorbital color homogeneity was statistically significant, but no statistically significant changes were observed in melanin content, stratum corneum hydration, wrinkles volume, and visibility index.
Mikhael and El-Esawy ¹² Case series	Skin rejuvenation with autologous concentrated platelet-rich plasma	Patients with different types of facial wrinkles	Intradermal injection of activated PRP (3ml) at six facial locations	Pre and post treatment	Good results were observed in the skin homogeneity and emotional status of the patient without serious side effects.

Table 1. (continued).

Author/Study design	Title	Problem/Population	Intervention	Comparison	Outcome
Shin <i>et al.</i> ¹³ Case-control study	Platelet-Rich Plasma Combined with Fractional Laser Therapy for Skin Rejuvenation	Korean women with skin phototypes IV–V	Combined topical application of PRP (3ml) and fractional laser treatment or fractional laser treatment alone	Study group who undergone combination of PRP and laser treatment with control group who had only laser treatment	PRP combined with fractional laser increased subject satisfaction and skin elasticity and decreased the erythema index.
Solafani ¹⁴ Case series	Safety, Efficacy, and Utility of Platelet-Rich Fibrin Matrix in Facial Plastic Surgery	Patients with fine rhytids & deep folds, acne scar, volume-depleted midface region	Intradermal and subdermal or preperiosteal plane injection of activated PRP (0.3ml to 2.5ml)	Pre and post treatment	Most patients were satisfied with the results of their treatments although 1 patient felt that there was limited or no improvement after 2 treatments. No swelling was observed lasting longer than 5 days, and minimal bruising was noted lasting for 1 to 3 days.
Amgar <i>et al.</i> ¹⁵ Case Series	Using objective criteria to evaluate cosmetic effects of platelet rich plasma	Class II or III on the Glogau scale of photoaging (Moderate to advanced wrinkle)	Intradermal injection of PRP (without CaCl ₂) (4ml) into the lower part of the face	Pre and post treatment	An average of 24% improvement in the anisotropy coefficient after the third week. The TEWL and micro-relief parameters also improved significantly
Redallei <i>et al.</i> ¹⁶ Case series	Face and neck revitalization with platelet-rich plasma (PRP): clinical outcome in a series of 23 consecutively treated patients.	Patients with skin wrinkle in face and neck	Intradermal injection of activated PRP (4ml)	Pre and post treatment	A good improvement of skin texture and elasticity, a volume increase at the injection site of nasolabial folds, forehead scars almost disappeared, acne scars were also treated with very good results. No serious and persistent side effects were detected.
Zenker ¹⁷ Case series	Platelet-rich plasma (PRP) for facial rejuvenation	Patient with wrinkle and loose skin in face and neck	Intradermal, superficial and deep dermal injection of PRP (4-6ml)	Pre and post treatment	The results obtained were age-dependent. The younger patients (less than 35 years) were found to respond more quickly. Their main indication was skin rejuvenation and the prevention of skin aging. For this group, treatment every 12 to 24 months was sufficient. Patients up to 45 years required a second treatment 9 to 12 months after the first one, as well as annual booster injections.
Solafani ¹⁸ Case series	Platelet-rich fibrin matrix for improvement of deep nasolabial folds	Patients with deep nasolabial folds	Intradermal injection of activated PRP (4ml)	Pre and post treatment	Maximal correction and significant long-term diminution of deep nasolabial folds with significant reduction in the mean WAS score. No patient noted any fibrosis, irregularity, hardness, restricted movement, or lumpiness.

Table 2. Comparison of sample size, participants' age, assessment methods and outcomes.

Author	No. of patients	Age range	No. of injection sessions	Duration of follow up	Assessment method (s)	Conclusion
Banihashemi <i>et al.</i> ⁹	30	35- 55 years (mean= 45.1)	two sessions with 3 months interval	3 and 6 months follow up	Personal judgment of patients and observation of before and after treatment photography by the physician and a dermatologist unaware of the order of photos	Best effects of PRP in rejuvenation were specified to improvement of periorbital darkness and decreasing skin wrinkles
Kapoor ¹⁰	50	30-63	3 treatment sessions 1 month apart	1 month after last injection (overall 4 months)	Comparing photographs from pre and post treatment, patient satisfaction score, physician satisfaction score	PRP is effective especially in small wrinkles and improves skin texture and elasticity
Mehryan <i>et al.</i> ¹¹	10	26-61 years (mean= 41.2)	One	1 week, 1 & 3 months	Melanin content of the infraorbital, epidermal stratum corneum hydration, global assessment by 3 independent and blinded investigators using before and after photographs, patient satisfaction	Platelet-rich plasma may have the potential to improve the infraorbital dark circle in terms of color homogeneity of the region.
Mikhael and El-Esawy ¹²	20	30-55 years (mean= 41.2)	3 sessions with one month interval	1 month after last session of injection	Patient satisfaction score & facial wrinkle scale for objective and subjective evaluation, and patient examination.	PRP is an effective treatment in skin rejuvenation without serious side effects.
Shin. <i>et al.</i> ¹³	11 case subjects + 11 controls	30-56 years (mean= 43.7)	3 sessions after fractional Laser at 4-weeks intervals	before the first treatment and 1 month after the last treatment session	Subjective satisfaction scale, improvement score according to blinded investigators (using standardized photography), biophysical measurements, and skin biopsies.	PRP with fractional laser treatment is a good combination therapy for skin rejuvenation. Keratinocyte and fibroblast proliferation and collagen production can explain the capacity of PRP to increase dermal elasticity.
Sciafani ¹⁴	50	23-72 (mean= 51.3)	average of 1.6 injections (range, 1-5 treatments)	3-30 months for a mean of 9.9 months	Serial photographs taken before and 3 and 12 months after a single treatment, patient satisfaction questionnaire	Autologous PRP treatment is a well-tolerated, excellent choice for use in the face.
Amgar <i>et al.</i> ¹⁵	37	40-60	Two sessions of injections	1, 3 or 4 months	Biometric parameters, including anisotropy, transepidermal water loss (TEWL), micro-relief, and hydration	A good anti-aging effect was observed after one PRP treatment which could last for up to 10 months. An additional predictor for a PRP treatment was found to be the initial hydration status of the skin. PRP repairs the skin characteristics which need repair more effectively and may be used as an anti-aging prophylactic method for other characteristics.
Redallei <i>et al.</i> ¹⁶	23	28-70 years (mean =47)	3 times	4 months	Comparing the pre and post treatment photography, by evaluating the spider improvement for 8 parameters of nasolabial folds, horizontal neck bands, skin micro-relief, homogeneity, texture and tonicity, snap test, crow's feet lines, final patient's satisfaction questionnaires, by the physician's impression	An easy-to-use and well tolerated technique that can be performed favorably in all small skin wrinkles, as well as in skin texture and elasticity. Good results in skin homogeneity. Objective clinical results were good. Patient satisfaction was very high.

Table 2. (continued).

Author	No. of patients	Age range	No. of injection session	Duration of follow up	Assessment method (s)	Conclusion
Zenker ¹⁷	418 from Germany, Japan, UK, Israel	38-79 years	2 to 4 times depend to the age of patient	3, 6, 9, 12 and 24 months following the primary injections.	Comparing the pre and post treatment photography	PRP is safe and creates an immediate, long lasting volumetric effect with natural looking results with high levels of patient satisfaction. The technique is easy to perform and has virtually no side-effects.
Solafani ¹⁸	15	30-56 years	4	1, 2, 6, and 12 weeks after treatment	Comparing photographs before and after treatment; NLFs were rated by the treating physician before and after treatment using WAS and patients rated their appearance at each post-treatment visit using the Global Aesthetic Improvement Scale.	PRP can provide significant long-term diminution of deep NLFs without the use of foreign materials.

such as effective concentration of platelet, mode of delivery, and application, direct injection or activation prior to injection need to be carefully investigated to achieve optimum, desired and consistent results. Inconsistency of practice and methodology in PRP therapy makes the standardization of this treatment method very challenging. Here, we discuss different variables present in PRP therapy for skin rejuvenation according to the findings from the selected articles. These studies focused on satisfying the need for alternative and safe skin rejuvenation methods either by injection or topical use of PRP alone or in combination with other aesthetic modalities. On the other hand, the present review critically evaluated the outcome of these studies to shed light on the safety and efficacy of PRP therapy for skin rejuvenation. The study design, age range of participants, number of injection sessions, duration of follow-up, technique of PRP application, and assessment methods were extracted from each study and compared.

In the selected articles, a study by Amgar *et al.*¹⁵ evaluated the effect of PRP without any activation prior to injection and a study by Shin *et al.*¹³ used PRP gel. The other eight studies used CaCl₂ for PRP activation. Thereafter, the resultant PRFM was injected to enhance skin rejuvenation. Since all of these studies reported some degrees of improvement for different skin conditions, it can be concluded that both activated and non-activated PRP demonstrate positive effects on skin regeneration. In line with this finding, Zandim *et al.*¹⁹ reported that 10% CaCl₂ was a suitable activating substance for platelets but PRP could also be injected without prior activation. It is believed that a high percentage of platelets can be fully activated after injection via routine procedures in the human body. In this review, PRP was used for wrinkle treatment in eight studies while the other two articles reported PRP treatment for the nasolabial fold (NLF). Restoration of the facial appearance using Botox and dermal fillers is considered safe and non-invasive. However, the application of the patient's own blood products such as PRP might be more desirable compared to Botox and dermal fillers. In addition, other skin characteristics such as periorbital darkness, skin texture and elasticity, acne scars, transepidermal water lost (TEWL), and skin homogeneity were also

Table 3. Details of PRP preparation and injection technique.

Author	Starting blood and PRP preparation	Technique of PRP injection	Commercial kit
Banihashemi <i>et al.</i> ⁹	Not clearly stated	Threading technique	No
Kapoor ¹⁰	20 ml blood, single centrifugation, activation by calcium chloride	Mesotherapy, linear threading, fan-like placement or cross hatching	No
Mehryan <i>et al.</i> ¹¹	10 ml blood, double centrifugation, activation by calcium chloride in the proportion of 0.1 ml of CaCl ₂ per 0.9 ml of PRP	Details is not mentioned	Tubex® MOOHAN
Mikhael & El-Esawy ¹²	10 ml blood, double centrifugation, activation by calcium chloride in the proportion of 0.1 ml of CaCl ₂ per 0.9 ml of PRP	Linear threading and fanning' injection in the nasolabial fold, 'serial puncture' for forehead and row's feet, 'linear threading' in the glabellar furrows	No
Shin <i>et al.</i> ¹³	12 ml blood, double centrifugation, activation by calcium chloride in the proportion of 0.1 ml of CaCl ₂ per 0.9 ml of PRP	Topical	No
Sclafani ¹⁴	9 ml blood, single centrifugation, activation by calcium chloride	Variety of methods depend to the indications	(Selphyl®; Aesthetic Factors, Wayne
Amgar <i>et al.</i> ¹⁵	Volume of blood not mentioned. Single centrifugation, no activation of PRP	Has not been mentioned	MyCells® kit
Redallei <i>et al.</i> ¹⁶	16 ml blood, single centrifugation, activation by calcium chloride	Depend to the area of face one of these techniques: microponfi, wave, "linear retrograde or tunnelling	CE marked RegenLab ® Kit
Zenker ¹⁷	10 ml blood, single centrifugation, no activation of PRP	Linear threading, fan technique or cross hatching technique.	MyCells® kit
Sclafani ¹⁸	9 ml blood, single centrifugation, activation by calcium chloride	Linear threading technique or serial puncture injections	(Selphyl®; Aesthetic Factors, Wayne

assessed after PRP therapy in the selected studies. All the studies reported a significant improvement in the skin texture and removal of the skin wrinkles. Both patients and physicians were satisfied with the outcomes. The results were also significant for the improvement of wrinkles when patients received a combination of PRP and laser therapy. In a study by Shin *et al.*¹³, a combination of fractional laser therapy and platelet concentrates produced better results when compared to mono-therapy with fractional laser. Fractional laser produces q micro thermal zone in the skin, which can increase the penetration depth of the platelet concentrate. Combination therapy was also reported to have better results in another study²⁰. Since topical application of PRP accelerates skin rejuvenation, it can be considered a superior method of application. As for the NLF, two selected studies showed that PRP had no effect on enhancing the skin volume, but improved the appearance of the NLF. The most common treatment for NLF augmentation is the injection of the dermal fillers which may lead to side effects such as granulomatous reaction, skin necrosis, and unwanted misplacement²¹. In contrast, platelet-rich fibrin matrix therapy showed no side effects. In these two studies, side effects

such as over-volumization, skin irregularity, and skin necrosis were not reported.

The age range of the study population was 23 to 72 years old. Both genders were included; however, females were the dominant group. Only one study conducted by Amgar *et al.*¹⁵ mentioned that improvement in the skin rejuvenation was age dependent and suggested the frequency as well as the intervals of PRP injection in each age group. It can be postulated that the age dependent results of PRP therapy might be associated with tissue repair mechanisms which are anticipated to work better in younger age groups. The regenerative capability of most tissues gradually declines with age due to both age-dependent changes in tissue-specific stem cells and also alterations of the environmental signals stimulating stem cells for tissue maintenance and repair²². Although there were no reports on the effect of age on skin rejuvenation in PRP therapy, age-dependent alterations in cellular responses to PRP therapy was previously reported in tissue engineering related researches^{23,24}. Some animal studies have shown a decrease in the expression of growth factor receptors due to aging. More specifically, a significant decrease has been observed in the expression of TGF-beta

receptor 1, FGF receptor, and VEGF receptor 2; and a less significant decrease has been noted in the expression of TGF-beta receptor 3 and PDGF receptor. An exception was VEGF receptor 1, a regulator of VEGF receptor 2 which did not show any age-dependent changes. These findings suggest that the decrease in the expression of growth factor receptors is a likely reason for the reduced PRP action with an increase in age²⁵. On the other hand, age-dependent skin fibroblast dysfunction, such as the reduced production of type I procollagen, is seen in aged fibroblasts. Laboratory studies conducted to stimulate the growth of fibroblasts have found that younger fibroblasts show a better response to growth factors²⁶. As fibroblasts are the main targets in PRP therapy, it is important to record whether the effect of this treatment is more prominent at a young age. In other words, it is necessary to investigate whether the duration of the beneficial effects of PRP therapy on skin improvement is longer in younger patients.

Other variables in these studies were the volume of the starting whole blood, single or double centrifugation, and the amount of injected PRP, number of sessions, use of ordinary test tubes or commercial tubes, and the method of injection. Since the normal platelet count has a wide range in humans, even if equal volumes of whole blood are used, the final concentration of platelets in PRP varies from one patient to another patient. However, none of the selected studies reported the final platelet concentration in PRP at the time of injection. It could be the primary reason for the difference in outcome in different patients in the same study who undergo the same treatment protocol because the injection of the same volume but different concentrations of PRP results in various amounts of growth factors and cytokines. Although the ideal concentration of platelets in PRP therapy is not identified, some studies have reported that concentrations 4 to 6 times more than the whole blood are sufficient to provide the benefit of PRP therapy²⁷. The higher concentration of platelet, up to 20 fold, had been reported to be obtained from whole²⁸. Generally, the composition of PRP and its preparation influence the cellular response of tissues and regulate its overall outcome in tissue repair²⁹.

One of the main limitations of the selected studies was their sample size except for one study that

recruited 418 participants¹⁷. The lack of a control group was a significant weakness of most studies. Only one study had matched case and control groups of 11 subjects.

A wide range of outcome assessments were used including the patient and physician satisfaction scale, blind clinical assessment, and the biophysical parameters of roughness, elasticity, and skin hydration, as well as erythema and melanin index. Biopsy and immunohistochemistry for matrix metalloproteinase were also carried out. However, most of these assessments were subjective, making it difficult to establish a sound comparison. However, all different assessment methods confirmed satisfactory results.

No study showed serious or permanent side effects. A burning sensation was a common finding in patients after the injection, which resolved without any treatment. It could be associated with adding calcium chloride to activate PRP. In addition, no study reported hyperpigmentation, hypopigmentation, serious infection, or hematoma. Based on the results of these studies, PRP therapy is a safe treatment method to improve the skin texture and remove the skin wrinkles.

With increased interest in using non-synthetic materials in different medical applications, PRP has attracted a lot of attention, especially in medical aesthetics which always deals with non-disease settings. Based on the results of this review, PRP therapy is a less invasive method compared to plastic surgery which demonstrated positive anti-aging effects on the skin. It is a simple technique which has favorable effects on all small skin wrinkles, skin texture, elasticity and homogeneity. Despite the existence of several PRP injection techniques, no significant differences have been reported. It is a safe treatment method for all skin types. The incidence of hyperpigmentation or hypopigmentation was not reported. This study showed PRP could be considered a safe, promising and effective method of skin rejuvenation. The results were significant when patients received a combination of PRP and laser.

The small sample size and lack of control group were the main limitations of the selected studies. Furthermore, the assessment method was not the same in all studies. As objective assessment of the wrinkles and skin texture is not easy to perform, most assessments are subjective and observation

is often the only evaluation, which calls for multi-centered well-controlled studies with larger sample sizes and longer follow-ups. Objective assessments should also be incorporated to confirm the efficacy and safety of PRP therapy in skin rejuvenation.

REFERENCES

1. The American Society for Aesthetic Plastic Surgery (ASAPS): Cosmetic Surgery National Data Bank Statistics. 2012. Available from: <http://www.surgery.org/media/statistics>. [Last Accessed: June 20, 2015]
2. Talwar HS, Griffiths CE, Fisher GJ, et al. Reduced type I and type III procollagens in photodamaged adult human skin. *J Invest Dermatol* 1995;105:285-90.
3. Fitzpatrick RE, Rostan EF. Reversal of photodamage with topical growth factors: a pilot study. *J Cosmet Laser Ther* 2003;5:25-34.
4. Fitzpatrick RE. Endogenous growth factors as cosmeceuticals. *Dermatol Surg* 2005;31:827-31.
5. Pietrzak WS, Eppley BL. Platelet rich plasma: biology and new technology. *J Craniofacial Surg* 2005;16:1043-54.
6. Lee JW, Kwon OH, Kim TK, et al. Platelet-rich plasma: quantitative assessment of growth factor levels and comparative analysis of activated and inactivated groups. *Arch Plast Surg* 2013;40:530-5.
7. Eppley BL, Pietrzak WS, Blanton M. Platelet-rich plasma: a review of biology and applications in plastic surgery. *Plast Reconstr Surg* 2006;118:e147-e59.
8. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol* 2009;27:158-67.
9. Banihashemi, M, Hamidi Alamdaran D, Nakhaeizadeh S. Effect of platelets rich plasma on skin rejuvenation. [Abstract]. The 2nd Annual Congress Stem Cells Research and Application. (22-23 May 2014, Mashhad-Iran). *Int J Pediatr* 2014; 2 (Supplement 3):55.
10. Kapoor S. Platelet rich plasma a novel treatment for skin rejuvenation. *Ann Geriatr Edu Med Sci* 2014; 1: 5-7.
11. Mehryan P, Zartab, H, Rajabi A, et al. Assessment of efficacy of platelet-rich plasma (PRP) on infraorbital dark circles and crow's feet wrinkles. *J Cosm Dermatol* 2014; 13: 72-8.
12. Mikhael NW, El-Esawy F. Skin rejuvenation with autologous concentrated platelet-rich plasma. *Egyptian J Dermatol Venereol* 2014, 34:5-9
13. Shin MK, Lee JH, Lee SJ, Kim NI. Platelet-rich plasma combined with fractional laser therapy for skin rejuvenation. *Dermatol Surg* 2012;38:623-30.
14. Sclafani AP. Safety, efficacy, and utility of platelet-rich fibrin matrix in facial plastic surgery. *Arch Facial Plast Surg* 2011;13:247-51.
15. Amgar G, Bonnet C, Butnaru A, Herault-Bardin F. Using objective criteria to evaluate cosmetic effects of platelet rich plasma. *PRIME* 2011;1: 30-41.
16. Redaelli A, Romano D, Marciano A. Face and neck revitalization with platelet-rich plasma (PRP): clinical outcome in a series of 23 consecutively treated patients. *J Drugs Dermatol* 2010;9:466-72.
17. Zenker S. Platelet rich plasma (PRP) for facial rejuvenation *J Médesthetchirderm* 2010;37:179-83.
18. Sclafani AP. Platelet-rich fibrin matrix for improvement of deep nasolabial folds. *J Cosm Dermatol* 2010;9:66-71.
19. Zandim BM, Souza MV, Magalhães PC, et al. Platelet activation: ultrastructure and morphometry in platelet-rich plasma of horses. *Pesq Vet Bras* 2012;32:83-92.
20. Zhu JT, Xuan M, Zhang YN, et al. The efficacy of autologous platelet-rich plasma combined with erbium fractional laser therapy for facial acne scars or acne. *Mol Med Rep* 2013;8:233-7.
21. Downie JB, Grimes PE, Callender VD. A multicenter study of the safety and effectiveness of hyaluronic acid with a cohesive polydensified matrix for treatment of nasolabial folds in subjects with Fitzpatrick skin types IV, V, and VI. *Plast Reconstr Surg* 2013;132:41S-7S.
22. Conboy IM, Rando TA. Aging, stem cells and tissue regeneration: lessons from muscle. *Cell Cycle* 2005;4:407-10.
23. Mastrangelo A, Magarian E, Palmer M, et al. The effect of skeletal maturity on the regenerative function of intrinsic ACL cells. *J Orthop Res* 2010;28:644-51.
24. Mastrangelo A, Haus B, Vavken P, et al. Immature animals have denser anterior cruciate ligament wound site cell repopulation than adolescent or adult animals. *J Orthop Res* 2010; 28: 1100-6.
25. Vavken P, Saad FA, Murray MM. Age dependence of expression of growth factor receptors in porcine ACL fibroblasts. *J Orthop Res* 2010;28:1107-12.
26. Goldstein S, Harley CB. In vitro studies of age-associated diseases. *Fed Proc* 1979;38:1862-7.
27. Driver VR, Hanft J, Fylling CP, et al. A prospective, randomized, controlled trial of autologous platelet-rich plasma gel for the treatment of diabetic foot ulcers. *Ostomy Wound Manage* 2006 52:68-70.
28. Araki J, Jona M, Eto H, et al. Optimized preparation method of platelet-concentrated plasma and non coagulating platelet derived factor concentrates: maximization of platelet concentration and removal of fibrinogen. *Tissue Eng Part C Methods* 2011; 2012;18:176-85.
29. Wasterlain AS, Braun HJ, Dragoo JL. Contents and formulations of platelet-rich plasma. *Op Tech Orthop* 2012, 22:33-42.