International Journal of Sciences: Basic and Applied Research (IJSBAR)

ISSN 2307-4531
(Print & Online)

http://gssrr.org/index.php?journal=JournalOfBasicAndApplied

Comparative Study: PRP Enhanced Fat Graft Versus Fat Graft Alone in Treatment of Postacne Scars with Clinical and Histopathological Eyes

Omar Ahmed Azzam[a], Maamoun Ismail[b], Laila Rashed[c], Ahmed Tarek Atta[d], Naglaa Sameh Zaki[e], Hamed M. Kadry[f], Pakinam Ibrahim Nabil Mostafa[g*]

[a,e,g] *Department of Dermatology, Kasr Alainy medical school, Cairo University, 11562, Cairo, Egypt*

[b,d,f] *Department of Surgery, Kasr Alainy medical school, Cairo University, 11562, Cairo, Egypt*

[c] *Department of Biochemistry, Kasr Alainy medical school, Cairo University, 11562, Cairo, Egypt*

[a]*Email: doc.omarazzam@gmail.com*

[f]*Email: hkadry@kasralainy.edu.eg*

[g]*Email: pakinamnabil@kasralainy.edu.eg*

Abstract

Fat grafting has a role in rejuvenation owing to its mesenchymal cell precursor content especially with growth factors added. Platelet Rich Plasma (PRP) is known for its high growth factor content. The objective of this study is to compare the effect of PRP when added to fat graft in acne scars. 28 patients were randomly divided into 2 groups. Group A was treated with fat grafting while group B was treated with PRP enhanced fat grafting. All patients received a single treatment session. Assessment was conducted by comparing digital photos and biopsies before and after 6 months of treatment. The results shows that acne scars improved with PRP enhanced fat graft (93%) more than fat graft (64%). The biopsy results also confirmed the significantly better improvement for PRP group (85.7%) than the fat graft group (58%) (p=0.042).

---

* Corresponding author.
pakinamnabil@kasralainy.edu.eg

PRP has provided an enhancement of fat grafting in treatment of post acne scars. Icepick scars were better treated by fat grafting alone, while rolling and boxcars showed better results with the addition of PRP.

Keywords: Fat graft; PRP; Acne scars

1. Introduction

1.1. Review of Literature

Acne scarring is an unfortunate, permanent complication of acne vulgaris, which may be associated with significant psychological distress [1]. Its treatment has traditionally had limited success [2]. There is no general recipe; each scar and each patient are treated individually according to their characteristics [3]. Fractional ablative lasers have been widely used in acne scars, showing a favorable outcome despite the possible drawbacks [4]. Also, radiofrequency has emerged recently and its devices with fractional technology proved equal results to fractional erbium in acne scars [5].

Autologous fat transplantation is now being used, not just as a filler but as a new method for rejuvenation [6]. Studies showed that during ischemia the preadipocytes in fat can differentiate to endothelial cells as well as cells of mesenchymal origin. Even adipocytes can dedifferentiate to help survival of tissues and can produce a cytokine profile [7]. Also, the addition of growth factors to the fat graft showed increased survival, mitogenesis for mesenchymal cells as well as angiogenesis [8].

Platelet Rich Plasma (PRP) has been used in multiple medical fields owing to its role in healing chronic ulcers, rejuvenation [9], and tendinopathies [10] as well as other muscloskeletal uses [11]. Furthermore, photoinduced wrinkles in mice improved when treated by PRP [12]. Several studies used PRP in combination with other therapies to gain synergistic effect. PRP was used as a part of a dermal scaffold with mesenchymal stem cells (bone marrow derived) which showed improved cell adhesion and spreading in addition to the stem cells acquiring a fibroblast like phenotype [13].

Platelets help wound healing, not only through matrix formation, but also through cell differentiation and proliferation. Moreover, it helps stimulation of new blood vessel formation by anchoring and recruiting endothelial progenitor cells at the site of damage [14]. All these changes were attributed to the growth factors in the PRP [10].

1.2. Aim of work

In the present study, fat grafting has been compared to fat grafting enriched with Platelet Rich Plasma for the treatment of acne scars. To the best of our knowledge, such a comparison has not been done before.

2. Materials and Methods

After approval of Dermatology Research Ethical committee (DermaREC) of the Faculty of Medicine, Cairo

University, this study was performed at the dermatology outpatient clinic and surgical operation room at Kasr Al-Ainy, Cairo University hospital in the period November 2013 – April 2014.

The study included 28 patients with acne scars, chosen at random using the closed envelope method. Patients >18 years old of both sexes with mixed atrophic acne scars were included in the study. Patients < 18 years old, with retinoid use in the past 6 months, with systemic disease (diabetes or hypertension), collagen disease, malignancy, photosensitivity, or keloidal tendency were excluded from the study.

All patients signed an informed consent and full history was taken.

They were divided into 2 groups. Group A (14 patients (6 females and 8 males)) were subjected to fat grafting only. Group B (14 patients (6 females and 8 males)) were subjected to fat grafting enhanced with PRP. Both groups received 1 session of treatment with 6 months follow up.

Group A: Fat grafting:

Fourteen patients were subjected to fat grafting. The procedure was done under local anesthesia at a surgical operation theatre under complete aseptic precautions.

Harvesting fat was done using tumescent anesthesia (20 cc xylocaine 2% + 20 cc saline + 1/200000 adrenaline) injected at the abdominal region using 20cc syringes. A 0.5 cm stab incision was done at the donor site to introduce the cannula (3) connected to a 10 cc syringe and fat aspirated by steady movements in subcutaneous tissues and the end point was the appearance of blood. The fat was placed in vacuumed laboratory plain tubes. The tubes were inserted in a centrifuge at a speed of 3000 rpm for 5 minutes and 3 layers were formed: an oily layer at the top, blood and fluid at the bottom, and the fat in between.

All layers were disposed except the fat layer, which was placed in 3 cc syringes with a screw lock. The whole face was sterilized using alcohol. Infraorbital nerve block was performed using 1 cc lidocaine 2% and 1/200000 adrenaline through the cheek. A 0.5 cm stab incision was executed preauricularly, in the hairline or in an already existing scar. The 3 cc syringe with the fat was connected to an injection cannula (1.4), which was inserted at the site of the incision. A fan shaped subcision of the scars was performed creating tracts for fat placement in subdermal regions. Fat was placed during cannula withdrawal in the bed created by the subcision tracts. Moulding was performed against the zygoma and maxilla.

Group B: Platelet rich plasma enhanced fat graft:

The other fourteen patients were subjected to Platelet Rich Plasma treatment added to fat grafting. PRP was prepared from 20 cc blood withdrawn from antecubital fossa (after site asepsis by an alcohol swab) into tubes containing 10% sodium citrate. The PRP was prepared according to a double-centrifugation protocol.

First centrifugation: The separation of the blood cell elements was performed using a laboratory centrifuge (Beckman Centrifuge, CA, USA). The tubes were centrifuged at 160 G for 20 minutes at room temperature

resulting in two basic components: Blood Cell Component (BCC) in the lower fraction and SErum Component (SEC) in the upper fraction.

Second centrifugation: A mark was made 6 mm below the line that separated the BCC from the SEC. To increase the total amount of platelets collected for the second centrifugation, all content above this point was pipetted and transferred to another 5 ml vacuum tube without anticoagulant. The sample was then centrifuged again at 400 G for 15 minutes resulting in two components: SEC and PRP. The PRP (approximately 0.5 ml) was separated from the SEC.

The separated PRP is added to the fat graft obtained from the patients as with group A. The fat:PRP (1cc:2cc) mix is inserted in 3cc syringes and injected in face as performed with Group A.

The procedure was a day-case surgery. Patient was prescribed antibiotics and anti-inflammatory drugs (NSAIDS) for a week. Compression garment was applied at site of harvesting for 48 hours and dressing with topical antibiotics. Steristrips were used at the incision sites in the face.

Follow up after 1 week and through the following 6 months for early (infection, hematoma and pain) and late (fat atrophy or hypertrophy) complications. Assessment of results was done through comparing photographs and biopsy performed before and after 6 months from the session, as well as patient satisfaction. Assessment of the photographs was conducted by a single blinded physician. The biopsy was assessed by a blinded dermatopathologist.

For the single blinded physician assessment and patient satisfaction of the overall scar improvement (pigmentation, erythema and fullness), the results were described using a scale of: {0-25% (mild), 25-50% (moderate), 50-75% (marked), 75-100% (excellent)}.

For the biopsies taken before and after treatment, they were assessed by a blinded dermatopathologist for dermal improvement, scar quality, as well as collagen thickness and homogenicity.

Statistical analysis

Results were expressed as a percentage (%). Comparison between categorical data was performed using the Chi square test. The data were considered significant if p value was equal to or less than 0.05. Statistical analysis was performed with the aid of the SPSS computer program (version 16 windows).

3. Results

To ensure the coherence of both groups for comparison, the characteristics of both groups were statistically insignificant (p= 0.638) when compared to each other. The type of predominant acne scars in both groups was studied, where the correlation between both groups was statistically insignificant (p=0.638) confirming the coherence of both groups.

Statistical analysis of the single blinded physician assessment (Figure1) and patient satisfaction for overall improvement in both groups was statistically insignificant (p=0.063, p=0.735 respectively).

The results of the biopsy assessment of scar improvement and collagen thickness and homogenicity, however, were statistically significant (p= 0.042) in favor of PRP enhanced fat group (Figure 2).

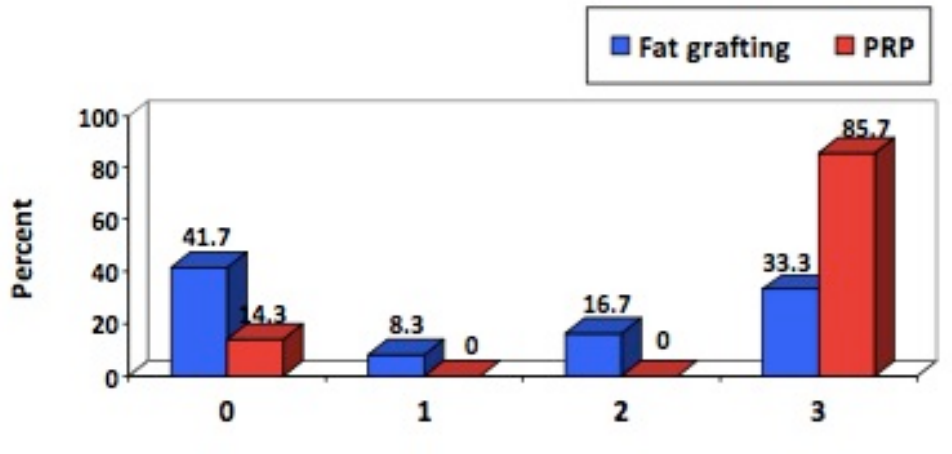

Figure 1: Graph presentation of single blinded assessment in both groups.

(1=0-25%, 2=25-50%, 3=50-75%, 4=75-100%)

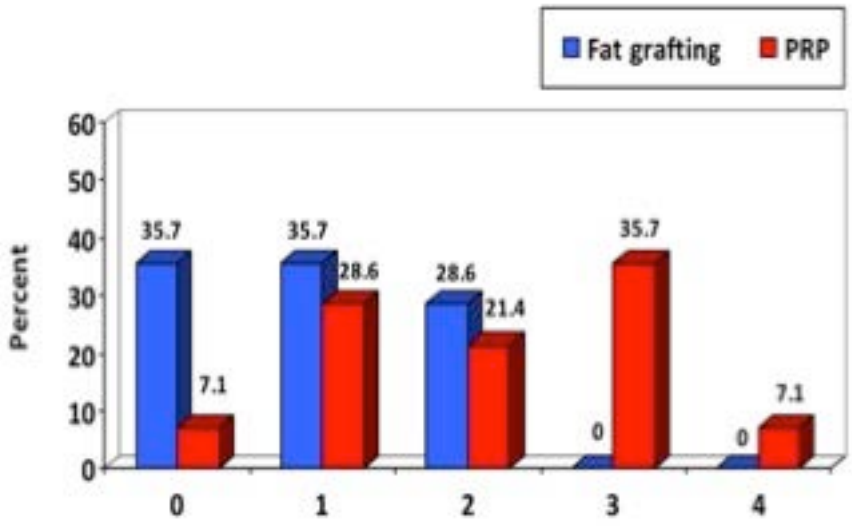

Figure 2: Graph presentation of biopsy results in both groups

(1=0-25%, 2=25-50%, 3=50-75%, 4=75-100%)

Furthermore, in an attempt to do a treatment protocol for acne scars treatment, each group was subdivided, according to the predominant scar in each patient, into boxcar, icepick and rolling (each patient had mixed atrophic acne scars with one type predominant). The overall improvement was correlated to the predominant scar in each patient of both groups, within the single blinded assessment frame as well as the biopsy result.

In group A, the single blinded assessment showed improvement of icepick scars in 80% of patients, while 50% of patients with predominant boxcar scars improved and 60% of patients with predominant rolling scars improved (Figure 3).

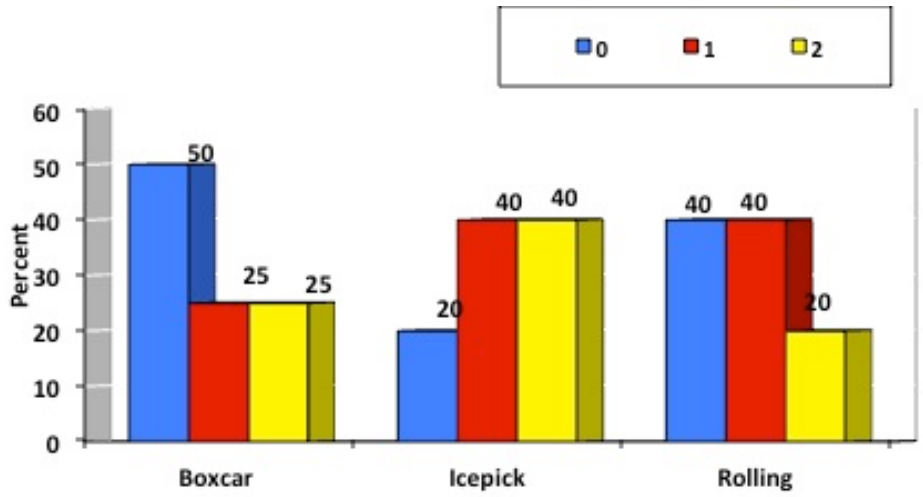

Figure 3: Graph presentation showing single blinded assessment of overall improvemnt in each of the predominant scar types in group A. (1=0-25%, 2=25-50%, 3=50-75%, 4=75-100%)

However, in group B, icepick scars improved in 66% of patients with predominant icepick scars, while more than 80% of patients with predominant boxcar scars improved and 80% of patients with predominant rolling scars improved (Figure 4).

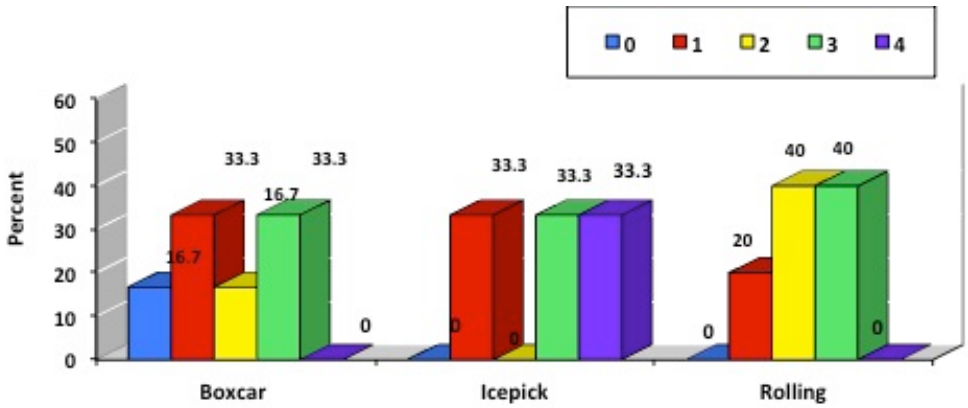

Figure 4: Graph presentation of single blinded assessment in each of the predominant scar types as regards the overall improvement in group B. (1=0-25%, 2=25-50%, 3=50-75%, 4=75-100%)

Regarding biopsy assessment, in group A, icepick scars showed improvement in 75% of patients with predominant icepick scars, while 50% of patients with predominant boxcar scars improved and 50% of the patients with predominant rolling scars improved (Figure 5). In group B, all patients (with predominant icepick scars as well as those with predominant boxcar scars as well as those with predominant rolling scars) improved (Figure 6).

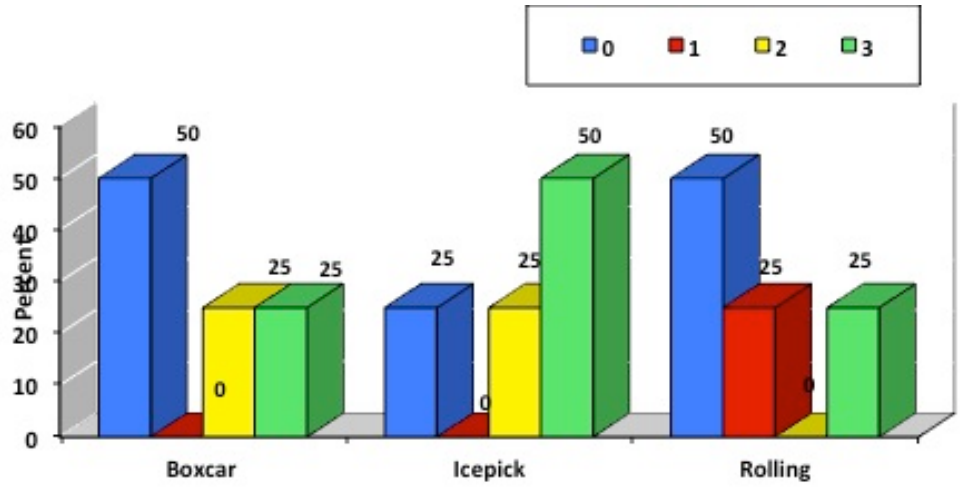

Figure 5: Graph presentation of biopsy assessment in each of the predominant scar types as regards the overall improvement in group A. (1=0-25%, 2=25-50%, 3=50-75%, 4=75-100%)

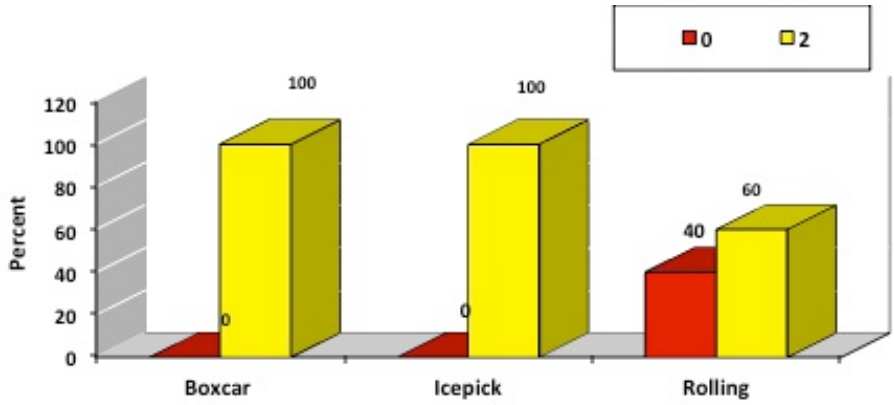

Figure 6: Graph presentation of biopsy assessment in each of the predominant scar types as regards the overall improvement in group B. (1=0-25%, 2=25-50%, 3=50-75%, 4=75-100%)

4. Discussion:

Multiple treatment modalities for acne scars have been tried, either singly or in combination. Different protocols were used with different outcomes reached, owing to the fact that there is no standardization of the starting point as well as the heterogenicity of acne scars, and no objective criteria for classification. This study compares fat

grafting to PRP enriched fat graft in treatment of acne scars, which, to the best of our knowledge, has not been previously attempted.

Our study chose the patients at random and the characteristics of the present study when analyzed, showed no statistical significance between the 2 study groups indicating the coherence of the 2 groups and hence, the fair comparison thereafter.

Aiming at designing a treatment protocol for acne scars, further analysis of the results was performed in our study. The predominant scar was observed for degree of improvement in both groups through clinical and histopathological assessment. Since both groups were coherent as regards the scar type, the comparison was achieved. All 3 types of atrophic acne scars showed improvement, to variable degrees, when the PRP was applied.

Icepick scars showed more improvement with the fat graft group (80%) than the PRP enhanced group (70%). Boxcars improved better with PRP enhanced treatment (less than 20% did not improve in group B, in contrast to 50% in group A). Rolling scars showed better improvement with the PRP enhanced group as well. This was confirmed using the results of a biopsy analysis.

The icepick scars improvement with fat grafting is contrary to the findings by authors in [4], where there was no improvement of icepick scars with fat grafting in contrast to the improvement achieved by fractional CO_2 laser. While authors in [1], recommended punch excision and CROSS chemical peels for icepick scars.

The overall assessment by a single blinded physician, when comparing both groups, was in favor of the PRP group. The single blinded assessment showed more than 92% of patients improved in the PRP group (Figure 7), to a variable degree from mild to excellent, whereas, in group A, 64% of the patients (mild to moderate improvement only) improved (Figure8), with 35% of patients showing no improvement.

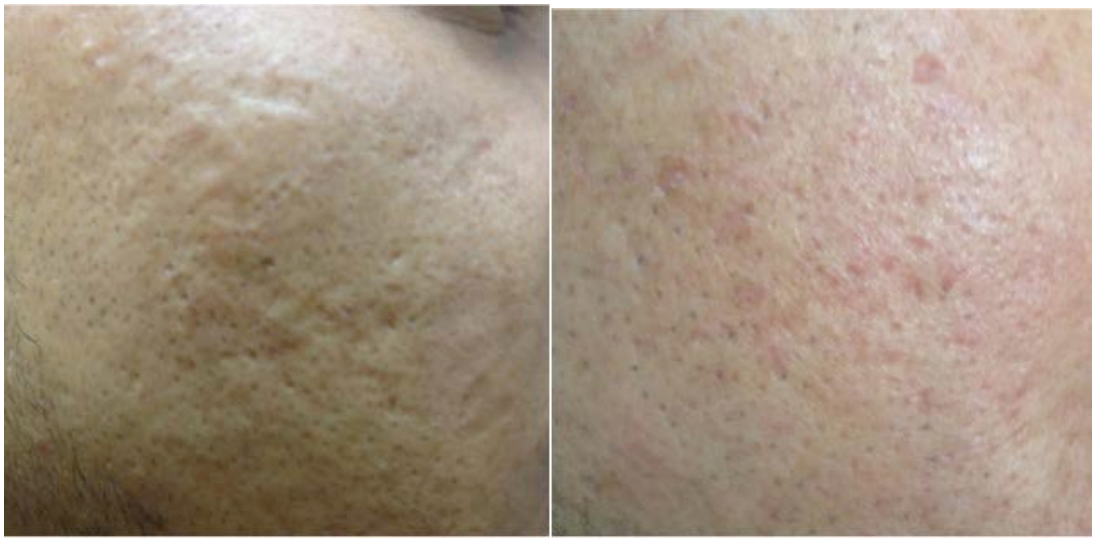

Figure 7: left: before treatment, right: after treatment, showing marked improvement (patient 17)

Similarly, such findings were further verified by a biopsy that was compared before and after the treatment. The PRP enriched fat graft group (B) showed higher improvement (Figure9) than the fat graft group (A) (Figure10), where 85% of patients showing marked improvement in group B and 33.3% of patients showed marked improvement in group A. This improvement was statistically significant regarding collagen quality and thickness all through the dermis. The relative improvement in group B can be explained by the role of growth factors in PRP on the fat graft.

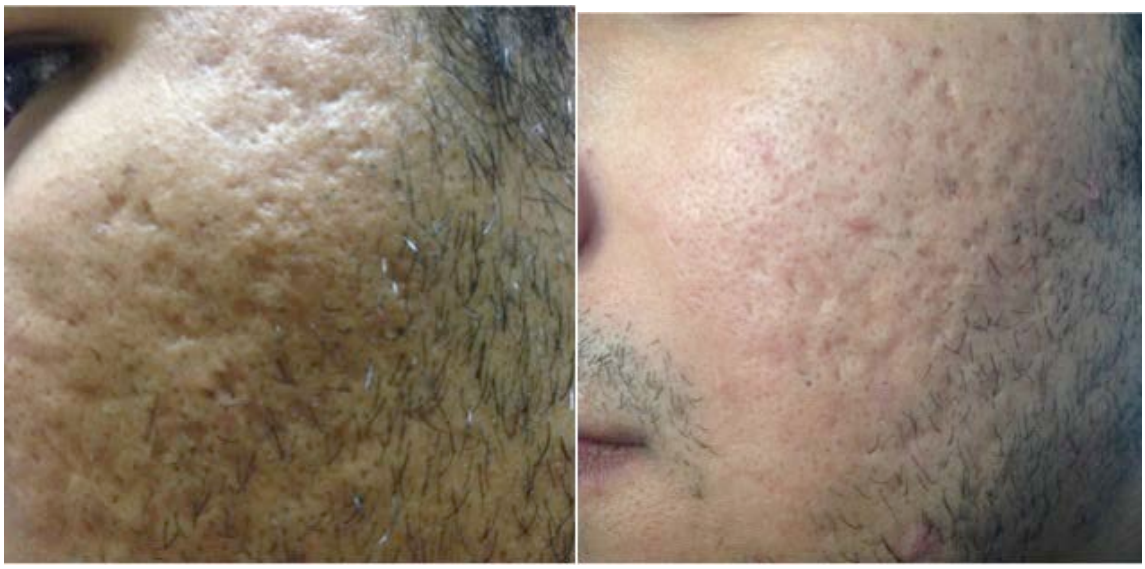

Figure 8: left: before treatment, right: after treatment, showing moderate improvement (patient 9)

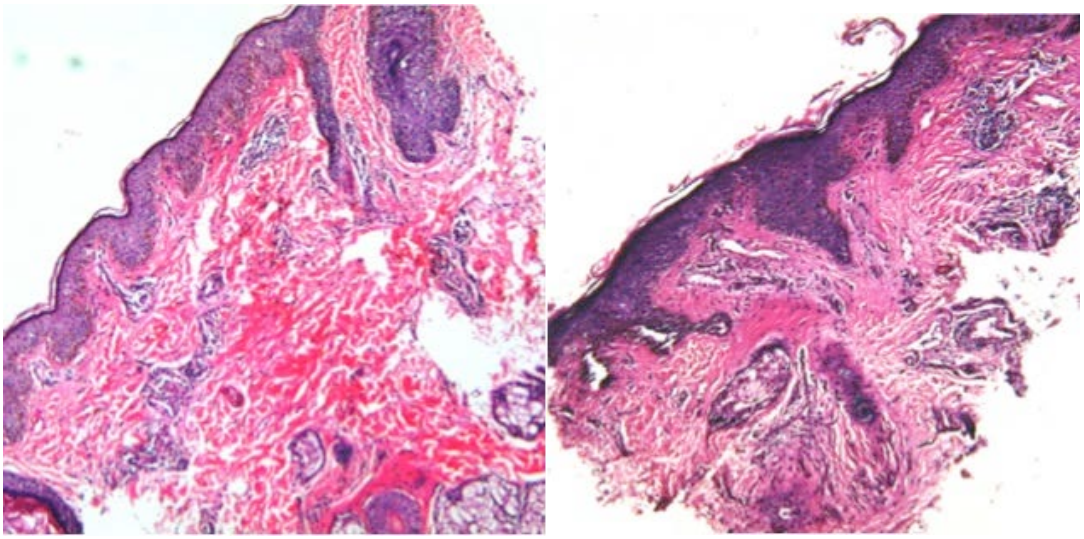

Figure 9: Biopsy in patient 3, left: before treatment, right: after treatment, note the improvement of collagen in the Upper dermis (group A)

The growth factors in PRP include Insulin like Growth Factor-1 (IGF-1), transforming Growth Factor Beta (TGF beta), Fibroblast Growth Factor (FGF), Platelet Derived Growth factor AB &BB (PDGF), Vascular Endothelial Growth Factor (VEGF) [10,15,16], Hepatocyte Growth Factor (HGF), Angiopoetins [15], Epidermal Growth Factor (EGF) [17], Neuroprotein 3, Nerve Growth Factor (NGF) and Growth associated protein 43 [18]. Also, PRP contains matrix metalloproteinases that proved to be important in remodeling [18].

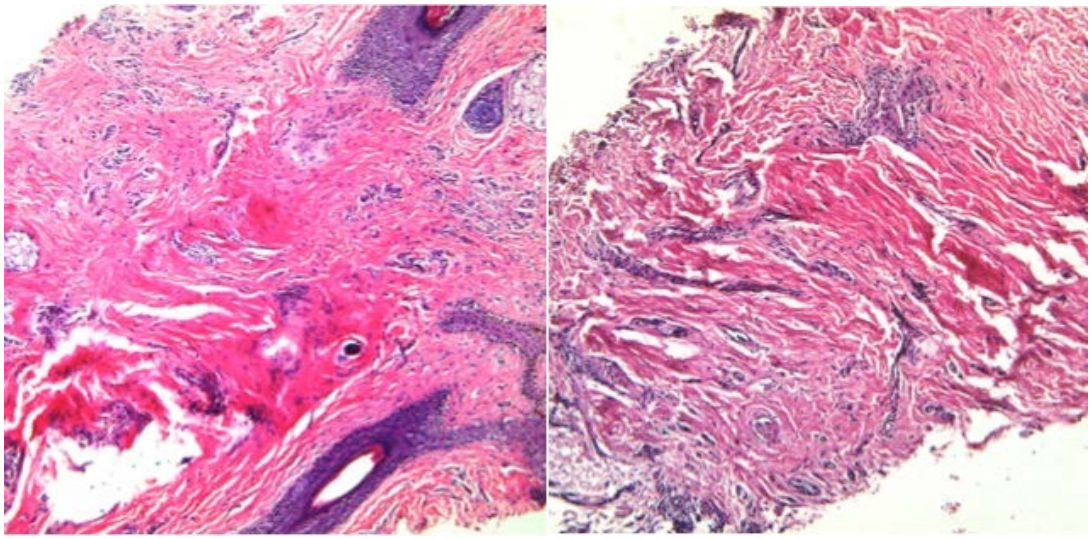

Figure 10: Biopsy in patient 22, left: before treatment, right: after treatment, note the improvement of collagen in the lower dermis (group B)

In the present study, the PRP addition to the fat graft appears to have a positive influence on the improvement. The percentage of unimproved patients was much less than the fat graft group and the range of improvement reached an excellent grade.

When the PRP was added to lipoaspirate on various animal studies, there were findings of endothelial cell proliferation, angiogenesis, neovascularization and granulation tissue formation with improved perfusion. Similarly in humans, PRP was added to fat grafts for chronic ulcers and showed marked improvement [17]. The fibrin matrix introduced upon injection of PRP in tissues provides a scaffold for healing [10] and when it was added to stem cells, showed transformation of the mesenchymal stem cells into fibroblast phenotype [13].

The adipose tissue contains preadipocytes which can differentiate into cells of mesenchymal cell lineage[7] in the presence of growth factors (as insulin (I), IGF-I (insulin-like growth factor I), bFGF (basic fibroblast growth factor), and mixtures of these factors [8]. However, the appropriate concentrations of these are yet to be determined [19].

Thus, the addition of PRP to the fat graft, with its growth factors, enhances the differentiation of the preadipocytes into fibroblasts, with the power for remodel as well as stimulate the resident fibroblasts to produce collagen, together with the fibrin matrix as a scaffold and the angiogenesis being stimulated. Thus in

the present study the improvement through the addition of PRP is better understood.

Authors in [20] showed fat resorption upon adding PRP to the fat graft. This did not happen in our study. Probably because the aim of our procedure was not filling, but rejuvenation, depending on the resident preadipocytes and adipose derived stem cells. This might be determined by the level (depth) of fat graft injection, i.e. we injected in deep dermis, while in filling usually the injection is in deeper layers such as the subcutaneous.

An incidental finding was the improvement of acne after treatment (Figure 11) in both groups. This occurred in another study by authors in [4] as well but could not be explained.

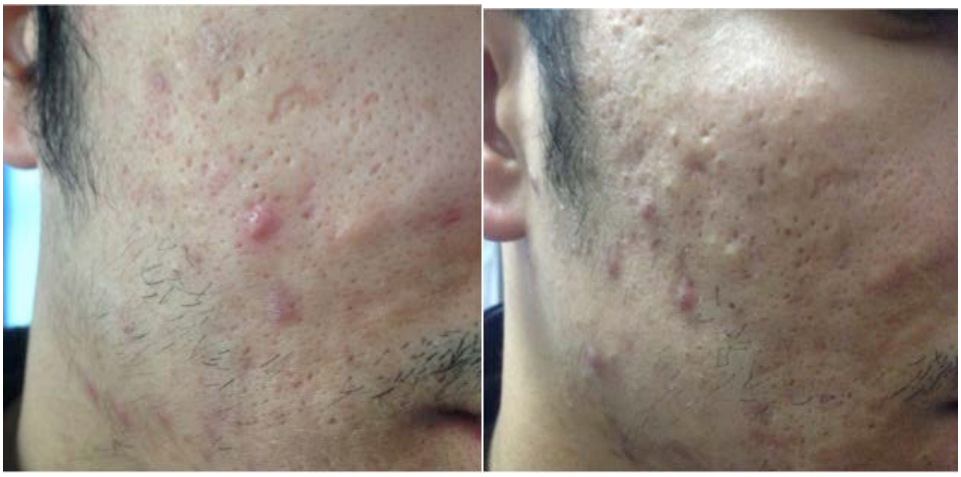

Figure 11: Left: before fat graft, Right: after fat graft showing no improvement (patient 5). Note the decrease in acne activity after treatment (group A).

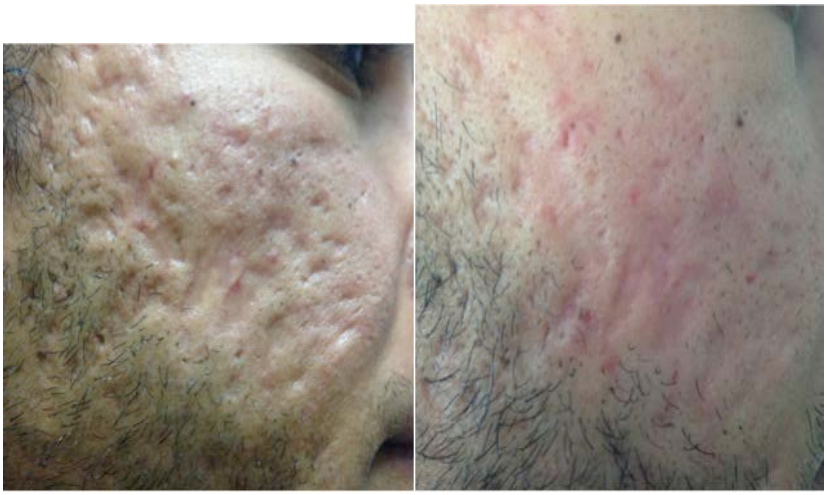

Figure 12: Right: before treatment, Left: after treatment, showing marked improvement (patient 22), note the residual erythema after treatment (group B).

Fat was harvested from the abdominal region in both groups. Fat tissue harvesting should be from the deeper layer, which is different genetically and metabolically from the subcutaneous layer [8]. Although authors in [21] showed no statistical difference in adipocyte viability among abdominal fat, thigh fat, flank fat or knee fat, Authors in [22] showed that the abdomen is the optimum site for harvest while the knee and medial thigh have the poorest adipocyte derived stem cells [23].

There was no incidence of complications as infection, hematoma, swelling or embolism in our study. However, erythema was a drawback in one patient in the PRP group *(Figure 12)*, probably due to superficial injection. The patient was not disconcerted. There was no downtime in both groups.

Even though both procedures are appealing, both are surgical procedures that needs a skillful operator with strict sterilization technique, unlike laser for example whose skills are relatively quicker to master.

A problem we faced was the difficult fat harvest in thin patients. We managed, however to obtain a practicable amount of fat.

However, some limitations were met in the study as the sample size. We intended to do the study on a larger number of patients but the biopsy taking made many patients refuse to join the study. This made us unable to perform the trial on a third group of patients to be treated with PRP only. Also, financial restrictions prevented us from examining further histopathological variables and analysis.

5. Conclusion

In conclusion, both groups showed improvement of acne scars with obvious higher results in the PRP enriched group. As for overall improvement and regarding the individual scars, the results were in favor of PRP enriched fat graft. This study being the first comparative study between fat graft and PRP enhanced fat graft in acne scars, we recommend further studies on a larger group of patients with more histological variables regarding treatment of atrophic acne scars with fat grafts whether enriched with other treatment modalities or alone. We recommend PRP enhanced fat grafting for the treatment of both boxcar and rolling acne scars to be put into future guidelines of acne scars treatment.

Acknowledgements

We would like to thank Prof. Mohammad Eldarouti, Fellow of dermatopathology NYU and professor of dermatology and dermatopathology, Faculty of Medicine, Cairo University, for being the blinded dermatopathologist in our study. Also, we would like to thank Professor Doaa Elderwi for doing the statistical analysis in our study.

References

[1] D. Fife. “Practical Evaluation and Management of Atrophic Acne Scars, Tips for the General Dermatologist”, The journal of clinical and aesthetic dermatology, 4(8): 50-57, 2011

[2] E.P. Tierney. “Treatment of acne scarring using a dual spot size ablative fractionated carbon dioxide laser: review of the literature”, Dermatologic surg, 37:945-961, 2011

[3] G.J. Goodman. “Postacne scarring: A review of its pathophysiology and treatment”, Dermatologic surgery, 26:857-871, 2000

[4] O.A. Azzam, A.T. Atta, R.M. Sobhi, P.I.N. Mostafa. “Fractional CO2 laser treatment vs autologous fat transfer in the treatment of acne scars: A Comparative study”, Journal of drugs in dermatology, 12(1): e7-13, 2013

[5] N. Rongsaard and P. Rummaneethorn. “Comparison of a fractional bipolarbradiofrequency device and a fractional erbium doped glass 1550 nm Device for the treatment of atrophic acne scars: A Randomised split face clinical study”. Dermatologic surgery, 40:14-21, 2014.

[6] A. Mojallal, C. Lequeux, C. Shipkov, et al. “Improvement of skin quality after fat grafting, Clinical observation and an animal study”, Plastic and Reconstructive Surgery, 124(3): 765-774, 2009

[7] B. Cousin, V. Planat, G. Charriere l., et al. “Adipose tissue, physiology and regenerative medicine”, In: Injection Treatments in Cosmetic Surgery. Benjamin Ascher, editor. London: Informa UK limited; p. 339-352, 2008.

[8] A. Mojallal and J.L. Foyatier. “The effect of different factors on the survival of transplanted adipose tissue and global approach and techniques of fat grafting”, In: Injection Treatments in Cosmetic Surgery, Benjamin Ascher, editor. London: Informa UK limited; p. 357-370, 2008.

[9] D.H. Kim, Y.J. Je and Y. Lee. “Can Platelet-rich Plasma Be Used for Skin Rejuvenation? Evaluation of Effects of Platelet-rich Plasma on Human Dermal Fibroblast”, Anndermatol, 23(4):424-431, 2011

[10] A.S. Wasterlain, H.J. Braun and J.L. Dragoo. “Contents and formulations of platelet rich plasma”, Oper Tech Orthop, 22:33-42, 2012

[11] D. Dionyssiou, E. Demiri, P. Foroglou, et al. “The effectiveness of intralesional injection of platelet-rich plasma in accelerating the healing of chronic ulcers: an experimental and clinical study”, Int Wound J; 10:397–406, 2013

[12] S.B. Cho, S.J. Lee, S. cho, et al. “Non ablative 1550 nm erbium glass and ablative 10,600 nm carbon dioxide fractional lasers for acne scars: a randomized split face study with blinded response evaluation”, J Eur Acad Dermatol Venereol, 24:921-5, 2010

[13] L. Formigli , S. Benvenuti , R. Mercatelli , et al. “Dermal matrix scaffold engineered with adult mesenchymal stem cells and platelet-rich plasma as a potential tool for tissue repair and regeneration”, J Tissue Eng Regen Med, 6: 125–134, 2012

[14] J. Textor. “Platelet rich plasma as a therapeutic agent: Platelet biology, Growth factors and a review of the literature”. In: Platelets-Rich Plasma, Lecture notes in bioengineering. Lana JFSD, Andrade Sanata MH, Dias Belangero W, Malheiros Luzo AC, editors. Berlin: Springer, p. 61-94, 2014.

[15] E. Anitua, M.M. Zalduendo, MH Alkhraisat and G.Oriv. Release kinetics of platelet-derived and plasma-derived growth factors from autologous plasma rich in growth factors. Annals of Anatomy,195: 461– 466, 2013.

[16] H.B. Park, J.H. Yang and K.H. Chung. “Characterization of the cytokine profile of platelet rich plasma (PRP) and PRP-induced cell proliferation and migration: Upregulation of matrix metalloproteinase-1 and -9 in HaCaT cells”, Korean J Hematol, 46(4): 265–273, 2011.

[17] C.E. Sommeling, A Heyneman, H. Hoeksema, et al. “The use of platelet-rich plasma in plastic surgery:A systematic review”, Journal of Plastic, Reconstructive & Aesthetic Surgery, 66, 301e312, 2013.

[18] X. Xie, S. Zhao, H. Wu, et al. “Platelet-rich plasma enhances autograft revascularization and reinnervation in a dog model of anterior cruciate ligament reconstruction”, Journal of surgical research, 183, 214e222, 2013.

[19] M.R. Kaufman, J.P. Bradley, B. Dickinson, et al. “Autologus fat transfer national consensus.trends in techniques for harvest, preparation and application and perceptionof short and longterm term results”, Plast Reconstr Surg,119(1):323-331, 2007.

[20] S.O. Keyhan, S. Hemmat, A.A. Badri, et al. “Use of Platelet rich fibrin and platelet rich plasma in combination with fat graft: which is more effective during facial lipostructure?”, Journal of Oral and Maxillofacial Surgery, 71(3):610-621, 2012.

[21] R.J. Rohrich, E.S. Sorokin and S.A. Brown. “In search of improved fat transfer viability: a quantitative analysis of the role of centrifugation and harvest site”, Plast Reconst Surg, 113:391-395, discussion 396:397, 2004.

[22] A.V. Padoin, J. Braga-Silva, P. Martins , et al. “Sources of processed lipoaspirated cells: Influence of donor site on cell concentration”, Plast Reconstr Surg, 122, 614-618, 2008.

[23] A. Wilson, P.E. Butler and A.M. Seifalian. “Adipose derived stem cells for clinical applications: a review”, Cell proliferation, 44(1), 86-98, 2011.