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Original Article

Comparison of outcome of microneedling with autologus platelet rich plasma verses microneedling with topical insulin in the treatment of post-acne atrophic scars

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Abstract

Objective To compare the outcome of micro-needling with autologous platelet rich plasma versus micro-needling with topical insulin in the treatment of post-acne atrophic scars.

Methods 80 patients fulfilling the inclusion criteria were enrolled. Goodman and Baron's Qualitative Scarring Grading System was used to calculate grade at enrollment and at a monthly interval for total 4 sessions and follow up visit after 2 months of last session. Following micro-needling with a derma roller, topical applications of 2ml of human actrapid insulin was done in group-A and 2ml of PRP in group-B. Percentage reduction of acne scar grade was calculated. Data was analyzed in SPSS v25.0. Chi-square test was applied for Comparison of outcomes in terms of post-treatment percentage reduction of grades from patient's baseline grade. P-value of <0.05 was considered significant.

Results Males and females were 10(25.0%) and 30(75.0%) respectively in group-A, while 13(32.5%) males and 27(67.5%) females were enrolled in group-B. The mean age of patients was 23.68±5.03 years and 24.48±4.75 years in group-A and B correspondingly. The mean duration of scar was 4.5±2.1 years in group A and 4.9±2.3 years in group B. In group A the mean exposure to sunlight was 4.9±2.3hours and in group B was 4.7±2.1hours. Mean percentage reduction of grades of scar in group-A was 55.42±12.74% and 23.33±16.79% in group-B.

Conclusion Micro-needling with insulin has more efficacy than micro-needling with Platelet Rich Plasma in treating acne scars. This combined procedure is cost effective, favourable for all skin types with minimal post-inflammatory hyperpigmentation. Also this novel combination procedure is convenient for both doctors and patients as no high skills are required, no need to take I/V line and less time consuming.

Key words
Acne vulgaris; Micro-needling; Platelet Rich Plasma; Insulin, Post-acne atrophic scar.

Introduction

Acne vulgaris is a disease involving inflammation or blockage of pilosebaceous units.[1] Post-acne scars are formed as a result of very inflamed and nodulocystic acne.[2] Most common type of acne scars are atrophic scars and they are further classified on the basis of depth and size of destruction into ice pick, boxcar and rolling scars.[3-4] There are many procedures to treat post-acne scars including lasers, platelet rich plasma, fillers, chemical peeling, pulsed dye lasers, fractional CO_2 lasers,

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subcision and punch techniques, but almost all lead to additional scarring and pigmentation.[5]

Nowadays micro-needling therapy is being used in the treatment of many dermatological conditions like post-acne scars, wrinkles and dyschromia.[6] The drug is delivered to skin in minimally invasive way by using this therapy.[7]In post-acne scars type 1 collagen is present predominantly as compared to type III collagen.[2] Micro-needling induces the type III collagen production in the normal framework, so reducing the grades of scars. It is safer for darker skin types and often is combined with PRP for better results.[8-9]

PRP has gained importance in dermatology recently.[10] It contains autologous growth factors comprising platelet derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), which improves acne scars by increasing the synthesis of collagen and up-regulating tissue growth.[11-13] Manoj Pawar *et al.* conducted a split face comparative study in which micro-needling and topical insulin (Human actrapid 40IU/ml) on the right s and micro-needling with autologous PRP was done on left side of face. They enrolled 16 patients of post-acne scars having Fitzpatrick skin types IV to VI.

The results showed 45% and 26% improvement on right and left sides of face in terms of reduction in number of scars after monthly four treatments. Topical insulin therapy was effective for boxcar scars (51.2%) as compared to PRP therapy (24.7%). Mild erythema, pain and edema were the side effects.[14]Mohamed Ali Mahmood Abbas *et al.* also conducted a similar study on 30 patients with atrophic scarring.

After micro-needling on each side of face, Human topical insulin was introduced on left with Vitamin C serum application on right side. Acne Scar Assessment Scale (ASAS) and Scar Quartile Grading Scale (SQGS) were used to assess the scars. ASAS value on both facial sides showed significant result (2.13 and 1.83) comparison with baseline (3.03 and 2.93) (p=0.005; p=0.001 respectively).[15]

The mechanism of action of topical insulin is to activate phosphatidyl inositol 3-kinase/ protein kinase B pathways and increase growth factors including VEGF. Thus it augments the synthesis of type III collagen fibers and improves the acne scars by reducing the depth and area.[16-17]

The major purpose of our study is comparison of outcome of microneedling and PRP as opposed to combining it with topical insulin in atrophic scars due to acne, as topical insulin is natural component of body, cheap, easy to use, minimally invasive and a new therapy for post-acne scars that showed good results in the studies mentioned. No local study was found in literature research. Hence, any effect of this potentially very effective therapeutic modality needs to be investigated.

Methods

Patients at Clinical setting at Department of Dermatology (Unit-II), Mayo Hospital, Lahore were enrolled. This was a randomized controlled trial with non-probability consecutive sampling. The sample size of 80 patients estimated through 80% power of study, 5% level of significance and i.e. 51.20% improvement in boxcar scars with insulin and 24.74% improvement in boxcar scars with PRP was made into account, including men and women age (18-40 years) with atrophic scarring (as per operational definition). Fitzpatrick skin type IV to VI 2 to 4 grades of post-acne atrophic scars was calculated by Goodman and Baron's Qualitative Scarring Grading System. Presence of active infection, Pregnant or lactating females, or on

oral or topical retinoid, ones with previous history of keloids or bleeding disorders (platelet count less than 150000/microliter), and Deranged blood glucose levels were excluded. The procedure and data collection on a pre-designed proforma was done by the author.

After approval from the hospital's Ethical Committee a total of 80 patients (men and women) were included. Written informed consent. Demographic data including age at enrollment, address, Fitzpatrick skin type was collected. The patients were then assessed and every patient's face was photographed at 45 degrees side lighting at 50cm from the scars from both sides at every visit.

Goodman and Baron's Qualitative Scarring Grading System was used to calculate grade on enrollment followed by monthly interval for total 4 sessions and then at follow up visit after 2 months of last session. Any improvement in grade was recorded along with the time taken/visit no. for the improvement to occur. Patients were randomly divided into two groups.

During each treatment session, the patient's affected skin was wiped clean with alcohol swab followed by half an hour EMLA®- lidocaine 2.5%, prilocaine 2.5% anesthetic application later followed micro-needling with a dermaroller. Ice pack was applied to treated areas of face. Topical application of 2ml of human actrapid insulin was done in group-A and topical application of 2ml of PRP was done in group-B thereafter.

Face was washed after 30 min. Patients were instructed to follow strict photo-protective measures (use of sunscreens and avoidance of sun exposure for at least one day after the procedure). Blood glucose was checked prior to and 30 mins following procedure. Any side effects were asked and treated as per standard treatment protocols.

Percentage of reduction of acne scar grade was calculated by subtracting post-treatment grade from pre-treatment grade and dividing it by pre-treatment grade and multiplying with 100. The effects of confounding variables like exposure to sunlight or smoking, duration of scars age of the patient were noted. The results were stratified with respect to these variables

Data analysis was done in SPSS v25.0. Quantitative variables as age, duration of scarring were termed as mean and SD. Qualitative variables as gender, type of post-acne atrophic scars, pre- and post-treatment grades, and percentage reduction in grades, Fitzpatrick skin types and smoking were presented as frequency and percentages. Comparison of outcome of microneedling with both insulin and platelet rich plasma as post-treatment percentage reduction of grades from patient's baseline grade, Data stratification according to the gender, duration of scar, age, exposure to sunlight, scar type, skin type and smoking and post-stratification analysis was performed to look for effect on grade reduction by applying Chi-square test. P-value ≤ 0.05 was considered significant.

Results

Male and female patients in Group A were 10 (25.0%) and 30 (75.0%) respectively, while 13 (32.5%) males and 27 (67.5%) females were enrolled in group B.

The mean age of patients in group A and Group was 23.68±5.03 years and 24.48±4.75 years respectively. In group A, 27 (67.5%) patients were aged between 18-25 years and 13 (32.5%) between 26-40 years, while in group B, 24 (60.0%) patients had ages between 18-25 years and 16 (40.0%) between 26-40 years.

The mean duration of atrophic scarring in group A and B was 4.5±2.1 years and 4.9±2.3 years correspondingly. In group-A, 17 (42.5%) patients had scar for >3 years and 23 (57.5%) for ≤3 years, while in group-B, 19 (47.5%) patients had scar for >3 years and 21(52.5%) for ≤3 years.

In group-A, 2 (5.0%) had ice pick scars, 34(85.0%) had boxcar scars and 4 (10.0%) had rolling scars, while in group-B, 5 (12.5%) had ice pick scars, 30 (75.0%) had boxcar scars and 5 (12.5%) had rolling scars. In both groups, no. of patients with boxcar scars were more. In group-A, 13 (32.5%) patients had grade-III scar and 27 (67.5%) had grade-IV scar at baseline, while in group-B, 11 (27.5%) patients had grade-III scar and 29 (72.5%) had grade-IV scar at baseline. In both groups, more patients with grade IV acne scars at baseline enrolled.

In group-A, 35 (87.5%) had type-IV skin, 4 (10.0%) had type-V and 1 (2.5%) had type-VI skin, while in group-B, 36 (90.0%) had skin type IV, 3 (7.5%) had type V and 1 (2.5%) had type VI.

In group-A, 5 (12.5%) were smokers, while in group-B, 4 (10.0%) were smokers.

The mean exposure to sunlight in group A and group B was 4.9±2.3hours and 4.7±2.1 hours respectively. In group A, 29 (72.5%) were exposure to sunlight for ≤3hours and 11 (27.5%) for >3hours, while in group-B, 27 (67.5%) patients had exposure to sunlight for ≤3hours and 13 (37.5%) for >3 hours.

In group-A, 33(82.5%), 7 (17.5%) and 0 (0.0%) of patients had grade II, III and IV scar respectively, after completion of therapy, while in group-B, 2 (5.0%) patients had grade-II scar, 34 (85.0%) had grade-III and 4 (10.0%) had grade-IV scar after completion of therapy **(Table 1)**.

The mean reduction in grades of scar in group-A was 1.50±0.51 and 0.68±0.47in group-B. The mean percentage reduction in grades of scar in group-A was 55.42±12.74% and 23.33±16.79% in group-B. In Micro-needling plus Insulin group, 20 (50.0%) had marked improvement, 20 (50.0%) moderate and 0 (0.0%) showed mild improvement, while in Micro-needling plus PRP group, marked, moderate and mild improvement was signified as 0 (0.0%), 27 (67.5%) and 13 (32.5%) respectively with a statistically significant p-value 0.005 **(Table 2)**.

Table 1 Comparison of grade of scar after completion of therapy between groups.

Grade of scar after completion of therapy	*Groups*				*Total*	
	Group A Micro-needling plus Insulin		*Group B Micro-needling plus PRP*			
	No. of pts.	*%age*	*No. of pts.*	*%age*	*No. of pts.*	*%age*
Grade-II	33	82.5%	2	5.0%	35	43.8%
Grade-III	7	17.5%	34	85.0%	41	51.2%
Grade-IV	0	0.0%	4	10.0%	4	5.0%
Total	40	100.0%	40	100.0%	80	100.0%

Table 2 Comparison of percentage improvement after completion of therapy between groups.

Percent of improvement after therapy completion	*Groups*				*Total*		*p-value*
	Group A Micro-needling plus Insulin		*Group B Micro-needling plus PRP*				
	No. of pts.	*%age*	*No. of pts.*	*%age*	*No. of pts.*	*%age*	
Marked (>50%)	20	50.0%	0	0.0%	20	25.0%	0.001
Moderate (25-50%)	20	50.0%	27	67.5%	47	58.8%	
Mild (<25%)	0	0.0%	13	32.5%	13	16.3%	
Total	40	100.0%	40	100.0%	80	100.0%	

Table 3 Stratification of percentage improvement after completion of therapy between groups with respect to type of post-acne atrophic scar.

Type of post-acne atrophic scar	*Percentage improvement after completion of therapy*	*Groups*				*Total*		*p-value*
		Group A		*Group B*				
		No.	*%age*	*No.*	*%age*	*No.*	*%age*	
Ice pick	Marked (>50%)	1	50.0%	0	0.0%	1	14.3%	0.019
	Moderate (25-50%)	1	50.0%	3	60.0%	4	57.1%	
	Mild (<25%)	0	0.0%	2	40.0%	2	28.6%	
	Total	2	100.0%	5	100.0%	7	100.0%	
Boxcar	Marked (>50%)	16	47.1%	0	0.0%	16	25.0%	0.001
	Moderate (25-50%)	18	52.9%	19	63.3%	37	57.8%	
	Mild (<25%)	0	0.0%	11	36.7%	11	17.2%	
	Total	34	100.0%	30	100.0%	64	100.0%	
Rolling	Marked (>50%)	3	75.0%	0	0.0%	3	33.3%	0.018
	Moderate (25-50%)	1	25.0%	5	100.0%	6	66.7%	
	Total	4	100.0%	5	100.0%	9	100.0%	

Group A: Micro-needling plus Insulin; Group B: Micro-needling plus PRP.

Table 4 Stratification of percentage improvement after completion of therapy between groups with respect to Fitzpatrick skin type.

Fitzpatrick skin type	*Percentage improvement after completion of therapy*	*Groups*				*Total*		*p-value*
		Group A		*Group B*				
		No.	*%age*	*No.*	*%age*	*No.*	*%age*	
Type-IV	Marked (>50%)	19	54.3%	0	0.0%	19	26.8%	0.001
	Moderate (25-50%)	16	45.7%	25	69.4%	41	57.7%	
	Mild (<25%)	0	0.0%	11	30.6%	11	15.5%	
	Total	35	100.0%	36	100.0%	71	100.0%	
Type-V	Marked (>50%)	1	25.0%	0	0.0%	1	14.3%	0.350
	Moderate (25-50%)	3	75.0%	2	66.7%	5	71.4%	
	Mild (<25%)	0	0.0%	1	33.3%	1	14.3%	
	Total	4	100.0%	3	100.0%	7	100.0%	
Type-VI	Moderate (25-50%)	1	100.0%	0	0.0%	1	50.0%	0.157
	Mild (<25%)	0	0.0%	1	100.0%	1	50.0%	
	Total	1	100.0%	1	100.0%	2	100.0%	

Group A: Micro-needling plus Insulin; Group B: Micro-needling plus PRP.

Stratification of percentage reduction in grades of scar after completion of therapy distribution between groups with respect to different variables were done and showed significant difference between groups with respect to variables ($p<0.05$) **(Table 3,4)**.

Discussion

Minimally invasive treatment modalities are effective for scar remodeling in post acne atrophic scarring, allowing extra-cellular matrix proteins in dermis to prosper without ablating the epidermal layer, hence, have been preferable for lesser downtime and least reported side effects.[16]

Several studies have been directed to determine the efficacy of minimally invasive procedures, most reveal a subjective assessment of the outcomes. However, only a few effective treatments for scars have been recognized, and micro-needling is considered as the newest addition for treating post-acne atrophic scars.[17]

Most of the times a derma roller is utilized in determining the advantages of micro-needling on scars to a clinical and histological level.

Micro-needling procedure enhances wound healing properties of skin,[18] effectively induces neocollagenesis without ablating epidermal layer therefore minimizing post procedure downtime.[19]

This procedure creates tiny channels that aid in absorption of numerous growth factors in PRP including epidermal growth factor, platelet-derived growth factor, transforming growth factor beta, and vascular endothelial growth factor, acting incoherent with growth factors induced by skin needling, enhancing collagen remodeling and wound healing cascade.[20]

Skin needling through controlled epithelial injury also induces potassium ions and proteins to be released from epithelial cells, eventually altering electrical potential and conductivity of interstitium resulting in migration of fibroblasts and formation of neocollagen at the site of epithelial injury.[21]

Several studies in literature support the role of microneedling in effectively inducing collagen in acne scars. Aust *et al.* showed a 40% increase in epidermal thickening with significant collagen deposition at one year post microneedling therapy.[22] Similarly Fernandes and Signorini also supported a thicker collagen deposition improving atropic acne scars.[23]

The present study showed a mean age of enrolled population to be 24.48±4.75; with a larger ratio of females to males. Porwal S *et al.* also stated similar results.[24] Our study showed most of the patients belonged to age group 18-25 years. Majid *et al.* observed age range from 13 to 34 years, with the mean age of 22.4 years.

In our study, scarring was persistent for less than 3 years in 55% of patients while more than 3 years in 45% of patients. Both treatment modalities (microneedling with topical insulin and microneedling with PRP) were more effective in scar age <3 years as compared to scar age >3 years. However microneedling with topical insulin (52.2% patients showed marked improvement) was more effective in scar age <3 years as compared to microneedling with PRP (66.7% patients showed moderate % improvement and no patient showed marked improvement) (p-value 0.001)

Most of the patients (80%) included in our study had boxcar scars. Microneedling with topical insulin was more effective in boxcar scars, ice pick scars and rolling scars as compared to microneedling with PRP.

Fitzpatrick skin type IV was present in 88.8% of patients included in our study. Both treatment modalities were more effective in skin type IV as compared to Fitzpatrick skin type V and VI. However microneedling with topical insulin was more effective (54.3% patients showed marked improvement) as compared to microneedling with PRP (69.4% showed moderate % improvement and no patient showed marked % improvement) in skin types IV (p-value 0.001).

In our study 88.7% patients were non-smokers and 11.3% were smokers. Both treatment modalities were more effective in non-somkers as compared to smokers. However microneedling with topical insulin showed good results (54.3% patients showed marked % improvement) as compared to microneedling with PRP (no patient showed marked % improvement) in nonsmokers (p-value 0.001).

Duration of sun exposure in 70% patients of our study was <3hours/day while it was >3hours/day in 30% patients. Both treatment modalities were more effective in patients having <3 hours/day duration of exposure. However microneedling with topical insulin was more effective as compared to microneedling with PRP.

In Micro-needling plus Insulin group, improvement was graded as marked, moderate and mild in 20 (50.0%), 20 (50.0%) and 0 (0.0%) respectively, while in Micro-needling plus PRP group, none had marked whereas 0 (0.0%), 27 (67.5%) and 13 (32.5%) had moderate and mild improvement with a p-value 0.005.

Side effects we studied including mild pain, erythema and edema were noted that got resolved on the same day in most of the patients. However no patient complained of post inflammatory hyperpigmentation or additional scarring. Blood glucose levels were monitored both 30 minutes before and 30 minutes after the procedure in group A. No change in blood glucose levels were noted.

There are only two studies available in the literature that used the procedure of microneedling and topical insulin in treating atrophic scarring due to acne.

Manoj Pawar *et al.* did a split face comparative study utilizing micro-needling and topical insulin (Human actrapid 40IU/ml) on the right and micro-needling with autologous PRP was done on left side of face. They enrolled 16 patients of post-acne scars having darker skin types.

The results showed 45% and 26% improvement on right and left sides of face in terms of reduction in number of scars after monthly four treatments. Topical insulin therapy was effective for boxcar scars (51.2%) as compared to PRP therapy (24.7%). Mild erythema, pain and edema were the side effects.[14] Similar results and adverse effects were noted in our study.

Mohamed Ali Mahmood Abbas *et al.* also conducted a similar study on 30 patients with atrophic scarring. After micro-needling on each side of face, Human topical insulin was introduced on left with Vitamin C serum application on right side. Acne Scar Assessment Scale (ASAS) and Scar Quartile Grading Scale (SQGS) were used to assess the scars. ASAS value on both facial sides showed significant result (2.13 and 1.83) comparison with baseline (3.03 and 2.93) (p=0.005; p=0.001 respectively).[15]

Conclusion of this study was that topical insulin and vitamin C combined with microneedling may cause comparable significant improvement in atrophic scarring and insulin can be efficacious in treatment for acne scars.

Conclusion

Combined treatment of Microneedling and insulin is more efficacious as compared to microneedling and PRP in acne scarring. This combined procedure is cost effective, favorable for all skin types with minimal post-inflammatory hyperpigmentation. Also this novel combination procedure is convenient for both doctors and patients as no high skills are required, no need to take Intravenous line and is

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