A Comparative Study between Fat Cell Grafting Alone and Fat Graft Augmented with Stromal Vascular Fraction in the Management of Postburn Hypertrophic Scarring

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ABSTRACT

Background: Post burn hypertrophic scarring represents a challenge to both surgeon and patient. Recently fat grafting has been used for regenerative purposes, taking advantage of the presence of adipose-derived stem cells. To compare the efficacy of fat graft alone and fat graft enhanced with stromal vascular fraction (cell assisted lipotransfer) in improving post burn hypertrophic scars clinically and histologically.

Patients and Methods: 20 patients suffering from post burn hypertrophic scars were divided into 2 groups; Group A: 10 patients, the scars were injected with fat only Group B: 10 patients, the scars were injected with fat enhanced with stromal vascular fraction. Evaluation was done preoperatively and postoperatively after 3 months through Vancouver scar scale, histological evaluation and photographic evaluation.

Results: Clinical improvement of the scar injected as regard elasticity, vascularity, pigmentation, scar height as assessed by Vancouver scar assessment scale. There was no statistical difference between the 2 groups.

Conclusion: Fat grafting alone superior to enriched fat as it is more simple and less expensive procedure.

Key Words: Fat cell grafting – Stromal vascular fraction – Hypertrophic – Postburn – Scarring.

INTRODUCTION

Burn injury is often a devastating event with long-term physical and psychosocial effects. Burn scars after deep dermal injury are cosmetically disfiguring and force the scarred person to deal with an alteration in body appearance (Van Loey et al., 2003).

Post burn hypertrophic scarring represents a challenge to both surgeon and patient. Hypertrophic scar is fibro-proliferative disorder of the skin that does not grow beyond the boundaries of original wound (Ogawa, 2010).

It is characterized histologically by a decrease in the thickness of epidermis, loss of differentiation between reticular and papillary dermis, increased angiogenesis, fragmented collagen with absence of whorl appearance and increased immature collagen and scanty count of elastic fiber (Wolfram et al., 2009).

The exact mechanism by which inflammation promotes scarring is not known; however, it appears that the development of scar is programmed during the inflammatory process (Peled et al., 2003).

Hyper trophic scars is principally associated with the overexpression of transforming growth factor-β1 (TGF β1), as it inhibits ECM (extracellular matrix) degradation by downregulating matrix metalloproteinase-1 (MMP-1) and upregulating tissue inhibitors of matrix metalloproteinases (TIMPs). The excessive deposition of collagen fibrils in ECM and the lower expression of remodeling enzymes e.g: Collagenase and MMPs, which mediates collagen degradation is the biological basis of scar formation, understanding mechanism of scar formation at molecular level may have a potential role in preventing and controlling scar formation (Ma et al., 2014).

Treatment algorithm includes surgical and non surgical modalities; surgical treatment includes scar revision, release by z-plasty and five flaps, tissue expansion, excision and coverage by split or full thickness skin graft and local, regional or free flaps. On the other hand, non surgical treatment includes; silicone gel or sheets, corticosteroids injection, pressure garments.

Fat grafting is a technique that allows the improvement of the quality of scar. In 1997, Coleman’s described his technique, an atraumatic method for fat harvesting, where cannula, syringe and centrifuge were used. Recently fat grafting; taking ad-
The advantage of the presence of adipose-derived stem cells; has been used for regenerative purposes as treatment of scars, wounds and ulcers.

We performed this study to compare the efficacy of fat graft alone and fat graft enhanced with stromal vascular fraction (cell assisted lipotransfer) in improving post burn hypertrophic scars clinically and histologically.

**PATIENTS AND METHODS**

This is a controlled clinical trial study with two comparison groups. The study was done at Plastic and Reconstructive Surgery Department and Burn Unit Ain Shams University Hospitals in the period from 2014 to 2016.

A total of 20 adult patients, suffering from post burn hypertrophic scar for at least 6 month duration, were selected for this study. Age ranged from 20-40 years. Selection criteria had no sex preference, patients with no associated comorbidities and nonsmoking patients.

Patients were divided into two groups; Group A: In these 10 patients, the scar was injected with fat only. Group B: In the other 10 patients, the scar was injected with fat enhanced with stromal vascular fraction (cell assisted lipotransfer technique).

The procedure was explained to the patient, its potential risks and complications informed consent was obtained from all patients at study entry and it was approved by the committee for ethics and research.

Preoperative assessment:

**Clinical assessment:**

History was taken from patient as regard the etiology, the causative agent, duration of scar and the type of treatment received.

Preoperative assessment of scar included its site, whether or not it was causing any functional disability. The scar itself was assessed using Vancouver scar assessment scale. Attributes were analyzed for vascularity, height, pliability and pigmentation, with a scoring system 0-13.

**Photography:** The camera used was a Canon Power Shot SX 170, preoperative photographs were taken for the scar using the same parameters in order to be compared with postoperative photo.

**Surgical technique:**

**A- Fat harvesting:**

Local anesthesia with sedation was used in most cases. General anesthesia was performed in some cases. Tumescent technique was used for harvesting. Fat harvesting by liposuction was standardized using 3mm blunt tip cannulas. Following aspiration the syringes filled with the collected aspirate is placed into a centrifuge run at 3000rpm for three minutes.

**B- Preparation of SVF:**

Patients in Group B were treated by fat graft injection enhanced with stromal vascular fraction which was prepared according to Yoshimura et al., 2008 with some modifications. The lipoaspirate centrifuged at 3000rpm for 3 minutes then divided into two halves, one of them used for isolation of SVF and the other half was used as a fat graft.

Isolation of stromal vascular fraction was obtained by collagenase digestion of the fatty portion. Digestion with 0.075% collagenase in buffered saline was done for 30 minutes on a shaker at 37°C. In some cases it took much longer up to 45min. Centrifugation 800g (2586r.p.m) 10min to separate the SVF, and then rinsing three times with buffered saline, sometimes more rinsing with phosphate buffered saline was needed to obtain clear sample.

The fluid portion then will be centrifuged 800g (2586r.p.m) for 5 minutes, and the pellets then resuspended in hypotonic water to lyse erythrocytes. The fluid portion is added to the graft material and, after gentle mixing and waiting for 10 to 15 minutes for cell adherence to the aspirated fat, the cells supplemented fat will be put into an injection syringe.

Determination of the presence of adipose derived stem cells (ASCs) was performed by (1) morphological identification in 10-15 days culture period as being a small cell body with a few cell processes that are long and thin (Fibroblast like). (2) CD 34 antibodies Fig. (1).
C- Fat injection:
Using 1ml syringe attached to sharp cannula injection was done at intrascar and subscar level for each 1cm² of the scar 1cc was injected, multiple injection at different sites were needed. Half of the prepared material was injected in the middle of the thick scar and the other half was injected at the subscar level.

Prophylactic antibiotics were given intraoperatively. A broad spectrum antibiotic was prescribed in all cases for the first 5 days postoperatively.

D- Biopsy:
Incisional biopsy measuring (1 X 1/2cm) was taken at the time of the operative procedure. The biopsy included the scar tissue and a layer of subcutaneous fat. They were placed in 10% saline buffered formalin to prevent their autolysis. After fixation, tissue samples are rinsed to remove excess fixative and were then dehydrated clarified then cut by microtome and placed on glass slides stained by following stains:
1- Hematoxylin-eosin for epidermis and dermis.
2- Mason trichrome for collagen.
3- Orcein for elastic fibers.

E- Evaluation:
Patients were followed-up for 1 year.

I- Clinical evaluation:
As in the preoperative evaluation Vancouver scar scale was used. This included scar vascularity, height, pliability and pigmentation.

II- Histological evaluation:
Epidermal thickness and elastic fibers count were calculated by an image analyzer Leica Q win V.3 program. The computer was connected to a Leica DM2500 microscope (Wetzlar, Germany).

F- Statistical analysis:
Mean ± standard Deviation (±SD) and range for parametric numerical data, while median and Interquartile Range (IQR) for non parametric numerical data. Frequency and percentage of non-numerical data was done for descriptive statistics.

Analytical statistics was done through; student T: This test was used to assess the statistical significance of the difference between two study group means. Mann Whitney Test (U test): Was used to assess the statistical significance of the difference of a non parametric variable between two study groups. Fisher's exact test: Was used to examine the relationship between two qualitative variables when the expected count is less than 20% of cells. Paired t-test: This test was used to assess the statistical significance of the difference between two means measured twice for the same study group.

RESULTS

During the course of study, 20 patients underwent injection of post burn hyertrophic scar with fat, we compared between two groups the 1st group was injected with fat only and the 2nd group was injected with fat enhanced with stromal vascular fraction.

There was no statistically significant difference between both groups as regard gender, etiology and site (Table 1).

There was no statistically significant difference between both groups as regard age, scar size and duration of scar (Table 2).

Follow-up was done for 3 months, after 3 months another tissue biopsy was taken. Post operative complication include edema, bruises at site of injection which subside within 1 week, no postoperative infection was reported neither in recipient site nor in donor site.

Postoperative follow-up showed improvement of the scar injected as regard elasticity, texture, pigmentation and overall scar appearance. Patients were satisfied with the overall result of operation especially the improvement of scar elasticity Fig. (2).

Immediately after the operation no change in the scar is observed, later on scar elasticity is much improved followed by color, texture and height.

After the operation some patients complained of itching at the injected site which subsided within two weeks at maximum.

Histological evaluation was done based on a biopsy stained by hematoxylin and eosin, masson trichrome, orcein stains for assessment of epidermis and dermis, collagen and elastic fibers respectively, also morphometric study was done for epidermal thickness and elastic fibers count.

In Group A: Preoperative finding showed: As regard Vancouver scar scale (mean ± SD) 7.7±2.45, epidermal thickness (mean ± SD) 163.82±32.3 and elastic fibers count (mean ± SD) 3.7±2.67.
Postoperative finding showed: As regard Vancouver scar scale (mean ± SD) 4.4±2.22, epidermal thickness (mean ± SD) 186.3±25.96 and elastic fibers count (mean ± SD) 13.58±6.69.

This table shows statistically significant improvement in VSS, increase in both epidermal thickness, increase in elastic fibers count by paired t-test.

In Group B: Preoperative finding showed as regard Vancouver scar scale (mean ± SD) 7.2±2.53, epidermal thickness (mean ± SD) 174.55±25.81 and elastic fibers count (mean ± SD) 4.26±3.82.

Postoperative finding showed: As regard VSS (mean ± SD) 3.2±2.35, epidermal thickness 233.73±68.62 and elastic fibers count 11.56±4.59.

This table shows statistically significant improvement in VSS, increase in both epidermal thickness and elastic fibers count by paired t-test Figs. (4-6).

Clinical evaluation showed overall improvement in the scar.

Tissue biopsy of scarred tissue before injection stained with H & E showed decrease in the thickness of epidermis (falttening of the epidermis), epithelial cells are not well arranged with disarray of basal cell layer and the granulous layer less evident, increased cellular degeneration, increase pyknotic cells, evidence of cellular mitosis, loss of differentiation between reticular and papillary dermis and angiogenesis.

Mason Trichrome stain showed fragmented collagen with absence of whorly appearance and increased immature collagen. Orcein stain showed scanty number of elastic fibers which are thin and short together with their absence in papillary dermis.

Three months following fat injection the tissue biopsy in both groups showed increase in the thickness of epithelium together with epithelial hyperplasia, dermal papillae become clearly visible, basal layer more arranged, increase cellular infiltration, decrease in pyknotic cells, decrease in the scar thickness, and neoangiogenesis in dermis as shown by hematoxylin-eosin.

Also in post injection tissue biopsy showed reappearance of skin appendage e.g: Sebaccous gland, sweat gland and hair follicle.

As regards collagen post injection biopsy; showed reorganization of collagen fibers where the whorly appearance of collagen bundles reappear after injection.

Elastic fibers increase markedly after injection especially around bvs with invasion of papillary dermis.

As mentioned before our study compared two groups the 1st group (Group A) only injected with fat processed according Coleman technique and the 2nd group (Group B) injected with fat enhanced with stromal vascular fraction (cell assisted lipo-transfer).

The previous table shows no statistically significant difference between the studied groups as regard different outcomes using Mann Whitney test.

Table (1): Comparison between the studied group as regard gender, etiology and site.

<table>
<thead>
<tr>
<th>Variables</th>
<th>A</th>
<th>B</th>
<th>Fisher exact test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>3</td>
<td>0.65 NS</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>7</td>
<td></td>
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<tr>
<td>Etiology:</td>
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<td></td>
<td></td>
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<tr>
<td>Chemical</td>
<td>3</td>
<td>2</td>
<td>0.729 NS</td>
</tr>
<tr>
<td>Flame</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Scald</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Site:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extremities</td>
<td>6</td>
<td>6</td>
<td>0.093 NS</td>
</tr>
<tr>
<td>Trunk</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Table (2): Comparison between the studied group as regard age, scar size and duration of the scar.

<table>
<thead>
<tr>
<th>Variable</th>
<th>A</th>
<th>B</th>
<th>t-test</th>
<th>p-value</th>
<th>Sig.</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>27.5±5.52</td>
<td>26.3±4.95</td>
<td>0.615</td>
<td>NS</td>
<td></td>
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<tr>
<td>Scar size cm²</td>
<td>16.2±5.33</td>
<td>16±7.72</td>
<td>0.947</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Duration of scar</td>
<td>2.68±2.07</td>
<td>2.55±2.21</td>
<td>0.891</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Table (3): Comparison between the preoperative and postoperative data of Group (A) as regards vancouver scar assessment scale, epidermal thickness and elastic fibers count.

<table>
<thead>
<tr>
<th>A</th>
<th>Before Mean ± SD</th>
<th>After Mean ± SD</th>
<th>Paired t-test</th>
<th>p-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancouver scar scale</td>
<td>7.7±2.45</td>
<td>4.4±2.22</td>
<td>0.001</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Epidermal thickness</td>
<td>163.82±32.3</td>
<td>186.31±25.96</td>
<td>&lt;0.001</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Elastic fibers count</td>
<td>3.7±2.67</td>
<td>13.58±6.69</td>
<td>&lt;0.001</td>
<td>S</td>
<td></td>
</tr>
</tbody>
</table>
Table (4): Comparison between the preoperative and postoperative data of Group (B) as regards vancouver scar assessment scale, epidermal thickness and elastic fibers count.

<table>
<thead>
<tr>
<th></th>
<th>Before Mean ± SD</th>
<th>After Mean ± SD</th>
<th>Paired t-test p-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancouver scar scale</td>
<td>7.2±2.53</td>
<td>3.2±2.35</td>
<td>&lt;0.001</td>
<td>S</td>
</tr>
<tr>
<td>Epidermal thickness</td>
<td>174.55±25.81</td>
<td>233.73±68.62</td>
<td>0.009</td>
<td>S</td>
</tr>
<tr>
<td>Elastic fibers</td>
<td>4.26±3.82</td>
<td>11.56±4.59</td>
<td>&lt;0.001</td>
<td>S</td>
</tr>
</tbody>
</table>

Table (5): Comparison between Group A and Group B as regard postoperative outcome.

<table>
<thead>
<tr>
<th>% of change</th>
<th>A Median (IQR)</th>
<th>B Median (IQR)</th>
<th>Mann Whitney p-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancouver scar scale</td>
<td>35.41 (25-60)</td>
<td>55 (44.4-75)</td>
<td>0.096</td>
<td>NS</td>
</tr>
<tr>
<td>Epidermal thickness</td>
<td>9.89 (8.69-14.97)</td>
<td>26.88 (8.6-39.97)</td>
<td>0.174</td>
<td>NS</td>
</tr>
<tr>
<td>Elastic fibers</td>
<td>272.12 (187.54-567.5)</td>
<td>264.81 (146.02-485.61)</td>
<td>0.496</td>
<td>NS</td>
</tr>
</tbody>
</table>

Fig. (2): 21 yrs old patient, 5 yrs scar duration, fat only group, above to the rt preoperative, (A) 3 months postoperative, (B) 6 months postoperative.

Fig. (3): 25 yrs old patient, 1 year duration, fat injection only group, (A) Preoperative, (B) 3 months after.

Fig. (4): Comparison between the score vancouver scar assessment scale preoperative and postoperative in both groups.
Fig. (5): Comparison between the epidermal thickness preoperative and postoperative in both groups.

Fig. (6): Comparison between the elastic fibers count preoperative and postoperative in both groups.

Fig. (7): Scar tissue stained by H & E showing flattening of the epidermis, disarray of basal layer of the epidermis with absence of granulous layer, presence of pyknotic cells and mitotic cells and undifferentiated reticular and papillary layers of dermis.
Fig. (8): Group A patient's biopsy stained with H & E: Rt photo: Preinjection biopsy shows thick scar, cells are not well arranged with ill defined border between them, Lt photo: Postinjection biopsy shows increase in epithelium thickness, basal layer of epithelium is more defined.

Fig. (9): Group B patient's biopsy stained with H & E: Right photo: Preinjection biopsy showing shows thick scar, cell are not well arranged no defined borders between cells, loss of differentiation between reticular and papillary dermis, Lt: Postinjection biopsy shows increase in epithelium thickness, basal layer of epithelium become more defined, differentiation between reticular and papillary dermis, increase of angiogenesis.
Fig. (10): Group B patient's post injection biopsy stained by H & E: Showing increased angiogenesis.

Fig. (11): Group A patient's biopsy stained by H & E: Rt photo preinjection biopsy showing absence of hair follicles and sebaceous glands. Lt photo postinjection biopsy: Showing reappearance of hair follicles and sebaceous glands.

Fig. (12): Group A patient's biopsy stained by Masson trichrome stain: (A) Preinjection biopsy showing wavy pattern of collagen fibers with absence of whorly appearance (B) Postinjection biopsy showed reorientation of collagen fibers in form of bundles. Fig. (C) Showing collagen fibers whorly appearance surrounding b.v.s.
Fig. (13): Group B patient's biopsy stained by Masson trichrome: Rt photo preinjection biopsy showing disorganized collagen fibers, Lt photo postinjection biopsy showing collagen reorientation.

Fig. (14): Tissue biopsy stained by orcein stain: The right photo: Preoperative biopsy shows scanty no of elastic fibers, left photo: Postinjection biopsy showing increase in the no of elastic fibers with their invasion of papillary dermis.

Fig. (15): Postinjection tissue biopsy stained by orcein: Showing invasion of papillary dermis by elastic fibers.

Fig. (16): Comparison between the 2 groups regarding percent of change of Vancouver scar assessment scale.
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Fig. (17): Comparison between the 2 groups regarding the percentage of change in epidermal thickness.

![Graph showing comparison between 2 groups](image1)

Fig. (18): Comparison between the 2 groups regarding percentage of change in elastic fibers.

![Graph showing comparison between 2 groups](image2)

**DISCUSSION**

Fat injection improves healing in different types of wounds most likely by the growth factor present in injected fat as well as the adipose-derived stem cells themselves they diminish fibrosis and inflammation and favor healing processes [8].

Ranganathan et al., [9] stated that fat grafting also improves aesthetic outcome of burn and radiation injury. It can be enriched with stromal vascular fraction or platelet rich plasma or mesenchymal stem cell.

In our study we evaluated the treatment of hypertrophic scar with fat grafting comparing two groups one injected with fat graft only and the other injected with fat graft enriched with stromal vascular fraction.

Evaluation of fat grafting as therapeutic option for management of post burn scarring discussed in previous studies. Klinger et al., [10] performed his study on three patient with hypertrophic scars located in face of 2-13 year duration were treated with fat grafting only processed according to Coleman’s technique a punch biopsy was taken from the scar and adjacent skin.

Bruno et al., [11] in his study included 93 post burn scars, mean age of the scars was 2.3 years, the first half of the scar injected of fat processed according to Coleman technique the other half is control group.

Gentile et al., [12] underwent study including 30 scars of traumatic and burn etiology he compared three groups the 1st group scar were treated with fat enhanced with stromal vascular fraction, the 2nd group fat mixed with platelet rich plasma and the 3rd group is control group where fat processed according to Coleman technique, his evaluation of scars was based on their volume restoration rather than their quality.

Piccolo et al., [13] his study included 240 patients with post burn scarring, venous and diabetic ulcers, he evaluated the efficacy of grafting in wound healing as well as improving scars, 87 patient with post burn scarring treated by fat grafting processed according Coleman technique, no control group included in the study.

In our study clinical evaluation of the scar was done after 3 months by Vancouver scar scale as it is widely used scale and can be easily applied that was unlike Pallua et al., 2014 who evaluated their patients clinically by Patient and Observer Scar Assessment Scale (POSAS).

During the course of our study we observed improvement in all parameters of the scale especially the pliability. Scar improvement continued improvement overtime however our assessment was done after 3 months. Most of patient reported their satisfaction especially regarding the scar elasticity.

Klinger et al., [10] on their clinical follow for their cases they reported improvement in texture, softness, thickness and elasticity no scoring system was used. Gentile et al., 2014 didn’t compare between the 2 groups as regard elasticity, pigmentation or thickness also no histological evaluation was done although they mentioned that patient reported improvement in texture and softness.

In our study, tissue biopsy of scarred tissue before injection stained with H & E showed decrease in the thickness of epidermis, epithelial cells are not well arranged with disarray of basal cell layer and the granulous layer less evident, increased cellular degeneration, loss of differentiation be-
etween reticular and papillary dermis and angiogenesis.

In literature few studies evaluate the effect of fat grafting on scar histologically. Klinger et al., 2008 in his study punch biopsy taken from the scar 6 months after the initial treatment with fat grafting stained with H & E showed dermal hyperplasia, hypervascularity, normal appearance of adnexal structure and new collagen deposition.

Bruno et al., [11] in their study tissue biopsy were taken at 3 and 6 months stained by histochemical and immunohistochemical stains, their result showed 6 months after treatment there were collagen eruption with better organization, reappearance of dermal papillae, decrease melanocytic activity, increase in elastic fibers number.

In our study the tissue biopsy was taken 3 months after the procedure, the results showed increase in the thickness of epithelium together with epithelial hyperplasia, dermal papillae become clearly visible, basal layer of epithelium became more arranged, increase cellular infiltration, decrease in pyknotic cells, decrease in the scar thickness, neoangiogenesis in dermis and reappearance of skin appendage as shown by H & E stain, reorganization of collagen with reappearance of whorly appearance of collagen bundles as shown by Masson Trichrome stain, increase in elastic fibers count as shown by Orcein stain.

Bruno et al., [11] in their study suggested that fat injection result in slowly long acting that trigger histological changes which reach its maximum 6 months after the injection. However in our study the biopsy was taken three months after the procedure with evident change.

The pathophysiological, cellular, and molecular mechanisms involved in scar remodelling have not been defined yet; however fat grafting procedure seems to improve the structural features of the extracellular matrix and increase its production.

Also Bruno et al., in their study assessed vascular endothelial growth factor expression it was markedly expressed before treatment and was not expressed after treatment however that finding doesn't explain the presence of angiogenesis in our study before and after treatment although it may be explained by the fact that our biopsy was taken after 3 months.

Based on previous result performed by by Piccolo et al., [13] who injected fat in scar treated by coleman technique they stated that Although there are apparent advantages in enrichment of fat with stromal vascular fraction they believe that there are enough stem cells in the centrifuged fat to warrant the obvious benefits noticed on patient treated by coleman technique, fat injection improve scars most likely through mesenchymal cells and numerous growth factors already contained in the lipoaspirate, which contribute to skin and scar remodeling.

Fat injection should be considered as a therapeutic option in management of hypertrophic scar as it is a simple procedure with minimal or no complication, however long term follow-up is needed as scar continue to improve over time following injection and repeated injection should be considered to achieve better outcome.

REFERENCES


