Evaluation of linear scars revision with and without platelet-rich fibrin and autologous unprocessed bone marrow injection

Original Article

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ABSTRACT

Introduction: There are many modalities of traditional methods of linear scar treatment including derma abrasion, chemical ablation, laser therapy, and use of surgical excision and grafting. However, surgical treatments, with or without supplementary nonsurgical treatments offers a confusing picture of widely variable 'success' rates, recurrence rates, patient populations, and follow-up periods.

Aim: Our main objective was to improve the results of treatment of linear scars. Also to evaluate of the results of adding platelet-rich fibrin (PRF) and autologous unprocessed bone marrow in surgically revised linear scars.

Patients and Methods: Total study number of 16 patients (nine men, seven women), aged 22–52 years were enrolled in this study. Six patients had the scar in the abdomen, four patients had the scar in the forearm, three in the leg and three in the neck. Assessment of scar was done including history, clinical examination using Vancouver Scar Scale, patient' and doctor' scar satisfaction. All patients were treated with scar revision by injecting half of the wound with the aspirated autologous unprocessed bone marrow and PRF. On follow-up, the patients were photographed at the start of the study (preoperative), weekly for first 2 weeks (postoperative), and monthly for the next 6 months.

Results: Adding heparinized autologous unprocessed bone marrow and PRF; may improve the pattern of scar revision. This preliminary work suggests that there were differences in the time of healing, scar appearance (100%) as P value was 0.021, pliability, height (62.5%) a *P value* was (0.009), vascularity and satisfaction (43.8%) between both groups of the study.

Conclusion: This novel treatment appeared to be safe and effective for scar treatment. To illustrate significant statistical differences, we need a larger sampling and longer follow-up periods.

Key Words: Bone marrow, mesenchymal stem cells, platelet rich fibrin, scars revision, wound healing.

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INTRODUCTION

Normal skin contains bone marrow–derived cells that are involved in host defense and inflammatory processes, including wound healing. Hematopoietic and mesenchymal stem cells are mobilized from the bone marrow into circulation after tissue injury. These cells will be hosted at the site of injury. After that they regulate the migration and proliferation of epithelial and dermal cells during the inflammatory phase[1].

Stem cells derived from the bone marrow could home to injured tissues and act on wound repair and tissues regeneration[2–6]. Adult bone marrow derived hematopoietic stem cells are the precursor to all blood cells, 'fibrocytes' and 'endothelial progenitor cells'. Stem cells have been shown to home in the site of injury improving healing process[6–12].

Platelets have many functions beyond that of simple hemostasis. They secrete growth factors which are responsible for increasing cell divisions, collagen production, attracting other cells, starting vascular growth, and initiating cell differentiation[13–16].

Platelet-rich fibrin (PRF) can hold these growth factors in a fibrin network. So, a gradual sustained release can accelerate and improve wound healing over a period of time. PRF has found a place in the regenerative field owing to its advantages over platelet-rich plasma (PRP)[17,18].

Lundquist R and colleagues reported that the platelet counts of PRF and PRP are similar but with low cost and great ease of the procedure[19,20]. Also fibrin has been shown to be an excellent provisional scaffold providing a conductive surface for cell attachment, adhesion, and migration during the initial phase of the healing process[21].

In our community, linear scars are problematic to patients and we know that the results obtained by traditional interventional methods are not satisfactory, so we tried in this study to compare the traditional surgical

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revision techniques of linear scars with injection of both PRF and autologous unprocessed bone marrow to enhance the healing process and minimize the formation of scar tissue in this lesion.

This technique is safe, easy, cheap, and may improve the results of linear scars surgical revision.

PATIENTS AND METHODS:

Patients

The current prospective comparative controlled clinical study was conducted at the outpatient clinic of plastic surgery of Suez Canal University Hospitals, Faculty of Medicine, Suez Canal University in the period between August 2015 to September 2016. after the approval of the Research Ethical Committee (REC), Faculty of Medicine, Suez Canal University was obtained. A written informed consent for treatment together with photography from all participants before enrollment in the study was obtained.

A total of 16 patients with scars fulfilling the inclusion criteria were included in the study.

The selection of the patients in this study was done according to the following criteria:

Inclusion criteria

(a) Adult patients with 18–60 years of age and of both sexes.

(b) Mature (nonhypertrophied) linear scars, indicated for revision.

(c) Treated area: linear scars all over the body.

Exclusion criteria

(a) Scars needing other surgical intervention (contracted, unstable scars., etc.).

(b) Severe Chronic medical diseases for example diabetes or hypertension.

(c) Patients with known bone marrow related disorders.

(d) Noncompliant patients.

(e) Postoperative infection.

(f) Incomplete follow-up period.

Procedure

Questionnaire designed to collect data about the personal data, preoperative, intraoperative and postoperative evaluation. All patients were interviewed and their personal data taken, and recorded.

After obtaining informed consent from the patients, Under local or general anesthesia, intralesional infiltration of 1/100 000 adrenaline, scar revision, with suturing of the dermal layer with Vicryl 5/0 sutures and the skin with 6/0 proline subcuticular suture. Proximal halves of the revised wounds were the control group, while the distal halves were the interventional group.

(a) PRF preparation: It included collection of whole venous blood (2 ml blood for each 1 cm of the wound) in sterile vacutainer tubes (6 ml) without anticoagulant and the vacutainer tubes were then placed in a centrifugal machine at 3,000 round per minute (rpm) for 10 min, after which it settled into three layers and the middle part representing platelets trapped massively in fibrin meshes was collected and applied into the interventional side of the wound.

(b) Bone marrow aspiration from posterior iliac spine crest in a heparinized syringe. The interventional half of the wound was injected immediately by the aspirated bone marrow (1 ml bone marrow for each 2 cm of wound).

The whole area was dressed by betadine ointment, Vaseline gauze and occlusive dressing.

Antibiotics, analgesics, antihistaminic and anti-inflammatory drugs were used as well as day after day dressing by Betadine ointment and Vaseline gauze till complete healing.

(a) Bone marrow aspiration and intralesional injection was repeated every week till complete healing of the wound.

(b) Silicon therapy, and pressure garment were applied for six months.

(c) Standardized clinical photographs were taken for the treated sites weekly in the first month and monthly in the following 6 months throughout the follow-up period.

(d) Record time of complete healing.

(e) Record complications (e.g. pain, discharge, infection, and scarring).

Aesthetic and functional evaluation of the treated area were done by means of questionnaire filled by the surgical staff (Scars will be assessed objectively using the Vancouver Scar Scale (VSS)).

RESULTS:

Total study number of 16 patients (9 men, 7 women), aged 22–52 years (mean age: 36.8) were enrolled in this

study. Six patients had the scar in the abdomen, four patients had the scar in the forearm, three in the leg and three in the neck.

The 16 patients were treated with scar revision with injecting half of the wound with the aspirated autologous unprocessed bone marrow (1 ml B.M.) for each 2 cm of wound length and PRF.

All patients were assessed clinically at the time of enrolment and at the end of the study by a qualitative grading score (VSS). The appearance and grading of scars were then compared with those in the pretreatment period as shown in (Fig. 1).

On the objective lines, an improvement of scarring by two grades or more was labeled as excellent response, whereas a good response means an improvement by a single grade only. Any invisible change in scarring response was labeled as poor response.

Patients and doctors' scar satisfaction was assessed on a scale of zero to ten (0=not satisfied, 2=poorly satisfied, 4=fairly satisfied, 6=satisfied, 8=very satisfied, 10=excellent).

The results of patient's and doctor's satisfaction are shown in (Figs. 2, 3). In Fig. 2 Fourteen (68.5%) patients stated that they were not satisfied preoperatively. (18.7%) of them were satisfied or very satisfied on the treated side, (50%) of them were very satisfied on autologous non processed BM side more than the scar revision only side, while (50%) described were fairly satisfied of the treated group.

Figure 3 show the difference in patients' scar satisfaction post-operative between both sides of the scar with good response only in the control group most of cases (56.2%) while most of cases in the intervention group showed excellent response (43.8%) with a statistically significant difference between both groups. All results were statistically significant.

Regarding VSS, (Table 1) summarizes the scar characteristics, percentages (%) on the VSS. preoperatively. Cases shows different percentages of skin height, pigmentation, pliability and vascularity on presentation preoperatively, while (Tables 2–5) shows the difference in patients' scar characteristics postoperatively.

Table 2 shows the height postoperative between both groups. Patients showed different scar height in the control group with most of cases (37.5%) showed a scar height 1~2 mm. While most of the cases in the intervention group showed excellent response as the scar height was normal (62.5%) with a statistically significant difference between both groups as *P value* is (0.009).

Table 3 shows the difference in scar pigmentation between both groups. Six cases presented with hypo pigmented scars, other 6 cases with hyper pigmented scars and 4 cases with mixed pigmentation. No changes were seen when scar revision only was done (37.5%), while all cases (100%) which were treated with autogenous unprocessed bone marrow and PRF showed no altered pigmentation postoperative. There's a statistically significant difference between the two study groups as *P value* is 0.021.

Table 4 show the difference in scar pliability postoperative between both groups. Most of cases had a firm (43.8%) or adherent (37.5%) scar to the surrounding tissues in the control group while most of cases (62.6%) showed a supple scar to the surrounding tissues in the intervention group. There's a statistically significant difference between the two study groups as *P value* is (0.003).

No marked improvement in scar vascularity was noticed in scar revision only (control) side, while all cases showed good to excellent vascularity on the BM treated side with normal to pink color. There's a statistically significant difference between the two study groups as *P value* is (0.037) as shown in Table 5.

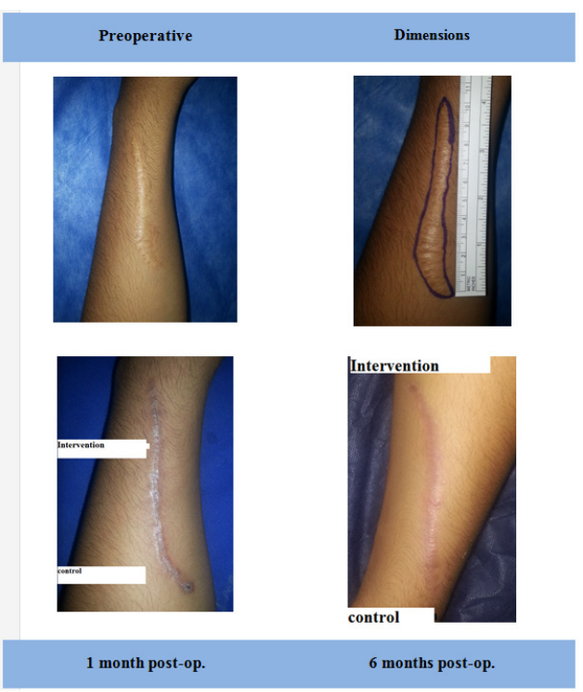

Fig. 1 A: 22-year-old male patient presented with a mature scar at the left forearm after fixation of fracture radius with plate and screws of 3 years duration.

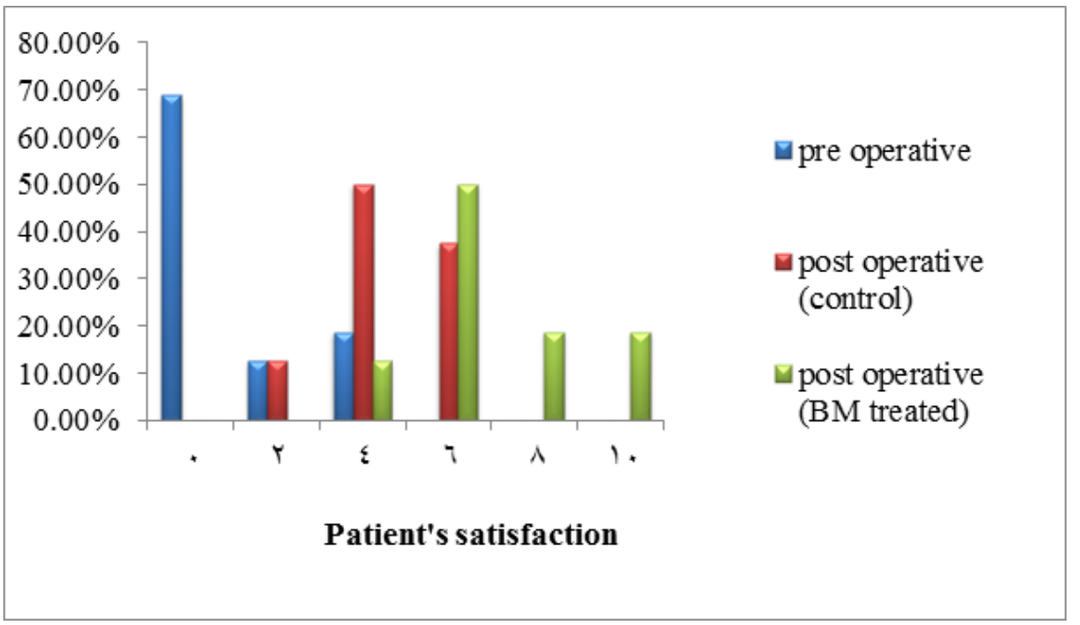

Fig. 2: Comparison of patients' satisfaction preoperative and postoperative for both groups.

Table 1: Summary of the scar characteristics preoperatively on vancouver scar scale

Characteristic	Scale	% cases	characteristic	Scale	% cases
Skin height	0	18.7	Scar pliability	0	0
	1	37.6		1	0
	2	25		2	18.7
	3	18.7		3	43.8
	4	0		4	37.5
Scar pigmentation	0	0	Scar vascularity	0	37.5
	1	37.5		1	0
	2	25		2	0
	3	37.5		3	62.5

Table 2: Difference of scar height between both groups

Characteristic	Control	Intervention	*P* value
Scale	**% cases**	**% cases**	**0.009**
Scar height			
0	18.7	62.5	
1	37.5	37.5	
2	25	0	
3	18.7	0	
4	0	0	

Table 3: Difference of scar pigmentation between both groups

Characteristic	Control	BM injection	*P* value
Scar pigmentation			
Scale	% cases	% cases	**0.021**
0	**0**	**100**	
1	**37.5**	**0**	
2	**25**	**0**	
3	**37.5**	**0**	

Table 4: Scar pliability comparison between both groups postoperative

Characteristic	Control	Intervention	*P* value
Scale	**% cases**	**% cases**	**0.003**
Scar pliability			
0	0	18.7	
1	0	62.6	
2	18.7	18.7	
3	43.8%	0	
4	37.5	0	

Table 5: Scar vascularity comparison between both groups postoperative

Characteristic	Control	BM injection	*P* value
Scale	**% cases**	**% cases**	**0.037**
Vascularity			
0	**37.5**	**56.3**	
1	**0**	**43.7**	
2	**0**	**0**	
3	**62.5**	**0**	

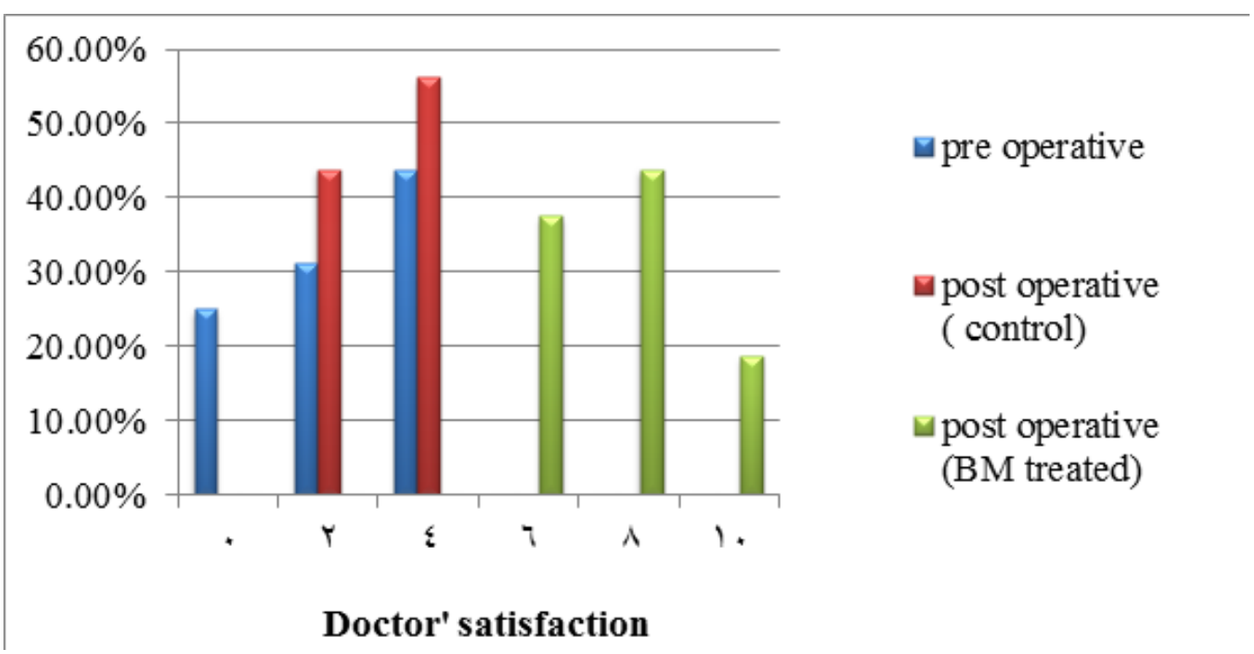

Fig. 3: Comparison of doctor' satisfaction preoperative and postoperative for both groups.

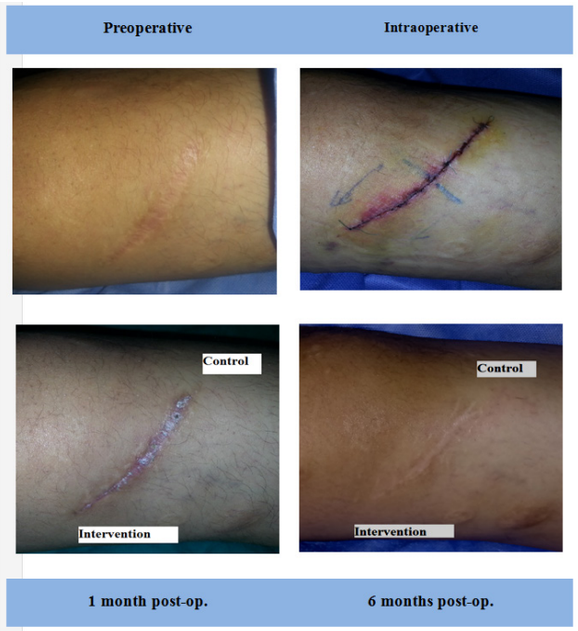

Fig. 4 A: 26-year-old female patient presented with a mature scar on the right leg after right knee cruciate ligament repair of 2 years duration.

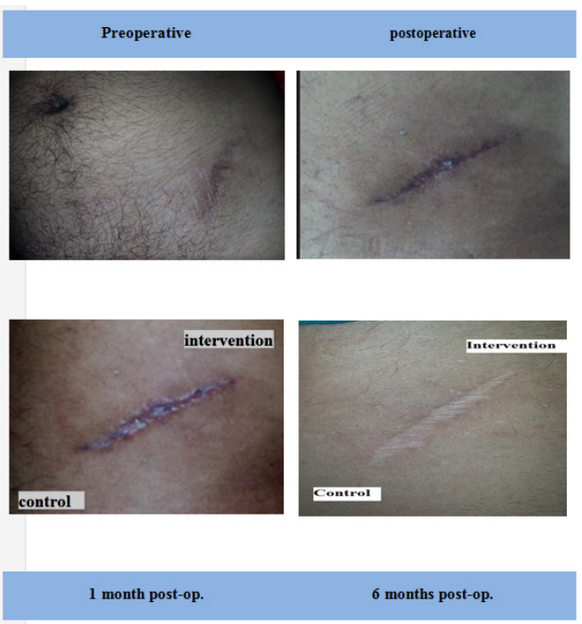

Fig. 5 A: 29-year-old male patient presented with a mature scar at the right groin after varicocelectomy of 5 years duration.

DISCUSSION

Wound healing has three principal phases: inflammatory, proliferative, and remodeling. Platelet-derived growth factor (PDGF) is released initially by platelets in the inflammatory phase during the formation of the initial thrombus. These growth factors attract, recruit, and activate additional macrophages. Transforming growth factor beta (TGF-β) is released by macrophages and platelets stimulating collagen formation (Li *et al*.)[22].

Many studies tried to combined cells from bone marrow and PRP to enhance healing. In 2011, Ravari and colleagues reported that a combination of bone marrow stem cells, platelet-derived wound healing factors, fibrin glue, and bone marrow-impregnated collagen matrix can improve the management of diabetic foot ulceration[23]. Heffner and colleagues, in 2012, concluded that addition of bone marrow derived mesenchymal stromal cells and PRP on a collagen matrix may reduce incisional hernia formation in rats[24].

Also in 2014, Lee and colleagues stated that bone marrow aspirate concentrate and PRP helped to improve bone healing in distraction osteogenesis of the tibia in humans. The combination of MSCs and PRP has many advantages. It is safe with minimal side effects because both MSCs and PRP are autologous, nontoxic, less invasive, and have no or limited immunogenicity[25].

So, we tried in this study to bring 'artificially' all factors needed for optimal wound healing to the site of injury. These factors include bone marrow mesenchymal stem cells, bone marrow hematopoietic stem cells, paracrine factors of both bone marrow and platelets, and fibrin network. The results were matching most of the literatures, but the point here is that we tried to compare the results in two groups subjectively as shown in (Fig. 4).

According to this study, treatment of patients with linear scars by intralesional PRF and B.M. injection was found to be better than treatment of the patients by scar revision only, especially in height, pigmentation, pliability, and vascularity of the scar as shown in (Fig. 5).

We are aware of limitations of this study, namely the small number of patients, lack of experience with applications of platelet concentrate in scars and still insufficient number of publications dealing with the scarring processes after PRF and B.M. injections.

CONCLUSION

Adding heparinized autologous unprocessed bone marrow and PRF; may improve the pattern of scar revision. This improvement can be documented objectively by means of questionnaire 'VSS' filled by the surgical staff, standardized clinical photographs patients, and doctor' scar satisfaction scales.

This preliminary work suggests that there were differences in the time of healing, scar appearance,

pliability, height, vascularity, and satisfaction between both groups of the study. To illustrate significant statistical differences we need a larger sampling and longer follow-up periods. There will be much to do to investigate and document these effects on biological and biochemical basis.

CONFLICT OF INTEREST

There are no conflicts of interest.

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