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Free Fat Grafting; Efficacy in Healing of Chronic Non Healing Ulcers

Col Shavinder Dogra[1], Air Cmde G S Bhatia[2], Lt Col Vibhu Sharm[3], Surg Lt Cdr Jishnu Raj(retd)[4]

[1]Dept Of Plastic Surgery, Command Hospital Western Command, Chandimandir (First Author)
[2]Dept Of Surgery, Command Hospital Western Command, Chandimandir (Second author)
[3]Dept of General Surgery, 181 Military Hospital, India (Third author)
[4] Dept Of Surgery, Command Hospital Western Command, Chandimandir (Corresponding author)

ABSTRACT

This study was carried out at two tertiary care hospitals. Patients were randomly placed in two groups - Group A (Saline dressings) and Group B (Free fat transfer) with 20 patients in each group. Eight patients , 4 from each group were lost to follow up, hence thirty two patients completed the study. In Group A, the wound was dressed with saline soaked dressings, changed daily till the end point. In Group B, fat graft harvest was done from the thigh and the prepared fat was injected into the base and margins of the ulcer. Wound size (cm2), presence of clinical signs of infection, percentage of granulation tissue covering the wound bed, percentage of non-viable tissue on the wound surface and other parameters recorded as per Bates Jensen Wound Assessment Tool (BJWAT) score were recorded. The scores were compared at initiation and end point (complete healing of wound or wound becoming fit for surgical intervention) of treatment. Free fat grafting was found to be effective in improving the overall wound condition and accelerates wound healing process in chronic non healing wounds. To conclude, this study has tried to achieve the objective of studying the efficacy of free fat transfer in healing of chronic non healing ulcers when compared to traditional saline dressings.

INTRODUCTION

Chronic wounds are wounds which have failed to proceed through an orderly and timely reparative process to produce anatomical and functional integrity over a period of three months(1,2). Common chronic wounds are diabetic foot ulcers, pressure sores, venous ulcers, arterial insufficiency ulcers and non-healing ulcers due to burns and infections, managed by dressings with agents like povidone iodine, EUSOL, acetic acid, hydrogen peroxide, silver sulfadiazine, local antibiotic ointments etc. meant for preventing infection or reducing bacterial load and promoting granulation tissue thus promoting wound healing(3). Conventional dressings take longer time to heal and drain resources(4,5). In this study efficacy of free fat transfer in management of chronic wounds was assessed compared with traditional saline dressings.

AIM & OBJECTIVE

To assess the safety and efficacy of free fat grafting in chronic non healing ulcer and poorly formed scars and demonstrate any statistically significant clinical improvement as a result of use of free fat grafting when compared with traditional saline dressings.

METHODOLOGY

The study was conducted at two tertiary care hospital over a period of 24 months from Jan 2019 to Dec 2021.This prospective study included all patients presenting to the plastic surgery OPD with chronic wounds irrespective of etiology. Institutional Ethical Committee clearance was obtained.

Sample size estimated based on assumption that incidence of chronic wounds in general population is 1.114 %. To estimate this proportion with a 95% confidence interval of proportion & margin of error as 5 % the sample size required was 17 subjects using the formula n0 = (z)2(p)(q)/(d)2 where: n0 sample size, z the value for the selected alpha level, e.g. 1.96 for (0.05) i.e at 95 percent confidence level. p was the estimated proportion of an attribute that is present in the population. q was 1-p. d was the acceptable margin of error for proportion being estimated, for possible dropouts it was decided to include 40 patients in total.

Forty patients were included for study and randomly placed in two groups- Group A (Saline dressings) and Group B (Free fat transfer) with 20 patients in each. Four patients from each group lost to follow up. 32 patients completed the study. Detailed history pertaining to duration, etiologic factors (trauma, burn, infection, diabetes, peripheral arterial disease etc.), prior treatment taken, evidence of any systemic disease and genetic susceptibility obtained. No attempt made to divide them based on etiology. Informed consent was obtained from each patient.

All patients with chronic wounds in the age group of 18-65 yrs who presented to plastic surgery OPD, at two selected tertiary care hospitals during the study period were included while patients below the age of 18 years and above the age of 70 year, patient involved in other study protocols, pregnancy or lactation,chronic renal dysfunction, acute lung infection, clinically manifested arrhythmia and epilepsy, inability to return to hospital for follow-up visits and patients taking chemotherapy, immunosuppressant or corticosteroids were excluded. They were divided into two study groups namely A and B by randomization coding system derived from computer generated randomization table.

Demographic parameters like age, sex, etiology, site of lesion recorded. Wound size (cm2), presence of clinical signs of infection, percentage of granulation tissue covering wound bed, percentage of non-viable tissue on wound surface, physician perception of treatment (improved/worsened/unchanged), patient perception of treatment (pain, discomfort, soothing, other) and adverse events recorded first at initiation of intervention and then at weekly interval.

It was a prospective study of 20 patients in each group in the age group of 18-70 years. At screening visit, subjects underwent detailed history taking and physical examination to characterise burn ulcer/scar. Ulcers/ Scars with evidence of pus, gangrene or vascular compromise excluded. Ulcer/scar measured using graph paper and photographed and placed in one of the two treatment groups, Saline dressing group (group A) and Free Fat grafting group (group B). Group A: wound dressed with saline soaked dressings, changed daily till the end point. Group B: Fat graft harvested from thigh or lower abdomen under local anaesthesia following sterile precautions using Leur-Lok syringe attached to 3 mm cannula, with two 3 mm side openings distally after infiltrating site with tumescent made by mixing 30 ml lignocaine and one ampule of adrenaline with 1 litre of RL. Compression dressing done on donor site. Harvested fat centrifuged at 3000 rpm for 3 minutes on 30 degree angle centrifuge, separating fat into three layers, top layer of oil, middle layer of fat(with Stromal Vascular Fraction(SVF) at its lower

portion) and an aqueous lower layer. Fat prepared for injection by barbotage of middle layer between two 20 ml syringes using 3-way cannula. Prepared fat injected into base of ulcer and margins subcutaneously/intradermally under aseptic precautions, after giving a regional block if required and the wound dressed using paraffin gauge dressing. Dressing changed every third day till healing. Single sitting of Free Fat Grafting done for each patient in Group B. Wounds observed at 72 hr, bi-weekly for the first four weeks and at 3 months(6).

Assessment of wound

At end of treatment sessions and during follow up visits, observation and comparison of wound done by another independent experienced observer, blinded to treatment received by patient.

During course of study cases with increase in size of ulcer on follow-up/ failure to completely heal at end of three months, evidence of frank infection such as cellulitis or pus at the ulcer base and evidence of sepsis, qSOFA score >2 were considered as failure of treatment(7).

STATISTICAL ANALYSIS

Data analysis was been done using SPSS (Statistical package for social sciences) statistical software

1. Analysis of pre-procedural variable.

a) Epidemiological data - Age: The participants varied from 54 to 74 years of age with a mean of 61.78 years. There was no statistically significant difference between the two study groups. Sex: A predominance of male patients was seen which is consistent with the previous known epidemiology of the disease. Both the groups were evenly matched with respect to the no of participants of either sex(8).

b) Clinical data- Location of Ulcer: All the ulcers included in the study were located over the lower limb. Smoking: History of smoking was seen in 21.9% of all individuals participating in the study. The difference between the distribution of individuals with history of smoking between two groups was not statistically significant (P value= 0.083). Hypertension: Overall proportion of hypertensives within the study population was 21.9%. Hypertensives were evenly distributed between two study groups (P value = 0.083). Peripheral Arterial Disease: Peripheral arterial disease was present in 18.8% of the individuals participating in the disease. The difference between the two groups was not statistically significant(P value = 0.172). Cardiac Disease: 18.8% of all study subjects suffered from cardiac diseases. Difference between two groups was not significant (P value = 0.172). Chronic Renal Failure: None of the patients included suffered from chronic renal failure. Other co-morbidities: The frequencies of other co-morbidities. Anaemia had a statistically significant incidence with a P value of 0.043. Body Mass Index: The variation in Body Mass Index between the two groups was significant with a P value of 0.048. Neuropathy: Both the groups were well matched with respect to patients testing positive for neuropathy (P value = 0.479)(15). Ankle brachial pressure index (ABPI): There was no statistically significant variation between the indices for control and test group subjects (P value = 0.120)(10).

Ulcer characteristics- Ulcer duration(months): The ulcer duration was recorded in months as reported by the patient. The data was skewed and its distribution between the two groups was found to be statistically significant (P value = 0.009). Ulcer size (cm2): Ulcers were measured using a graph paper. The analysis however found not to be significant (P value = 0.296 distribution within the study population was found to be skewed, therefore subjected to non-parametric). Ulcer grade: Wagner's system of grading diabetic foot ulcers was used. The two groups did not have a statistically significant difference with respect to this characteristic (P value = 0.527)(11). Wound infection: Wound swabs were taken from the ulcer floor to guide the antibiotic prophylaxis given to the patient(12,13,14)

(2) Outcome and results: Four cases from 'Test' group and five cases from 'Control' group lost to follow up. Further three cases from 'Control' group excluded as ulcers developed evidence of frank infection. A total of sixteen 'Test' cases and twelve 'Control' cases were available for analysis

(a) Primary outcome measures

Wound Healing: Days taken for wound healing measured. It was recoganized that various other factors affect rate of healing other than parameter under consideration such as initial size of ulcer (larger ulcers take longer to heal), duration of ulcer (older ulcers might take longer to heal), duration of diabetes (longer duration of diabetes would result in more severe micro and macro-angiopathic changes resulting in longer duration for healing), body mass index (BMI) (as higher body mass could be related to higher atherosclerosis), pallor (anaemia result in decreased nutrition hence slower healing) Considering multiple variables which could additionally affect primary outcome and statistically significant difference between test and control groups it was decided to subject the results to univariate analysis in order to eliminate all possible confounding factors. Results were found to be statistically significant with a P value of 0.023 and predictability power of 65%.

b) Secondary outcome measures

Pain at donor site was measured for test group using Visual analogue scale. Mild to moderate intensity pain was experienced by subjects and controlled using oral analgesics(15). Haematoma formation(at donor site in Test group) was not seen in any. Paraesthesia (at donor site in Test group)- five out of sixteen subjects reported parasthesia(31.25%) Scar quality at three months was assessed using Vancouver scar score. There was a statistically significant difference between two groups. Breakdown at 6 months of healing: None of the healed wounds showed any breakdown at the end of six months however two patients died within 2months after the ulcer had healed.

c) Other complications

Two out of sixteen subjects in 'Test' group developed surgical site infection at donor site, accounting for 12.5% of subjects.Two out of twenty cases in 'Test' group developed pain at recipient site, accounting for 10% of cases.

Figures:-

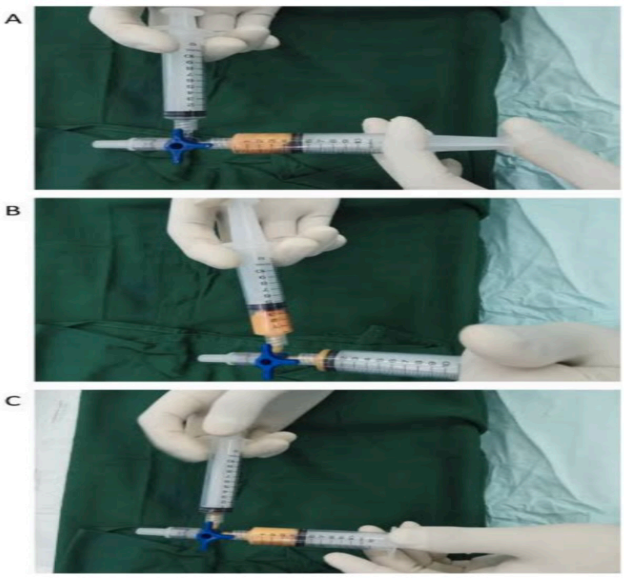

Fig 1. Fat preparation by barbotage of middle layer of centre using syringe and 3way cannula

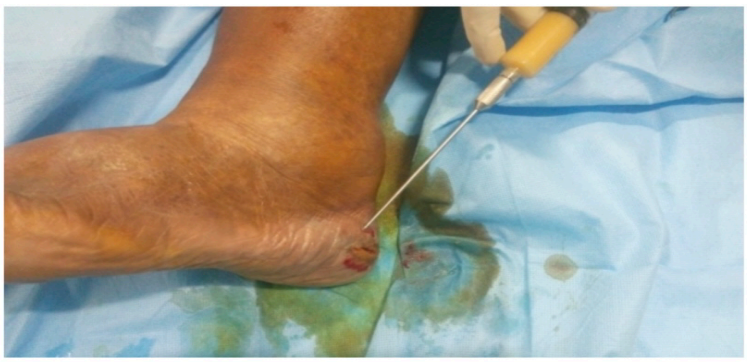

Fig 2. Injection of processed fat into the margins and base of the ulcer

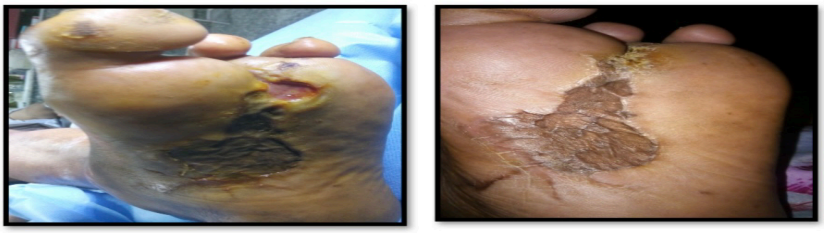

Fig 3 & 4. REPRESENTATIVE CASE 01

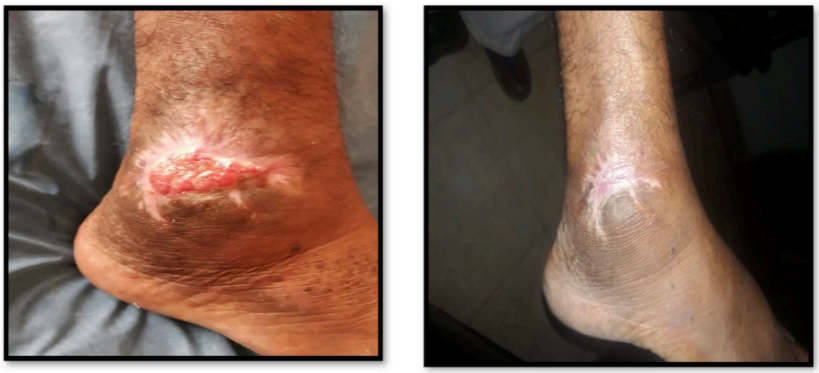

Fig 5 & 6 REPRESENTATIVE CASE 2

DISCUSSION

Chronic non healing ulcers while being a major source of morbidity to patient, continue to be a tricky situation for general surgeon, given the poor results despite varied efforts towards wound healing.

This study is an attempt at assessing efficacy of fat grafting in assisting wound healing in chronic non healing wounds. It is a comparative analysis done under the aegis of Surgical Division and Reconstructive Surgery Department at two tertiary care hospitals over a span of two year. Twenty cases each were recruited to the two groups viz 'Test' and 'Control' as per a pre-determined randomization plan. So as to avoid any confounding factors, pre-determined inclusion and exclusion criteria were strictly followed. After procedure patients were admitted to the hospital till the first dressing change and

thereafter discharged on regular follow-up. Pre-determined Primary and secondary outcome measures were assessed and any additional findings duly recorded.

PRIMARY OUTCOME MEASURES

In this study the ulcers managed with free fat grafting healed with in a mean of 43.25 ±17.46 days which was significantly better as compared to 64.42 ± 8.35 days (p value = .023, accounting for other variables such as BMI, duration of diabetes, duration of ulcer, size of ulcer, pallor) for ulcers managed with saline dressings.

The results are comparable to Han et al's in "The treatment of diabetic foot ulcers with uncultured processed lipoaspirate cells: a pilot study" where they observed complete healing in 17 to 56 days (mean, 33.8 ± 11.6 days) in the Processed lipoaspirate cell-treated group and from 28 to 56 days (mean, 42.1 ± 9.5 days) in the control group ($p < 0.05$). The time to healing was slightly better and can be attributed to a more extensive processing than in our study.

Stasch et al in "Débridement and Autologous Lipotransfer for Chronic Ulceration of the Diabetic Foot and Lower Limb Improves Wound Healing" observed that 22 out of 25 chronic ulcers after being managed with lipotransfer healed in 68 ± 33 days. This study consisted of subjects suffering from Diabetes Mellitus, Peripheral Arterial Disease and Chronic Renal Failure when compared to our study, it was ensured that patients with peripheral arterial disease had an ABPI of 0.5- 1.3, moreover no patients with chronic renal failure were included in our study which has resulted in faster healing in our subjects as compared to this study.

The comparison further brings out the multifactorial nature of wound healing and how adequate attention to other possible factors must be paid before considering the effects of the factor under study.

SECONDARY OUTCOME MEASURES

Fat grafting resulted in statistically better quality of scar as compared to ulcers managed with saline dressings. Tolerable donor site pain was seen which was managed with oral analgesics which is well documented as mentioned by Kotaro Yoshimura et al in "Complications of Fat Grafting: How They Occur and How to Find, Avoid and Treat Them." Donor site paraesthesia was seen in 31.25% of the subjects undergoing fat grafting which was temporary, caused due to neuropraxia of the subcutaneous nerves caused during liposuction. None of our subjects reported haematoma formation at the donor site. No breakdown of scar was seen at six months after the procedure for either of the groups implying no significant advantage with regards to stability of scar.

OTHER COMPLICATIONS

Donor site surgical site infection was seen in 12.5% of subjects which re-emphasizes the need for stringent asceptic precautions. Pain at recipient site seen in 10% of individuals was another complication of the procedure observed which was in case of fat grafting over the heel. The pain was managed satisfactorily with oral analgesics.

LIMITATIONS OF STUDY

1. Selected centre study.
2. Not a blinded study.
3. Not a randomized control trial.

4. Wound swabs used for assessment of infection status rather than ulcer base biopsy.
5. Comparison groups not matched with respect to location of ulcer.
6. No previous similar studies available, it is difficult to verify results.
7. Histopathological examination of healing ulcers and scars not carried out, which could provide a more substantial evidence.

CONCLUSIONS

Prospective randomised study to study the effects of free fat grafting in chronic non healing ulcers in comparison to traditional saline dressings.At the end of the study it is suggested that fat grafting resulted in healing of chronic non healing ulcers faster as compared to when managed with saline dressings. The scar quality was assessed as per the Vancouver scale and observed that free fat grafting resulted in better quality of scars subjectively. It is therefore recommended that fat grafting may be considered in selective patients with chronic non healing ulcers without overt infection to enhance wound healing.

RECOMMENDATION

Use of free fat transfer in chronic non healing wounds is a promising treatment modality. Its use can negate the need for complicated surgical procedures. Useful method for treating Ulcers at peripheral centres.

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