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Original Research Article

Effect of moist dressing, collagen sheet dressing and epidermal growth factor in healing of chronic wounds

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ABSTRACT

Background: Surgical literature is full of innumerable solutions to the problems of wound healing and it speaks of itself that the problem is not so simple and straight forward to tackle with. The aim of the present study was to compare three modalities moist saline dressing, collagen sheet dressing and epidermal growth factor in early epithelization and healing of chronic wounds. to study the effect of various dressing modalities on epithelization of chronic wound in terms of time required for healing and the quality of scar it forms, the functional results both early and late, post-healing morbidity and complications and the practicality and the cost involved in using these modalities.
Methods: Prospective randomized controlled study. Study including chronic wound cases admit to AVBRH Sawangi over period of 3 years.
Results: Reduction in size of wound by 70-100% was found highest in Epigrof group. In Epigrof treated group 88% of wounds healed within 3 weeks while 80% in collagen group and 56% in moist dressing group it. Collagen dressing is the most cost effective of the three whereas Epigrof was most costly due to the initial cost of purchase. The scar quality was satisfactory in 19 of Epigrof group and 17 of the collagen sheet group and 15 of the moist dressing group.
Conclusions: Epidermal growth factor is superior in epithelization, collagen is the next best local applicant, but collagen sheet is more cost effective than Epigrof and non-adherent dressings.

Keywords: Chronic wound healing, Collagen sheet dressing, Epidermal growth factor, Epigrof, Moist saline dressing, Scar quality

INTRODUCTION

Wound healing has been matter of concerned since dawn of civilization. It dates back to 2000 BC when Sumerians who described wound healing as spiritual and physical. Later as studies were carried out these concepts were modified. Then came the concept that the body's response to injury leads to release of various chemicals so called mediators of healing which helps in wound healing. Knowledge of wound healing and various promoters of wound healing allow the physicians to manipulate the wound to achieve an optimal result in a rapid period of time.

Surgical literature is full of innumerable solutions to the problems of wound healing and it speaks of itself that the problem is not so simple and straight forward to tackle with. Among various substances studied, tissue therapy has proved to be the most starlit and revolutionary. These biological stimulators help in wound healing and cure a wide array of ailments by stimulating the inborn vital defense processes of the body.

Modalities used in present study are moist non-adherent dressing, epigrof ointment (epidermal growth factor) and collagen sheet.

Moist dressing

Fine and wide meshed weaved cotton gauze has been used for many years for debridement of heavily contaminated exudative and necrotic wounds. As the dressing dries fibrin from the wound bed causes temporary bonding of the dressing to the wound. The dressing is usually changed after 24 hours, the wound is lavaged with a sterile diluted antiseptic solution which is delivered to the wound surface. Virginia A C et al, also supported the theory that saline dressing is efficacious in promoting wound healing.[1] Choice of dressing or tropical agent affects the healing of surgical wounds by surgical intention as per Vermeulen H, Kunugiza Y found that gauze encourages scab formation, which impairs epithelization and increases VEGF expression.[2,3] Topical negative pressure dressing help in faster healing of chronic wounds and better graft take-up and reduce hospital stays compared to conventional gauze dressing by Francis TL.[4] Xalellis GC stated that cost of hydrocolloid treatment was significantly less expensive.[5]

Collagen sheet dressing

R Krishnan studied role of collagen sheet as a temporary cover for raw area on dogs and concluded that it prevents exogenous infections, promotes rapid epithelization, frequent dressing is not required, lesser time to heal as compared to other conventional dressing.[6] Jeschke G concluded that collagen matrix accelerates epidermal regeneration and locally increases growth factor concentration.[7] Snap L et al studied chronic ulcer with collagen sheet to conclude that it encourages early healing with uniformity in granulation.[8] Chengcan Yao et al, found that wound healing was enhanced in traumatic ulcers with application of absorbable collagen sponge.[9] P Halankar found that there was hematoma beneath the collagen dressing but there was complete re-epithelization beneath the hematoma.[10]

Epidermal growth factor

Epidermal growth factor enhances in vivo resurfacing of porcine wounds. Nanney LB concluded that topical application of EGF stimulates epithelization of partial thickness wounds and produces a positive impact on the underlying dermis during the early phases of wound repair.[11] Ingo Haase et al, demonstrated that EGF can influence different components of the keratinocyte migration determining the speed of wound epithelization.[12] X B Fu et al, stated that after application of EGF in local wound, the wound healing velocity can be accelerated and wound healing quality improved with their powerful mitogenic and non- mitogenic effects.[13] Hoa Le Tuyet evaluated the efficacy and safety of recombinant human epidermal growth factor in healing foot ulcer in diabetic patients with positive response of granulation.[14] Hence the present study was conducted with objectives to study the effect of various dressing modalities on epithelization of chronic wound in terms of time required for healing and the quality of scar it forms, to study the functional results both early and late, to study post- healing morbidity and complications and to study the practicality and the cost involved in using these modalities.

METHODS

Comparative study of healing and epithelization of 150 cases done, admitted in Acharya Vinoba Bhave Rural Hospital Sawangi (Meghe) Wardha from June 2008 to August 2010.

Materials to be compared

- Dressing materials (saline soaked gauze, vaseline gauze, paraffin gauze)
- Epidermal growth factor ointment (Epigrof)
- Collagen sheet

Moist saline dressing

Meshed cotton gauze soaked in normal saline placed over wound and changed daily or as required according to the wound condition.

Collagen sheet

Material used is collagen in sheet form produced from Bovine sources composed mostly Type 1 and Type 3 collagen. Collagen is packed in neutral glass vials containing sterile preservative liquid medium sterilized by Ethylene oxide and available in various sizes. Expose denuded area thoroughly cleaned. Selected right dimension collagen sheet is washed thoroughly in sterile normal saline. Apply local collagen sheet firmly on raw area with no air bubble in between. No repeat dressings.

Epidermal growth factor

Wound cleaned thoroughly then Epigrof ointment applied over the wound surface of approx. 2mm thickness. The wound is secondarily dressed with dry cotton gauze and changed daily.

RESULTS

In present study, patients of all age were included and grouped at 10 years interval. About 60 % were above 30 years, suggesting that chronic wound is common in the middle aged and the elderly depending on their etiology. When the types of wounds were studied on basis age groups the findings were traumatic wound and varicous ulcer may be seen in any age group. Diabetic wounds were found more in elderly with maximum cases detected after 40 years of age. This may be depending on the fact that they are mostly insulin dependent diabetes mellitus.

Abscess and cellulitis related wound gape is found to be common in all age groups.

While looking at the gender distribution present study included 76% males and 24% females. Traumatic ulcer, varicose ulcer and wound dehiscence are found to be common in male patients. Abscesses are common in both the sexes. Various types of wounds were randomly selected for local treatment with non-adherent dressing, collagen sheet and Epigrof. 5 patients of varicose ulcer were treated with collagen sheet and 7 patients were treated with epidermal growth factor. Table 1 shows that 60% patients treated with Epigrof application showed 70-80% reduction in size. In present study 52% of the patients treated with local application of collagen showed 70-100% of reduction in size of wound as shown in Table 2.

Table 1: Wound reduction in epigrof group.

Time in week	Percentage of reduction in size										No. of patients	Percentage
	No response	10-20%	21-30%	31-40%	41-50%	51-60%	61-70%	71-80%	81-90%	91-100%		
0-1	--	--	--	1	--	--	--	--	--	1	2	8%
1-2	--	--	--	--	1	1	2	1	--	2	7	28%
2-3	--	--	--	--	--	2	2	--	--	9	13	52%
3-4	--	--	--	--	--	--	--	--	--	2	2	8%
4-5	--	--	--	1	--	--	--	--	--	--	1	4%
Total	--	--	--	2	1	3	4	1	--	14	25	100%
%	--	--	--	8%	4%	12%	16%	4%	0%	56%	100%	

Table 2: Wound reduction in collagen sheet group.

Time in week	Percentage of reduction in size										No. of patients	Percentage
	No response	10-20%	21-30%	31-40%	41-50%	51-60%	61-70%	71-80%	81-90%	91-100%		
0-1	--	--	--	--	--	--	--	--	--	--	--	0%
1-2	--	--	1	--	1	--	2	--	--	5	9	36%
2-3	--	--	--	--	1	1	3	--	--	6	11	44%
3-4	--	--	--	1	--	--	--	--	1	1	3	12%
4-5	--	1	1	--	--	--	--	--	--	--	2	8%
Total	--	2	2	1	2	1	5	0	1	12	25	100%
%	--	8	8	4	8	4	20	0	4	48	100%	

Table 3: Wound size reduction in moist dressing group.

Time in week	Percentage of reduction in size										No. of patients	Percentage
	No response	10-20%	21-30%	31-40%	41-50%	51-60%	61-70%	71-80%	81-90%	91-100%		
0-1	--	--	--	--	1	--	--	--	--	--	1	4%
1-2	--	--	--	--	--	--	--	--	--	4	4	16%
2-3	--	--	--	1	--	1	1	1	1	4	9	36%
3-4	--	--	--	3	1	2	3	--	1	1	11	44%
Total	--	--	--	4	2	3	4	1	2	9	25	100%
%	--	--	--	16%	8%	12%	16%	4%	8%	36%	100%	

Present study showed that 48% of patients treated with non-adherent dressing showed 70-100% of reduction in size of wound (Table 3). It was observed that 36%, 48% and 56% of patients treated with non-adherent dressing, Collagen and Epigrof respectively showed 90-100% of reduction in size of wound where the mean size of the wound before treatment in the non-adherent dressing group was 7.64 cm^2, 13.36 cm^2 in collagen sheet treated group and 10.4 cm^2 in Epigrof group. When all three modalities were compared non-adherent dressing group 56% of patients showed healing completely by 3 weeks (Table 4). In collagen group 80% patients healed within 3 weeks as was seen in present study.

88% of patients were healed in 3 weeks in Epigrof group in present study. Average cost of non-adherent dressing

was found to be 912 rupees which was more than collagen dressing. Average cost of dressing for collage was 675 rupees which was depicted to be less due to less number of dressing changes though the duration remains longer. Epigrof group had average cost of 1226 rupees in the present study. The average hospital stay in the non-adherent group is 15 days, in collagen group was 14.9 days and in Epigrof group is 15.8 days. This study was conducted in rural hospital where patients were admitted for such treatment to prevent them from lost to follow-up. Total 61 patients came for follow up at 6 months while 39 patients came at 1 year. The patient who came for follow up at 6 months out of 25 patients in each group gross scar thickening was absent in 15 patients of moist non-adherent dressing group, 17 patients of collagen sheet group and in 19 patients of Epigrof group. In non-adherent dressing group 4 patients, collagen sheet group 3 patients and Epigrof group 3 patients showed sensitivity and pain. Amongst the 39 patients who came for follow up at 1 year 6 had unstable scar, these were the patients who were paraplegic/ quadriplegic or diabetic Table 5.

Table 4: Duration of complete treatment.

Total duration of complete treatment (weeks)	Non-adherent dressing	Collagen	Epigrof
0-1	1	0	2
1-2	4	9	7
2-3	9	11	13
3-4	11	3	2
4-5	--	2	1
Total	25	25	25

Table 5: Scar characteristics.

Local application	6 months follow-up				1 year follow-up	
	Gross scar thickness		Sensitivity/pain		Unstable scar	
	Present	Absent	Present	Absent	Present	Absent
Non-adherent dressing	5	15	4	16	3	10
Collagen	3	17	3	17	2	12
Epigrof	2	19	2	19	1	11
Total	10	51	9	52	6	33

In present study 17 patients of collagen sheet group had a satisfactory scar. In Epigrof group 19 patients had satisfactory scar while 2 had non-satisfactory scar.

The practical problem faced in present study was loss of patients to follow up. The reasons detected are lack of awareness, lack of transport and communication. Reasons for this are patients living in remote areas and moreover they are daily wages workers with low income.

DISCUSSION

Present study shows that middle age is commonly affected with chronic ulcers which co-relates to the study by Mustoe T et al, who states that chronic wounds mostly affects elderly age group mostly above 60 years of age.[15] Crovetti G et al, states that more incidences of injuries are seen in the age group of more than 60 years.[16] Kumar P and present study shows that traumatic and venous ulcer can be seen in any age group.[17] Diabetic ulcer being common in elderly group co-related to the study by Ch. Manes et al, in which the mean age was significantly higher in neuropathic patients than non-neuropathic patients.[18] Male predominance for ulcer co-relates with the study by Francis TL et al, in which ratio of male to female is 1.24: 1 and Pramod Kumar et al 201017 where the results suggest that the male to female ratio was 17:3.[4]

Patient selection was supported by the study by Snap L et al, where 92% improvement was seen in venous ulcer treated with collagen and a study by Falagen V which suggests a greater reduction in size and a larger number of healed ulcer with the use of h-EGF.[8,19] Veves A et al, stated that moistened gauze was comparable to Promorgan in promoting wound healing in diabetic ulcers.[20] 70-80% reduction in size of ulcer with Epigrof dressing co-relates with Brown GL patients healed completely with epidermal growth factor in an average of 34±26 days Tsang MW as 20-21 patients out of 61 patients showed complete wound healing.[21,22] Sundarrajan CR et al, suggested use of collagen sheet for the treatment of burns after removal of eschar with a rate of epithelization of 7-15 days in collagen group as compared to 10-20 days in control group.[23] Also in other study Long MA found 61% decrease in wound area treated with pure collagen dressing by the end of 2 weeks.[24] 70-100% reduction in size of ulcer in non-adherent dressing group closely co-relates to the study by Dagilaitis R et al, who found out that rate of epithelization at 3 months to be 98% for ulcers <3 cm^2 in size.[25] Also Xakellis GC et al, found that the mean dressing time was greater in gauze treated group than hydrocolloid group for complete healing.[5] Healing rates in non-adherent dressing group co-relates with the results

of study by Ubbink DT et al 2008.[26] Similar were the findings in study by Dagilatis R et al.[25]

The present study results of collagen group are correlating with studies by Sundarrajan CR et al showing epithelization in 7-15 days.[23] Whereas Jansson K et al found complete epithelization in 7 days.[27] Epigrof group results were similar to study by Tsang MW who found it to be 50% in 3 weeks and complete healing by 12 weeks.[22]

Cost of treatment results correlates with finding of Virginia et al, who found that overall cost of wound care was significantly higher for patients in normal saline group due to higher number and cost of dressings.[31]

Less cost of collagen dressing was also stated by Umesh Shah.[28] Epigrof group cost effectiveness has not been evaluated by any clinical trial as stated by R Eldor et al.[29]

Most of the patients in the mentioned literature Virginia AC et al, Vermeulen H and Xakellis GC have been treated as out-patients hence could not be directly correlated with present study.[1,2,5]

Pain and sensitivity observation in the present study co-relates to the study by P Halankar who found hypertrophic scarring in 2 patients treated with collagen sheet.[10]

Scar status had similar findings as was seen in study by Tuyet HL where only 1 female patient had over-granulation.[14]

The rising cost of health care delivery is universal and can be afforded only by a few so newer modalities like Epigrof and collagen should be welcomed in this field of treating wounds.

The present study consisted of 150 patients of various wounds of which patients who lost to follow-up were excluded from the study. Hence 75 patients of various type of wounds like traumatic (19%) diabetic ulcer (12%) varicose veins (16%) abscess (21%) wound dehiscence (21%) and cellulitis (7%) were included in the study.

Amongst the included patients 76% were males and 24% were females. Equal number of patients were randomly selected for treatment with local application of moist dressing, collagen and Epigrof. Reduction in size of wound by 70-100 % was found in 60%, 52% and 48% of patients in Epigrof, collagen and moist dressing group respectively.

Epigrof is the most efficacious in epithelization of the chronic wounds followed by collagen and then is moist non-adherent dressing.

In Epigrof treated group 88% of wounds of patients healed within 3 weeks while 80% of wounds of patients healed within 3 weeks in collagen group and in moist dressing group it was complete healing in 56% by 3 weeks.

The average cost of treatment in non-adherent dressings, collagen and Epigrof was 912, 675 and 1226 respectively. Collagen dressing is the most cost effective of the three modalities whereas Epigrof was most costly due to the initial cost of purchase.

The scar quality was satisfactory in 19 of the patients of Epigrof treated group and 17 of the collagen sheet treated group and 15 of the patients had a satisfactory scar in moist dressing group.

CONCLUSION

- Local application of Epigrof in wound management is found to be effective in wound healing as:
    a) It promotes early epithelization of wound
    b) There is formation of satisfactory scar after healing
- Collagen was the most cost effective of the three modalities and decreased the morbidity of the patients as compared to the other modalities.
- In a rural setup, in view of cost factor and awareness of the patient population, collagen sheet should be used for dressing of diabetic and various ulcers whereas epidermal factor in traumatic and diabetic ulcers as it decreases the cost of ulcer.

As per the present study in comparison, epidermal growth factor is superior in epithelization, collagen is the next best local applicant, but collagen sheet is more cost effective than Epigrof and non-adherent dressings.

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