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COMPARATIVE STUDY OF EFFICACY OF EPIDERMAL GROWTH FACTOR WITH NEGATIVE PRESSURE DRESSING IN HEALING OF PRESSURE SORES

Surgery

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ABSTRACT

Constant pressure resulting in 'distortion or deformation damage' is probably the most accurate description of a pressure ulcer. In the present study we compared the efficacy of Recombinant human epidermal growth factor (rhEGF) with negative pressure dressing and daily twice regular gauze dressing for healing of pressure sores. Patients > 18 years age, of either gender, hospitalized & diagnosed case of pressure sore/decubitus ulcer/bed sore, ulcer volume ranging between 8 – 200 cm3, were divided into three groups as Study group (A) receive rh-EGF along with gauze dressing, study group (B) received Negative pressure wound therapy (NPWT) dressing & control group (C) received twice daily simple gauze dressing changes. Total 60 patients were recruited, 20 in each group. In group A, B & C there was significant decline observed in wound length & width at 1, 2 and 3 weeks as compared to 0 week. In group A & B there was significant decline observed in wound depth, area & volume at 2 and 3 weeks while no difference at 1 week as compared to depth at 0 week. Use of growth factors has shown beneficial effect in wound healing considering the depth parameter when compared with conventional methods.

KEYWORDS

Pressure sore, Epidermal growth factor, NPWT, wound

INTRODUCTION

Pressure injuries, previously called pressure ulcers, result from local trauma to the skin and/or underlying tissues due to pressure with shear or friction or unrelieved pressure for certain period causing tissue ischemia, cessation of nutrition and oxygen supply to the tissues and eventually tissue necrosis. Constant pressure resulting in 'distortion or deformation damage' is probably the most accurate description of a pressure ulcer. [1]

Apart from health conditions (mental or physical) that encourage immobility, those with immune compromised states and are more common in patients aged > 65-70 years additional risk factors appear to increase the likelihood of developing a pressure ulcer, including poor nutrition, comorbid conditions, such as diabetes mellitus and peripheral arterial disease (PAD), immunodeficiency or the use of corticosteroid therapy, and smoking. Any prior pressure ulcer increases the risks for additional ulcers. [1,2]

Various methods have been used to study the treatment of patients with pressure ulcers, with negative pressure wound therapy (NPWT), maintained through the film dressing, which is semi-permeable to maintain moisture in the wound area and facilitate recovery.[3,4,5] Growth factors are endogenous signaling molecules that regulate cellular responses for wound healing process. These proteins are upregulated in response to tissue damage and are secreted by platelets, leukocytes, fibroblasts, and epithelial cells. Once growth factors are secreted, they act through autocrine, paracrine, or endocrine mechanisms by binding to membrane or cytoplasmic receptors. [6]

The present study was aimed to compare the efficacy of Recombinant human epidermal growth factor (rhEGF) with negative pressure dressing and standard method of dressing i.e., daily twice regular gauze dressing for healing of pressure sores.

MATERIAL AND METHODS

Present prospective observational study was conducted in department of General Surgery, at Bharati Vidyapeeth (DTU) Medical College and Hospital, Pune, India from September 2019 to August 2021. Study was approved by institutional ethical committee and informed consent was obtained from each participant before enrollment.

Patients above 18 years age, of either gender, hospitalized & diagnosed case of pressure sore/decubitus ulcer/bed sore, ulcer volume ranging between 8–200 cm^3, willing to participate & follow up were included in the study. The patients with arterial, venous disorder as cause for ulcerated wound, with malignant Ulcers, recent use of chemotherapy, and/or patient refusal to continue participation, patient gets discharged, or DAMA were excluded from study.

Patients were divided into three groups - two study groups and one control group in a sequential manner (A->B->C) to the patients regardless of the pressure sore grade.

1. Group A: Receive rh-EGF along with gauze dressing. Recombinant human epidermal growth factor (rhEGF) (gel base) of strength 60 pg/gm, was applied twice daily for all grades of pressure sores,.
2. Group B: Receive Negative pressure wound therapy dressing. Vacuum assisted closure (VAC) device containing sterile sponge, translucent air seal dressing (IOBAN), centralized suction pump system with tubing (RYLE'S TUBE). NPWT dressings was applied for all grades of pressure sores and changed after 48 hours.
3. Group C: Control group received twice daily simple gauze dressing changes.

Ulcer grading was done according to 'European Pressure Ulcer Advisory Panel Grading System'. [7] Routine blood investigations including complete blood count, blood sugar, urea, Serum creatinine & special investigations like pus culture and sensitivity or tissue culture and sensitivity, colony count, histological analysis of wound tissue were done at the start and at the end of the study.

Initial sharp debridement was done to remove any necrotic tissue and slough followed by application of the Drug and Special dressing as per group allocation, if required. The maximum and expected duration of study of treatment was 4 weeks (28 days). Standard pressure-relieving devices (air-fluidized bed) were used, if required. Patients not on air-fluidized beds were repositioned rigorously at 2-hour intervals throughout the treatment period. Treatment outcome assessed (by week 1, 2, 3 and 4) were wound contraction achieved, wound surface area (length × width × depth), wound Volume (area × depth × 0.327), pain by VAS Scoring. Final outcome was reported as either healing by secondary intention (no requirement of intervention) or requirement of STSG/Surgery (intervention)

Statistical Analysis:

All the Quantitative data was presented as mean ± standard deviation (SD) and means between the 2 groups was compared by using students

't' test and between 3 groups ANOVA test was used, followed by Post hoc Tuke's test. The analysis was done using SPSS version 26.0 software. 'p' value of <0.05 was considered significant.

RESULTS

Total 60 patients were recruited with mean age of 54.53 ± 12.90 years, and distributed among 3 groups, viz. Group A: used Recombinant Human Epidermal Growth Factor for healing of pressure sores, Group B: Using Negative Pressure Wound Therapy and Group C: standard method of dressing, each group comprised of 20 patients, with mean ages of 55.90 ± 11.30, 53.40 ± 13.78 and 54.30 ± 13.99 years respectively.. Among all 40 (66.67%) were males and 20 (33.33%) were females. Majority of wounds in group A, B & C were grade 3 (80%), grade 3 (60%) and grade 2 (80%) respectively. Above data is summarized in table 1.

Table 1: General Characteristics

Characteristics	Group A	Group B	Group C
Mean age (years)	55.90 ± 11.30	53.40 ± 13.78	54.30 ± 13.99
Gender			
Female	7 (35 %)	8 (40 %)	5 (25 %)
Male	13 (65 %)	12 (60 %)	15 (75 %)
Grade			
2	4 (20 %)	7 (35 %)	16 (80 %)
3	16 (80 %)	12 (60 %)	4 (20 %)
4	0	1 (5 %)	0

In group A, B & C there was significant decline observed in wound length (in cm) at 1, 2 and 3 weeks as compared to 0 week. The means of wound length (in cm) at respective weeks was compared among the 3 study groups by ANOVA test & no significant difference in the means of wound length noted at 0, 1, 2, 3 and 4 weeks between any of the group. Above data is summarized in table 2.

Table 2: Wound Length (in cm) Within The Study Groups

Interval	Group A (n=15)	Group B (n=8)	Group C (n=7)	p value
0 week	8.60 ± 3.04	7.75 ± 3.62	7.63 ± 3.54	0.24
1week	7.97 ± 2.92	7.50 ± 4.06	7.06 ± 3.21	0.25
2 weeks	6.97 ± 2.68	6.44 ± 3.66	6.63 ± 3.15	0.56
3 weeks	6.10 ± 2.47	6.13 ± 3.36	6.25 ± 2.88	0.99
P value	0.001*	0.003*	0.018*	

In group A there was significant decline observed in wound width (in cm) at 2 and 3 weeks while no difference at 1 week as compared to 0 week. In group B there was significant decline observed in wound width (in cm) at 2 and 3 weeks as compared to 0 week. In group C there was no significant decrease observed in wound width at 1, 2 and 3 weeks as compared to 0 week. The means of wound width at respective weeks was compared among the 3 study groups by ANOVA test & no significant difference in the means of wound width noted at 0, 1, 2, 3 and 4 weeks between any of the group. Above data is summarized in table 3.

Table 3: Wound Width (in cm) Within The Study Groups

Interval	Group A (n=15)	Group B (n=8)	Group C (n=7)	p value
0 week	6.13 ± 2.88	6.38 ± 4.00	5.38 ± 2.26	0.39
1week	5.80 ± 2.68	6.13 ± 4.40	5.39 ± 2.11	0.72
2 weeks	5.27 ± 2.55	5.31 ± 3.83	5.13 ± 1.87	0.89
3 weeks	4.67 ± 2.66	4.75 ± 3.54	4.94 ± 2.01	0.98
P value	< 0.001*	0.02*	1.0	

In group A & B there was significant decline observed in wound depth (in cm) at 2 and 3 weeks while no difference at 1 week as compared to depth at 0 week. In group C there was no significant decrease observed in wound depth at 1, 2 and 3 weeks as compared to 0 week. The means of wound depth (in cm) at respective weeks was compared among the 3 study groups by ANOVA test. At 0 weeks there was significant (p<0.0001) difference found between the study groups. While there was no significant difference in the means of wound length noted at 1, 2, 3 and 4 weeks between any of the group. Above data is summarized in table 4.

Table 4: Wound Depth (in cm) Within The Study Groups

Interval	Group A (n=15)	Group B (n=8)	Group C (n=7)	p value
0 week	2.30 ± 0.59	2.50 ± 0.80	1.88 ± 0.44	<0.001*
1week	2.00 ± 0.68	2.13 ± 0.52	1.88 ± 0.44	0.39
2 weeks	1.58 ± 0.48	1.69 ± 0.53	1.75 ± 0.38	0.82
3 weeks	1.11 ± 0.51	1.13 ± 0.44	1.60 ± 0.49	0.07
P value	< 0.001*	0.01*	0.78	

In group A & B there was significant decline observed in wound area (in cm^3) at 2 and 3 weeks while no difference at 1 week as compared to area at 0 week. In group C there was no significant decrease observed in wound area at 1, 2 and 3 weeks as compared to 0 week. The means of wound area (in cm^3) at respective weeks was compared among the 3 study groups by ANOVA test & no significant difference in the means of wound area noted at 0, 1, 2, 3 and 4 weeks between any of the group. Above data is summarized in table 5.

Table 5: Wound Area (in cm^3) Within The Study Groups

Interval	Group A (n=15)	Group B (n=8)	Group C (n=7)	p value
0 week	129.30 ± 88.57	139.06 ± 143.31	81.75 ± 66.72	0.13
1week	100.40 ± 99.08	140.45 ± 208.32	75.80 ± 59.86	0.54
2 weeks	64.67 ± 51.97	84.44 ± 127.88	66.25 ± 55.05	0.98
3 weeks	37.33 ± 38.40	52.38 ± 83.53	57.81 ± 53.64	0.67
P value	< 0.001*	0.05*	0.8	

In group A there was significant decline observed in wound volume (in cm^3) at 2 and 3 weeks while no difference at 1 week as compared to volume at 0 week. In group B and C there was no significant decrease observed in wound volume at 1, 2 and 3 weeks as compared to 0 week. The means of wound volume (in cm^3) at respective weeks was compared among the 3 study groups by ANOVA test. There was no significant difference in the means of wound volume noted at 0, 1, 2, 3 and 4 weeks between any of the group. Above data is summarized in table 6.

Table 6: Wound Volume (in cm^3) Within The Study Groups

Interval	Group A (n=15)	Group B (n=8)	Group C (n=7)	p value
0 week	101.75 ± 55.12	92.61 ± 76.52	49.69 ± 39.59	0.08
1week	77.03 ± 102.00	109.45 ± 173.11	45.94 ± 35.89	0.64
2 weeks	37.51 ± 32.99	53.20 ± 84.05	38.79 ± 32.91	0.9
3 weeks	16.98 ± 19.95	24.80 ± 42.25	32.85 ± 33.44	0.51
P value	< 0.001*	0.096	0.175	

DISCUSSION

The pressure sore also known as pressure injury is the local injury to skin and/or underlying tissues, often over bony prominence, caused by pressure or pressure with shear. The tissue and/or skin injury typically due to immobility but can also be due to medical equipment or device pressures on mucosal tissues. [8, 9] These wounds are mostly neglected and they result in significant morbidity and leads to prolonged hospital stay. [10]

Recombinant human epidermal growth factor (REGEN-DTM 150), which was cloned and over expressed in E. coli, has shown enhanced healing of chronic diabetic foot ulcers (DFU) by significantly reducing the duration of healing in addition to providing excellent quality of wound healing and reepithelization. [11] NPWT on the other hand is a popular treatment for the management of both acute and chronic wounds. NPWT is commonly used in place of more traditional dressing techniques using cotton gauze. Whilst cotton gauze is an inexpensive product which is able to keep wounds clean and covered whilst absorbing exudate, many clinicians feel that NPWT is a more dynamic alternative that reduces infection and promotes early closure. [12]

In the present study the wound characteristics in 3 groups were measured in the form of length, width, depth, area and volume at presentation, 1, 2 and 3 weeks and compared between the groups. 1 patient each in group A & B and 2 patients in group C at 2nd week lost follow up, at 3 weeks total 5 in group A and 12 each in group B & C lost for follow up, while only 7, 4 and 3 patients followed up at 4th week. The decline in follow up was observed due to the situation of COVID pandemic during the study period.

Within the group comparison indicated a significant decrease in the length of the wound at 1, 2 and 3 weeks as compared to 0 week in group A, while in group B and C there was significant decline observed in wound length at 2 and 3 weeks as compared to 0 week. The decline in length in group A at 4 weeks than at presentation was much higher as compared to group B & C.

Comparison of groups yield no significant difference in wound length, width, depth, area and volume reported between all 3 groups. There was only significantly lower wound depth in group C than groups B &

C, but it showed poor decline in depth as compared group B & C. The length was significantly declined within the group at 3 weeks than baseline (0 weeks), while there was significant decrease noted in wound width, depth and area at weeks compared to baseline in group A & B, and volume was declined only in group A only.

Rao BAR [10] et al reported no significant better effect of human epidermal growth factor in healing of pressure ulcers as compared to placebo group, but there was significant percentage of complete healing of the ulcers in rhEGF group. In an experimental animal study Gonul B [13] et al showed increased levels of serum zinc and plasma PGE2 levels after EGF administration, indicating effectivity of EGF on wound healing. The better efficacy of NPWT was reported by Song YP [14] et al, than the standard wound care, with significant low healing time. Similar results were reported by Ikura K [15] et al. Dumville JC [16] et al, reviewed 4 studies with a total of 149 participants, with uncertainty of effect of NPWT with conventional wound healing method about the potential benefits or harms, or both, of using this treatment for pressure ulcer management. Mustoe TA [17] et al., assessed the role of recombinant platelet-derived growth factor—BB (rPDGF-BB), in the treatment of deep pressure ulcers, they reported decrease in the ulcer volumes by 83%, 29%, and 40% of the initial size in the groups receiving placebo, rPDGF-BB, 100 µg/dL, and rPDGF-BB, 300 µg/mL, respectively at the end of 28 days of follow up. The volume was decreased in both rPDGF-BB groups after 28 days compared with the placebo group.

The use of EGF in treatment of diabetic foot ulcer was investigated by Zhang K [18] et al, against nano-silver dressing, the combined group, and the saline control group. Compared with the control group, combined group achieved a shorter time, while the EGF group had even shorter healing time for wound repairing. The EGF and silver nano particles showed the anti-bactericidal effect, compared to control group.

Aktaş Ş [19] et al, showed the efficacy of EGF-IL, in treatment of diabetic foot ulcers after failing the treatment with hyperbaric oxygen therapy and NPWT. The intralesional application of EGF-IL then proved to prevent amputation in 9 out of 11 patients with advance diabetic foot ulcers. As per knowledge, literature review has shown that previous studies using other growth factors in comparison to conventional methods in diabetic foot has shown promising results but there are limited studies on use of growth factors in treatment of bed sores, hence, we think ours Is a novel study comparing use of epidermal growth factor with negative pressure dressing and conventional method in healing pressure sores. The emergence of growth factors has given new hope, its use in treatment of diabetic foot ulcers has promising effect.

Limitations of present study were single center study, decrease in sample size due to covid-19 pandemic & Non randomized study design and selection bias. Further studies with larger sample sizes and considering different factors affecting wound healing in future studies will prove more beneficial.

CONCLUSION

Present study reported no beneficial effect of human epidermal growth factor in treating pressure ulcers as compared to NPWT and conventional dressing of the wound. Use of growth factors have shown beneficial effect in wound healing considering the depth parameter when compared with conventional methods, hence, we recommend the use of growth factors in pressure sores.

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