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To Study the Efficacy of Placental Extract Gel in Chronic Non Healing Foot Ulcer

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Introduction

Wound healing is a complex and regulated process that is critical in maintaining the skin barrier function. The numerous disease processes can affect the events involved in wound healing, resulting in chronic, non-healing wounds. These would subject them to significant discomfort and distress and drain the medical system resources enormously.[1,2]

A chronic wound can be defined as that does not heal in an orderly set of stages and in a predictable amount of time or within three months. They remain in the inflammatory phase for too longand never heal or may take years.[3,4] Chronic leg and foot ulcers occur in many adults with diabetes, chronic venous insufficiency, arterial disease, prolonged pressure, or neuropathy.[5]

Chronic ulcers may last for 12 to 13 months and even recur in 60-70% of cases. They cause loss of function and decreased quality of life and significant morbidity.[6,7] These chronic ulcers are predominantly seen in elderly, becoming more prevalent and more difficult to treat and are associated with high treatment costs.[8]

So wound care has become essential in these ulcers, and surgical debridement and dressings are the corners stones. Many wound dressings like gauge, films, hydrocolloids, gels, foams etc. were developed to both protect the healing wound from infection and to promote the healing process.[1]

Placental extract gel is a rich source of various peptides, amino acids, nucleotides, PDRNs and carbohydrates, which are believed to support the healing process.[9] Application of placental extract preparation increases collagen synthesis, increases tissue protein, accelerates neoangiogenesis, and epithelialization.[10] It has an immunotropic effect and causes the release of Epidermal growth factor, Fibroblast growth factor at the tissue level. It also reduces surrounding tissue inflammation and oedema and reduces microbial burden.[11] Its application accelerates healing because of amino acids, nucleotide and vitamins that improve healing.

Diabetes mellitus is the common cause of foot ulceration and is thought to affect 15% of people with diabetes at some time in their lives.[12] This is because of the complex association of various factors like-Ischemia, Neuropathy and Infection. Micro-angiopathy, hypercoagulable status, atherosclerosis, and hyperglycemia may lead to the above complex, thus leading to the diabetic lesion and its complications.[13,14,15] People with diabetes are between 15 and 70 times more likely to undergo lower-limb amputations than people without diabetes.[16]

As diabetes is the common cause of non-healing ulcers in our setting, we considered patients with diabetic foot and the dressing was done with Placental extract gel to determine its efficacy

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in healing the ulcer compared to conventional dressing techniques.

Materials and Methods

Type of Study: A Prospective Interventional study to determine the efficacy of Placental Extract Gel in chronic non-healing foot ulcer.

Study Setting: Department of general surgery, Tertiary Care Centre

Study Period: November 2017 to September 2019

Study Sample: 100 cases, divided into two groups by random allocation technique. Group A and Group B with 50 cases in each group.

Inclusion criteria

- Male and female patients between 20 to 75 years.
- Patients with chronic lower limb ulcers due to diabetes in the non-weight-bearing area of the foot, and <5% total body surface area.
- Patients who gave consent for the study.

Exclusion criteria

- Patients of age group < 20 and >75years.
- Chronic lower limb specific ulcers due to malignancy, TB, Leprosy, arterial and venous pathology.
- Chronic Renal Failure, chronic liver failure patients.

Methodology

Institute Ethical Committee clearance certificate obtained for the study. Patients attending the surgical outpatient department with diabetic foot ulcer formed the study subjects.

Demographic data of the patients, recorded in the proforma. Investigations like haemoglobin, renal function test; screening, fasting, postprandial sugars were sent and recorded. All cases underwent debridement to remove the slough and antibiotics given according to culture and sensitivity. Cases were considered for the study once the wound is sterile as evident from culture and sensitivity report, was recognised as the study start point.

Patients were then grouped into two by Random Allocation Technique. Group A (cases) patients had a conventional method of dressing along with the application of Placental extract gel. Group B (controls) patients had a traditional way of dressing with povidone-iodine, peroxide alone.

The dressing was done every day. The wound progress studied in two groups, with the following parameters wound size, time taken for the appearance of healthy pink granulation tissue, the total duration of hospital stay with the endpoints like SSG, secondary healing depending on the size of the ulcer.

Wound size measured with a graph paper plotting the wound edges on it and measuring the large and small boxes measured in $cm.^2$ Size is measured at the study start point and on the day of appearance of red granulation tissue. At the end of the study, the results of the two groups measured comparing the following events.

- Percentage reduction in the surface area of the wound at the time of starting and endpoint of the study.
- Days took for the full granulation, i.e. pink, pinpoint velvety tissue that bleeds on touch to appear.
- The total duration of hospital stay, taken from the start point to endpoint i.e. after SSG or secondary closure or secondary healing of the wound.
- Complications if any encountered in each group.

Statistics

Microsoft Excel was used to construct a master chart using SPSS 22.0. Mean, and percentages for descriptive analysis. 'p' values are used to determine the significance in the difference noted between the two groups.

Results

Age Distribution

Table 1: Age Distribution in the Study Groups (N=100).

Age in Years	No. of Cases		
	Group A	Group B	Total
21-30	1 (1%)	0	1
31-40	13 (13%)	9 (9%)	22
41-50	6 (6%)	9 (9%)	15
51-60	20 (20%)	18 (18%)	38
61-70	9 (9%)	14 (14%)	23
>70	1 (1%)	0	1
Total	50	50	100

The mean age of cases in Group A is 51.68 years. The mean age of cases in Group B is 53.94 years.

Table 2: Sex Distribution in the Study Groups (N=100).

Sex	Group A	Group B	Total
Male	38	34	72
Female	12	16	28
Total	50	50	100

Male to female ratio in the study was 2.6:1.

Table 3: Initial Surface Area of ulcer in the Study Groups (N=100).

Area of ulcer in cm^2	Group A	Group B
<10	4	8
10 -15	18	8
15-20	6	11
20-25	7	6
25-30	4	5
>30	11	12

Table 4: Mean ulcer size in the Study Groups (N=100).

Mean ulcer size in cm^2	Group A	Group B
Initial size	20.7	21.8
At end of second week	16.1	19.6
At end of third week	11.2	18.5

Table 5: Mean% Reduction of ulcer size in the Study Groups (N=100).

Mean % reduction in ulcer size	Group A at 2nd week	Group B at 3rd week
Split skin graft	17.24%	14.6%
Secondary Healing	36.7%	29.6%
Over all cases	30.9%	24.5%

Table 6: Mean days of the appearance of granulation tissue, hospital stay, Final treatment.

	Group A	Group B
Mean days of the appearance of granulation tissue	11.9 days ± 2.4	24.4 days ± 2.8
Mean days of hospital stay	16.2 days ± 4.5	29.1 days ± 3.05
Skin Grafting	15	35
Secondary healing	17	33

Discussion

As the chronic wound has deranged normal healing process, application of placental extract gel has the following effects.

- Increases the epithelial proliferation from the edges.
- Accelerates neoangiogenesis by providing growth factors.
- Stimulates the fibroblast proliferation and thus the formation of granulation tissue.
- Helps in the contraction of the wound.

In the cases where there appeared an excellent granulation tissue culture was done and was posted for skin grafting if the size of the wound is more. If the wound size is less and if the patient is ready for follow up, cases were followed regularly on an outpatient basis, and regular application of placental extract gel decreased the wound size and contracted it allowing for secondary healing.

Management of diabetic foot is mainly by controlling the sugars, preventing infection, appropriate and timely debridement, adequate closure of the wound surface with a skin graft or allowing the wound to heal spontaneously. The placental extract increases collagen synthesis, increases tissue protein, accelerates neo-angiogenesis, and epithelialization. It has immune-tropic effect, EGF, Fibroblasts and growth factors. It supports ossification and reduces surrounding tissue inflammation and edema.[17,18,19]

Conclusion

Foot ulcers are the common morbidities noted in diabetic patients. A timely intervention like debridement and appropriate dressing care will reduce the amputation rates. Among the several dressing techniques available from my study I conclude that Placental Extract Gel application along with Povidone-iodine instead of Povidone-iodine and normal saline will

- Decrease the wound size significantly
- Allows granulation tissue formation at an early stage
- Help in early wound coverage by skin grafting.

Table 7: Comparison of Sample Size & Mean Age.

Study	Group A				Group B			
	Sample size	Mean age	Male	Female	Sample size	Mean age	Male	Female
Sudhir et al[20]	30	57	23	7	30	56.8	21	9
Vivek Vardhan et al[21]	50	55.7	35	15	50	57.9	37	13
Present study	50	51.68	38	12	50	53.94	34	16

Table 8: Comparison of Mean Reduction in Wound Size, Appearance of Granulation Tissue, Hospital Stay, Final Outcome.

Study	Group A				Group B			
	Mean reduction	Granulation tissue	Hospital stay	Final outcome	Mean reduction	Granulation tissue	Hospital stay	Final outcome
V. Vardhan et al[21]	65.4	14.9	20	SSG 44 SH 6	72.7	20.2	25	SSG 19 SH 31
Sudhir et al[20]	-	14.2	19.8	-	-	23.4	28.2	-
Present study	30.9	11.9	16.2	SSG 15 SH 35	24.5	24.4	29.1	SSG 17 SH 33

- Thereby decrease the duration of hospital stay there by the cost of the patient.

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Conflict of Interest: Nil

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