Original Article

Efficacy Of Topical Recombinant Human Platelet Derived Growth Factor- Bb In Wound Healing

DR. SUDHIR S[1] , DR. HARISH KUMAR P[2] , DR. YAMUNA VS[3] , DR. PRATEEK PRASOON (CORRESPONDING AUTHOR)[4]

[1]PROFESSOR & UNIT HEAD, DEPARTMENT OF GENERAL SURGERY, JSS MEDICAL COLLEGE & HOSPITAL, JSSAHER MYSURU, KARNATAKA, INDIA
[2]ASSISTANT PROFESSOR DEPARTMENT OF GENERAL SURGERY, JSS MEDICAL COLLEGE & HOSPITAL, JSSAHER MYSURU, KARNATAKA, INDIA
[3]ASSISTANT PROFESSOR, DEPARTMENT OF GENERAL SURGERY, JSS MEDICAL COLLEGE & HOSPITAL, JSSAHER MYSURU, KARNATAKA, INDIA
[4]POST GRADUATE, DEPARTMENT OF GENERAL SURGERY, JSS MEDICAL COLLEGE & HOSPITAL, JSSAHER MYSURU, KARNATAKA, INDIA ADDRESS:1297, 3RD MAIN, 4TH CROSS, KRISHNAMURTYPURAM, MYSURU, KARNATAKA 570004, INDIA MAIL: PRTKPRSUN@MAIL.COM
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Abstract

Wound healing is a complex process that aims to reestablish the functional and structural integrity of disrupted tissue. Recombinant DNA technology can be used to create some growth factors, which can hasten ulcer healing. Platelet derived growth factor (PDGF) is a growth factor that exerts its action on fibroblasts, endothelial cells, and smooth muscle cells.

AIM: To assess the efficacy of rhPDGF BB as compared to normal moist surgical dressings in patients with chronic wounds.

OBJECTIVE: To assess wound contraction, appearance of granulation tissue and time leading up-to split skin grafting between the study groups.

METHODS: A single centre, prospective randomised control trial was conducted on 60 patients, diagnosed as Chronic wounds from Department of General Surgery, JSS Hospital, Mysuru from January 2021 to June 2022. Patients were randomly divided into test and control group of 30 patients each. On Days 1, 7, and 14, wounds were compared on wound healing-related characteristics, including single largest dimension, granulation tissue and time taken to reach end point.

RESULTS: The study's findings indicate that males are mostly affected by extremity ulcers, which are more prevalent in middle age. Platelet derived growth factor was used to treat cases and normal saline alone to treat controls. The average duration of hospital stay was shorter in test group as compared to control group (14.9 v/s 17.8 days). On all days, there was a difference in ulcer size measured in terms of length. Over days, the test group saw a greater decline in ulcer size than the control group did (5.7 to 5.0 and 8.04 to 7.02, respectively, p= 0.008). The granulation tissue in the control and test groups had same quality at the beginning of the trial. At day 7, the granulation's better granulation was noted in test group, but by day 14, both groups' outcomes were comparable. Also, the test group took lesser time to reach end point than the control group (14 days as compared to 19 days).

CONCLUSION: This study found a correlation between topical Platelet-derived growth factor use and accelerated time to split skin grafting and quicker wound healing. However, both groups had a relatively similar granulation look. Considering the cost-benefit analysis and the aforementioned data, topical PDGF can be used as a substitute to standard dressings in the therapy of chronic wounds.

Key words: Chronic ulcers, rhPDGF, wound healing, Original research paper, 2691 words

INTRODUCTION

The burden of chronic wounds causes a great challenge both in terms of prevalence and in quality of life. In an epidemiological study conducted in India the prevalence of wounds was observed to be was 15.03 per 1000. The acute and chronic prevalence were 10.55 and 4.48 per 1000 respectively. Lower extremity wounds are primarily due to diabetes (43%), venous disease (25%) and trauma (27%).

Wound healing is a complex process that aims to reestablish the functional and structural integrity of disrupted tissue. Neutrophils, macrophages, mast cells, lymphocytes, and fibroblasts are among the cells involved, along

with cytokines, growth factors, and metalloproteinases. Local and systemic variables can roughly be categorised into those that impact wound healing.
Recombinant DNA technology can be used to create some growth factors, which can hasten ulcer healing. Platelet derived growth factor (PDGF) is a powerful chemoattractant and mitogen that exerts its action on fibroblasts, endothelial cells, and smooth muscle cells. The resultant protein becaplermin has been observed to have a biological activity similar to the endogenous PDGF-BB.
Various studies conducted internationally and in India have shown that recombinant human platelet derived growth factor (rhPGDF) in the form of Becaplermin gel. However, most of these studies have been done for diabetic or traumatic ulcers alone and there is not enough evidence for efficacy of rhPDGF with respect to other chronic ulcers. Hence, the current study aims to study the efficacy of plermin gel on chronic wound healing of lower extremity ulcers chronic venous ulcers, diabetic foot ulcers, traumatic ulcers measured as wound contracture, appearance of granulation tissue and time leading up-to split skin grafting between the study groups.

OBJECTIVES OF THE STUDY

- Primary objective: To assess the efficacy of rhPDGF BB as compared to normal moist surgical dressings in patients with chronic wounds.
- Secondary objective: To assess wound contraction, appearance of granulation tissue and time leading up-to split skin grafting between the study groups.

MATERIALS AND METHODS

DESCRIPTION OF STUDY

A single centre, prospective, comparative, interventional, randomised control trial conducted on a study population of 60 patients from Department of General Surgery, JSS Hospital, Mysuru. It was carried out over 18 months from January 2021 to June 2022. Patients diagnosed with chronic wounds were included in this study by simple random sampling and divided into test and control groups of 30 patients each. They were followed up from the time of presentation to the EMD/OPD till the time of discharge

SUBJECT ELIGIBILITY

- **Inclusion Criteria**
  - All patients presenting with Stage II to Stage IV chronic wounds – Wagner classification
  - Lower extremity ulcers including Diabetic foot ulcers, venous ulcers, traumatic ulcers.
- **Exclusion Criteria**
  - Patients below the age of 18 years.
  - Patient refusal
  - Patients with necrotic wounds.
  - Patients with osteomyelitis.
  - Exposed osseous tissue.
  - Acute wounds.
  - Ulcer size <2cm

STUDY CONDUCT

Wound swabs were taken for culture and sensitivity and after thorough debridement and wound bed preparation, culture was repeated, positive wounds were additionally prepared by giving appropriate antibiotics and wounds with negative cultures were included in the study. Sample was randomly categorised into two groups of 30

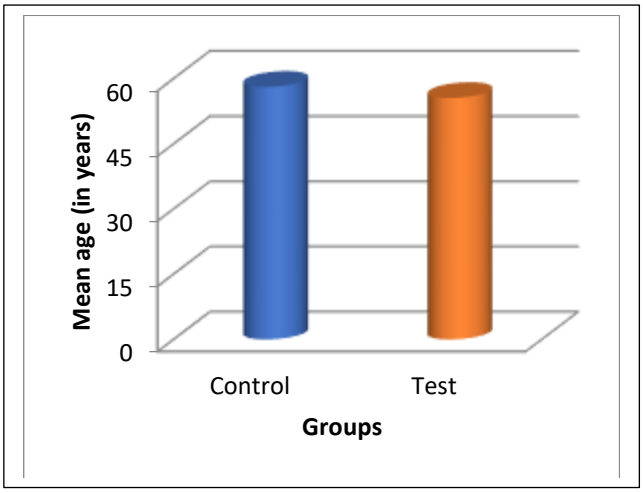
participants each with group 1 being normal moist being the control group undergoing normal moist surgical dressings and group 2 being the experimental group undergoing dressing with Plermin gel. Assessment of wounds was done at the end of 7 and 14 days, on the following parameters, Wound contraction as reduction in single largest dimension. Appearance and quality of granulation tissue, time taken to reach end point i.e. Split Skin Grafting.

RESULTS

DEMOGRAPHIC CHARACTERISTICS

AGE-

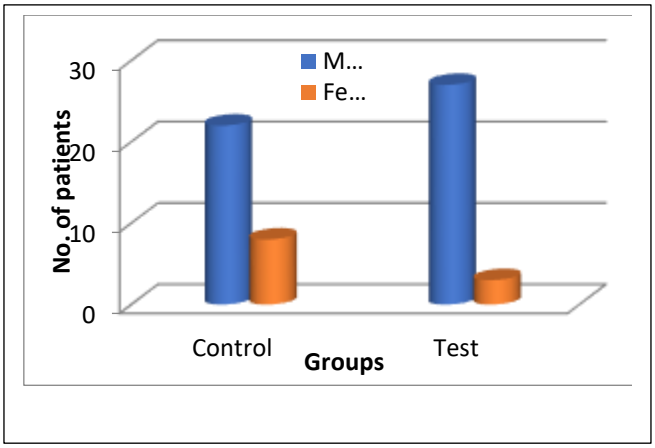
- The mean age in control group was 58.13 vs 55.56 in test group



Graph 1: Age distribution

GENDER DISTRIBUTION

- 26.7% of subjects in control group and 10% in test group were females whereas, 73.3% in control group and 81.7% in test group were males



Graph 2 : Gender distribution

MODE OF ONSENT

- Spontaneous and traumatic wounds were evaluated, spontaneous wounds included diabetic foot ulcers, venous ulcers and pressure sores.
- 29 cases and 1 traumatic ulcers were evaluated in control group and 25 spontaneous and 5 traumatic ulcers were evaluated in the test group.

	Group	
	NORMAL SALINE DRESSING	PDGF DRESSING
	Count	Count

Mode of onset	Spontaneous	29	25
	Trauma	1	5

Table 1 : Mode of onset

DURATION OF STAY IN HOSPITAL (IN DAYS):

- Shorter duration of stay was noted in PDGF Dressing group as compared to normal saline dressing group.

	Group			
	NORMAL SALINE DRESSING		PDGF DRESSING	
	Mean	SD	Mean	SD
Duration of stay	17.80	11.65	14.96	9.05

Table 2 : Duration of stay

DURATION OF ULCER:

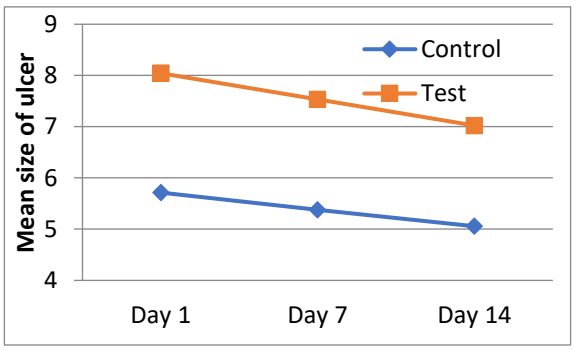
- The mean duration of ulcers in control group was 46.66 days v/s 48.03 days in test group

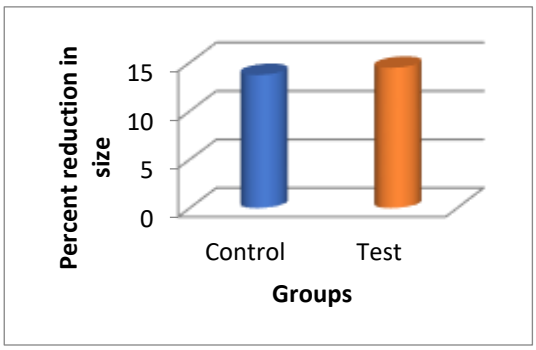
	Group			
	NORMAL SALINE DRESSING		PDGF DRESSING	
	Mean	SD	Mean	SD
Duration of ulcer	46.66	29.68	48.03	2

Table 3 : Duration of ulcer

ULCER SIZE COMPARISON

- Difference in size was noted in control and test group on all days, however over time the decrease in ulcer size was more in test group v/s control group(p= 0.008 at day 14), however no significant difference was noted in percent decrease in ulcer size.

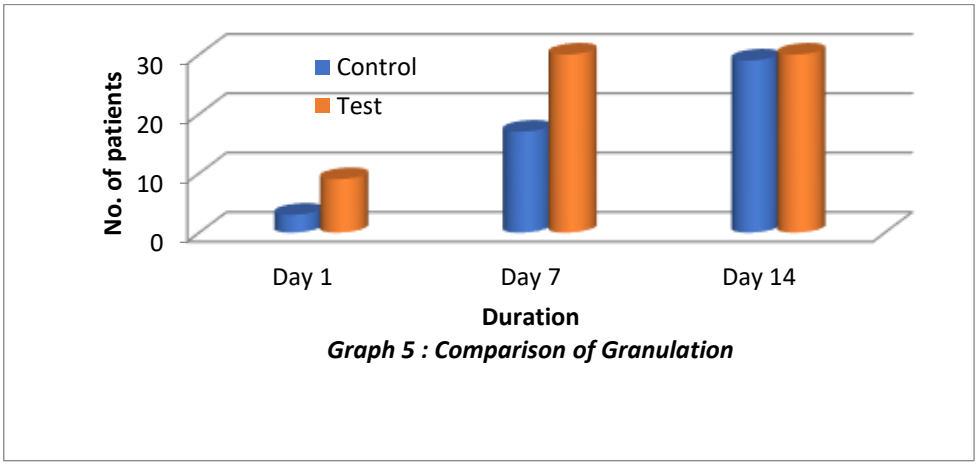




Graph 3 : Ulcer size comparison **Graph 4 : Percent reduction in size**

COMPARISON OF GRANULATION:

- On day 1 no significant difference was noted between control and test groups, on day 7 test group developed significantly better granulation and on day 14 the difference was minimal.



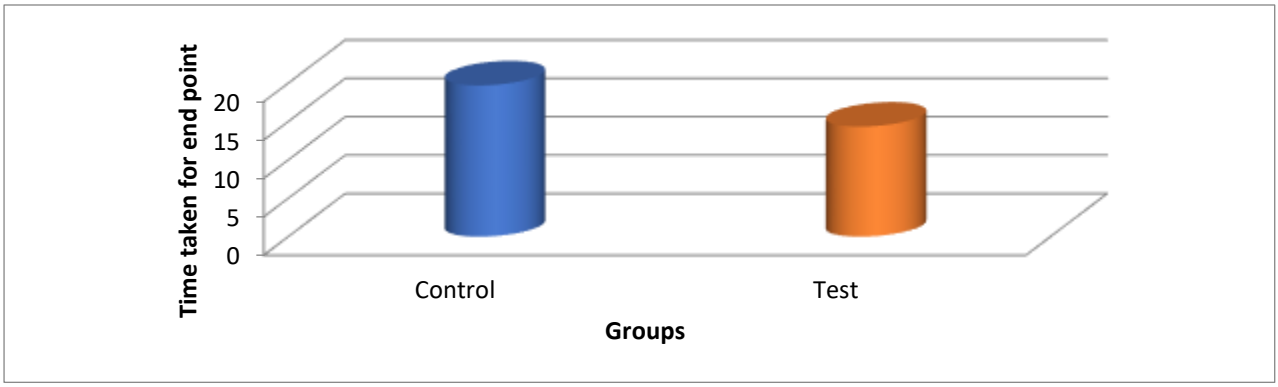
Graph 5 : Comparison of Granulation

COMPARISON OF NUMBER OF DAYS TO END POINT AND NO OF DRESSINGS:

- Significant difference was noted in time taken to reach end point in test group as compared to control group(p=0.005)
- Fewer number of dressings were needed in test group as compared to control group.

	GROUPS	N	Mean	Std. Deviation	P
Number of days to end point	Control	30	19.7000	8.04792	0.005
	Test	30	14.3333	5.86829	
No of dressings	Control	30	9.3000	3.60220	0.004
	Test	30	6.9000	2.50998	

Table 4 : Comparison of number of days to end point and no of dressing



Graph 6 : Comparison of number of days taken to reach end point.

DISCUSSION

India has a high incidence and prevalence of extremities ulcers, which has a major negative impact on morbidity and mortality. Even though higher generation antibiotics and thorough wound debridement have recently reduced mortality, extremity ulcers, especially those connected to or resulting from Type II Diabetes Mellitus and Peripheral Vascular Disease, continue to be associated with significant morbidity and therefore there is a need to treat these ulcers appropriately and think about newer modalities in treatment of chronic ulcers.

Local wound management is significant and is frequently cited as being at least as essential as systemic antibiotics and supportive care in the healing of wounds.

This 18-month study recruited 60 participants who were randomly assigned into two equal groups of controls and cases in an effort to investigate the effects of topical Platelet derived growth factor on wound healing. Platelet derived growth factor was used to treat cases, whereas normal saline dressings alone were used to treat controls.

The study's findings indicate that extremity ulcers are more commonly seen in males, particularly middle aged males, with controls and cases being on average 58 and 55 years old, respectively.

The average duration of hospital stay was shorter in test group as compared to control group (14.9 v/s 17.8 days)

After complete debridement, chronic wounds were assessed on days 1, 7, and 14 for variables such as a reduction in the single largest dimension, the presence of granulation tissue, and the amount of time required to achieve the end point.

On all days, there was a difference in ulcer size measured in terms of length. Over days, the test group saw a greater decline in ulcer size than the control group did (5.7 to 5.0 and 8.04 to 7.02, respectively). Similarly, in a study by Steed et al. in , twenty-nine (48%) of 61 patients randomized to the rhPDGF-BB group achieved complete wound healing during the study compared with only 14 (25%) of 57 patients randomized to the placebo group ($p = 0.01$). The median reduction in wound area in the group given rhPDGF-BB was 98.8% compared with 82.1% in the group given placebo ($p = 0.09$). However, there was no discernible difference in percentage reduction of length. [19]

At the beginning of the study, there was no difference in the quality of the granulation tissue between the control and test groups. At day 7, there was a noticeable change in the appearance and quality of the granulation, but on day 14 similar results were noted in both groups. This result was similar to a study conducted by Langer et al. in which the mean number of days it took for granulation tissue to form in the 155 wounds under study was 13.81 +/- 2.68 in the test group and 13.36 +/- 3.81 in the control group ($P = 0.401$). [2]

Additionally, the test group took lesser time to reach end point than the control group (14 days as compared to 19 days)

CONCLUSION

In conclusion, to encourage wound healing, chronic ulcers require strong local care in addition to systemic antibiotic therapy and supportive therapies. According to this study, topical Platelet derived growth factor usage is linked to faster wound healing and enhanced time leading upto Split skin grafting. However the appearance of granulation was somewhat similar in both the groups. In light of the above evidence, topical PDGF can be an alternative to conventional dressings in chronic wound management, keeping in mind the cost to benefit ratio analysis.

LIMITATIONS

This study has certain limitations, much like other randomised prospective studies do, specifically:

1. The expense of the interventional drug might be a barrier to broad use, particularly in a developing nation like India.
2. Confounding variables in the research may have included anaemia and nutritional status, which both have a role in wound healing.
3. The fact that this study was done on a limited scale and had a sample size of 60 patients, 30 of whom were in the therapy group, may mean that it is not typical of the general population.

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