Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(6F):2302-2306 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i06.090

Original Research Article

A Comparative Study on Wound Healing with Topical Application of Human Epidermal Growth Factor verses Application of Povidone-Iodine in Diabetic Wounds

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Abstract: Diabetic wounds or ulcers are major complication of diabetes mellitus. Diabetes is a metabolic disorder that impedes the normal steps of wound healing process Major increase in morbidity in diabetic patients is due to macro and micro vascular complications including failure of wound healing process. Diabetes is the cause for more than 3/4th lower limb amputation Increased glucose in the tissue precipitates infection. The aim of this study is to establish whether topical application of human epidermal growth factor enhance wound healing better than conventional povidone-iodine dressing in diabetic wounds. For one group of patients, topical application of recombinant human epidermal growth factor gel over the wound and wound dressing was done twice daily For other group of patients, topical application of povidone-iodine over the wound and wound dressing done twice daily. The Human Epidermal Growth Factor Application group patients equally belonged to the male gender class interval (n=15, 50%). In the Conventional Povidone Iodine Dressing group patients, majority belonged to the male gender class interval (n=15, 50%). The association between the intervention groups and gender distribution is considered to be not statistically significant since $p > 0.05$ as per fishers exact test. The results of the study conclude that the topical application of human epidermal growth factor enhances wound healing significantly and is better than conventional povidine iodine dressing.
Keywords: Wound healing, Diabetes mellitus, Topical application

INTRODUCTION

The earliest accounts of wound healing date back to about 2000 B.C., when the Sumerians employed two modes of treatment: a spiritual method consisting of incantations and a physical method of applying poultice-like materials to the wound [1]. The Egyptians were the first to differentiate between infected and diseased wounds compared to no infected wounds. Wounds are classified as either acute or chronic. Acute wounds heal in a predictable manner and time frame [2]. The process occurs with few, if any, complications, and the end result is a well-healed wound. Surgical wounds can heal in several ways. An incised wound that is clean and closed by sutures is said to heal by primary intention. Often, because of bacterial contamination or tissue loss, a wound will be left open to heal by granulation tissue formation and contraction; this constitutes healing by secondary intention [3]. Delayed primary closure, or healing by tertiary intention, represents a combination of the first two, consisting of the placement of sutures, allowing the wound to stay open for a few days, and the subsequent closure of the sutures [4].

Acute Wounds

The healing spectrum of acute wounds is broad. In examining the acquisition of mechanical integrity and strength during healing, the normal process is characterized by a constant and continual increase that reaches a plateau at some point post injury. Wounds with delayed healing are characterized by decreased wound-breaking strength in comparison to wounds that heal at a normal rate; however, they eventually achieve the same integrity and strength as wounds that heal normally. Conditions such as nutritional deficiencies, infections, or severe trauma cause delayed healing, which reverts to normal with correction of the underlying pathophysiology. Impaired healing is characterized by a failure to achieve mechanical strength equivalent to normally healed

wounds. Patients with compromised immune systems, such as those with diabetes, chronic steroid usage, or tissues damaged by radiotherapy, are prone to this type of impaired healing [5].

Chronic Wounds

Chronic wounds are defined as wounds that have failed to proceed through the orderly process that produces satisfactory anatomic and functional integrity or that have proceeded through the repair process without producing an adequate anatomic and functional result [6]. The majority of wounds that have not healed in 3 months are considered chronic. *Skin ulcers*, which usually occur in traumatized or vascularly compromised soft tissue, are also considered chronic in nature, and proportionately are the major component of chronic wounds. Repeated trauma, poor perfusion or oxygenation, and/or excessive inflammation contribute to the causation and the perpetuation of the chronicity of wounds [7]. Unresponsiveness to normal regulatory signals also has been implicated as a predictive factor of chronic wounds. This may come about as a failure of normal growth factor synthesis, and thus an increased breakdown of growth factors within a wound environment that is markedly proteolytic because of overexpression of protease activity or a failure of the normal antiprotease inhibitor mechanisms [8]. Fibroblasts from chronic wounds also have been found to have decreased proliferative potential, perhaps because of senescence or decreased expression of growth factor receptors. Chronic wounds occur due to various etiologic factors, and several of the most common are discussed in the following sections [9]. Malignant transformation of chronic ulcers can occur in any long-standing wound (Marjolin ulcer). Any wound that does not heal for a prolonged period of time is prone to malignant transformation. Malignant wounds are differentiated clinically from non-malignant wounds by the presence of overturned wound edges. In patients with suspected malignant transformations, biopsy of the wound edges must be performed to rule out malignancy. Cancers arising de novo in chronic wounds include both squamous and basal cell carcinomas [10].

MATERIALS AND METHODS

All units in general surgery in Government Stanley Medical College and Hospital, Prospective, Non-randomized control trial. The Study Duration was between July 2014 to June 2015 Sample Size was around 50 Data was collected from all patients who was admitted in Government Stanley medical college and patients was included those who come under the inclusion criteria. For one group of patients, topical application of recombinant human epidermal growth factor gel over the wound and wound dressing was done twice daily. For other group of patients, topical application of povidone-iodine over the wound and wound dressing done twice daily. The study end point was the complete closure of the wound. Failure to heal was arbitrarily defined as incomplete healing after 12 weeks. Results are tabulated and analyzed. Inclusion Criteria**:** All patients who are diagnosed as type 2 diabetes mellitus with a non-healing ulcer, Both males and females, Age between 35 to 75 years, Size of the wound - 5cm to 15cm. Exclusion Criteria **:** Recurrent ulcers, Non-diabetic wounds, Malignant ulcers

STATISTICAL METHOD

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analyzed with the unpaired t test. Categorical variables were analysed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analyzed using SPSS version 16 and Microsoft Excel 2007

RESULTS AND OBSERVATIONS

Figure 1 Majority of the Human Epidermal Growth Factor Application Group patients belonged to the 61-70 years age class interval (n=19, 38%) with a mean age of 60.60 years. In the Conventional Povidone Iodine Dressing group patients, majority belonged to the same age class interval (n=8, 32%) with a mean age of 57.24 years. The association between the intervention groups and age distribution is considered to be not statistically significant since $p > 0.05$ as per unpaired t test.

Figure 1, If you are in Epidermal Growth Factor Application Group, your probability of wound healing in 7 weeks is 100%. If you are in Conventional Povidone Iodine Dressing Group , your probability of wound healing at the same time is slightly more than 76%.It is statistically significant with a p-value of 0.033 as per log-rank test

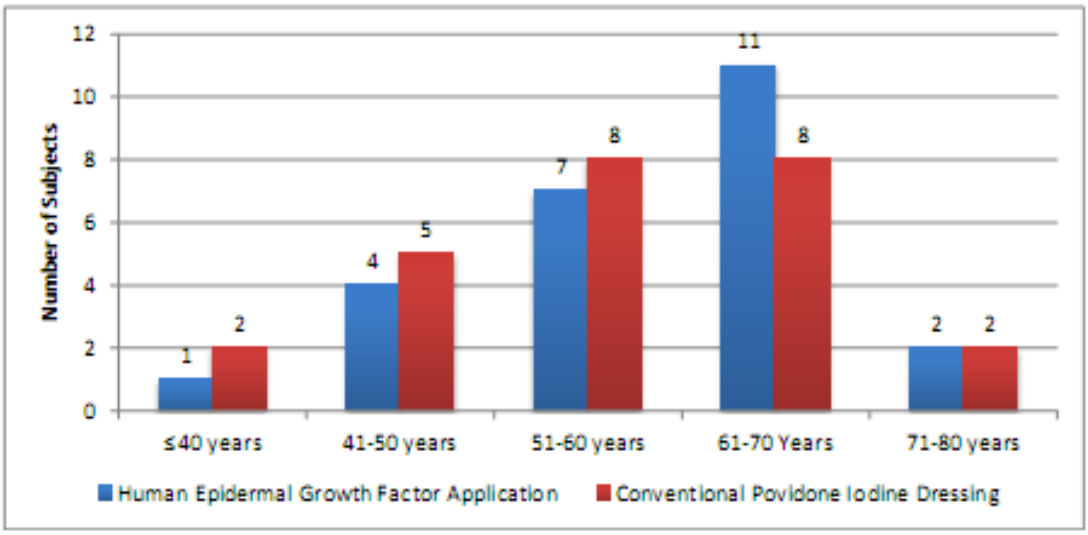

Fig-1: Age distribution

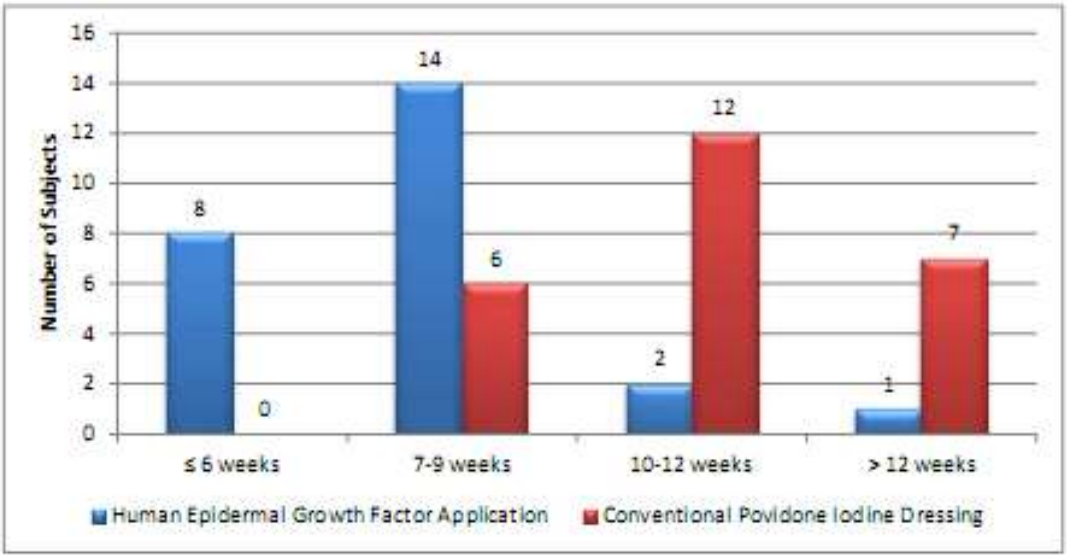

Fig-2: Shows the wound healing weeks among two groups

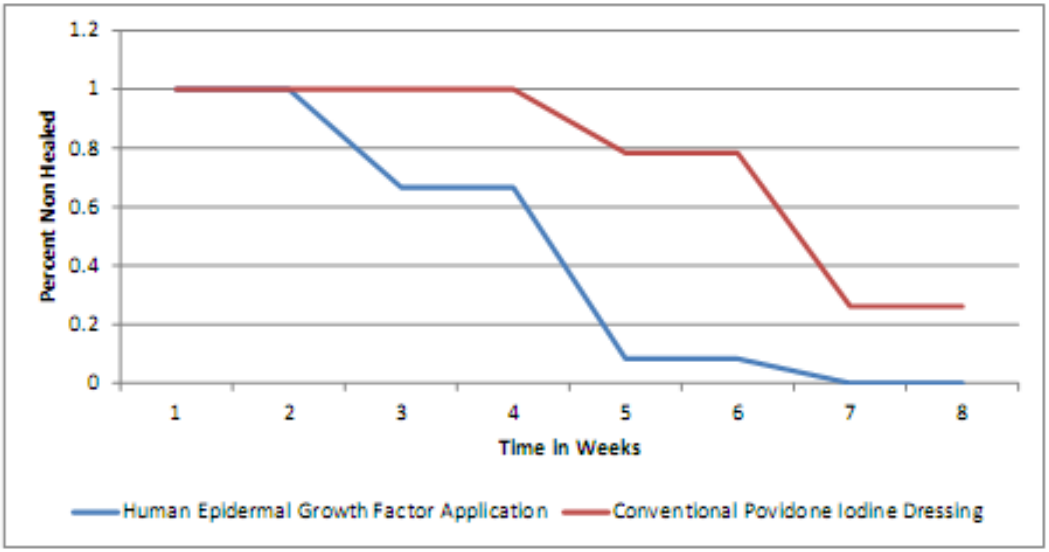

Fig-3: Kelan meier estimate curve- non healing of ulcer

DISCUSSION

Wound and wound healing is an important discussion topic for centuries. Wound healing is hindered by many factor. One of the most important hindrance to wound healing or that impedes the steps of wound healing is associated Type 2 Diabetes Mellitus [11]. Major factor in diabetes that delays or hinder with wound healing are obesity, uncontrolled hyperglycemia, renal compromise, and insulin resistance. Uncontrolled diabetes results in reduced inflammation, angiogenesis, and collagen synthesis. Additionally, the large- and small-vessel disease that is the hallmark of advanced diabetes contributes to local hypoxemia. Defects in granulocyte function, capillary in growth, and fibroblast proliferation all have been described in diabetes. Obesity, insulin resistance, hyperglycemia, and diabetic renal failure contribute significantly and independently to the impaired wound healing observed in diabetics [12]. The diabetic wound appears to be lacking in sufficient growth factor levels, which signal normal healing. It remains unclear whether decreased collagen synthesis or an increased breakdown due to an abnormally high proteolytic wound environment is responsible. Careful correction of blood sugar levels improves the outcome of wounds in diabetic patients. Increasing the inspired oxygen tension, judicious use of antibiotics, and correction of other coexisting metabolic abnormalities all can result in improved wound healing [13]. Diabetes is still one of the major cause for limb amputations mainly in lower limb [14]. Increased level of glucose in tissues or uncontrolled level of glucose in tissues precipitates infection, and lead to vascular compromise which in turn results in a non-healing wound or even may lead to amputation if it is in extremities, mainly in lower extremities [15]. Human epidermal growth factor stimulates cell growth, differentiation, and proliferation by binding to it EGFR receptor. In case of T2 DM previous studies has shown that topical application of epidermal growth factor is enhancing the wound healing than other conventional methods. In our study, we found that in patients we used human epidermal growth factor, 16% healed within 6 weeks of time, another 56% healed by 9 weeks of time, 8% healed by 12 weeks and only 4% went for non-healing wound [16]. In case of patients we used povidine-iodine dressing we found that no patients healed by 6 weeks of time, 24% patients healed by 9 weeks of time, another 48% healed by 12 weeks time and 28% patients did not heal, and went for non-healing wound [17]. The decreased mean duration of wound healing in Human Epidermal Growth Factor Application Group compared to the Conventional Povidone Iodine Dressing Group is statistically significant as the p value is 0.0001 as per unpaired t-test indicating a true difference among study groups. The mean duration of wound healing was meaningfully less in Human Epidermal Growth Factor Application Group compared to the Conventional Povidone Iodine Dressing Group by 3.16 weeks [18]. This significant difference of 29% decrease in mean duration of wound healing in Human Epidermal Growth Factor Application Group compared to the Conventional Povidone Iodine Dressing Group is true and has not occurred by chance [19].

CONCLUSION

The results of the study conclude that the topical application of human epidermal growth factor enhances wound healing significantly and is better than conventional povidine iodine dressing. Results of the study also concludes that the topical application of human epidermal growth factor causes significant reduction in number of non-healing ulcers.

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