

Original article

Role of topical insulin in healing of chronic ulcers

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Abstract

The prevalence of chronic wounds such as diabetic ulcers, pressure sores, surgical site wounds is around 4.5 per 1000 in India which is approximately half that of acute wounds[1]. Chronic wounds by definition are wounds that have failed to proceed through a timely and orderly reparative process to produce anatomic and functional integrity over a period of 3 months. Wound healing is a complex biological process influenced by several agents such as insulin-like growth factor (IGF) and human acidic fibroblast growth factor (rh-a FGF) [2]. In vitro studies have shown that IGF can stimulate the proliferation and differentiation of endothelial cells and fibroblasts and thus promote granulation tissue regeneration.

Keywords: Topical insulin, Chronic ulcers

Introduction

Chen X et-al in may 2012 published the role of topical insulin in improving wound healing in mice. G.J.Hardman et-al in 2001 and Panuncialman J In 2010 have demonstrated that daily injection of insulin were used to improve bone healing in rats, incision wounds of the skin, healing in the distal limb of horse and in cutaneous ulceration in mice [3,4]. Greenway SE and Filler LE through a randomized double blind placebo-controlled trial in 1999 showed improved wound healing in humans by topical application of insulin[5].

Insulin regulates neutrophil function by binding to cell membrane receptors and regulating the function of neutrophil adhesion thereby signaling their migration and phagocytosis[6]. Insulin treatment retards the systemic inflammatory response by inhibiting the expression of monocyte chemoattractant protein (MCP-1) and cytokine induced neutrophil chemoattractant (CINC-1 and CINC-2)[7]. In the proliferative phase of wound healing, low dose topical insulin causes migration of vascular endothelial cells and keratinocytes through insulin receptor mediated PI3k-Akt-Rac1 signal pathway thus causing angiogenesis and re-epithelization subsequently promoting wound healing[8]. IGF, which has been shown through in-vivo studies to stimulate the proliferation, migration and extra cellular matrix excretion by keratinocytes, endothelial cells, fibroblast and even promote the formation of granulation tissue[9]. Insulin causes advanced infiltration and resolution of macrophages which correlated with the expression of monocyte chemoattractant protein-1, a potent chemotactic factor for macrophages.

Aims and Objectives

The study is carried out :

1. To assess the role of topical insulin in healing of chronic ulcers.
2. To compare the healing time and healing rates in study and control groups.

Materials and Methods

This prospective study was conducted from January 2014 to June 2015 involving a cohort of 60 patients who had chronic ulcers. The study required regular hospital follow up with strict inclusion and exclusion criteria.

Inclusion criteria:

- Age between 20-70 years
- Wound area less than 20 cm²
- Chronic wounds of more than 3 months duration

Exclusion criteria:

- Age <20 years and >70 years
- Patients with immune-deficient states
- Pregnancy
- Osteomyelitis
- Varicose ulcers and burns
- Liver or renal failure
- Ischemic limbs

Patients qualifying the criteria were randomized into two groups, Group A which received topical human soluble actrapid dressing 4 units in 1 ml of normal saline for each 10 cm² of wound (study group) and Group B received normal saline dressing (control group). Glycemic control was achieved for all diabetic patients with appropriate anti-diabetic therapy. Before enrolling the patients for study, wound swab culture and sensitivity of all the ulcers were taken. Surgical debridement of dirty wounds were done before being included in the study. Time required for preparing the ulcers from the time of admission till enrollment in the study was considered as wound preparation time and was not taken into study duration.

The wound area was measured using a sterile transparent paper placed on the wound to mark the borders and two longest perpendicular dimensions were multiplied to obtain the wound area. Ulcer area was measured once a week on day 7,14,21,28 till 4 weeks or till the complete healing and re-epithelization, whichever was earlier.

Rate of wound healing :

Area on day 1 – Area on day of evaluation x 100

Area of wound on day 1

Observation and Results

The wounds in both the groups were inspected everyday during dressing and measurements were noted on days 7,14,21,28. Out of the 60 patients 30 were diabetic and 30 were nondiabetic. Both the groups were comparable in terms of age distribution with mean age of Group A being 45 years and Group B being 42 years. The average area of Group A wound was 8.11 cm² and that of Group B was 8.125 cm². It was observed that 9 patients out of 30 in Group A showed complete healing of the wound as indicated by full epithelization of wound surface as compared to 8 patients in Group B. The average healing time as determined by complete wound coverage by epithelization was

21.22 days in Group A as compared to 22.25 days in Group B. These findings and p-value of 0.000714 is statistically significant.

Discussion

Insulin has long been recognized as an important contributor to wound healing. Insulin like growth factor (IGF) , which as a high sequence similarity to hormonal insulin , has been shown through in-vivo studies to stimulate the proliferation and migration of endothelial cells and fibroblast and even promote formation of granulation tissue. In the later half of 20th century, topical insulin was used in an attempt to control local hyperglycemia of peripheral tissues[10]. Later investigations have focused on topical insulin application as it relates to IGF. According to Niazi AK et-al, insulin also has beneficial effects on other organ systems of the body such as sensory organ, central and peripheral nervous system, vestibule, hair follicles, sweat and sebaceous gland and eyes[11]. After the exudate and necrotic tissue has been removed, insulin accelerates the metabolism of adjacent layer and stimulates it to regenerate and proliferate. It also arrests bacterial growth and enhances phagocytosis, thus lowering the chances of infectio[11]. In our studt it was found that there was lower incidence of infection in patients recieving insulin dressings as compared to patients recieving saline dressings as confirmed by culture and sensitivity report of wound swab.

Conclusion

Daily topical application of insulin on chronic ulcers reduces the time required for healing in such wounds. Insulin dressings are cost effective than other conventional methods of dressing like collagen, polymeric films, foams, hydrogels and colloids and holds a prespective cheap alternative to traditional methods of dressing. Insulin application probably reduces the possibility of wound site infection.

Conflict of interest

There were no financial implications or conflict of interest involved in the current study.

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