



## DIABETIC WOUND HEALING MANAGEMENT- A PEER REVIEW

Harshavardhan Pathapati<sup>1</sup>, T.E. Gopala Krishna Murthy<sup>2</sup>, B. Ramanaiah<sup>3</sup>, Davu Srinivas<sup>4</sup>

<sup>1</sup>Research Scholar in Bapatla college of Pharmacy, Bapatla- 522101, Guntur-522017, Andhra Pradesh, India.

<sup>2</sup>Principal of Bapatla college of Pharmacy, Bapatla- 522101, Guntur-522017, Andhra Pradesh, India.

<sup>3</sup>Research Scholar in Bapatla college of Pharmacy, Bapatla- 522101, Guntur-522017, Andhra Pradesh, India.

<sup>4</sup>Research Scholar in Bapatla college of Pharmacy, Bapatla- 522101, Guntur-522017, Andhra Pradesh, India.

Email- harshapropharma@gmail.com

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### ABSTRACT

**Objectives:** Diabetes is a metabolic disorder mainly impairs the body glucose utilization capacity due to this perforce repressing the immuno-dysfunction (decreases chemotaxis, phagocytosis and intracellular killing actions) and collagen synthesis which are essential in wound debridement management of diabetic patients. Delayed wound healing is considered as one of the most repulsive disabling and costly complication of diabetes. People with diabetes have attenuated circulation, poor resistance to infection and mitigate local nutrition, thus their wounds are meticulously susceptible to infection. Moreover diabetes agonizes the equilibrium exists between accumulation of extra-cellular matrix components and their re-modeling by matrix metallo-proteinases (meltrin), due to this extenuated proliferation action of fibroblasts and finally freezes the progress of wound healing frequency in hyper glycemics. However in diabetic persons the nervous system becomes numb and all feasible actions of neurons are skipped, that condition is called as diabetic neuropathy. In that situation patient body features elevated a glucose level which stiffens the arteries and lack of pain sensation in foot resulting in commencement of new wounds. **Conclusion:** Consider all problems associated with wound healing in diabetic persons, a proper wound healing management which includes controlling measures like optimized systemic and local factors as well as implement suitable wound dressing for necessary wound in diabetes patients.

**Keywords:** Delayed wound healing, Diabetic wound healing management, Diabetic neuropathy, Immuno-dysfunction, Wound dressings.

### INTRODUCTION

Topical wound healing is a complex and deligent matter of fact in the restoration of tissues formation and remodeling of wounded tissues. Commonly wound debridement is a dynamic instinct in which extensive extra-cellular matrix components act in concert to exquisite deposition of injured tissues. Wound healing process is extenuated by the free-radicals and air borne contaminants present in wound site. These free-radicals noxiously causing enzymatic degradation, lipid peroxidation and lastly affects the DNA breakdown by sizzering the cells and most importantly the airborne contaminants like microbes decrepit the status of the wound and eventually freezes the wound healing frequency. In order to deduce the intensity of the wound status there is a provision to implementation of effective wound healing managements and treatment technologies and finally encourage the tissue regeneration.

Diabetes is one of the most prevalent human metabolic diseases, reaching pandemic proportions[1]. The morbidity of diabetes has increased dramatically over the past few years, and afflicts more than 100 million people worldwide. Delayed wound healing is considered one of the most common, disabling, and costly complications of diabetes. People with diabetes have poor circulation, poor resistance to infection, and poor local nutrition, thus their wounds are highly susceptible to infection[2]. This impairment in diabetic wound healing represents a significant clinical problem, leading to chronic non-healing ulcers ultimately resulting in infection, gangrene, or even amputation[3]. Thus, accelerating wound healing must be the primary goal of wound care.

Diabetic foot ulcers can be divided into two groups: those in neuropathic feet (so called neuropathic ulcers) and those in feet with ischaemia often associated with neuropathy (so called neuroischaemic ulcers). The neuropathic foot is warm and well perfused with palpable pulses; sweating is diminished, and the skin may be dry and prone to fissuring.

The neuroischaemic foot is a cool, pulse less foot; the skin is thin, shiny, and without hair. There is also atrophy of the subcutaneous tissue, and intermittent claudication and rest pain may be absent because of neuropathy [4].

### WOUND HEALING MANAGEMENT IN DIABETIC PATIENTS

#### Diabetic Wound Healing (DWH)

Wound healing is a multifunctional dynamic process of regenerating damaged tissue layers and cellular organelles. Generally wound healing management plays a crucial role in repairing of lost cells in case of acute and chronic wounds. Diabetes is a condition in which the body does not effectively use sugar in body and approximately 15% of the diabetic world population develops diabetic foot ulceration at some point in their lives [4]. Generally wound healing can be slowed down and eventually worsen rapidly in case of diabetic patients.

Delayed wound healing as occurs in diabetes mellitus results from dysregulation of the normal healings pathways. The diabetic wound is complex with contribution from infection, neuropathy and impaired vascular supply. There are many physiological defects in diabetic wound includes decreased or impaired growth factor production, angiogenic response, macrophage function, collagen accumulation, epidermal barrier function, quantity of granulation tissue, keratinocyte, fibroblast migration and proliferation and bone healing. There is an imbalance between the accumulation of extra-cellular matrix components and their re-modeling by matrix metallo-proteinases. In addition fibroblasts from diabetic wounds become senescent and show a decreased proliferative response to growth factors [5]. This is associated with a persistent increase in pro-inflammatory cytokines by various immune and non-immune cells and it is hypothesized that this blunts the acute, focused cytokine response needed to progress through the normal phases of wound healing [6].

## Factors Affecting Wound Healing in Diabetic Patients [7-10]

### i. Systemic Factors

	Drug
Steroids	Interrupts macrophage function which leads decreasing of inflammatory response. Inhibit prolyl/lysyl hydroxylase which interns collagen bonds formation and it is rectified by anabolic steroids and vitamin-A. . Executes T and B cell dysfunction. Impairs leucocyte bactericidal activity.
Anti-Neoplastic agents	Reduced WBC's, fibroblast proliferation, wound contraction and protein synthesis. Colchicine - decreases collagen precursors, collagen secretion (cellular constipation) and elevates collagenases activity. Penicillamine – Deceives Calcium activity which helps in collagen formation.
NSAIDs	Progress of collagen synthesis lessens around 45% even at normal dose.
Vitamin A	Elevates collagen synthesis and improves wound healing ability. Capable of clenching the deleterious disquiet of steroids and Vit-E.
Vitamin C	Plays co-factor role in proline hydroxylation. In deprived of Vit-C (scurvy) enhances the noxious consequences like capillary fragility and wound healing problems.
Vitamin E	Vitamin E agonize the collagen synthesis and wound healing frequency.
Zinc	Enzyme constituent and cofactor for collagen synthesis.
Copper	Extracellular cofactor necessary for collagen cross linking.
Magnesium	Supports cofactor role in glycolization.
Nutritional Status	
<ul style="list-style-type: none"> <li>• Catabolic state (net -ve nitrogen balance) reduces wound debridement.</li> <li>• Protein depletion – which plays a rate limiting step in inflammatory phase and impairs fibroplasia.</li> <li>• Methionine is essential for capacitate disulfide bonds in collagen synthesis.</li> <li>• Carbohydrates – power generators for WBC's.</li> <li>• Fats have no significant effect in wound healing.</li> </ul>	
Associated Illnesses/Immunity	
Cancer, Infection, Peripheral vascular disease, COPD/ hypoxia, obesity and smoking etc.,	All deduces wound healing progress.
Patient Age	
<ul style="list-style-type: none"> <li>• Associated with delayed onset of healing, protraction of phases and an inability to reach same level of healing.</li> <li>• Upon ageing debilitate chivalry actions such as tensile strength and wound closure rate.</li> </ul>	

### ii. Local Factors

#### Blood glucose levels

Most importantly elevated blood glucose levels play a vital role in the wound healing in diabetic patients. When rise in the blood sugar levels causes the stiffening of arteries and narrowing of blood vessels. Due to this far reaching and includes the origin of wounds as well as risk factor to proper wound healing.

#### Diabetic neuropathy

When blood glucose levels are uncontrolled, nerves in the body are affected and becomes numb due to this the patients losses the sensing ability, particularly this situation considered as diabetic neuropathy. Whenever this condition is predominant patient develops lack of pain sensation in blistering, infection or

surgical wound problem. Because a diabetic patient may not able to feel a change in the status of a wound or the actual wound, the severity can progress and there may be complications with wound healing.

#### Immune system deficiency

Diabetes lowers the efficiency of immune system of the body against infection. A rise in blood sugar levels predominantly limits the efficacy of the host immune system due to this the individual highly susceptible to infections and more over it skips the healing process. Studies states that particularly enzymes and hormones that the body produces in response to an elevated blood glucose levels suffocates the immune system in diabetes which prolongs wound healing frequency.

#### Infection [11]

The status of the healing process in the inflammatory phase will be ensured by the infection at the wound site. When the pathogen microbes compete with the macrophages and fibroblasts for limited resources they cause necrosis in the wound bed. Serious condition of this infection can lead to sepsis and death. The infection is diagnosed when bacterial counts of micro-organisms per tissue are in excess as demonstrated by wound culture. In diabetics functioning of immune system is predominantly reduced thus influences the risk of infection and raises many health complications eventually slow down the wound healing frequency. If untreated wound status becomes worsen and developing life threatening complications like gangrene, sepsis and bone infection like osteomyelitis and ended with severe trauma finally leads to death.

#### Mechanical stress Factors [12]

This stress occurs due to pressure friction and shear. Pressure may be due to immobility such as bed rest (or) local pressure generated by a tight fitting shoe on a diabetic patient's foot. The granulation tissue damage and blocking of blood vessels may occur due to shear forces. The wound may return to inflammatory phase when the newly formed epithelium or granulation tissue wears away due to friction.

#### Foreign Body

Necrotic tissue or foreign materials like sutures, dressing residues, fibers shed by dressings and foreign materials introduced during the wounding process such as dirt or glass constitute debris. In order to allow the progression of wound healing process from inflammatory stage to proliferative stage of healing, the materials that are deposited as debris should be removed.

#### Temperature

The rate of chemical and enzymatic processes occurring within the wound is influenced by the wound temperature. Generally greater than 30°C temperature encourages the tensile strength of wound layer in wounded persons.

#### Wound Hydration

Wound gets soften when soaked in the secreted fluids, and becomes broaden, which is more susceptible to increase the mechanical forces and infection. In order to protect the skin around the wound from sweat or inconvenience, the moisture is removed. For this, modern wound products are designed.

#### Influence of Oxygen level in wound area

In diabetic person nutritional status and oxygen level are rate limiting step (requires sufficient inspired oxygen, Hemoglobin for transport and capacity to perfusion into even micro vessels) in healing wound. Efficient oxygen levels enable collagen synthesis, proline hydroxylation, collagen secretion and finally help in wound debridement. Oxygen levels also execute leucocyte killing capacity (phagosomal peroxidation), growth factor stimulation and fibroblast proliferation which initiate neo vascularization.

### Chemical stress

Daily use of antiseptic and cleansing agent may impale the wound healing frequency which leads to chemical stress. Most of the antiseptic and cleansing agents have the ability to induce oxidative stress causes cell damage because these agents consists peroxide, chlorhexidine, iodine, alcohol and acetic acid etc.

### Pressure [8]

Under pressure may lead to ischaemia of the wound, therefore, all wounds, particularly chronic wounds, should be off-loaded and reduced wound healing progress is reported. In patients with peripheral neuropathy, it is important to offload at-risk areas of the foot in order to redistribute pressures evenly. Inadequate offloading leads to tissue damage and ulceration. The gold

standard is the total contact cast (TCC). This is a well molded, minimally padded foot and lower leg cast that distributes pressures evenly over the entire plantar surface of the foot. It ensures compliance because it is not easy for the patient to remove. Using a TCC in patients with a unilateral uncomplicated plantar ulcer can reduce healing time by around six weeks.

### 3. Clinical Approach to Diabetic Patients in Wound Healing Management

The multitude of factors affecting wound healing should be examined for every individual. In general, to provide for optimal wound healing one should strive to eliminate underlying causative and/or contributory factors and stimulate positive physiologic factors required for the healing process.

**Table 1: Systemic and Local approaches in Diabetic Wound Healing Managements [13, 14]**

Systemic Factors	
Nutritional status	Eating a healthy diet and maintaining good nutrition will help to regulate blood glucose levels. Adequate protein, carbohydrates and vitamin C intake are important factors to aid healing.
Psychological status	Depression inhibits drug compliance and wound healing.
Biochemical status	Acid base balance Endocrinologic status, blood sugars, hypo-thyroidism. Correct renal failure, liver failure
Perfusion and Oxygenation	Cardiac status Pulmonary status Anemia Maintaining good habits like stop drinking and smoking etc., Vascular bypass surgery if required
Drugs	Effective utilization of ant diabetic drugs with antibiotics and vitamin constituents.
Local Factors	
Wound Environment	Exquisite display of applying wound dressings. Eliminate foreign bodies, dead space and necrotic tissue Elimination of infection by using systemic/topical antimicrobials and P <sup>H</sup> active agents. Reduce edema Decrease load pressure Provide moist wound environment.
Weight management and Exercise	Engaging in regular aerobic exercise, chronic inflammation can be reduced. Exercise lowers the blood sugar and also helps with weight management.

**Table2: Best Wound Healing Dressings for Diabetic Persons [15-17]**

Type	Actions	Use	Precautions/contraindications
Alginates/CMC	Absorb fluid, promotes autolytic debridement, moisture control, and Conformability to wound bed.	Moderate to high exuding wounds.	Do not use on dry/necrotic wounds. Use with caution on friable tissue (may cause bleeding). Do not pack cavity wounds tightly.
Foams	Absorb fluid, Moisture control and Conformability to wound bed	Moderate to high exuding wounds.	Do not use on dry/necrotic wounds or those with minimal exudates.
Honey	Rehydrate wound bed, promote autolytic Debridement and Antimicrobial action	Low to moderate exuding wounds and Critically colonized wounds or clinical signs of infection.	May cause 'drawing' pain (osmotic effect) and Known sensitivity.
Hydrocolloids	Absorb fluid Promote autolytic debridement	Clean, low to moderate exuding wounds	Do not use on dry/necrotic wounds or high exuding wounds. May encourage over granulation and maceration.
Hydrogels	Rehydrate wound bed, Moisture control, cooling effect and promote autolytic debridement	Dry/low to moderate exuding wounds	Do not use on highly exuding wounds or where anaerobic infection is suspected and May cause maceration
Iodine	Antimicrobial action	Critically colonized wounds or clinical signs of infection and Low to high exuding wounds	Do not use on dry necrotic Tissue. Known sensitivity to iodine. Short-term use recommended (risk of systemic absorption)

Low-adherent wound contact layer (silicone)	Protect new tissue growth, A traumatic to periwound skin and Conformable to body contours.	Low to high exuding wounds	May dry out if left in place for too long and Known sensitivity to silicone.
PHMB	Antimicrobial action	Low to high exuding wounds, Critically colonized wounds or clinical signs of infection and May require secondary dressing.	Do not use on dry/necrotic wounds and Known sensitivity.
Odor control (eg: activated Charcoal)	Odor absorption	Malodorous wounds (due to excess exudates) and May require antimicrobial if due to increased bio burden.	Do not use on dry wounds.
Protease modulating	Active or passive control of wound protease levels	Clean wounds that are not progressing despite correction of underlying causes, exclusion of infection and optimal wound care.	Do not use on dry wounds or those with leathery eschar.
Silver <sup>[18]</sup>	Antimicrobial action	Critically colonized wounds or clinical signs of infection and Low to high exuding wounds.	May cause discoloration, Known for sensitivity and Discontinue after 2 weeks if no improvement.
Polyurethane film	Moisture control, Breathable bacterial barrier and Transparent.	Primary dressing over superficial low exuding wounds and Secondary dressing over alginate or hydrogel for rehydration of wound bed.	Do not use on patients with fragile/compromised periwound skin and Do not use on moderate to high exuding wounds.

**Table 3: Treatment Optimization approaches depending upon Status of Wound in Diabetic Persons [18-20]**

Type of tissue in the wound	Therapeutic goal	Role of dressing	Treatment options		
			Wound bed preparation	Primary dressing	Secondary dressing
Necrotic, black and dry	Remove devitalized tissue, do not attempt debridement if vascular insufficiency suspected and keep dry and refer for vascular assessment	Hydration of wound bed and promote autolytic debridement	Surgical mechanical debridement	or Hydrogel Honey	Polyurethane film dressing
Sloughy, yellow, brown, black or grey Dry to low Exudates	Remove slough and provide clean wound bed for granulation tissue	Rehydrate wound bed, Control moisture balance and promotes autolytic debridement	Wound cleansing (consider antiseptic wound cleansing solution)	Hydrogel Honey	Polyurethane film dressing Low adherent (Silicone) dressing.
Sloughy, yellow, brown, black or grey Moderate to high exudates	Remove slough Provide clean wound bed for granulation tissue exudate management	Absorb excess fluid Protect periwound skin to prevent maceration Promote autolytic Debridement	Surgical mechanical debridement if appropriate wound cleansing barrier products	or Absorbent dressing for deep wounds, use cavity strips, rope or ribbon versions.	Retention bandage or polyurethane film dressing
Granulating, clean, red, dry to low exudates	Promote granulation and provide healthy wound bed for epithelialisation	Maintain moisture balance and protect new tissue growth	Wound cleansing	Hydrogel, Low adherent dressing and for deep wounds use cavity strips, rope or ribbon versions	Pad and/or Retention bandage.
Granulating, clean, red moderate to high exudates.	Exudate management and provides healthy wound bed for epithelialisation	Maintain moisture balance and ensures new tissue growth	Wound cleansing and consider barrier products	Absorbent dressing, Low adherent dressing and for deep wounds, use cavity strips, rope or ribbon versions.	Avoid bandages that may cause occlusion and maceration. Tapes should be used with caution due to allergy potential and secondary complication
Epithelialising, red, pink, No to low exudates	Promote epithelialisation and wound maturation.	Protect new tissue growth	—	Hydrocolloid (thin), Polyurethane film dressing and Low adherent (silicone) dressing.	
Infected, Low to high exudates	Reduce bacterial load Exudate management Odor control.	Antimicrobial action, Moist wound healing, Odor absorption.	Wound cleansing and barrier product (consider antiseptic wound cleansing solution)	Antimicrobial dressing	

## CONCLUSION

Diabetes is a well known burdening disability worldwide, but it is not an invincible complication, unless blood glucose levels are raised predominately. Wound healing is a complicated process in normal persons, in case of diabetic individuals wound healing is a worsen phenomenon sometimes it is even life threatening aspect. In order to treat diabetic wound healing salutary diabetic wound healing management approaches which includes perfect Medication, optimistic treatment measures and more importantly convenient wound dressings with respect to status and morphology of wounds are propagated accurately. Considering all facts about diabetes current article gives a brief awareness, problems associated with diabetes in wound healing and best treatment options in diabetes persons.

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