Recent Advances in Management of Chronic Non-healing Diabetic Foot Ulcers

Ashok Damir
MD, Foot Fellowship, Chicago, USA, Sr. Diabetic Foot Specialist & Stem Cells Therapist
Fortis C-DOC, Chirag Enclave, New Delhi, India

INTRODUCTION

Foot ulcers in diabetic patients are common. It is estimated that 15% of diabetes patients will develop Diabetic foot ulcer once in their lifetime, and approximately 14% of diabetic ulcers lead to amputation unless a prompt, rational, multidisciplinary approach to therapy is taken.

Factors that affect development and healing of diabetic patient’s foot ulcers include the degree of metabolic control, the presence of ischemia or infection, and continuing trauma to feet from excessive plantar pressure or poorly fitting shoes. Appropriate wound care for diabetic patients addresses these issues and provides optimal local ulcer therapy with debridement of necrotic tissue and provision of a moist wound-healing environment.

A wide variety of advanced treatments for diabetic foot ulcers, such as topical growth factors, bioengineered skin grafts, VAC(Vacuum Assisted Closure) Therapy, and hyperbaric oxygen therapy(HBOT), are available commercially now in India, and clinical studies of these products have shown some evidence of improved wound healing compared to standard wound care.

During the prolonged healing process of a chronic wound, rapid and accurate evaluation of the healing progress is critical so that unsuccessful treatments can be discontinued and alternate treatments be initiated as soon as possible.

Though recent advances in the management of Diabetic Foot Ulcers have increased our abilities to salvage the lower limb, the best management still remains prevention. This can only follow with intense patient education about foot care and a proactive role in treating the factors which lead to these foot problems.

MANAGEMENT OF DFU CAN BE DISCUSSED BY FOLLOWING HEADINGS

A. Microbiological Control
B. Wound Control
C. Metabolic Control
D. Vascular Control
E. Mechanical Control
F. Educational Control

A. Microbiological Control

Certain principles should be followed while giving antibiotics when diabetic foot infection cases are suspected. Most of the Diabetic Foot Infections are poly microbial.

So broad spectrum Antibiotic are to be used for longer duration. Because of Immunopathy there is a Poor immune response in diabetics hence normal skin commensals can cause serious infection. Wide spectrum of antibiotics should always be used even at initial presentation because it is Impossible to predict type & no. of microorganisms clinically, there is no way of predicting rapidly ascending or Life threatening Diabetic Foot Infection and Triopathy of DM reduces local resistance to invading bacteria.

B. Wound Control

After exposing the wound you should irrigate the wound with saline or diluted solution of Povidone iodine. Never use concentrated solution of Povidone iodine who damages normal granulation tissue to grow.

VASHE WOUND CLEANSING SOLUTION

VASHE is solution of Hocl (Hypochlorous Acid). It Kills important wound pathogens like Gram +ve, Gram -ve bacteria, Anaerobes & Fungi.

A gauze soaked in VASHE solution is wrapped around wound for 10-15 mnts. which cleans, irrigates, moistens & debrides the wound.
and removes bacteria & fungus along with bed odor from wound.  

**DEBRIDEMENT** (REMOVAL OF DEVITALIZED TISSUE FROM ULCER)  

Once you have cleaned the wound, it should be debrided thoroughly. There are different ways of debridement like Sharp, blunt, Surgical, Chemical & Auto debridement but I’m going to discuss here only two new modalities i.e. Ultrasonic debridement & Biodebridement (also known as Maggot Rx).

**ULTRASONIC DEBRIDEMENT**  

With ultrasonic debrider there is Ultrasonic formation & collapse of Vapor Bubbles who fragments & emulsify the necrotic tissue without disturbing the viable tissue. Ultrasonic debridement is effective in removal of particulate matter and reduction of bacterial counts. Good thing about this modality of debridement is that there is hardly any blood loss. This type of debridement is particularly useful in handling deep and tunnelling wounds where debridement with other technique is difficult.

**BIODEBRIDEMENT OR MAGGOT Rx**  

Medicinal maggots of Lucilia sericata (Green Bottle fly) are used for debriding the dead necrotic & infected tissue of wound. Beauty of these maggots is that they donot eat or disturb normal host tissue. Benefits of Maggot’s therapy are good debridement with removal of dead necrotic tissue and elimination of infection. Shortcomings of Maggot’s therapy are that Medicinal maggots are costly & difficult to get. They have short shelf life, pt. can have uncomfortable crawling sensation & once move out of dressing, Maggots can create lot of neusense.

**VAC (VACCUM ASSISTED CLOSURE)/ NPWT (NEGATIVE PRESSURE WOUND THERAPY)**  

VAC or NPWT device comprises  
1. Granufoam Dressing  
2. Plastic Tubing  
3. Canister

**Indications for Maggot’s Rx**

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Infected or sloughy wounds</td>
</tr>
<tr>
<td>2.</td>
<td>Necrotic area on diabetic foot</td>
</tr>
<tr>
<td>3.</td>
<td>Necrotizing fasciitis</td>
</tr>
<tr>
<td>4.</td>
<td>Infection with MRSA</td>
</tr>
</tbody>
</table>

**Contraindications for Maggot’s Rx**

<table>
<thead>
<tr>
<th>S.No</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Fistulae</td>
</tr>
<tr>
<td>2.</td>
<td>Wounds that connect with vital organs such as Brain</td>
</tr>
<tr>
<td>3.</td>
<td>Wounds near cavities eg. Abdomen, Thorax</td>
</tr>
<tr>
<td>4.</td>
<td>Wounds near large blood vessels</td>
</tr>
</tbody>
</table>
4. Computerized Rx Unit
After cleaning & debriding the wound a special granufoam dressing is applied over wound which is connected to special Computerized Rx Unit with a plastic tubing. This Computerized Rx Unit applies 125mmHg negative pressure to wound which draws exudates etc. into a special canister attached to Unit. VAC therapy helps in reducing oedema, exudates and bacterial load & also helps in regeneration of granulation tissue & neo vascularisation.

AUTOLOGEL-AUTOLOGUS PLATELET RICH PLASMA (PRP) GEL
This new modality for wound healing is based upon principle of Platelets containing components & properties for wound healing & Plasma containing fibrin matrix.
Procedure- Depending upon the size of ulcer, around 5 to 30 ml patient’s blood is centrifuged & Platelet Rich Plasma is separated. This PRP is taken into a syringe having different reagents [Thrombin(CaCl2) & Vita C], who activate platelets & make gel consistency. This is known as Autologel. This gel like material is applied over wound twice a week for 12 weeks & it was observed by Vickie R. Driver etal. that 68.4% of those wounds which were treated with Autologel healed in comparison to 42.9% of Control wounds.

O2 MISLY
After Cleaning & Debriding the wound pt. puts his lower limb in a canister of O2 Misly machine & wound is exposed to 4 Cycles of 100% O2(5 mnt.each) alternatively with Vapor of water & antibiotic(10 mnt.each). This therapy is given Twice a week for 12 to 20 weeks. Ubbink DT et al found that in comparison to standard wound care proportion of healed Wounds with use of O2 Misly were 200% better at 12 to 20 week.

LLLT(LOW LEVEL LASER THERAPY)
LASER is Light Amplification by Stimulated Emission of Radiation. There have been lot of medical indications of using Laser & one indication is nonhealing Diabetic Foot Ulcer. Wound is exposed to Low Level Laser Therapy which activates Microcirculation & Macrophages leading to Anti-inflammatory, Analgesic, Regenerative, Bacteriostatic & Bactericical clinical effects on wound. Martinez-Sanchez G et al. Found Low Level Laser Therapy very effective in healing of Chronic Nonhealing diabetic Foot Ulcer.

GROWTH FACTORS
The term growth factor refers to a naturally occurring protein capable of stimulating cellular proliferation and cellular differentiation. There are different types of Growth Factors which are involved in wound healing.

Growth Factors involved in wound healing

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Growth Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Epidermal growth factor (EGF) – US FDA approved</td>
</tr>
<tr>
<td>2.</td>
<td>Platelet derived growth factor (PDGF) – US FDA approved</td>
</tr>
<tr>
<td>3.</td>
<td>Hepatocyte growth factor (HGF)</td>
</tr>
<tr>
<td>4.</td>
<td>Vascular endothelial growth factor (VEGF)</td>
</tr>
<tr>
<td>5.</td>
<td>Fibroblast growth factor 1 and 2 (PDGF-1, -2)</td>
</tr>
<tr>
<td>6.</td>
<td>Transforming growth factor alpha (TGF-α)</td>
</tr>
<tr>
<td>7.</td>
<td>Transforming growth factor - β (TGF-β)</td>
</tr>
<tr>
<td>8.</td>
<td>Keratinocyte growth factor(KGF)</td>
</tr>
</tbody>
</table>

US FDA has so far approved only two types of growth factors for use in Chronic Wounds. They are Platelet derived growth factor (PDGF) and Epidermal growth factor (EGF). Most commonly used plermin (rh PDGF BB, Recombinant human Platelet derived growth factor) has Chemo tactic, mito genic, angio genic, and stimulatory effects and helps in wound healing if used in noninfected superficial wounds.

OZONE THERAPY
Ozone is “active oxygen”. It is triratomic allotrope of oxygen formed by recombination of oxygen atoms. It is a Colourless pungent-odor gas. Ozone disinfects, oxidizes, deodorizes and decolorizes. Ozone is very strong oxidant and is found to be more than 3000 times powerful disinfectant than chlorine. Peripheral Ozone Therapy is very effective for badly-infected and non-healing Ulcers like chronic Diabetic foot ulcers. Technique of giving Peripheral Ozone Therapy is known as “Bagging”. That means after preparing the wound, limb is covered with a plastic bag & a tube from Ozone generator is tightly secured in upper portion of bag. Wound is exposed to Ozone for 20 to 30 mnt.
HYPERBARIC O2 (HBO) THERAPY

Hyperbaric oxygen therapy means exposing pt. to 100% oxygen under increased atmospheric pressure.

Indications of HBO Therapy

<table>
<thead>
<tr>
<th>No.</th>
<th>Pediatric Indications</th>
<th>General Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Ch. Non healing wound of &gt;90 days (Wagner Gr. 3 or more)31-33</td>
<td>CO Poisoning (Carbon Monoxide Poisoning)26</td>
</tr>
<tr>
<td>2.</td>
<td>Gas Gangrene(30,21)/Embolism</td>
<td>Decompression Syndrome27</td>
</tr>
<tr>
<td>3.</td>
<td>Necrotizing Fasciitis (23)</td>
<td>Intracranial Abscess,Stoke(24),Multiple Sclerosis(29,30)</td>
</tr>
<tr>
<td>4.</td>
<td>Refractory Osseous Myelitis(23-25)</td>
<td>Skin grafts and flaps (compromised)31</td>
</tr>
</tbody>
</table>

Monoplace HBOT Chamber

Two types of HBO chambers are available. Monoplace & Multiplace Chambers. In Monoplace chamber one person can lie down inside glass chamber and he is exposed to pressurised oxygen for a prescribed limit of time. While Multiplace chamber is like a big Oil-tanker in which number of patients can simultaneously be exposed to HBO. Pt. is placed in Monoplace / Multiplace HBO Chamber & he breathes 100% oxygen under increased (2 to 3 times) atmospheric pressure for 90 to 120 mnts. This Increases tissue oxygen tension, angiogenesis, fibroblast proliferation, collagen deposition and enhanced bacterial killing32.

This Rx is given for 5 days a week & total such 20 to 40 treatments are given depending upon size & severity of wound. Improved wound healing & reduced rate of amputations were observed in significant no. of cases of DFU by Stone JA et al.33

SKIN GRAFTS – APLIGRAF

Whenever size of wound is large & it is superficial & well granulated, it needs skin grafting. Skin graft can be natural skin grafts or Bioengineered grafts. Apligraf is Bioengineered Epidermis & Dermis Graft, developed from foreskin of Newborn. Indication of using Apligraf are Ch. Non healing (non infected) DFU34 or Superficial Venous Ulcers35.

C. METABOLIC CONTROL

Controlling Blood sugar and other general parameters are equally important for comprehensive management of Ch. Non healing Diabetic Foot Ulcer.

If wound is small & superficial one can use OHAs (Oral Hypoglycemic Agents) for controlling Blood sugar in Type II DM. Pt. should be put on Insulin if wound is large. Infected, necrotic & patient has septicemia, looks toxic and or has Diabetic Keto acidosis. DKA should be treated & hydration should be maintained. Take care of pt’s nutrition, if hypo proteinemia, treat it.

D. VASCULAR CONTROL

Whenever pt of DFU comes always put your fingers on peripheral arteries like DP,PT,Pop & femorals. If two or more than 2 arteries are impalpable & or ABI (Ankle Brachial Index) is low get Peripheral Vascular Doppler & Angiography done, if need arises. If arterial occlusion is less than 10 cm then different options available are-Intraarterial Thrombolysis, Endarterectomy & Angioplasty which can be conventional Balloon Angioplasty with or without Stents, Sub intimal angioplasty, Lasers Angioplasty and Rotablaters for Hard Plaque.

If arterial occlusion is more than 10 cm then different types of Vascular Grafts (Natural or Synthetic) are applied to bypass the occlusion & to achieve good circulation distal to occlusion leading to healing of ulcer.

E. MECHANICAL CONTROL - OFF LOADING

Offloading is cornerstone of managing Chronic Nonhealing diabetic foot ulcer36 which is most of the time overlooked by clinicians. No matter what ever modalities so far I have mentioned (Old or New) are used for treating Ch. Nonhealing Diabetic Foot Ulcer, if proper offloading of the wound is not done, one will not be able to achieve ultimate target that is complete healing of Diabetic Foot Ulcer.

Depending upon site, size & severity of wound pt. may be advised for complete bed rest or may be advised of using different offloading devices. Pt. should be asked not to bear weight until wound is healed up. Every step which is taken will delay the wound healing until otherwise optimal offloading is instituted.

Different offloading devices could be Crutches, Wheel Chair, different types of Offloading Shoes, Scotch Cast boot, Removable Cast Walker(RCW) & Air Cast walker which is latest in armamentarium.
TCC (Total Contact Cast) is just like applying plaster around fracture of foot or leg. TCC can be made of plaster of Paris (POP) or Fiberglass. Although best offloading is achieved by TCC, it is cumbersome, time consuming & needs expertise & one cannot follow the trend of wound.

Most of these shortcomings of TCC can be overcome by using ITCC i.e. Instant Total Contact Cast which was developed by Dr. David G Armstrong et al. of Chicago.

**SUMMARY**

Most Common Cause of hospitalization in Diabetics is Diabetic Foot Problems. Since n.o.o. Diabetics is increasing hence different complications related to diabetes are also increasing including non healing diabetic foot ulcers. Minor ulcer can lead to Amputation so one should be cautious since its beginning. Newer & more advanced techniques are now available for better wound care including Vac therapy, Hyperbaric Oxygen Therapy, Growth Factors, Bioengineered Skin grafts, Maggot’s therapy etc. If Diabetic Foot Ulcer is not improving one should refer case to Podiatrist or specialist.

The holistic care of diabetic foot ulcer requires a multidisciplinary team approach. Apart from blood sugar control, treatment of ulcer involves debridement, offloading, appropriate dressings, vascular maintenance and infection control.

**REFERENCES**