Special Article

[Simplified Wound Care/Management - Excerpts from 7th National Wound Care Workshop 2021]

New Modalities and Challenges in Diabetic Foot Management

Milind Ruke[1], Anup Sharma[2], Ramananda Saikia[3], Triloc Chand Agrawal[4], Rajendra Kumar Maskara[5], Manoj D Togale[6], Rahul Rathod[7], Seetharam V[8]

Management of diabetic foot ulcer is critical and a multidisciplinary approach. New investigative modalities for diagnosis of diabetic foot ulcer include biothesiometer, hand held Doppler, calculative AVI for vascular studies, podoscan for fore foot pressure and footwear. TIME concept comprising of evaluation of pathology, comorbidities involved and offering wound careis frequently used to manage diabetic wounds. Debridement, effective antiseptics, hydration, biomechanics, offloading and biofilm management are important aspects of rapid wound healing. Negative pressure wound therapy is used frequently for diabetic wound healing.

[*J Indian Med Assoc* 2021; **119(5):** 64-9]

Key words **: Biofilm, Debridement, Diabetic wounds, Offloading.**

Several diabetes-related infections occur frequently such as laparoscopic port infections, mesh infection due to polymicrobial infections and diabetic foot ulcer (DFU) leading to amputation. A few years ago, amputation was just cut and done, leading to contralateral foot amputation, increased load on decompensated heart in diabetes resulting in myocardial infarction and death. Anesthetists were not aware about the role of regional blocks in DFU that would decrease the complications and physicians were adapting to newer drugs of diabetes and insulin. Incidence of retinopathy and DFU are much greater than other diabetic complications among patients with longer duration of diabetes.

It is understood by clinicians that management of DFU is a multidisciplinary approach. Insulin infusion is recommended for glucose control during emergency surgical management of DFU. In case of hyperglycemia, if insulin is not provided the patient undergoing surgery develops a state of hormonal catabolism with increased levels of hormones and chemical mediators such as growth hormone, cortisol, glucagon, adrenaline, cytokines, fatty acids and increase glucose. It is observed that with insulin in-hospital mortality, bloodstream infection and acute renal failures are reduced. Consensus statement on inpatient glycemic control suggest insulin therapy for treating persistent hyperglycemia and intravenous insulin infusions are ideal for achieving and maintaining glycemic control. However, frequent glucose monitoring is crucial to prevent hypoglycemic events and achieve optimal glucose control[1].

Understanding wound healing in DFU is critical. Normal wound healing occurs in four stages hemostasis, inflammation, proliferation, remodeling. Wound arrest occurs between inflammation and proliferation. Accumulation of metalloproteins occurs during wound closure. Wound arrest occurs in first week after the onset of wound. Wound debridement should occur with lot of inflammation and should progress to proliferation without any hindrance of vascular supply, infection, foreign body or osteomyelitis.

A 15% reduction in wound area on a weekly basis

Editor's Comment :

- Difficult to treat diabetic wounds occur in patients with osteomyelitis, vascular insufficiency, renal foot, biofilms, immunocompromised, and Charcot neuropathic ulcers.
- Debridement, effective antiseptics, hydration, offloading and biofilm management are important aspects of rapid wound healing.
- Negative pressure wound therapy is used frequently and is very effective. If surgery fails, hyperbaric oxygen therapy is implemented which improves circulation and granulation ensuring faster wound healing.

[1]MS, DHA, FICS, FIAGES, FDFM (UTMB), CWS (USA), PGCDFM (AIMS), Consultant General Surgeon, Diabetic Foot & Limb Salvage, Associate Professor, Government Grant Medical College, Mumbai 400008

[2]MBBS, MS, Consultant Surgeon, Matoshree Clinic, Dhanbad 828127, Jharkhand

[3]MBBS, MS, Consultant Surgeon, NC Das Nursing Home, North Lakhimpur 787001, Assam

[4]MS, MCh, Professor, Department of Plastic Surgery, Hansaraj Memorial Hospital, Gwalior 474008 Madhya Pradesh

[5]MBBS, MS, Consultant Surgeon, Paras Spring Meadows Hospital, New Delhi 110065

[6]MS, Associate Professor, Department of Surgery, JNMC KLE University Campus, Nehru Nagar, Belgaum, Karnataka 590010

[7]MD, MBA, Cluster, Head, Medical Affairs, Dr Reddy's Laboratories Ltd, Ameerpet, Hyderabad 500016

[8]MBBS, PG(Surgery) FMAS, Consultant Surgeon, Seetharam Hospital, Coimbatore 641007, Tamil Nadu

Received on : 05/05/2021
Accepted on : 08/05/2021

is considered as a normal healing rate. The wounds that respond below the normal healing rate should be considered for alternative therapies or further investigations. A 12-week prospective multicenter clinical trial in patients with diabetes determined that the percent change in foot ulcer area after 4 weeks is a robust predictor of healing at 12 weeks. Prevention of DFU involves detecting high risk foot in diabetes mellitus. New investigative modalities for diagnosis of DFU include biothesiometer, hand held Doppler, calculating ABI for vascular studies, podoscan for fore foot pressure and footwear. TIME concept comprising of evaluation of pathology, comorbidities involved and offering wound care frequently is used as a part of the comprehensive approach to manage wounds (Fig 1)[3].

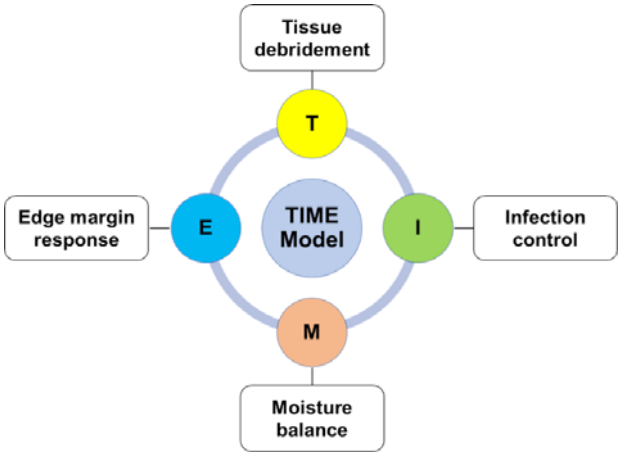

Fig 1 — Time concept for wound healing[3]

Diabetic foot infection and biofilm micro diversity-Indian perspective :

Biofilm comprises of mixed strains of microbes, and other cellular debris, formed when these microorganisms adhere themselves to the wound surface. It is difficult to get rid of them with traditional antimicrobial agents as they have several potential antimicrobial resistance mechanisms. Biofilm process occurs in five phases wherein phase 1 Formation within 1-2 hrs after contamination, with biofilm adherence in 6-12 h, Growth & multiplication 24 hrs, maturation occurs in 2-4 days. In phase 5 (dissemination), biofilm splits creating new colonies[4]. About 77.1% patients with DFU are infected with biofilm producing organisms, particularly the gram-negative organisms with mixed infection. Most commonly biofilm causing gram-negative organisms include *Escherichia coli* (42.2%), *Pseudomonas aeruginosa* (23.7%), *Klebsiella oxytoca* (11.3%) and *Klebsiella pneumonia* (9.2%) while few gram-positive bacteria species include *staphylococcus* and *streptococci*[5].

World Health Organization has identified the need for antibiotic resistant bacteria and provided a priority list of these organisms, driving the research for developing new antibiotics with novel mechanism of action, absence of cross-resistance, new chemical scaffolds and novel multi-molecular targets. The moderator also highlighted the presence of resistance to all the organisms in the culture list during his routine clinical practice making it difficult to salvage them[6].

Diabetic Foot Osteomyelitis :

It is usually a consequence of soft tissue infection that spread to bone and any bone from the foot may be involved. Clinical manifestations may be acute in the form of fever, swelling, pain, or chronic in the form of DFU. Diabetic foot ulcer is more common in osteomyelitis when they are >2 cm in size or depth is >3 mm. Bone testing is performed clinically, radiologically and using imaging techniques such as magnetic resonance imaging (MRI). X-ray can detect cortical abnormalities, periosteum or bony destructions. Additional evaluations including microbiological investigations, swab culture, bone biopsy, bone culture, inflammatory markers in the form of increased complete blood count (CBC), erythrocyte sedimentation rate (ESR), CRP, and procalcitonin measurement may support diagnosis. Panel suggested conservative or surgical management for osteomyelitis. Medical management with appropriate antibiotics for 4-6 weeks is effective to salvage patient. After 2-3 weeks, antibiotic review should be taken. Some patients may not respond, so they can undergo conservative management such as meta-tarsal head resection and supportive antibiotics. Major resections like amputation may be carried out.

Current gapsin wound care management

- Saline is the most economical option for wound irrigation; however, it is not sufficient for cleaning large and complex wounds complicated with extensive necrotic tissue, exudate, biofilm, and high microbial load.
- Currently one wound irrigation solution (squeeze bottle 350 ml/L) and gel containing Polyhexa-methylene biguanide (PHMB) surfactant is available but is very expensive (INR 750 for 350 mL bottle). Hence, cheaper alternative is required.
- Other shortfalls include unavailability of economical and safe antimicrobial formulation that requires fewer dressing changes.

- Most antimicrobial formulations are less or ineffective against biofilms.
- Overall cost of irrigation vacuum-assisted closure (VAC) therapy per week is INR 25,000 per person. Hence, in post-surgical debridement, a topical product which has maintenance debridement property would be beneficial and economical.
- Following surgical debridement, a product having attributes such as cleansing action, maintenance debridement, antibiofilm with sustained antimicrobial action and efficacy in early wound closure with faster epithelization are desired.

Biofilm Management :

A non-healing wound is indicative of the presence of biofilm. The participating Panel suggested meticulous debridement in the form of surgical, mechanical, biological, and using newer modalities. Offloading, managing infection with adequate antibiotic and finally using ideal antiseptics and dressings are the key strategies in biofilm management (Fig 2).

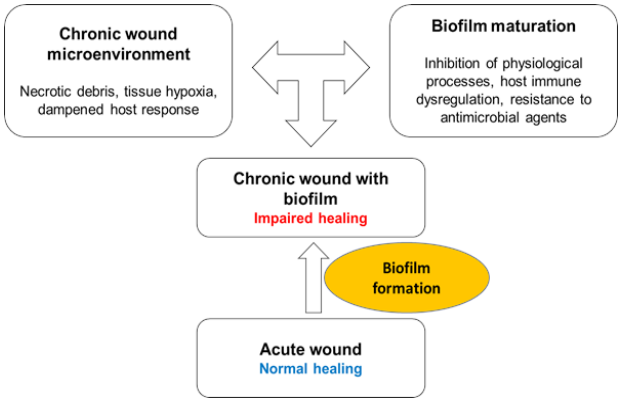

Fig 2 — Impaired healing with biofilm formation

Silver Solution/colloid :

Colloidal silver solution disrupts and penetrates bacterial biofilm. It kills 91% of MRSA within 10 minutes of application[7]. It provides comprehensive infection control in lesser time with 50% faster wound repair. It provides an effective scar reduction. Owing to its anti-adherent properties, it assists in easy dressing removal and has no cytotoxicity.

Smart Bead Technology :

Bead technology is capable of acting for 72 h that prevents the formation and breaking of biofilm. Iodine is physically bound to beads (matrix) and released only when required. Controlled release of iodine prevents accumulation thereby minimizing complications. It contains poloxamer (surfactant) that cleans wound and breaks the biofilm, cadexomer absorbs exudate and prevents biofilm formation and iodine is a broad-spectrum antimicrobial agent.

Case Study :

Treatment Modalities :

Surgery types —

The different types of surgeries include Class1 elective, Class 2 prophylactic, Class 3 Curative, and Class 4 emergency surgery. Preventive surgeries lengthening of tendon, excision of metatarsal heads, charcoat foot surgery, ilizarov external fixator, surgery for claw foot, vascular stents, and bypass surgery decrease the probability of wound formation in patients with diabetes. Several preventive foot care clinics are coming up in India. Hammer toe correction, bunion and claw feet, charcoat foot, pre-operative stenosis is some of the deformity corrective surgeries performed in patients with DFU.

Negative Pressure Wound Therapy (NPWT) :

Negative pressure wound therapy is a process of extraction of fluid and infection from a wound using a special dressing (bandage) with a vacuum pump attached. It is used in myriad of wound types such as open abdominal wounds, traumatic wounds, venous ulcers, skin grafts, pressure ulcers, DFU, and chronic ulcers. This therapy is safe and gives excellent results in healing wounds. Several randomized clinical trials have investigated the safety and efficacy of this therapy in diabetic foot wounds[8,9]. A comparison of indigenous NPWT system with commercially available NPWT has shown equivalent results at a fraction of expenses in the treatment of DFU for limb salvage (Table 1)[10].

A 47-year-old female presented with DFU and also had hypertension, IHD, and peripheral neuropathy.
Cadexomer iodine was applied for weeks, would granulated well. VAC therapy continued for three sittings at three-day interval with continuous pressure of 125 mmHg. A STSG was performed for would closure. As the wounds healed the patient was mobilized four weeks after surgery with orthotic shoes. Modified footwear was given to walk.

Fig 3 — Wound care in Diabetes

Steps involved in NPWT method of application :

1. Debride and clean the wound with isotonic solution
2. Cut the foam dressing in shape of wound and place it on the wound bed
3. Seal the wound with semi-permeable drape and make a small hole in the center
4. Keep the multipotent adult progenitor cells (MAPC) to bring distal end in symmetry with the hole in centre and connect with negative pressure source.

Reconstructive Ladder :

It is the spectrum of options available for wound closure. It helps to match the complexity of wound with appropriate level of treatment. The more complex and challenging the wound the higher up you climb (Fig 4)[11].

Extracellular Wound Matrix (ECM)[12] :

In chronic wounds, body's naturally occurring ECM fails. Hence, these exogenous ECM helps generation of key components of basement membrane and epidermal cells, stimulates cell proliferation and migration to assist in modulation of cellular response. Although costly, they play a vital role in wound care and management.

Table 1 — *Characteristics of commercial vs indigenous group treatment*[8]

Characteristics	Commercial Negative Pressure Wound Therapy	Indigenous Negative Pressure Wound Therapy
Cost of 12-day therapy	INR 22,000 or $440	INR 400 or $8
Average time	10-15 days	12-16 days
Availability	Only metropolitan areas	All rural areas
Foam pore size	131 μ	330 μ
Thickness	>400 μ	130-200 μ
Suction pressure	125-150 mmHg	150-200 mmHg

Common ECM products :

- Epicel-cultured epidermis
- Integra-2 layered, bovine collagen and outer silicone
- AlloDerm-human cadaver
- Biobrane-porcine collagen and semipermeable silicone membrane
- Dermagraft
- Apligraph and OrCell
- Acell matrix

Biomechanics and Offloading :

Diabetic foot ulcers frequently result from abnormal mechanical loading of the foot, hence early identification of the foot at risk can help mitigate DFU. Understanding biomechanics is crucial in the management of DFU and accordingly mechanical or surgical offloading is recommended. Neuropathy, structural deformity, gait abnormalities, and limited joint mobility are contributing factors to abnormal biomechanics of diabetic foot, high plantar pressures and neuropathic ulceration (Table 2). Offloading to counter altered biomechanics include procedures such as appropriate foot wear modification, deformity correction surgeries, tonsillectomy and adenoidectomy (TA), gastric release, tendon transfers and prosthesis.

Table 2 — *Factors contributing to abnormal biomechanics of diabetic foot*

Neuropathy	Structural deformity	Gait abnormality	Limited joint mobility
Mononeuropathy			
Polyneuropathy	Primary (Idiopathic)	Foot drop	Collagen glycosylation
Sensory	Secondary	Equinus	reduced mobility
Motor	- Muscle atrophy	Intrinsic muscle	Reduced shock
Autonomic	- Equinus	atrophy	absorption
	Amputations	Clawtoes	Increased
	Charcot	Amputations	pressures

Hyperbaric Oxygen for Diabetic Foot Wound :

Hyperbaric oxygen has multi-factorial benefits in managing DFU asthe chief cause of diabetic wound is hypoxic tissue. It has a direct and indirect antimicrobial activity, so potency of antibiotics can be increased. It helps in post-operative wounds in case of thicker skin grafts and can reduce tissue edema, improve vascular angiogenesis thus making healthier grafts. This therapy does not depend on haemoglobin values andhence, it can be use in patients with anemia and renal failure.

Transcutaneous oximetry measurement of tissue oxygen levels can determine whether this therapy will work and if patient requires this therapy or not. There is modified Wagners grade where patients with grade III are observed to benefit from hyperbaric oxygen. In necrotizing wounds and vascular tissues, if transcutaneous oximetry is done and if oxygen level is around 30-40 mmHg then this therapy will work. If 100% oxygen is given and if oxygen level improves by 10 mmHg then it will work. Hyperbaric oxygen therapy is contraindicated in patients with chronic obstructive pulmonary disease (COPD), upper respiratory tract infection, and pregnant particularly in COVID-era in patients with COPD and respiratory infection.

Stem Cell Therapy :

Fig 4 — Reconstructive ladder

Stem cell therapy is a promising therapeutic approach for treating diabetic wounds and a favorable option to amputation for some patients having no other substitute for revascularization. These products are recommended only if primary wound healing is unsatisfactory even after standard wound care procedure after 12 weeks.This therapy is implemented after debridement, when wound becomes vascular and healthy. Morbidity period is less with this therapy and patients are satisfied in terms of cost and recovery. It improves healing without surgery.

Rehabilitation :

The participating Panel discussed about biomechanical correction for fore foot ulcer healing. Limited joint mobility commonly causes hallux valgus and depending on the degree of rigidity, foot wear modification or callus procedure is beneficial in patients. Footwear like frontal orthowedge shoes can be used but again depends on balancing of patients. If the patient is unable to balance, shoes with two insoles are recommended so that ulcer sits in an opening and wound starts healing without much pressure on it. In addition, podoscan can be done to determine the types of pressures to give different kinds of inserts.

Newer adjunctive technologies for DFU management :

- Ultrasound
- Monochromatic infrared therapy
- Transcutaneous electrical nerve stimulation (TENS)
- High Voltage Pulsed Current (HVPC)
- Pulse irrigation
- Negative pressure wound therapy (NPWT) with instillation
- Stem cell
- Maggots
- Growth factors
- Gene therapy
- Lasers

References

1 Moghissi ES, Korytkowski MT, DiNardo M, Einhorn D, Hellman R, Hirsch IB, *et al* — American Association of Clinical Endocrinologists; American Diabetes Association. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care* 2009; **32(6):** 1119-31.

2 Sheehan P, Jones P, Caselli A, Giurini JM, Veves A — Percent change in wound area of diabetic foot ulcers over a 4-week period is a robust predictor of complete healing in a 12-week prospective trial. *Diabetes Care* 2003; **26(6):** 1879-82.

3 Harries RL, Bosanquet DC, Harding KG — Wound bed preparation: TIME for an update. *Int Wound J* 2016; **13 (Suppl 3):** 8-14.

4 Galanakos SP, Papadakis SA, Kateros K, Papakostas I, Macheras G — Biofilm and orthopaedic practice: the world of microbes in a world of implants. *Orthopaedics and Trauma* 2009; **23(3):** 175-9.

5 Zubair M, Malik A, Ahmad J, Rizvi M, Farooqui KJ, Rizvi MW — A study of biofilm production by gram-negative organisms isolated from diabetic foot ulcer patients. *Biology and Medicine* 2011; **3(2) Special Issue:** 147-57.

6 Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL, *et al* — WHO Pathogens Priority List Working Group. Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. *Lancet Infect Dis* 2018; **18(3):** 318-27.

7 Colloidal silver composition having antimicrobial properties. Available at https://patents.google.com/patent/WO2005000324A2/en. Accessed on 15 April 2021.

8 Eginton MT, Brown KR, Seabrook GR, Towne JB, Cambria RA — A prospective randomized evaluation of negative-pressure wound dressings for diabetic foot wounds. *Ann Vasc Surg* 2003; **17(6):** 645-9.

9 Armstrong DG, Lavery LA — Diabetic Foot Study Consortium. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. *Lancet* 2005; **366(9498):** 1704-10. doi: 10.1016/S0140-6736(05)67695-7.

10 Ruke M, Puranik S, Pawar A — Indigenous Negative Pressure Wound Therapy for poor patients in India-an observational case series. *The Journal of Diabetic Foot Complications* 2013; **5(3):** 73-7.

11 Simman R — Wound Closure and the Reconstructive Ladder in Plastic Surgery. *J Am Col Certif Wound Spec* 2009; **1(1):** 6-11. Published online 2009 May 1.doi: 10.1016/j.jcws.2008.10.003

12 Mac Neil S — What role does the extracellular matrix serve in skin grafting and wound healing? *Burns* 1994; **20:** S67-70. doi: 10.1016/0305-4179(94)90094-9.