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REVIEW

Choice of wound care in diabetic foot ulcer: A practical approach

Karakkattu Vijayan Kavitha, Shalbha Tiwari, Vedavati Bharat Purandare, Sudam Khedkar, Shilpa Sameer Bhosale, Ambika Gopalakrishnan Unnikrishnan

Karakkattu Vijayan Kavitha, Podiatry Department, Chellaram Diabetes Institute, Pune 411021, India
Shalbha Tiwari, Research Department, Chellaram Diabetes Institute, Pune 411021, India
Vedavati Bharat Purandare, Sudam Khedkar, Shilpa Sameer Bhosale, Ambika Gopalakrishnan Unnikrishnan, Diabetes and Endocrinology Department, Chellaram Diabetes Institute, Pune 411021, India
Author contributions: Unnikrishnan AG and Kavitha KV contributed to the idea behind the manuscript and to the writing, modification of content, and final approval of the draft; Tiwari S contributed to writing of the manuscript, its modification, and final approval; Purandare VB, Khedkar S and Bhosale SS contributed to writing of the manuscript and its final approval.
Correspondence to: Dr. Ambika Gopalakrishnan Unnikrishnan, Chief Endocrinologist, Diabetes and Endocrinology Department, Chellaram Diabetes Institute, 1st Floor, Lalani Quantum, Bavdhan, Pune 411021, India. unnikrishnanag@gmail.com
Telephone: +91-20-66839717 Fax: +91-20-66839701
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Abstract

Diabetic foot ulcers are the consequence of multiple factors including peripheral neuropathy, decreased blood supply, high plantar pressures, *etc.*, and pose a significant risk for morbidity, limb loss and mortality. The critical aspects of the wound healing mechanism and host physiological status in patients with diabetes necessitate the selection of an appropriate treatment strategy based on the complexity and type of wound. In addition to systemic antibiotics and surgical intervention, wound care is considered to be an important component of diabetic foot ulcer management. This article will focus on the use of different wound care materials in diabetic foot. From a clinical perspective, it is important to decide on the wound care material depending on the type and grade of the ulcer. This article will also provide clinicians with a simple approach to the choice of wound care materials in diabetic foot ulcer.

Key words: Diabetes; Foot; Wound; Debridement; Topical

Core tip: Diabetic foot ulcers are an important complication of diabetes. There is no conventional guideline regarding the selection of wound care materials in diabetic foot wounds. This article includes fundamental aspects of wound care and management with special emphasis on the selection of appropriate wound care materials depending on the type of wound tissue. Risk factors for foot ulceration, classification and grading of wounds, bacteriology, multidisciplinary team approach, types of debridement, importance of offloading, wound care and choice based on the complexity of the wound and properties of the dressing regime in each category based on clinical experience and practice are discussed.

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INTRODUCTION

The increasing prevalence of diabetes has resulted in concomitant illness[1]. The critical effects of hyperglycemia include micro-vascular complications (nephropathy, neuropathy and retinopathy) and macro-vascular complications (coronary artery disease, stroke and peripheral arterial disease). Diabetes is a leading cause of non-traumatic lower extremity amputation, which is often

Figure 1 Wound classification based on the Red-Yellow-Black wound classification system by Marion Laboratories. A: Necrotic tissue; B: Sloughy tissue; C: Granulating tissue; D: Epithelializing tissue.

preceded by a non-healing ulcer. The lifetime risk of foot ulceration in people with diabetes is 15%-20%[2]. More than 15% of foot ulcers result in amputation of the foot or limb[3]. Several other population-based studies indicate a 0.5%-3% annual collective incidence of diabetic foot ulcers. The prevalence of foot ulcers reported varies from 2% to 10%[4]. Approximately 45%-60% of all diabetic foot ulcerations are purely neuropathic, whereas 45% have both neuropathic and ischemic components[5]. It has been estimated that around 15%-27% patients with diabetes require lower limb amputations predominantly (50%) due to infection[6].

DIABETIC FOOT

Definition

Infection, ulceration or destruction of deep tissues associated with neurological abnormalities and various degrees of peripheral vascular diseases in the lower limb (World Health Organization definition, 1995).

Risk factors

Diabetic foot ulcers are a consequence of many factors including loss of protective sensation due to peripheral neuropathy where the feet become numb and the injury goes unnoticed. Also, arterial insufficiency complicates the neuropathic ulcer which leads to poor wound healing. Foot deformity and calluses can result in high plantar pressure, which results in additional risk. Mechanical stress at the wound site is hypothesized to affect wound healing[7]. Many other factors contribute to the risk of foot ulceration and its subsequent infection in patients with diabetes. Uncontrolled hyperglycemia, duration of diabetes, trauma, improper footwear, callus, history of prior ulcers/amputations, older age, blindness/impaired vision, chronic renal disease and poor nutrition have also been demonstrated to play a role in the pathogenesis and progression of diabetic foot ulceration. Infection further deteriorates the diabetic foot resulting in a non-healing chronic wound. Recently, vitamin D deficiency was proposed as a risk factor for diabetic foot infection[8].

Classification

Based on the Red-Yellow-Black[9] wound classification system by Marion Laboratories, wounds can be classified as follows[10]: (1) Necrotic tissue-either dry or infected and usually black or dark green in color as shown in Figure 1A; (2) Sloughy tissue-combination of wound exudate and debris forming a glutinous yellow layer of tissue over the wound which is often mistaken for infection as shown in Figure 1B; (3) Granulating tissue-highly vascularized, red in color and sometimes highly exudating as shown in Figure 1C; and (4) Epithelializing tissue-Epithelium grows over a wound formed by migration of keratinocytes from the wound margins, which looks pink in color as shown in Figure 1D.

Debridement of necrotic tissue is an integral component in the treatment of chronic wounds as they do not heal in the presence of unviable tissue, debris, or critical colonization[11,12] and may be contraindicated in arterial ulcers[13]. Excision of necrotic tissue is necessary for wound healing. Calluses or thickened skin surrounding the ulcer

need to be excised. Necrotic tissue removed on a regular basis can expedite the rate at which a wound heals and has been shown to increase the probability of attaining full secondary closure[14,15].

Grading

Grading can be done using Wagner's or the Texas wound classification system[16]. The most common is the University of Texas wound classification system, which describes the wound with regard to depth, presence or absence of infection or ischemia or both. A description of the wound is important for wound care choice and includes the location, stage, dimension in length, breadth and depth (length and breadth can be measured in centimeters by tracing it on a sterile acetate sheet and depth can be taken by inserting a sterile swab gently into the deepest part of the wound), wound edges (undermining), wound base description, drainage (heavy or low), color, odor, pain and progression, *etc*[17].

Microbiology

Hyperglycemia, impaired immunologic responses, neuropathy, and peripheral arterial disease are the major predisposing factors leading to limb-threatening diabetic foot infections[18-20]. The prevalence of infection in India was 6%-11%, whereas the prevalence of amputation was 3% in patients with type 2 diabetes[21]. Both aerobic and anaerobic bacteria have been shown to infect diabetic foot wounds[22-25]. Fungal infections are also common in diabetic foot[26-28]. Polymicrobial etiology of diabetic foot infections has been widely reported[22-25,29]. However it is not uncommon to have a predominance of mono-microbial infection in diabetic foot[30]. Researchers have shown the predominance of both gram negative[30] and gram positive[26] bacteria in diabetic foot infections. Various studies have reported a high prevalence of *Pseudomonas*[31], *E. coli*[30], and *S. aureus*[26,30] infections in diabetic foot. The pattern of microbial infection in patients with diabetic foot infections is inconsistent and therefore evaluation of microbial characteristics and their antibiotic sensitivity is necessary for the selection of appropriate antibiotics for management of diabetic foot infection.

MANAGEMENT TECHNIQUES

The foot is a complex structure, which acts as a foundation for the whole body, and it is important to prevent progression of diabetic foot problems. The integration of knowledge and experience through a multidisciplinary team approach promotes more effective treatment, thereby improving outcomes and limiting the risk of lower extremity amputation[32,33]. Therefore the following specialists play an important role: (1) Endocrinologist/Diabetologist (optimize blood glucose control); (2) Podiatrist (focus on the foot including prevention and treatment of diabetic foot wounds); (3) Vascular surgeon (manage vascular issues); (4) Microbiologist (look into microbiological etiology and antibiotic selection based on cultures); (5) Orthotist (ensures that therapeutic or custom made footwear aids in minimizing pressure); and (6) Nutritionist (concentrates on diet which helps in the management of diabetes as well as wound healing).

Wound healing is a complex process involving highly regulated responses of specified cell types, which harbor locally secreted growth factors that play a key role in wound healing[34]. Treating a diabetic foot infection requires proper wound care and appropriate antibiotic therapy[19]. The fundamentals of good clinical care includes adequate frequent debridement, offloading, moist wound care, treatment of infection, and revascularization of the ischemic limb[35]. In addition, wound healing can be enhanced by the appropriate choice of a topical regime (mixed range of standard and advanced topical therapies), however, adequate training and significant clinical experience are essential for making this choice. Many factors including assessment of the wound, its classification, and the need for debridement including sharp surgical, mechanical, chemical, *etc*., have to be taken into consideration before proceeding with the appropriate selection of topical regimen.

Debridement

Debridement involves removal of dead, damaged, or infected tissue, which improves the healing potential of the remaining healthy tissues. Depending on the wound tissue type, different debridement techniques are recommended[36,37]: (1) Surgical debridement or sharp debridement-recommended for necrotic and infected wounds. The terms surgical debridement and sharp debridement are often used synonymously, some clinicians refer to surgical debridement as being performed in an operating room, whereas sharp debridement is performed in a clinic setting[38]. Sharp surgical debridement is the most effective and fastest method of debridement; (2) Autolytic debridement-a selective process in which the necrotic tissue is liquefied. A wound covered with an occlusive dressing allows accumulation of tissue fluids containing macrophages, neutrophils, and enzymes, which remove bacteria and digest necrotic tissues. This is achieved by a moist wound healing environment[36]. Autolytic debridement is not advisable for the treatment of infected pressure ulcers[39]; (3) Mechanical debridement-involves removal of unhealthy tissue using a dressing, which is changed regularly by wound irrigation (pressure: 4-15 psi), without damaging healthy/new tissues[40]. Scrubbing the wound aids in removal of exudates and devitalized tissues, however this leads to bleeding as well as pain resulting from wound trauma. This technique is used in the management of surgical wounds and venous leg ulcers. The drawbacks of the method is that it is time consuming and expensive; (4) Enzymatic debridement-a method of debriding devitalized tissue by topical enzymes such as collagenase, fibrinolysin, or papain. Recommended for sloughy, infected, necrotic wounds where surgical debridement is contraindicated[41]; and (5) Maggot debridement-a technique in which maggots or fly larva that

Table 1 Antibiotic recommendation based on the severity of the infection

Site	Severity or extent	Route of administration	Duration of therapy
Soft tissue only	Mild	Topical or oral	1-2 wk may extend up to 4 wk if slow to resolve (outpatient)
	Moderate	Oral (or initial parenteral)	1-3 wk (Outpatient/inpatient)
	Severe	Initial parenteral, switch to oral when possible	2-4 wk (Inpatient, then outpatient)
Bone or joint	No residual infected tissue (*e.g.*, post-amputation)	Parenteral or oral	2-5 d
	Residual infected soft tissue (but not bone)	Parenteral or oral	1-3 wk
	Residual infected (but viable) bone	Initial parenteral, then consider switching to oral	4-6 wk
	No surgery, or residual dead bone post-operatively	Initial parenteral, then consider switching to oral	⩾ 3 mo

are raised in a sterile environment are used. The most commonly used fly is Lucilia sericata, which is used for human wound treatment when conventional treatments fail[42]. Maggots are placed on the wound followed by wrapping with secondary dressing. The larvae feed on the necrotic (dead) tissue and bacteria present at the wound site and secrete antimicrobial enzymes, which help in the wound healing process.

Offloading

Completely or partially relieving pressure from the weight bearing area of the foot by providing mechanical support with the intention of giving rest to the wound area aids in healing. Repetitive trauma and high plantar pressure on the ulcer bed are two primary reasons for the persistence of ulcers once they have developed[43]. Offloading is very important in diabetic wound healing. There are many types of offloading techniques including total contact casts, removable cast footwear, wedge footwear, half shoes, mobilization by wheelchair, *etc*. Total contact casts are considered to be the gold standard method of offloading and treating diabetic patients with neuropathic ulcers[32,44-46].

Wound care

Wound care plays a pivotal role in the management of diabetic foot ulcer, which comprises cleaning the wound with normal saline following aseptic techniques and the use of modern wound care techniques that promote a moist wound healing environment[47,48]. Although topical treatment is an important aspect of wound care, it is always considered secondary to surgical and systemic care[49]. There are numerous topical regimens and devices available for the management of diabetic foot wounds including hydrogels, hydrocolloids, alginates, foam, silver impregnated dressings, growth factors, silicon impregnated atraumatic dressings, vacuum aided devices, hyperbaric oxygen therapy, *etc*. However, before choosing a regime one should consider factors such as the general health of the patient, the process of tissue repair, assessment of the wound by means of grading, description and classification of the wound, local environment of the wound, knowledge on specific properties of the dressing materials and devices as well as their availability, affordability, and accessibility.

The ideal characteristics of a wound dressing are as follows[50,51]: (1) Sterile, easy to use, cost effective; (2) Maintain a moist wound healing environment; (3) Absorb excess exudate; (4) Non-adherent/non-toxic, non-allergic; (5) Not contaminate the wound with foreign particles; (6) Protect the wound from microorganisms; (7) Allow gaseous exchange and control wound odor; and (8) Provide thermal insulation and mechanical protection.

Antibiotic selection

The principle of antibiotic treatment is based on evidence provided by reports on bacteriological culture and sensitivity from different centers worldwide[52,53].

Use of anti-infectives/antibiotics must be guided by appropriate cultures. Inappropriate use of antibiotics could lead to resistance and adverse effects.

Oral and parenteral antibiotics are prescribed for mild soft tissue infections and moderate to severe infections, respectively (Table 1)[54]. Evidence-based regimes should be followed for the management of infection in diabetic foot. Appropriate dosage, optimal duration, identification and removal of the infective focus and recognition of adverse effects should be critically evaluated in all outpatients and inpatients with diabetic foot infections[54-56].

Every hospital should develop an institutional antibiotic policy containing guidelines and protocols for antibiotic use. It is advisable to have different sections for treatment and prophylaxis including surgical procedures as well as how to treat different infections[57].

Three levels of antibiotic prescribing are generally recommended: (1) First line of choice - antibiotics prescribed by all doctors; (2) Restricted antibiotic group - for resistant pathogens, polymicrobial infections, special conditions, and expensive antibiotics. When prescribing antibiotics from this group, the prescriber should discuss with the committee and head of the department; and (3) Reserve antibiotics-for life-threatening infections, to be used after obtaining permission from the committee.

The institutional antibiotic committee should update their policy by collecting surveillance on antimicrobial resistance and data on antibiotic consumption, which will improve clinical and laboratory standards. The committee should monitor implementation of the policy,

Table 2 Choice of wound care materials for necrotic and sloughy wounds

Wound classification	Choice of wound care material	Advantages	Disadvantages
Necrotic wound	Wet to dry	Good debriding capacity and inexpensive	Frequent dressing change Painful if not soaked with saline prior to dressing change
	Topical antibacterial such as metronidazole	Very good antibacterial coverage Maintains a moist wound healing environment by promoting autolysis and controls odor	Chance of maceration Contraindicated in infected necrotic wounds
	Hydrogel	Hydrates the wound by promoting autolysis	Chance of maceration Contraindicated in infected necrotic wounds and is expensive
	Hydrocolloid	Maintains a moist wound healing environment, which helps in autolytic debridement	Expensive Contraindicated in infected necrotic wounds
Sloughy wound	Wet to dry	Good debriding capacity Absorptive, adhesive and cheapest	Frequent dressing change Painful if not soaked with saline prior to dressing change
	Topical enzymes such as collagenase, papain, fibrinolysis	Promotes autolytic debridement by desloughing Can be used in combination with metronidazole or hydrogel	Contraindicated in granulating or epithelizing wounds
	Topical antibiotics such as metronidazole	Very good antibacterial coverage Maintains moist wound healing environment by promoting autolysis and controls odor	Chance of maceration
	Polyurethane Foam	Very effective in desloughing Maintains a moist wound healing environment by promoting granulation	Sometimes painful if not soaked with saline prior to dressing change
	Hydrogel	Hydrates the wound by promoting autolysis	Chance of maceration and is expensive
	Hydrocolloid	Maintains a moist wound environment, which helps in autolytic debridement	Chance of maceration and is expensive

receive feedback information, assess the outcome, and discuss with various specialty doctors. The policy should be reviewed every year based on the experience of prescribers and the susceptibility reports of microbiology and laboratory.

Revascularization

With advances in both vascular and orthopedic reconstructive surgeries, limb salvage has become an option for limbs that previously would have been amputated. Patients with both diabetes and peripheral arterial disease are more prone to ischemic ulceration than those without the disease[58,59]. Several endovascular options, including percutaneous transluminal angioplasty (PTA), balloon-expandable stents, self-expanding stents, and covered stents are now available. The success rate after stent implantation in the iliac arteries is greater than 95%[60]. Revascularization plays a crucial role in the treatment of ischemic lower extremity wounds and should be performed before drainage or debridement[61]. Endovascular techniques such as cryoplasty, drug eluting stenting, plaque debulking lasers, *etc*., are being investigated and are potentially useful adjuncts to PTA. Subintimal angioplasty for arterial lesions below the ankle in diabetic patients could achieve a limb salvage rate of 94.6%[62]. Several retrospective studies report considerably better results of transmetatarsal amputations performed after a revascularization procedure[63,64].

CHOICE OF TOPICAL REGIME

Choice of wound care materials should be based on wound tissue type, complexity, and its properties (Tables 2 and 3).

Wet to dry dressing or simple saline

This dressing has a good debriding action and helps in wound bed preparation. Wet-to-dry dressings are described in the literature as a means of mechanical debridement[65]. It is very absorptive as well as adherent and one of the cheapest dressings used throughout the world, but requires frequent dressing change (twice or thrice a day) based on wound severity. Dressings should be moistened before removal to minimize any chance of bleeding. A gentle cleanser (normal saline or neutral-pH cleanser) will minimize wound irritation and discomfort[66]. When treating a granulating or epithelizing wound one should soak the dressing thoroughly with normal saline for five minutes (based on our clinical experience) to prevent trauma and heavy bleeding.

Antibacterial agents

Used solo or in combination for each category except dry necrotic wounds. Topical antibiotics have broad-spectrum antibacterial coverage which lasts for 12 h and are less toxic. Metronidazole gel [Ornidazole (IP-10 mg and water soluble gel base quantity sufficient)] has good anaerobic coverage and helps in maintaining a moist wound healing environment. By weight, gels are mostly liquid, yet they behave like solids due to a three-dimensional cross-linked network within the liquid. It is the crosslinking within the fluid that gives a gel its structure (hardness) and contributes to its adhesion[67]. Both by

Table 3 Choice of wound care materials for healing/sinus or cavity wounds

Wound classification	Choice of wound care materials	Advantages	Disadvantages
Granulating wounds	Non adherent dressing	Reduces trauma to the healing tissue Maintains a moist wound healing environment	Chance of shearing to new epithelium
	Wet to dry dressing	Promotes healing	Chance of bleeding if not soaked with saline before dressing change
	Polyurethane foam	Maintains a moist wound healing environment Promotes healing process	Chance of bleeding if not soaked before dressing change
	Topical antibacterial such as metronidazole, mupirocin, Tulle, Silver containing ointments, Acetic acid 0.5%-5% and povidone iodine	Maintains a moist wound healing environment, promotes epithelization and controls odor Effective against Gram positive cocci including MRSA. Silver sulfadiazine has broad antibacterial coverage, accelerates epithelization, and is very effective in burns. Acetic acid is very effective against Pseudomonas. Povidone iodine is very effective for gangrene as it hastens demarcation	Silver containing ointments cannot be used in Sulfa allergy patients Povidone iodine is cytotoxic to fibroblasts and delays the healing process
	Platelet derived growth factor	Faster healing and very effective	Expensive
	Hydrogel	Promotes healing	Chance of maceration and is expensive
	Hydrocolloid	Promotes healing Reduces the interval of dressing change	Chance of maceration and is expensive
Epithelizing wounds	Non adherent	Reduces trauma to the healing tissue Maintains a moist wound healing environment	Chances of shearing
	Wet to dry dressing	Promotes faster healing	Soaking of dressing is required prior to dressing change
	Topical antibacterial	As mentioned in granulating wounds	As mentioned in granulating wounds
	Epidermal growth factor	Effective and faster healing	Expensive
	Hydrogel	Effective	Chance of maceration and is expensive
	Hydrocolloid	Effective	Chance of maceration and is expensive
Cavity/Sinus wounds	Alginate	Highly absorbent and non-adherent Maintains a moist wound healing environment	Needs adequate padding and is expensive
	Hydrogel	Effective in promoting granulation tissue	Needs adequate padding and is expensive

weight and volume, gels are mostly fluid in composition and thus exhibit densities similar to those of their constituent liquids, such as hydrogels. Topical metronidazole gel (0.75%-0.80%) is frequently used directly on the wound once per day for five to seven days or more often as needed[68,69], and metronidazole tablets can be crushed and placed onto the ulcer bed[66,70]. There are numerous other articles (case studies or anecdotal experience) reporting the reduction of wound odor with topically applied metronidazole[71-73]. Antibiotics such as Neomycin, Gentamycin, and Mupirocin have good antibacterial coverage when used topically. Silver containing dressings come in different formulations and have very good antibacterial coverage. Silver dressings and polyherbal preparations have shown good results in healing diabetic foot wounds[74]. They are very effective in burn wounds and can also be used in infected or colonized wounds. Sisomycin (0.10%) and acetic acid at concentrations between 0.5% and 5% are effective against *Pseudomonas*, other gram-negative bacilli, and beta hemolytic streptococci wound infections. Povidone iodine solution dressings are very effective in healing sutured wounds and hypergranulating wounds to suppress or hamper further granulation. Povidone iodine soaked gauze is a good dressing for dry gangrene which hastens the process of demarcation. Iodine has been found to be toxic to human cells as well as bacteria and fungi at high doses[75,76]. Also, it should not be used on granulating or epithelizing wounds because it slows down the healing process and is cytotoxic to keratinocytes and fibroblasts.

Tulle dressings

These are gauze dressings impregnated with paraffin, which lowers the dressing adherence, but this property is lost if the dressing dries out. Tulle dressings are mainly indicated for superficial clean wounds and skin grafts. They can be used in granulating and epithelizing wounds. Tulle dressings not only prevent trauma to the new and delicate epithelium during dressing removal, but also provide a good moist environment, which is preferred for epithelial cell proliferation and migration[77]. This concept is well supported by evidence from many previous studies which showed faster re-epithelialization rates when moist environment dressings were compared with traditional dry dressings[77-79]. Evidence shows that gauze-based dressings still have a place in wound care[80].

Polyurethane films

These films are coated with an adhesive (water-proof dressing) and are comfortable. The vapor-permeable films allow diffusion of gases and water vapor which helps in maintaining a moist wound healing environment. Their transparency allows for wound monitoring without dressing removal, but there is a chance of maceration of surrounding skin. They can be used for low exudating wounds.

Polyurethane foam

These dressings are extremely absorbent, non-adherent, and have a semi-permeable backing which allows moisture to escape. Polyurethane foam dressings loosen slough by creating a moist wound environment, assisting in proper wound bed preparation, and promoting wound healing[81]. They maintain a moist wound environment which implies that they can be easily removed without pain. They are also used as outer dressings after application of topical antibiotics, such as metronidazole, or hydrogels. Polyurethane foam is widely used in diabetic foot wounds and is capable of absorbing light to heavy amounts of exudate, thereby preventing maceration, facilitating removal of slough, and promoting the proliferative stage of wound healing[82].

Hydrogel dressings

These dressings consist of cross-linked insoluble starch or carboxymethylcellulose polymers and water (96%). The term hydrogel implies that the material is already swollen in water. Hydrogels donate fluid to dry necrotic and slough wounds and promote autolysis. They apparently debride by rehydrating the wound. These dressings are the best choice for the treatment of dry wounds with necrotic eschar, and the hydrogel reaches a 50% debridement level more quickly than wet-to-dry dressings and are more cost-effective[83-85]. The hydrogel hydrates, cools the wound and provides an analgesic effect.

Hydrocolloid dressing

These dressings are a combination of polymers such as gelatin, pectin and cellulose which form a waterproof adhesive dressing. Exudates produced by the wound are absorbed into the dressing and form a gel. Hydrocolloid dressings are capable of absorbing low to moderate levels of exudate and can be used to promote autolytic debridement of dry, sloughy, or necrotic wounds[86]. They maintain a moist wound healing environment and promote autolytic debridement of necrotic and sloughing tissues. They can be used as occlusive dressings and are very good at absorbing exudate. Hydrocolloid dressings should be avoided on plantar ulcers of the foot, as the periwound skin is susceptible to maceration. Additionally, hydrocolloids have been shown to retain growth factors under the dressing as well as promote granulation and epithelialization[87]. The low pH created by the hydrocolloid is effective for the treatment of wounds infected by *Pseudomonas* species[88].

Alginate dressings

Alginate dressings are highly absorbent and are available in two forms; calcium alginate and calcium sodium alginate. The use of alginate dressings as hemostatic agents was reported both *in vitro* and in clinical studies. The selection of an alginate dressing is usually to manage wound exudate, as it is claimed that they can absorb 15-20 times their own weight in wound fluid[89]. The alginate forms a gel when it comes into contact with the wound surface. It can be used in granulating, epithelializing, and cavity wounds. Cochrane reviews detail the role of alginate dressings in the treatment of diabetic foot ulcers[90,91].

Growth factors

Growth factors such as platelet-derived growth factor (PDGF), insulin-like growth factor, transforming growth factor (TGF)-β, TGF-α, epidermal growth factor (EGF), *etc*., are very effective in diabetic wound healing and have been reported to accelerate the formation of various components of healing. Growth factors stimulate different functions including angiogenesis, enzyme production, cell migration, and cellular proliferation[92]. Diabetic wounds are enriched in proteases and supports the premise that impaired growth factor availability may act as a rate limiting factor in diabetic wound healing[93]. PDGF regulates cell growth and division. It plays a significant role in blood vessel formation (angiogenesis). A recombinant human (rh)-PDGF dressing is an effective modality for facilitating wound healing in patients suffering from diabetes and can be used as an adjunct to the conventional mode of treatment for healing diabetic wounds[94]. It can be used in the granulating stage of the wound. EGF stimulates the proliferation of fibroblasts, keratinocytes, and vascular endothelial cells, which contributes to scar tissue formation. Local injections of rh-EGF offer a favorable risk-benefit balance in patients with advanced diabetic foot ulceration and was significantly enhanced by 75 μg EGF treatment in neuropathic *vs* ischemic ulceration[95].

Honey-impregnated dressings

Proposed to have antimicrobial and anti-inflammatory properties, these dressings can be used for acute or chronic wounds. The antimicrobial properties of honey have been demonstrated in the laboratory, however, *in vivo* evidence is scant, particularly in comparison to the literature on silver antimicrobial dressings[96,97].

Topical enzymes

Collagenase, fibrinolysin, or papain containing ointments help in the enzymatic debridement of sloughy tissues and thus promote granulation formation. Collagenase and papain/urea formulations have been demonstrated to have degrading effects on wound components, such as collagen, fibrin, and elastin both *in vitro* and clinically. Papain-urea and collagenase have proven efficacy in enzymatic wound debridement. Papain-urea (89.2%) is a better enzymatic debriding agent than collagenase (82.2%)[98].

Mechanical device

Vacuum-assisted closure generates a topical negative pressure over the wound bed. Pressure of 125 mmHg is the ideal pressure. Vacuum-assisted closure is extremely effective in removing exudate and reducing edema, while leaving the surface of the wound moist. It is contraindicated in avascular wounds or exposed tendons or bones. Some of the contraindications include untreated osteomyelitis,

non-enteric and unexplored fistula, presence of necrotic tissue, exposed organs or blood vessels, and malignancy in the wound[99]. Vacuum-assisted closure is effective in promoting wound closure in patients with treated osteomyelitis or soft tissue infections[100,101]. Hyperbaric oxygen therapy (HBOT) is another treatment which is used as an adjunct to standard wound care in the treatment of diabetic foot wounds. It has limited side effects, is relatively safe, and is widely used[102].

CONCLUSION

The successful management of diabetic foot wounds requires the multidisciplinary teamwork of specialists. The management of diabetic foot wounds needs timely detection of complications and frequent assessment of the wound. No wound should be treated as simple. It is important to take into account all the related causes, identify the problem, and treat it. There are various topical regimes available, but the choice depends only on the treating physicians, podiatrist, or clinical care nurse. While selecting wound care materials one should bear in mind the properties of the ideal wound care dressing which should maintain a moist wound healing environment, absorb exudates, control infection/odor and be effective in treating diabetic foot wounds. In addition to these wound care techniques, antibiotic therapy and offloading plays a very important role.

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