Proper Management of Diabetic Ulcers

Clinicians should be familiar with newer interventions, signs of infection, and the indications for surgical management.

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Diabetic ulcers are associated with a significant impact on morbidity and mortality along with exorbitant treatment costs. Their overall incidence is estimated at about 15-25 percent and climbs to 42 percent after patients have suffered from diabetes for 20 years. Up to 28 percent of diabetic ulcers result in limb amputation.1,2 Morbidity has been shown to be significant in people who suffer from ulcerations as a complication of diabetes. In addition, the cost of treatment over a two-year period has been estimated at $28,000 per individual.2 Understanding risk factors and pathogenesis is essential for prevention and optimal treatment. Knowledge of indications for surgery and proper wound care is crucial.

Risk Factors and Pathogenesis

Important risk factors for the development of diabetic ulcers include neuropathy, peripheral vascular disease, biomechanical factors, and poor glycemic control.3 Neuropathy, which has been found to be significant in over 40 percent of patients with type 2 diabetes mellitus (DM), represents an important cause of ulceration.4 The sensory, motor, and autonomic fibers are all affected. Important to note is that the clinical triad of neuropathy, foot trauma, and deformity is found in more than 63 percent of foot ulcers.5 Demyelination of sensory fibers contributes to loss of sensation, ultimately resulting in increased trauma to the foot.6 Sensory nerves have been found to release neuropeptides, which aid in local wound healing; when neuropeptides are diminished, there is a negative effect on the time of ulcer regression.7 Motor neuropathy leads to intrinsic muscle weakness and in turn an ataxic gait. As a result, significant structural changes can occur in the foot. These differing points of high pressure contribute to foot deformity and development of ulceration. The sensory and motor components, coupled with the autonomic effects of decreased sweating, vasodilation, and the formation of fissuring in existing calluses, provide increased potential for ulceration and promote microorganism entry into the foot.6

Glycemic control should be stressed in these patients. Increasing evidence links delayed wound healing with hyperglycemia.8 Impaired leukocyte function and increased oxidative stress have been found in patients with chronic hyperglycemia.9,8 Through various downstream molecular events, excessive glucose causes a preponderance of free radicals compared to antioxidant capability.9,10 This in turn inhibits healing by increasing inflammation and disrupting vascular function.11 Peripheral vascular disease, another prominent risk factor, is present in 30

Take-Home Tips. Debridement and antibiotic therapy form the standard intervention for non-healing ulcers. Clinicians should know evaluation techniques, advancements in dressing, and adjunctive treatments, like hyperbaric oxygen. Prevention of ulcers through glycemic control and regular skin/nail exams is the best “therapy.” ●
percent of foot ulcers. This plays a major role in delayed wound healing and gangrene. Diabetics are particularly prone to PVD due to the thickening of the arteriolar basement membrane. The risk factors are directly proportional to one’s chances of ulceration development. Therefore, proper management and evaluation in these patients is imperative.

Evaluation and Management

When presented with a diabetic ulcer, a problem-focused history and physical exam should be carefully taken. The skin of the legs and feet, including all of the toes, should be closely examined. In addition, the lower extremities should be compared to the skin on the upper extremities for a baseline measurement. Dermatologists should be able to promptly recognize a looming infection clinically, as management is affected by the severity and extent. Clinical diagnosis of infection is made on the presence of at least two of the cardinal signs of inflammation or through the presence of purulent secretions. According to IDSA guidelines, the goal of evaluating an ulcer should be to determine clinical extent, including systemic signs of infection, the microbes involved, the pathogenesis of the wound (see risk factors above), vascular compromise, and if present, the biomechanical contribution. The physician should assess for PVD, neuropathy, and any signs of osteomyelitis after debridement.

If an infection is present, then the severity of the wound should first be evaluated. One of the more common classifications is Wagner’s criteria, on which severity ranges from grade 0 (no ulcer in high risk foot) to grade 5 (gangrene involving the whole foot). The wound must first be cleansed and debrided for evaluation; proper cultures should be collected. Wound swab specimens are insufficient when from an aspirate from the abscess. Rather, curettage from the ulcer base or biopsy are preferred, as the specimens provide for a more definitive evaluation. Many different antibiotics have been administered as treatment; however, limited data exist regarding the comparison or standardization of specific antibiotic regimens. Initial treatment should at minimum cover gram-positive cocci. Further treatment should be dictated by the sensitivities that the wound culture yields, often necessitating the administration of a broader spectrum antibiotic. Treatment should continue until there is resolution of the infection. There is no evidence supporting the treatment of uninfected ulcers with antibiotic therapy.

With standard treatments, approximately 31 percent of ulcers have been shown to heal within 20 weeks. The goal of adjuvant treatment is to reduce the time to healing, the extent of the wound, and decrease the incidence of complications. Management of the ulcer begins with debridement and antibiotic administration. Debridement removes the necrotic tissue and calluses (source of pressure), thus converting a chronic wound into an acute one, and as a result, promoting normal healing. Sharp debridement is most commonly used and has been associated with quicker healing rates, especially with vigorous debridement. Yet, as Game notes, data is weak and warrants other randomized, controlled trials. Other debridement methods should be further examined. For example, hydrogel, a form of chemical debridement, has been found to advance healing when compared to saline dressing.

It is not as clear when to use more extensive surgical intervention. The ISDA recommends seeking a specialized surgeon when patients have a deep infection, idiopathic persistent pain, purulent discharge under pressure of an ischemic foot, and especially in limb-threatening infections. Also important is the correction of deformities in those with chronic ulceration in order to prevent new ulcer formation. Not controversial, however, is early surgery for revascularization (commonly femoral-distal bypass) of limbs with ischemic ulcers, especially in severe cases.

Role of Dressings

Dressings promote healing by providing a moist environment; in addition, some also have antimicrobial activity. Traditionally, wet-to-dry saline dressings are used, but newer dressings provide a moister environment and enhance tissue preservation. Since the 1960s, it has been well established that moist environments provide better healing results than dry environments, including prevention of eschar formation, increased rates of healing, and decreased pain.
A vast number of dressings exists, including hydrocolloid dressings, alginates, hydrogels, foam dressings, hydrofiber dressings, paraffin gauze, silver impregnated dressings, and nonadherent dressings, with few clinical studies to support one particular treatment as the gold standard.\(^2\) Those mentioned in this discussion have been found beneficial in randomized controlled trials. Zinc oxide tape is a self-adhesive, occlusive dressing providing a moist wound environment and a constant release of zinc onto the wound. Zinc has been shown to have antibacterial mechanisms and to aid in the elimination of necrotic tissue, as well as the migration of normal keratinocytes.\(^2\) Hydrocolloid is an occlusive dressing made of a matrix on a polymer base. On contact with the wound exudate, the hydrocolloid liquefies and provides a moist environment. Hydrogel dressings, mentioned above, consist of up to 80 percent water and have a starch polymer that allows for the absorption of wound exudates and rehydration. Hydrofibre is a non-woven, ultra-absorbent dressing that allows for maintenance of a stable environment with consistent temperature and moistness. Polymeric semi-permeable membrane dressings contain surfactant, glycerin, and a starch co-polymer that act as a cleanser, anti-adherent, and absorbent, respectively. The membrane allows for gas exchange but is impervious to bacteria.\(^2\) Among these dressings, zinc oxide tape has been shown to decrease the area of necrotic wound when compared to hydrocolloid.\(^2\) When compared to saline-moistened gauze, hydrogels, carboxymethylcellulose hydrofibre, and polymeric semi-permeable membranes have all been found to significantly reduce the ulcer area and advance healing.\(^2\)

Relief of pressure on the ulcer improves healing rates. Various orthotics exist, but a total contact cast offers best results because of better compliance and decreased mobility.\(^2\) This device helps remove pressure from the ulcer via redistribution and has been shown to have higher healing rates.\(^3\) The wound should not show signs of infection or ischemia. One disadvantage of the cast is that it can promote the formation of a new ulcer. In addition, its application requires special training. Another drawback is the compromise of daily activities due to immobility.\(^4\)

**Adjunct Treatments**

New adjuvant treatments have shown promise. Hyperbaric oxygen (HBO) has been used both topically and systemically (prolonged periods of time in a large hyperbaric chamber). In a systematic review of treatments in chronic diabetic ulcers, five different studies all showed that systemic HBO significantly reduces the rate of amputation and the ulcer area.\(^2\) A recent report of six cases strongly supports the use of transdermal sustained oxygen therapy in ulcers not responsive to previous treatment.\(^2\) Use of topical negative pressure or vacuum assisted therapy has been expanded to the treatment of diabetic foot ulcers, with the theory that it can help reduce surface debris and swelling, in a similar fashion to compression treatment. It can also be applied at home, in contrast to HBO systemic therapy. A large study showed benefit in the time of healing in those who had just undergone pedal surgery.\(^2\)

Another adjuvant treatment developed in light of increased awareness of molecular events in wound healing is growth factor. FDA-approved, the recombinant human platelet-derived growth factor becaplermin is dependent on proper wound care for successful outcomes.\(^1\) The only other factor showing promise has been trans-retinoic acid. All others, including platelets, platelet-derived products, and basic fibroblast factor, have shown little promise in advancing wound healing.\(^2\) G-CSF has not been shown to affect healing but has been shown effective in decreasing the need for amputation and other surgeries.\(^2\)

Skin grafts and bioengineered skin have also been used in the treatment of diabetic foot ulcers, including dermal fibroblast culture, fibroblast/keratinocyte co-culture, and keratinocytes. The most promising of these has been fibroblast/keratinocyte culture, with superior healing properties when compared to the traditional dermal fibroblast culture.\(^2\) Although these adjuvant treatments show promise, there is not enough data to standardize their use in specific treatment. More research is absolutely necessary in the field of advancing healing of diabetic foot ulcers.

**Recommendations**

Treatment of a diabetic ulcer involves a complex
interplay of many factors, necessitating good judgment and understanding of the pathophysiology of each case and available treatment options. A dermatologist must exercise good judgment in choosing a viable treatment option until more data are available. Prevention, then, prevails as the most important aspect of care in these individuals.

The ADA released guidelines this year outlining foot imaging for diabetic patients. Educating the patient annually about the clinical consequences and preventative measures of their disease is paramount and can clearly help minimize the risk of ulcers, which can lead to amputations. A foot examination, including a screen for peripheral arterial disease, skin integrity, severe nail pathology, neuropathy, altered biomechanics, and evidence of increased pressure, should be carefully done at least annually. Important to note is the condition of the skin, including the presence of impending breakdown or infection. If found to have an ulcer or high-risk foot (upon positive findings of exam), a multidisciplinary approach is recommended with more frequent foot examinations. Depending on the findings on foot exam, further steps should be taken to reduce the risk of ulceration. For example, if peripheral arterial disease is present or claudication is present or claudication is a complaint, then ABIs should be sought for the patient.

Although standardization of treatment is not yet available, we have presented an arsenal of viable treatment options that have been found to be helpful in a diabetic ulcer. Until further advancements are made, prevention and awareness of the possible consequences should be at the forefront of a dermatologist’s mind when encountering a diabetic patient.  

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