European Journal of Research Development and Sustainability (EJRDS)
Available Online at: https://www.scholarzest.com
Vol. 4 No 02, February 2023
ISSN: 2660-5570

MODERN APPROACH TO COMPLEX TREATMENT OF DIABETIC FOOT ULCERS. (LITERATURE REVIEW)

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Article history:

Received: 8th December 2022
Accepted: 8th January 2023
Published: 10th February 2023

Abstract:

Diabetic foot ulcer (DFU) is the most costly and devastating complication of diabetes mellitus, which affect 15% of diabetic patients during their lifetime. Based on National Institute for Health and Clinical Excellence strategies, early effective management of DFU can reduce the severity of complications such as preventable amputations and possible mortality, and also can improve overall quality of life. The management of DFU should be optimized by using a multidisciplinary team, due to a holistic approach to wound management is required. Based on studies, blood sugar control, wound debridement, advanced dressings and offloading modalities should always be a part of DFU management. Furthermore, surgery to heal chronic ulcer and prevent recurrence should be considered as an essential component of management in some cases. Also, hyperbaric oxygen therapy, electrical stimulation, negative pressure wound therapy, bio-engineered skin and growth factors could be used as adjunct therapies for rapid healing of DFU. So, it's suggested that with appropriate patient education encourages them to regular foot care in order to prevent DFU and its complications.

Keywords: diabetes mellitus; wound management; diabetic foot ulcer; amputation; foot care.

INTRODUCTION. Diabetes mellitus (DM) is one of the major health system problems and a global public health threat that has increased dramatically over the past 2 decades [1,2]. According to epidemiological studies, the number of patients with diabetes has increased from about 30 million cases in 1985, 177 million in 2000 to 285 million in 2010, and according to experts, if the situation persists by 2030, more than 360 people will suffer from diabetes. million people [3, 4].

Patients with DM experience multiple complications, one of which is diabetic foot ulcer (DFU). DFU is a frequent complication of DM, which tends to increase over the past decades [5-7]. In general, according to researchers, 15% of patients with diabetes will suffer from DFU during their lifetime [8]. Although it is difficult to obtain accurate data on the prevalence of DFU, the presence of this complication ranges from 4% to 27% [9-11].

The incidence of DM has shifted from developed countries in Europe and the United States to developing countries in the Middle East, Asia, Africa and the Caribbean [77].

To date, DFU is considered the main type of morbidity and the leading cause of hospitalization of patients with diabetes [1,5,12,13]. It has been estimated that approximately 20% of hospital admissions among patients with DM are the result of DFU [14]. Indeed, DFU can lead to infection, gangrene, amputation, and even death if the necessary care is not provided [14]. On the other hand, with the development of DFU, the risk of ulcer progression increases, which can eventually lead to amputation. In general, the incidence of lower limb amputations in patients with DM is 15 times higher than in patients without DM [8]. It has been estimated that approximately 50-70% of all lower limb amputations are due to DFU plasia [8]. In addition, it is reported that every 30 seconds, one leg is amputated worldwide due to DFUplasia [9].

Etiology of DFU. Recent studies have identified multiple risk factors associated with the development of DFU [18-21]. These risk factors are as follows: gender (male), duration of diabetes mellitus for more than 10 years, older age of patients, high body mass index and other comorbidities such as retinopathy, diabetic peripheral neuropathy, peripheral vascular disease, glycated hemoglobin (HbA1C), foot deformity, high plantar pressure, infections and improper foot care [1,12,20-22] (Fig. 1).

Figure 1. Risk factors for diabetic foot ulcers. Ulcers can be distinguished by general or systemic signs from those localized on the foot and its pathology.

Although a number of diabetes-related risk factors have been identified in the literature that contribute to lower limb ulceration and amputation, to date the majority of DFU has been caused by ischemic, neuropathic, or combined neuroischemic abnormalities [6,17] (Fig. 2). Ischemic ulcers probably account for only 10% of DFU and 90% are caused by neuropathy, alone or with ischemia. In recent years, the incidence of neuroischemic problems has increased, and neuroischemic ulcers are the most common ulcers currently seen in most diabetic foot clinics.

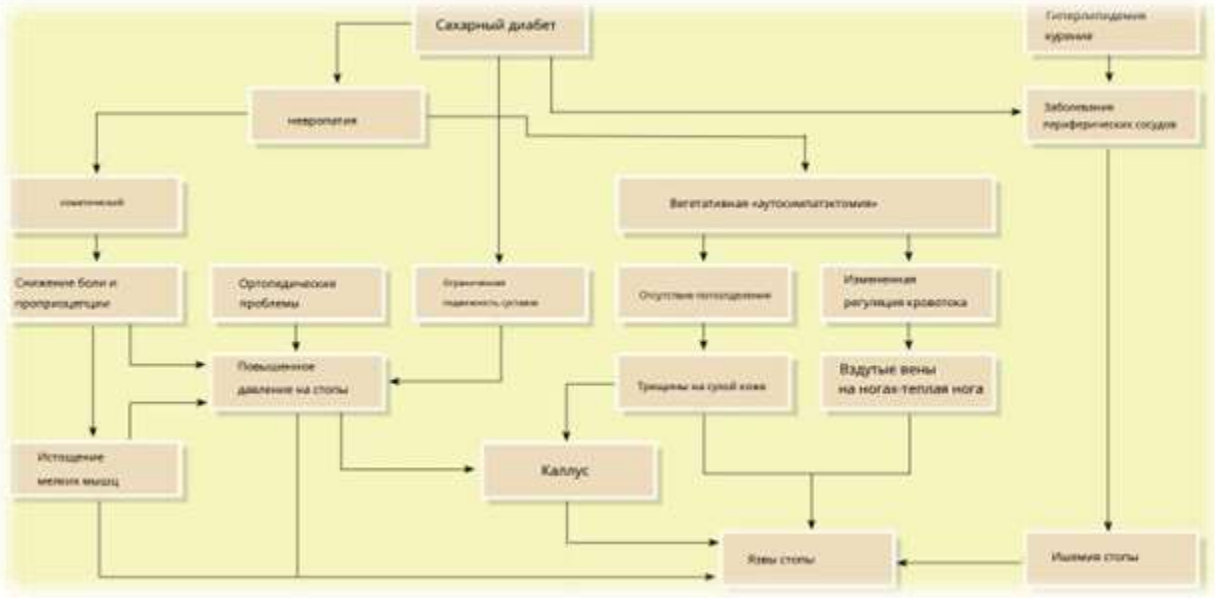

Figure 2. Etiology of diabetic foot ulcer. (Data adapted from Boulton et al [17]).

In general, the most common pathway for developing foot problems in diabetic patients is peripheral sensorimotor and autonomic neuropathy, which leads to increased pressure on the feet, foot deformities, and gait instability, which increases the risk of ulcers [24-26]. To date, numerous studies have shown that increased plantar pressure is associated with foot ulceration [27-29]. Data on the prevalence of neuropathy among people with DM vary from 28% to 65%, depending on the duration of the disease and diagnostic methods [78]. In addition, foot deformities and gait instability have been shown to increase plantar pressure, which can lead to foot ulceration [24,30].

Care And Control For Dyas. Unfortunately, often patients deny their disease and cannot take responsibility for their disease, as well as take the necessary measures to prevent complications and solve many problems associated with the treatment of DFU. However, numerous studies have shown that proper treatment of DFU can significantly reduce, delay, or prevent complications such as amputation, gangrene, and death [6,31,32]. Since diabetes is a multi-organ systemic process, all comorbidities that affect wound healing should be managed by an interdisciplinary team to achieve optimal results in the treatment of DFU [35–38]. In accordance with public health strategies, the clinical treatment of DFU should be carried out immediately by an interdisciplinary team consisting of a general practitioner, a nurse, an orthopedist, as well as consultations with other specialists such as vascular surgeons, infectious disease specialists, dermatologists, endocrinologists, nutritionists [39]. Today, numerous studies have shown that a multidisciplinary team can reduce amputation rates, reduce costs, and improve the quality of life of patients with DFU [39-41].

The American Diabetes Association has concluded that a preventive care team, defined as an interdisciplinary team, can reduce the risks associated with DFU and amputation by 50-85% [42]. DFU to consistently reduce the severity of complications, improve the overall quality and increase the life expectancy of patients [36]. In this article, we review the available evidence for the treatment of DFU as follows: education, blood sugar control, wound debridement, modern drug dressings, including the need for self-examination, foot temperature control, proper daily foot hygiene, use of comfortable and appropriate footwear, and monitoring blood sugar levels [47].

Education. Up to 50% of DFU cases have been shown to be preventable with effective education. In fact, educating patients about self-management of foot injuries is considered the cornerstone of prevention of DFU [12,43-45]. The control of blood sugar levels in patients with DFU is essential in the process of self-management. The blood glucose level is the most important metabolic factor. In fact, inadequate blood sugar control is a major cause of DFU [6,49,50]. The best indicator of glucose control over a period of time is the HbA1C level. This test measures the average concentration of sugar over a 90-day period in red blood cells in the peripheral circulation. The higher the HbA1C level, the more hemoglobin glycosylation will occur in erythrocytes. Studies have shown that blood glucose > 11.1 mmol/L (equivalent to > 310 mg/mL or HbA1C > 12) is associated with reduced neutrophil function, including leukocyte chemotaxis [50]. Indeed, a greater rise in blood glucose levels has been associated with a higher potential for suppressing inflammatory responses and a reduced host response to infection [6]. Pomposelli et al [51] indicated that a single blood glucose level >220 mg/dL on the first postoperative day was a sensitive (87.5%) predictor of postoperative infection. In addition, the authors found that patients with blood glucose levels >220 mg/dL had a 2.7-fold higher infection rate than those with lower blood glucose levels (31.3% vs. 11.5%, respectively) [51]. In addition, a mean 1% reduction in HbA1C has been reported to be associated with a 25% reduction in microvascular complications, including neuropathy [47]. Studies have shown that poor glucose control accelerates the onset of peripheral arterial disease (PAD). It has been shown that for every 1% increase in HbA1C levels, there is a 25-28% increase in the relative risk, which is the main cause of DFU [52].

Surgical intervention. Surgical debridement is the removal of necrotic and non-viable tissues, as well as foreign and infected materials from the wound, which is considered the first and most important surgical step leading to wound closure and reducing the risk of amputation of a limb in patients with DFU [53-56]. The use of CO2 laser allows to perform wound and bloodless necrectomy, improve wound repair, and also reduces the microbial contamination of a purulent wound. The CO2 laser has photocoagulating properties and a sterilizing effect on tissues [79]. Sanitation appears to reduce bacteria and stimulate the production of local growth factors. This method also reduces pressure, cleans the wound bed, and facilitates wound drainage [32,57]. There are various types of debridement, including surgical, enzymatic, autolytic, mechanical, and biological [58]. Among these methods, the highest efficiency of surgical debridement was found and that it is more effective in the healing of DR [54,59-62]. Surgical or acute debridement involves the excision of dead and infected tissue, followed by daily application of a cotton swab moistened with an antiseptic solution [53]. The main purpose of this type of debridement is to turn a chronic ulcer into an acute one. Surgical debridement should be repeated as often as necessary if new necrotic tissue continues to form [63]. There are reports that regular (weekly) acute debridement is associated with faster ulcer healing than less frequent debridement [59,64-66]. The method of debridement depends on the characteristics, preferences, and level of knowledge of the practitioner [54]. When surgical or acute debridement is not indicated, other types of debridement may be used. Despite the benefits of debridement, adequate debridement should always precede the use of topical wound healing agents, dressings, or wound closure procedures, which can be costly.

Unloading Methods. The use of unloading techniques, commonly known as pressure modulation, is considered the most important component in the treatment of neuropathic ulcers in diabetic patients [81,82]. Recent studies have provided evidence that proper unloading promotes healing of DFU [83-85]. Although many unloading methods are currently in use, only a few studies describe the frequency and speed of wound healing with some of the methods commonly used in clinical practice. The choice of these methods is determined by the physical characteristics of the patient and his ability to adhere to the treatment regimen, as well as the location and severity of the ulcer [42]. The most effective method of unloading for the treatment of neuropathic DFU is a total contact dressing (TCD) [42,46,51]. The TCD is minimally padded and conforms exactly to the shape of the foot with a walking heel (fig. 3). The dressing is designed to relieve pressure from the ulcer and distribute pressure over the entire surface of the foot, thus protecting the wound site.

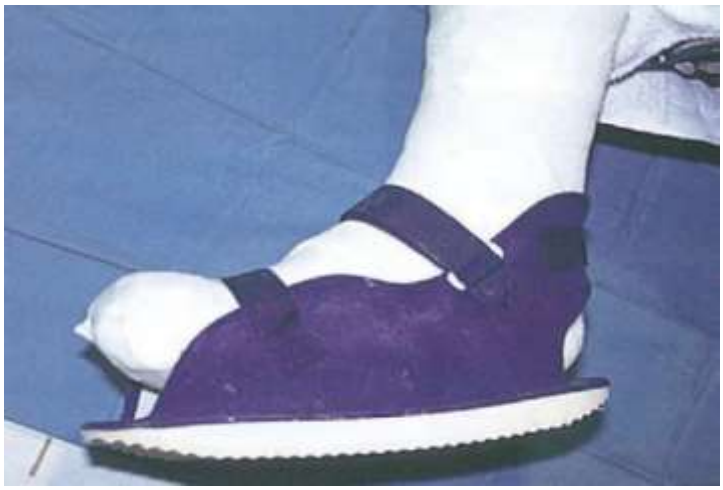

Figure 3. Total contact bandage

A study by Mueller et al [51] showed that TST healed a higher percentage of plantar ulcers at a faster rate than standard treatment. An important breakthrough in the treatment of DFU over the past decades has been an improved dressing [13]. Since this device does not require a skilled technician to use, it could revolutionize the treatment of plantar neuropathic ulcers in the future. It has been suggested that TCD will also dramatically change the treatment of non-ischemic, neuropathic, diabetic plantar ulcers and may replace TCD as the gold standard for relief of neuropathic plantar ulcers [42]. Ideally, dressings should provide moisture balance, protease sequestration, stimulation of growth factors, antimicrobial activity, oxygen permeability, and promote autolytic debridement, leading to granulation tissue formation and a re-epithelialization process. In addition, it should have a prolonged time of action, high efficiency and delayed release of the drug in the case of drug therapy [46,53]. Therefore, no dressing meets all the requirements of a patient with diabetes and a foot ulcer. The choice of dressing is largely determined by the causes of DFU, the location of the wound, the depth, the amount of scar or eschar, exudate, the condition of the wound edges, the presence of infection and pain, the need for adhesion and fit of the dressing [13]

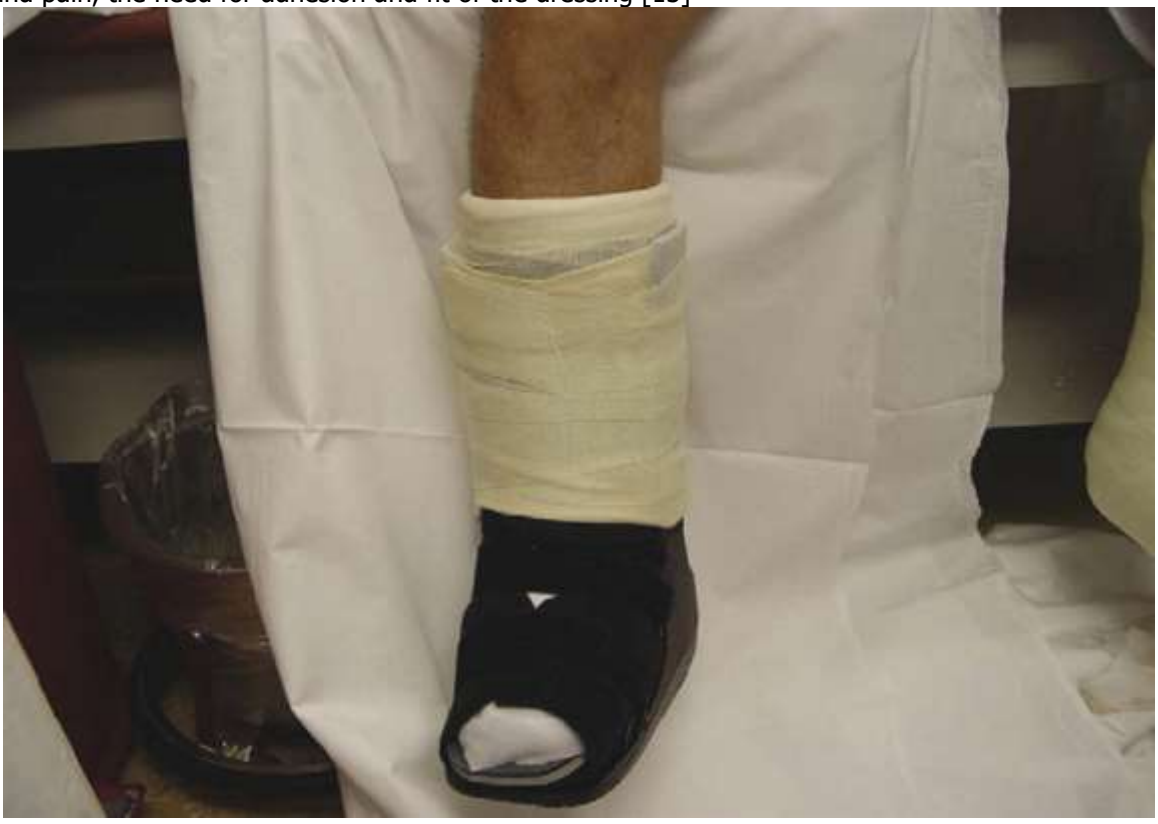

Figure 4. Instantaneous total contact dressing for patients with diabetic foot ulcers.

Diabetic foot surgery plays an important role in the prevention and treatment of DFU [52], and has been on the rise in the past 2 decades [53, 55]. Although surgical interventions in patients with DFU are associated with certain risks, selective correction of persistent foot ulcers may improve outcomes [53]. Typically, operations to heal DFU include

non-vascular foot surgery, vascular foot surgery, and in some cases, amputation. Avascular foot surgery is subdivided into elective, preventive, curative, and emergency, aimed at correcting deformities that increase plantar pressure [52]. Recently, vascular operations on the foot have been developed, such as femoral artery grafting to the pedal arteries and peripheral angioplasty to improve blood flow in the ischemic foot [60].

Modern therapy. Hyperbaric oxygen therapy - hyperbaric oxygen therapy (HBO) has shown promise in the treatment of severe cases of non-healing DFU plasia resistant to other therapeutic methods [55-57]. HBO includes intermittent pumping of 100% oxygen, usually in daily sessions [57]. During each session, patients breathed pure oxygen at 1.4–3.0 abs. atmosphere during 3 periods of 30 min each (90 min in total) with intercalation at 5-min intervals in the pressure chamber [34].

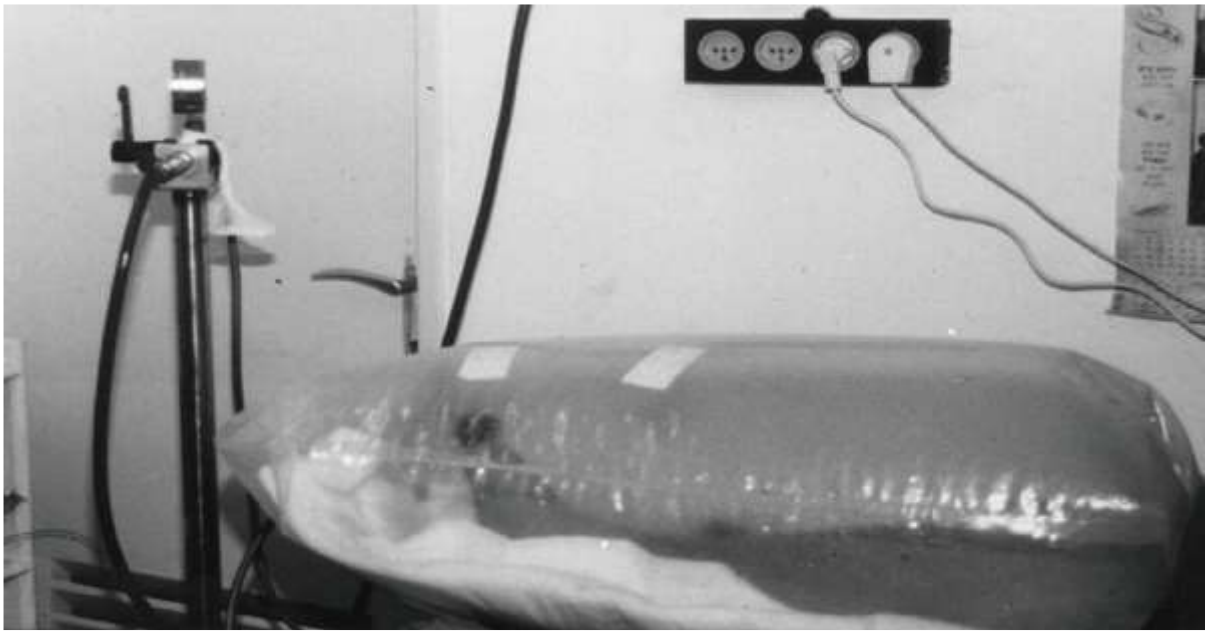

Figure 5. Polyethylene pressure chamber. Oxygen at a concentration of 100% was pumped into the bag through a conventional car wheel valve. The open end of the bag was fixed with an elastic bandage to the leg above the knee. Oxygen was passed through the bandage, and the pressure in the chamber was maintained at a level of 20–30 mm Hg. Art. (1.02–1.03 atm) above atmospheric pressure. (Data adapted from Landau [57]).

To date, numerous studies have reported positive effects of HBO [56]. The exact mechanism of HBO remains poorly understood. Some studies have reported that HBO reduces wound tissue hypoxia, enhances perfusion, reduces edema, reduces inflammatory cytokines, and promotes fibroblast proliferation, collagen production, and angiogenesis [57]. In addition, HBO has been shown to stimulate the mobilization of vasculogenic stem cells from the bone marrow and recruit them into the skin wound [54]. Despite reports of increased healing rates and reduced amputations with HBOT, the adjuvant use of this technique in DDD remains controversial.

Electrical stimulation. Electrical stimulation (ES) has been described in recent literature as an ideal adjunctive therapy for healing of DFU plasia. Currently, there is a significant amount of work confirming the effectiveness of ES for the healing of DFU [63-66]. ES does not replace antibiotic therapy. In a randomized, double-blind, placebo-controlled, 12-week study by Peters et al [63] in 40 patients with DFU, significant differences were found in the number of healed ulcers (65% in the treatment group versus 35% in the control group). Based on a review of the literature, it is suggested that ES may reduce the common deficiencies that have been associated with improper wound healing in DFU, such as poor blood flow, infection, and inadequate cellular response [63,67]. This therapy is a safe, inexpensive and simple intervention to improve wound healing in patients with DFU [67,68].

Bioengineered skin. Bioengineered skin (BIS) has been used over the past decades as a new therapeutic method for the treatment of DFU plasia [71]. This method replaces the degraded and destructive environment of the extracellular matrix with the introduction of a new ground substance matrix with cellular components to start a new healing trajectory [72]. Despite the advantages of BIS, they cannot be used in isolation for the treatment of DFU. Peripheral ischemia, which is one of the pathological characteristics of DFU, is a critical factor influencing BIS transplantation. In addition, this method requires infection control [71,75]. Thus, the above points may lead to high long-term costs and raise serious concerns about the use of this treatment [76].

CONCLUSION. Foot ulcers in diabetic patients are more common and often result in lower limb amputation unless a prompt, rational, multidisciplinary approach to therapy is adopted.

The main components of treatment that can ensure successful and rapid healing of DFU include education, blood sugar control, wound debridement, extended dressing, unloading, surg ery, and advanced therapies that are used in clinical practice. These approaches should be used whenever possible to reduce the high morbidity and risk of serious complications resulting from foot ulcers.

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