EDITORIAL

Diabetic Foot Ulcer: A short review of current management

Diabetes mellitus affects more than 415 million people worldwide[1] and upto 25% of diabetics patients will develop diabetic foot ulcer (DFU) over the course of the disease.[2] Approximately 20% of diabetic foot ulcer require amputation eventually.[3] Vascular and neural abnormalities are dominant predisposition to diabetic foot ulcer.

The pathogenesis of neuro-pathy and vasculo-pathy has been studied extensively. In 1912 L.C Maillard reported the formation of yellowish-brown product on heating a mixture of sugars and amino acids. In the 80s, other workers found that glucose can react non-enzymatically with amino groups on protein to form Schiff bases and Amadori products. These early glycation products undergo re-arrangement, dehydration and condensation to become ir-reversibly cross-linked, hetero-geneous fluorescent derivatives termed advanced glycation end products (AGEs). The formation and accumulation of AGE in various tissues and plasma have been known to occur in old age but are accelerated in Diabetes. Aminoguanidine has been used in experiments to block the receptor for AGE (RAGE) and this has been found to reduce AGEs and improve endoneural blood flow and Na-K+ ATPase activity. Preliminary clinical trials of anti-glycation agent, benfotiamime, showed some efficacy for diabetic neuropathy,[4] However, no effective drug has yet been developed that can suppress the formation of AGEs in vivo in humans.

Meggitt–Wagner classification of diabetic foot ulcers is widely used to access the severity of diabetic foot and treatment is offered according to severity of the disease. Grade-0 Wagner classification the foot is at risk needs prevention. In Grade-1Wagner there are localized, superficial ulcer and treatment is in the form of antibiotic and glycemic control. In Grade-II Wagner there are deep ulcers to bone, ligament, or joint, need good glycemic control, wound debridement, antibiotics. In Grade-III Wagner, has deep abscess and osteomyelitis treatment in the form of wound debridement and some form of amputation. In Grade-IV Wagner, has gangrene of toes and treatment in the form of forefoot amputation, wide wound debridement. In Grade-V Wagner classification there is gangrene of entire foot and it requires below knee amputation.

Aldose reductase increases sorbitol in the nerve cells and causes intra-cellular hyper-osmolarity and nerve damage via the polyol pathway. Accumulation of sorbitol also causes NA-K+ ATPase dysfunction. These contribute to neuropathy. Attempts to mitigate the effects of polyol have led to the development of Aldose Reductase Inhibitors. At the moment, epalrestat has been licensed in Japan alone. It was approved after a 3-month double-blinded trial,[5] which showed improvement of symptoms and nerve function.

The Meggitt and Wagner classification is the most widely used and incorporates 6 grades (0-5). Major disadvantage of the classification that it does not emphasize ischemia or neuropathy. In addition, only grade III addresses infection. Depth-Ischemic classification is a modification of Wagner-Meggit system and aims at more accuracy, rationality and differentiates between grades II and III. It correlates treatment with the grade.

According to a new guideline from the Infectious Diseases Society of America (IDSA), prompt response and early involvement of a multi-disciplinary team of clinicians in the care of patients with diabetic foot infections is crucial to preventing foot amputations.[6] Current treatment guidelines recommend standard treatment of a DFU to include off-loading, debridement, and the restoration of skin perfusion.[7] Removal of callus and dead tissue should be carried out by a podiatrist. Reducing pressure on the ulcer ("off-loading") is crucial and patients should be seen by foot specialist to prescribe an appropriate non-contact shoes. Of utmost importance are good wound care, good blood glucose control and good nutrition.

Evaluating the circulation in the legs should be by a vascular surgeon. If the ulcer is infected antibiotics should be given.

After exposure, irrigate the wound with saline or diluted solution of Povidone iodine. Never use concentrated solution of Povidone iodine because it damages normal granulation tissue. Hypochlorous solutions like VASHE solution have been found to be effective in sanitizing DFUs. VASHE is solution of Hocl (Hypochlorous Acid) which kills important wound pathogens like Gram +ve, Gram -ve bacteria, Anaerobes & Fungi. Gauze soaked in VASHE solution is wrapped around wound for 10-15 minutes. It cleans, irrigates, moistens & debrides the wound and removes bacteria & fungus along with bed odor from wound.[8]

Debridement is the key process of wound bed preparation. This serves to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures. Debridement is defined as the removal of necrotic tissue, bacteria, and other foreign bodies from the wound and is more generally defined as the removal of dead cells.[9] Saap and Falanga,[10] developed the Debridement Performance Index that found that healing was twice as likely with aggressive debridement. Their finding was supported by Williams et al in another study[11] on sharp debridement with a curette in an outpatient setting. Yet another study[12] concluded that frequent debridement of DFUs and venous leg ulcers (VLUs) may improve healing outcomes.

Debridement techniques include: autolytic, enzymatic, mechanical, surgical, and bio-surgical debridement.[13-15] Autolytic debridement is the breakdown of necrotic tissue by the body's own defense mechanism.[13,15] Enzymatic debridement applies enzymatic agents to break down the tissue within the wound only (not the surrounding area).[14] Mechanical debridement can consist of wet-to-dry dressing application on the wound, pulsed lavage, whirlpool therapy, and/or the surgical removal of the dead tissue.[13,14] Wet-to-dry dressings can be painful and cause bleeding, whereas pulsed lavage is painless and can be easily performed by nurses.

Conventional treatment of a DFU, with offloading and debridement, does not always result in complete wound closure for a significant percentage of patients. If a reduction in wound size is not observed after 4 weeks of standard wound therapy, one may need to add adjuvant treatment.[16] This may include advanced biological therapy. Examples of agents that have been studied are bi-layered living cell therapy (Apligraf), growth factor therapy with recombinant platelet derived growth factor–BB (becaplermin) and platelet releasate (Procuren) and human fibroblast-derived dermal substitute (Dermagraft).

A new device has been developed in the US and approved by FDA that delivers shock waves to the wound to stimulate healing.[17] Marketed as the Dermapace System, the device uses a handheld probe to deliver high-energy pulses similar to sound waves to the wound's surface. The device increases perfusion and arteriogenesis, angiogenesis, biofilm disruption, and growth factor upregulation, which help regenerate skin and musculoskeletal and vascular structures. Treatment lasts over 2 to 10 weeks.

There is paucity of data to measure outcomes of treatments of DFU. The incidence of amputations has been used as surrogate for such measurement. However, amputation is a form of treatment and not a true measure of disease outcome. Therefore its value is limited. Despite this limitation, however, the use of major amputation as an outcome measure[18] has shown evidence that the overall incidence of major amputation is falling in some countries with nationwide databases.[19,20] For instance, in the UK, there was a reduction of incidence of amputation from 3.0-3.5 per 1,000 people with diabetes per year in the 90s to 1.0 per 1,000 per year currently. However, evidence did not show this to follow any major change in the use of particular treatments but has coincided with the publication of National Institute for Health and Care Excellence guidelines on the management of DFUs in 2004, updated in 2010 and 2016.[21] This is a result of wider implementation of change in structure of care, including the establishment of a single multidisciplinary service and encouraging early referral of all new DFUs for expert assessment.[22,23]

In conclusion, there is clear evidence that healthcare structural changes that focus on clear policies that enable early assessment of DFUs by a specialist multi-disciplinary service and structured surveillance and care for those who have had a DFU and have healed would improve outcomes. If communities embrace these initiatives, it should be possible to trigger substantial improvement in outcomes relating to Diabetic Foot Ulcers. Care of the foot, therefore, needs to be considered a "superspecialty" instead of a subspecialty of diabetes.

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