

Editorial Article

CURRENT PERSPECTIVE IN THE MANAGEMENT OF DIABETIC FOOT ULCERS - AN OVERVIEW ON THE INDIAN SCENARIO

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Definition: Diabetic foot as defined by the World Health Organization (WHO) as, "The foot of a diabetic patient that has the potential risk of pathologic consequences, including infection, ulceration, and/or destruction of deep tissues associated with neurologic abnormalities, various degrees of peripheral vascular disease, and/or metabolic complications of diabetes in the lower limb" [1].

Epidemiology: India is slowly progressing to the top of the world with the largest volume of diabetic subjects and is being anticipated to be the "diabetes capital of the world". India will be the capital of diabetics by 2025. According to the Diabetes Atlas 2013 published by the International Diabetes Federation, the number of people with diabetes in India currently is 65.1 million, which is expected to rise to 142.7 million by 2035 unless urgent preventive steps are taken [2]. Up to 25% of patients with diabetes develop the corresponding ulcers of the foot. More than half of all foot ulcers become infected, requiring hospitalization, while 20% of infections result in amputation. Diabetes contributes approximately 80% of all non-traumatic amputations performed every year. After a major amputation, 50% of people will have the other limb amputated within two years time. People with a history of diabetic foot ulcer have a 40% greater 10-year death rate than people with diabetes alone [3]. Of the total lower limb amputations, 85% are due to DFU [4]. Although recent population based data for Diabetic Foot Ulcer (DFU) is not available, it is estimated that approximately 45,000 legs are amputated every year in India [5].

Diabetes cost a whopping USD 548 billion in health expenditure globally in 2013. In a report published by Gupta S (2012), an average Indian should spend approximately 1960 USD for the complete treatment of neuro-ischemic foot [6].

Pathophysiology: DFU is a complex pathological phenomenon in which neuropathy and vasculopathy play a vital role and are together termed as neuro-ischemic ulcer. In most of the cases, infection is a consequence of neuro-ischemia and termed as neuro-ischemic ulcers/DFU. In the majority cases of DFU in India, neuropathy (15%) and infections (7.6%) are foremost than vascular diseases (5%) [4].

The hyperglycemic condition in diabetes mellitus (Type 1 or Type 2) causes a range of pathological changes in diabetes patients, such as increased activity of protein kinase C, formation of advanced glycation end products and increased reactive oxygen species which leads to peripheral neuropathy. Micro and macrovascular diseases of blood vessels which supply blood to the foot lead to development of an ischemic state which engenders deficient nutrient blood supply to the foot and hence poor wound healing.

Peripheral vascular disease, diabetic peripheral neuropathy, nephropathy, retinopathy, tobacco chewing, cigarette smoking, and alcohol consumption are the significant risk factors associated with DFUs.

The treatment strategies available for DFUs include antibiotics (Piperacillin, Vancomycin), neuropathic drugs (symptomatic-anticonvulsants, mechanism based- PKC inhibitors), dressings

(collagen scaffolds), growth factors (rhEGF, PDGF, rhFGF), skin substitutes (Apligraf®, Dermagraft®), devices (hyperbaric oxygen therapy, Negative pressure therapy) and surgery (reconstruction and amputation).

Unfortunately, none of the current treatment strategies address all the requirements to treat DFUs and also, the overall costs of these treatment strategies are high. Hence a single treatment strategy (multi-mechanism based drug/product) to satisfy all the requirements needs to be addressed or developed.

The most important factor in minimizing the overall cost of therapy is the development of novel drug delivery systems which will not increase the total cost, despite their high unit cost, if they are applied less frequently.

In India, currently 12 clinical trials are underway (Table. 1), out of which 6 studies are topical, 4 studies are oral and 2 studies are observational. Of special importance is the fact that, of the 12 clinical trials initiated for diabetic foot therapy, herbal and homeopathic trials constitute a total of 4 trials [7].

Over the years, topical therapy has evolved with specific advantages to its reputation, which include high local concentration of the drug rather than systemic levels, restriction of total antibiotic usage and respite from the systemic toxicity. Established reports on collagen sponges and local application of gentamycin hint at it being a dependable method for the treatment of diabetic foot infections.

Resistance development to single antibiotic administration is a common phenomenon well studied for decades; so the logical conclusion arising out of this is to include a combination of antimicrobial agents in tandem with surgery, debridement or osseous resection.

"Every 30 seconds a lower limb is lost somewhere in the world as a consequence of diabetes" [8] - The concerns arising from DFUs are such that, aside from developing countries, developed countries are depicting high rates of amputation, thereby providing us with a clear picture of the scale of impact this disorder has had world over. In spite of this, the appeal of knowledge, attitude and practice of diabetic foot care has not picked up around the globe, with respect to DFU incidence, especially in India. The situation has so deepened, that a system of rapid prevention with maximum compliance must be established for immediate application for all patients. National programs that raise awareness on diabetes and its corresponding complications on the feet are the need of the hour.

"Prevention is better than cure"- There is no worthy situation for the application of this adage than in diabetic foot care. Constant risk assessment and its classification along with consecrated diabetic care by both health care specialists and others will help to achieve the ultimate goal of diabetic foot ulcer prevention. Typical situations of ulcer managements requires sound fundamental accesses to the multiple factors involved with special attention to the microbiology of the infections. For established ulcers an organized web of qualified practitioners is essential to guarantee viable treatment strategies that provide the best of both worlds; comply with clinical

guidelines and ensure patient satisfaction. Therefore, a technically capable practitioner is of utmost importance for patient specific diagnosis and therapy management. As a number of biochemical shortcomings/variations eventually cause DFUs, a single pronged

treatment strategy holds no promise. Management therapies of the future must take into consideration the inherent pathological complexities and ensure authentic redressal of the inadequacies arising out of DFUs and eventually, patient satisfaction.

Table 1: Medicines in clinical trials (India)

S. No.	Intervention/ Product Name	Type of trial	Mechanism
1.	ReliDerm®DT	Interventional	Allogeneic fibroblast graft. (Dermal tissue equivalent).
2.	HO/03/03	Interventional	PKCa activation and PKCd inhibition, migration of skin cells across the wound gap to provide complete re-epithelialization.
3.	Platelet derived growth factor (PDGF-BB)	Interventional	Stimulates chemotaxis and synthesis of fibroblasts and smooth muscle cells.
4.	Diperoxochloric acid	Interventional	Derived from dichloric acid, stimulate skin growth and disinfection.
5.	Granexin™ Gel	Interventional	Stabilizes gap junctions/ tight junctions of endothelial cells during the wound healing process
6.	Esmolol hydrochloride	Interventional	Increased vascular perfusion.
7.	Linezolid 1200mg SR Tablet	Interventional	Bactericidal activity on <i>Staphylococcus aureus</i>
8.	Katupila fresh leaf kalka with till taila	Interventional	Antiseptic and its paste is used in folklore to extract any extraneous materials from body tissues without surgery
9.	Homoeopathic medicines Sulph Sil Lyc Ars.	Interventional	-
10.	Homoeopathic medicine with ulcer dressing using Calendula Q	Interventional	Antioxidant activity
11.	A survey on awareness of foot problem and care among diabetic population in India	Observational	-
12.	Estimate of prevalence of depression in Type2 Diabetes patients as compared to non-diabetic patients	Observational	-

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