CLINICOPATHOLOGICAL STUDY OF DIABETIC FOOT ULCER - AN ACCOUNT OF 'THE ROLE OF FOCUSED WOUND CARE' AND 'PRESSURE RELIEVING MEASURES' IN HEALING

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ABSTRACT

BACKGROUND

Diabetes mellitus is the epidemic of current generation, and the diabetic foot ulcers are major complications. Though DFU formation itself indicates disease progression, the failure to treat it effectively contributes further to deterioration in patient's quality of life and increased mortality. DFU often leads to infections, osteomyelitis or gangrene, and consistently being ascertained as significant risk factor for lower extremity amputation.

MATERIALS AND METHODS

It was a prospective, observational study including 30 patients suffering from DM (Both type 1 and Type 2) with foot ulcers. After taking careful history and physical examination, complete haemogram, estimation of blood glucose and glycosylated haemoglobin (HbA1C) was done. Assessment of sensory impairment was done by using Semmes-Weinstein 5.07 monofilament nylon wires. Deep swabs or a tissue biopsy was taken for microbiological culture and microscopy. For imaging modalities, e.g. straight X-ray of the affected limb, bone scan, Doppler study of vascular system were done. The traditional classification system developed by Wagner and also Depth Ischaemia classification for grading diabetic foot ulcers has been used. Diabetic foot infections, divided into two categories known as non-limb threatening (NLT) and limb threatening (LT) infections are also taken into consideration. Patients were assessed for need for special rehabilitation measures, time need for mobilisation and return to routine/active life and amputation.

RESULTS

Among the study population (n=30), 26 patients were downgraded from Grade 3, Grade 2 ulcer to Grade 2 & Grade 1 ulcer respectively. 2 patients initially suffering from Grade 1 ulcer remained in the same grade. 2 patients (Grade 4 & 5 ulcer) did not show any clinical improvement and ultimately needed amputation.

CONCLUSION

Management of diabetic foot requires a multisystem approach that addresses the problems of the nervous, vascular, skeletal, immune and integumentary system. These include appropriate antibiotic, proper wound cleansing, debridement of any callus and necrotic tissue, focused wound care with application of tissue regenerators and specially off-loading of pressure.

KEYWORDS

Diabetes Mellitus, Foot Ulcer, Wound Care, Pressure Relieving Measures, Healing.

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BACKGROUND

Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases.[1] Diabetes mellitus occurs throughout the world, but is more common (Especially type 2) in more developed countries. The greatest increase in rates is, however, expected to occur in Asia and Africa, where most people with diabetes will probably be found by 2030.[2] Diabetes Mellitus (DM) is extraordinarily important to the primary care physician and has a profound impact in daily practice. There are two major forms of the disease- in type 1 DM, there is an immune mediated destruction of the pancreas, so that the body does not produce insulin; this develops most often in children. The more common form is type 2 DM which comprises 90% of cases of DM where the body does not use insulin properly and does not produce enough insulin; this commonly develops in adults. Both types of diabetes are characterised by high blood glucose level. These high blood glucose levels cause changes in organ and tissues that eventually cause devastating complications.

Foot infections in diabetes cause substantial morbidity. Prevention and care of diabetic foot continue to represent a major challenge to the physician. Neuropathy, infection, deformity and ischaemia are major threats to the diabetic foot and overall functional wellbeing of the diabetic patient.

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Diabetes is the leading cause of amputation worldwide and 6%-43% (Depending on ulcer severity) of patients with diabetic foot ulcers ultimately have the most severe diabetic foot outcome, amputation.[3] It occurs in 15% of all patients with diabetes and precedes 84% of all lower extremity amputations.[4]

Management of diabetic foot requires a multisystem approach that addresses the problems of the nervous, vascular, skeletal, immune and integumentary system. Providing optimal wound care is crucial for healing. These include appropriate antibiotic, proper wound cleansing, debridement of any callus and necrotic tissue, focused wound care with application of tissue regenerators and specially off-loading of pressure.

Aims

1. To identify and document the pathophysiological changes leading to the development of diabetic foot ulcer (DFU).
2. To assess and grade DFU with Wagner classification.
3. To evaluate the outcome of ulcers with "focused wound care" and "pressure relieving measure."

MATERIALS AND METHODS

The study was conducted in the Department of General Surgery in a busy Medical College and Hospital, Kolkata, over a period of 18 months. It was a prospective, observational study including 30 patients suffering from DM (Both type 1 and type 2) with foot ulcers attending the Outpatient Department, Emergency Department and also Indoor patients. After taking careful history and physical examination, complete haemogram, estimation of blood glucose and glycosylated haemoglobin (HbA1c) for assessment of long term blood glucose status were done. Assessment of sensory impairment was done by using Semmes-Weinstein 5.07 monofilament nylon wires. Deep swabs or a tissue biopsy was taken for microbiological culture and microscopy. For imaging modalities, e.g. straight X-ray of the affected limb, bone scan, Doppler study of vascular system were done. The traditional classification system developed by Wagner and also Depth Ischaemia classification for grading diabetic foot ulcers has been used. Diabetic foot infections, divided into two categories known as non-limb threatening (NLT) and limb threatening (LT) infections are also taken into consideration. Patients were assessed for need for special rehabilitation measures, time need for mobilisation and return to routine/active life and amputation.

Procedure was carried out after obtaining the valid consent and approval from the Independent Ethical Committee (IEC) of the institute. All the patients of DFU were included in the study and foot ulcers not associated with DM were excluded from this study.

RESULTS

Thirty (30) adult patients between 38-74 years of age were included in the present study; 16 (53%) were male and 14 (47%) were female suggesting that both the sexes are almost equally affected with the disease process. Twelve (40%) patients had type 1 DM and eighteen (60%) patients had type 2 DM suggesting both the types of diabetes suffer similar foot pathology. Among the study population, mean duration of DM mellitus was 9.8 years (Range: 4 to 20 years) and mean duration of DFU was 8 years (Range: 4 to 12 months). The glycaemic status of the study population was observed under three categories. The mean value of fasting plasma glucose (FPG) and post-prandial plasma glucose (PPPG) was 119.7 mg/dL (range: 86-142) and 213.3 mg/dL (Range: 168-266) respectively. The mean value of glycosylated haemoglobin (HbA1c) was 7.2% (Range: 6.2 - 8.4).

After initial assessment of glycaemic status, the patients under this study were evaluated for any sensory impairment over the wound area. Only 6 (20%) patients had intact sensation as evidenced with 5.07 (10 g) Semmes-Weinstein monofilament nylon wires. Among the study population, 20 (67%) patients had non-limb threatening (NLT) infections, and 10 (33%) patients had limb threatening (LT) infections. Five (17%) patients had ischaemic ulcers and rest twenty-five (83%) patients had no evidence of ischaemia.

Initially, 16 (53%) patients were treated with oral hypoglycaemic agents (OHA), either with single agents or in combinations, among which 4 (13%) patients also required insulin preparations for proper glycaemic control. Fourteen (47%) patients were treated with insulin preparations from the very beginning.

According to Wagner classification, pretreatment grading of the foot ulcers of the study population was as follows: Two (6.6%) patients had grade-1 ulcer, 18 (60%) patients had grade-2 ulcers, and 8 (26.6%) patients had grade-3 ulcers, one (3.3%) patient each with grade-4 and grade-5 ulcer. After proper debridement of the wound with simultaneous use of proper antibiotics, the wounds were rendered non-infective. Twenty five (83%) patients were given tissue regenerator PDGF to the wounds for a maximum duration of 10 weeks: three (12%) patients healed remarkably during this period without any subsequent intervention, seven (28%) patients were subsequently advised total contact cast as off-loading measure and fifteen (60%) patients were prescribed pressure relieving footwear.

At the end of our interventions, the outcome or post-treatment grading as per Wagner classification was as follows: eighteen (60%) patients were converted from grade-2 ulcer to grade-1 ulcer. Among the 8 patients of grade-3 ulcer, five patients were converted to grade-1 ulcer and three patients were converted to grade-2 ulcer. Two patients, initially suffering from grade-1 ulcer, though remained in the same grading after standard treatment, showed that the residual ulcers healed to some extent. Two (6.6%) patients, one suffering from grade-4 and another suffering from grade-5 ulcer did not show any clinical improvement and remained in the same grade. In spite of all available measures, these two patients ultimately needed amputations- one was left midtarsal amputation, and another was right below-knee amputation.

Total Number	Male	Female
n = 30	16	14
Row %	53%	47%

Table 1. Showing the distribution of male and female among the study population

Total Number	Type 1	Type 2
N = 30	12	18
Row %	40%	60%

Table 2. Showing distribution of type of diabetes mellitus (type 1 and 2) among the study population

Duration	Mean±Standard Deviation
DM Duration (Years)	9.8333±3.630
DFU Duration (Months)	8.0666±2.7029

Table 3. Showing the mean duration of diabetes mellitus in years and also diabetic foot ulcer duration in months with standard deviation in study population

	Mean±SD
Fasting Blood Sugar (FBS)	119.7000±14.3097
Postprandial Blood Sugar (PPBS)	213.0330±25.6588
Glycosylated Haemoglobin (HbA1C)	7.2533±0.5587

Table 4. Showing mean with standard deviation of fasting blood sugar, postprandial blood sugar and glycosylated haemoglobin among the study population

Total Number	Sensation-Intact	Sensation-Impaired
N=30	6	24
Row%	20%	80%

Table 5. Showing distribution of sensitivity to Semmes-Weinstein monofilament 5.07 (10 g) among the study group

Total Number	NLT infection	LT infection
n=30	20	10
Row %	67 %	33 %

Table 6. Showing number of patients with non-limb threatening (NLT) and limb threatening (LT) infections in the study group

Total Number	Ischaemic	Non-ischaemic
n=30	5	25
Row%	17%	83%

Table 7. Showing evidence of presence and absence of ischaemia among the study population

Treatment	Oral Hypoglycaemic Agents	Insulin	OHA+Insulin
n=30	12	14	4
Row %	40 %	47 %	13 %

Table 8. Showing the required treatment modalities for proper control of hyperglycaemia with oral hypoglycaemic agents, insulin or combination of both

	Limbs Saved	Amputation
n=30	28	2
Row %	93 %	7 %

Table 9. Showing the ultimate result of the study. In 93% of the study population with diabetic foot ulcer, limb salvations were possible by conservative therapy. Unfortunately, in 7% patients, amputation could not be avoided

DISCUSSION

Diabetes mellitus affects every organ system of the body. Foot ulcers are cutaneous erosions characterised by a loss of epithelium that extends into or through the dermis to deeper tissue. Considerable variation is reported in incidence and prevalence of diabetic foot ulcers. The life-time risk for foot ulcers in person with diabetes is estimated at 15%.[4] The disease appears to progress as a function of age, duration of diabetes or both. Neuropathy, infection, deformity and ischaemia are major threats to the diabetic foot and the overall functional wellbeing of the diabetic patient. As time progressed, diagnostic techniques have improved. The cost associated with adequate caring for these problems represent a significant monetary impact to the health care system.

The patients under this study evaluated for any sensory impairment showed 24 (80%) patients had intact sensation over the wound area. Laing PW et al[5] studied that sensory neuropathy is responsible for most foot ulcerations. As many as 60-70% of diabetic patients have neuropathy which usually occurs in stocking-glove distribution with initial symptoms beginning with paraesthesias or dysaesthesia and progressing to complete loss of sensation.

Brodsky J W[6] observed that ulcers of the foot are the single most common complication for which DM patients seek medical consultation and vast majority of plantar foot ulcerations are caused by the combination of underlying bony prominence coupled with insensitivity caused by neuropathy rather than by diabetic vasculopathy.

DM is the leading cause of amputation worldwide; constitutes 51% of patients needing LEA and more than 54,000 new LEAs are performed each year.[3] The long-and short-term prognosis for the diabetic undergoing amputation has always been poor. Post-operative morbidity is a frequent occurrence in these patients.

In our study, we assessed the results of the strategy used in avoiding major amputations in patients admitted to our hospital with multidisciplinary approach. Also aimed to identify the pathophysiological changes (e.g. neuropathy or ischaemia) leading to development of diabetic foot ulcer, to make an assessment of the ulcers as appropriate for grading them with Wagner classification and also on the basis of presence of infection, to evaluate the outcome of the ulcers in the baseline grading with "focused wound care" by application of tissue regenerators (PDGF) and "pressure relieving measures" by use of total contact casting (TCC) and footwear specially designed by the help of the Artificial Limb Centre (ALC) in our institute.

In the present study, pretreatment grading of the foot ulcers of the study population showed majority (86.6%) had grade-2 or grade-3 ulcers. One (3.3%) patient each with grade-4 and grade-5 ulcer. The outcome or post-treatment grading as per Wagner classification was as follows: eighteen (60%) patients were converted from grade-2 ulcer to grade-1 ulcer. Among the 8 patients of grade-3 ulcer, five patients were converted to grade-1 ulcer and three patients were converted to grade-2 ulcer. Two patients, initially suffering from grade-1 ulcer did not progress further. In spite of all available measures, two (6.6%) patients, one suffering from grade-4 and another with grade-5 ulcer did not show any clinical improvement and remained in the same grade. These two patients ultimately needed amputations. Wagner FW Jr.[7] traditionally classified and graded diabetic foot ulcers, and it has been widely accepted and used but the continuum from ulceration to gangrene has been disputed and has led to newer classification system. This result is in contrast to other reports[8] where they reported an occurrence of amputations in 15% cases of DFU.

Twenty (67%) patients had NLT infections and 10 (33%) patients had LT infections. After proper debridement of the

wound with simultaneous use of proper antibiotics and proper glycaemic control by OHAs and or insulin preparations, the wounds were rendered non-infective. Casqueiro J et al[9] in a review of pathogenesis of infections in patients with DM studied that in diabetic ulceration, granulocyte motility and activity is slowed and the epidermis is compromised, exposing deeper structures. Due to the suppressed immune state overall, diabetic foot ulcers tend to acquire rapid, polymicrobial infection, often a mixture of Gram-positive, Gram-negative and anaerobic strains. Karchmer AW and Gibbons GW[10] divided diabetic foot infections into two categories - non-limb threatening infections, and more severe limb-threatening infections. Although most of these infections are initially monomicrobial, the ulcers eventually tend to acquire a polymicrobial character including Gram-positive and Gram-negative bacteria as well as anaerobic strains.

Wound healing is the process by which tissue responds to an injury. Platelets that initiate the coagulation cascade in the wound, are the initial source of growth factors including PDGF, TGF-β, EGF, etc. PDGF is the most widely suited growth factor clinically; appears to be safe and efficacious and presently approved for use in the treatment of diabetic foot ulcers.[11]

In our study, tissue regenerator PDGF was given to 25 (83%) patients for a maximum duration of 10 weeks: three (12%) patients remarkably healed during this period without any further intervention, 7 (28%) patients were subsequently advised TCC as off-loading measure and 15 (60%) patients were prescribed pressure relieving footwear.

Knighton DR et al[12] performed different investigations that have shown that PDGF can be an important adjunct to healing wounds that have shown resistance to comprehensive approaches. Wieman J et al[13] studied in a trial using recombinant human PDGF in the treatment of patients of diabetic foot ulcers, PDGF–BB was found to increase the incidence of complete wound closure by 43% as compared with placebo (p=0.007). It also decreased the time to achieve complete wound closure by 32% (p=0.013) when compared with placebo gel.

Veves A et al[14] studied most (74%) diabetic plantar foot ulcers are located under the metatarsal heads suggesting that ulcerations do not occur in a random pattern over or under the foot but rather are found in areas of high-pressure distribution.

Among the various off-loading methods, TCC and specially designed footwear remain the "cornerstone" for healing of DFU and may be used in conjunction with other methods. Footwear is the primary means of protecting insensitive feet. Patients with an insensitive foot will always need life-long assistance to prevent tissue damage. With the proper use of appropriate footwear and instructions related to foot care, most diabetic patients can expect to avoid a skin wound on their feet. People seldom realise the kind of impression diabetes mellitus can leave on their feet.

Caputo G M et al[15] observed that most foot ulcers commonly fail to heal simply because the patients continue to put weight on their feet, and treatment must be directed at relieving pressure. Relief of pressure begins by debriding the hyperkeratotic callus that surround the ulcer, along with unhealthy and devitalised skin. The patient should be counselled that the ulcer requires debridement to initiate the healing process.

Brike JA et al[16] reported a 75% to 84% reduction in peak pressure at the 1st and 3rd metatarsal heads respectively, when a person walked in the total contact cast compared to normal shoes. Therefore, the utility of contact-casting is in reducing peak plantar pressures, through increasing the surface area of the foot. Coleman WC[17] studied that a rigid shoe sole can reduce shear stress on the foot. As much as 50% of the pressure can be reduced by use of a rigid rocker sole.

Some of the most common and least understood phenomena experienced by amputees are phantom pain, phantom sensation and residual limb pain. It is estimated that 85% of amputees will experience one or all three forms of pain or sensation at one time or another.[18]

Study on 'foot and ankle survey in adults with diabetes mellitus' showed that a low percentage of subjects with diabetes regularly have their feet examined and that a relatively high percentage (31%) wear shoes that are too narrow. Identifying these patients early may allow modification of habits that put their feet at risk.[19]

It is important to optimise holistic care of these patients to improve outcome. Despite correction of the underlying cause and best practice wound care, a proportion of these ulcers do not heal in a timely manner. The development of next-generation DFU therapies including: (i) topical growth factors, (ii) scaffolds, and (iii) cellular therapies have yielded measurable but modest improvements in DFU repair. Because DFUs arise as a result of multiple biochemical deficiencies, a singular treatment modality is unlikely to be effective.[20] The introduction of biologic alternatives (PDGF) and adjunctive treatments (TCC and footwear) has increased the potential of healing as reflected in this study.

CONCLUSION

Foot lesions, especially DFUs are common in a person with DM. The pathogenesis of diabetic foot lesion is multifactorial. Physicians involved in the management of diabetic foot must understand the pathogenesis and risk factors involved so that whenever possible the development of foot problems can be prevented. If treatment is delayed, or inappropriate, the ulceration can become infected and gangrene may develop.

Management of DFU demands a multidisciplinary approach. However, the opportunity exists to diagnose appropriately the common foot problems in a diabetic patient to manage them effectively to minimise complications, and most importantly, to educate, train and motivate them as how to take self-care of the feet. By these, although foot problems cannot be eradicated completely, it is certain that number of hospitalisations and health care costs directly attributable to such problems can be reduced.

REFERENCES

1. Melmed, Williams S, Hardin R. Williams textbook of endocrinology. 12th edn. Philadelphia: Elsevier/Saunders 2011:1371–435.
2. Wild S, Roglic G, Green A, et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27(5):1047–53.
3. Edmonds ME, Blundell MP, Morris ME, et al. Improved survival of the diabetic foot: the role of a specialized foot clinic. Quart J Med 1986;60(232):763-71.

4. Brem H, Tomic-Canic M. Cellular and molecular basis of wound healing in diabetes. Journal of Clinical Investigation 2007;117(5):1219–22.
5. Laing PW, Cogley DI, Klenerman L. Neuropathic foot ulceration treated by total contact casts. J Bone Joint Surgery Br 1992;74(1):133-6.
6. Brodsky JW. Outpatient diagnosis and care of the diabetic foot. In: Heckman JD (edr). Instructional course lectures. Park ridge III, American academy of orthopedic surgeons 1993:121-39.
7. Wagner FW. A classification and treatment program for diabetic, neuropathic, and dysvascular foot problems. In: St. Louis, Mosby CV. Instructional course lectures. American academy of orthopedic surgeons 1979:143-65.
8. Reiber GE, Boyko EJ, Smith DG. Lower extremity foot ulcers and amputations in diabetes. In: Harris MI, Cowie CC, Stem MP, et al. (eds) Diabetes in America. Washington, DC, US Government Printing Office 1995:409-28.
9. Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: a review of pathogenesis. Indian J Endocrinol Metab 2012;16(Suppl 1):S27-36.
10. Karchmer AW, Gibbons GW. Foot infections in diabetes: evaluation and management. Curr Clin Top Infevt Dis 1994;14:1-22.
11. Krupski WC, Reilly LM, Perez S, et al. A prospective randomized trial of autologous platelet-derived wound healing factors for treatment of chronic nonhealing wounds: a preliminary report. J Vasc Surg 1991;14(4):526-32.
12. Knighton DR. Growth factors and repair of diabetic wounds. In: Levin ME, O'Neal LW (eds). The diabetic foot. 5th edn. St. Louis: Mosby Year Book 1993.
13. Wieman TJ, Smiell JM, Su Y. Efficacy and safety of a topical gel formulation of recombinant human platelet-derived growth factor-BB (becaplermin) in patients with chronic neuropathic diabetic ulcers. A phase III randomized placebo-controlled double-blind study. Diabetes Care 1998;21(5):822-7.
14. Veves A, Ross VER, Boulton AJ. Foot pressure measurements in diabetic and nondiabetic amputees. Diabetes Care 1992;15(7):905-7.
15. Caputo GM, Ulbrecht JS, Cavanagh PR, et al. Assessment and management of foot disease in patients with diabetes. N Engl T Med 1994;331(13):854-60.
16. Brike JA, Sims DS, Buford WL. Walking casts: effect on plantar foot pressures. J Rehabil Res Dev 1985;22(3):18-22.
17. Coleman WC. The relief of forefoot pressures using outer shoe sole modifications. In: Patil KM, Srinivasan H (eds). Proceeding of international conference on biomechanics and clinical kinesiology of hand and foot. Indian Institute of Technology, Madras, India 1985.
18. Davis RW. Phantom sensation, phantom pain, and stump pain. Arch Phys Med Rehabil 1993;74(1):79-91.
19. Reveal GT, Laughlin RT, Capecci P, et al. Foot and ankle survey in adults with diabetes mellitus. Foot Ankle Int 2001;22(9):739-43.
20. Futrega K, King M, Lott WB, et al. Treating the whole, not the hole: necessary coupling of technologies for diabetic foot ulcer treatment. Trends Mol Med 2014;20(3):137-42.