

Mini Review

Management of Diabetic Foot Ulcer - A Pharmacist Perceptive

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Abstract

Diabetes is one among the leading cause of death in the world causing various other secondary complications associated with it. Neuropathy is a foremost primary cause of diabetic ulceration, which reduces sensation at the nerve endings. Diabetic foot ulcer is one of the increasing causes of morbidity and mortality in the present era with uncontrolled high incidence of diabetic conditions. In most of the cases it requires amputations posing a threat to the lower limbs excision. Increased hospitalizations, cost of therapy etc., pose unnecessary complications to the condition. In the present case, a seventy-year-old female patient with diabetic foot ulcer was admitted to the hospital and the therapy was initially started with intravenous antibiotics as per doses mentioned in guidelines. Further she was treated with Platelet rich plasma containing multiple growth factors for natural healing of her non-healing ulcer. Pharmacist could play keen roles in making the patients understand complications associated with diabetes, the administration of insulin and counseling on other oral hypoglycemic, ruling out antibiotic resistance by avoiding unnecessary use of broad spectrum-antibiotics without carrying out sensitivity testing. Pharmacists counseling on diabetes control, regular monitoring and check-up of extremities for any unseen wounds or neuropathic symptoms to be done from time to time.

Keywords: Amputation; Diabetics; Foot Ulcer; Ulceration

Introduction

Diabetes is the fourth leading cause of death worldwide due to secondary complications involving nerve and vascular damage. It involves pathological changes in tissues, vasculature or nerves. Major disorder of Diabetic foot is vascular disease, ulceration, and neuropathy. Neuropathy causes foot deformities and plantar pressure changes which are irreversible and instigate ulcer formation. Increased morbidity has been resulted from diabetic neuropathy with affecting quality of life. In patients with Diabetes Mellitus, autonomic neuropathy symptoms lead to secondary complications like cardiac arrhythmias and diabetic foot ulcers [1]. This condition is a challenge to surgeons with the loss of lower limbs. Increased damage to nerves and vascular supply occurs due to neuropathy with no sensation in the lower limbs as a result of which any trauma occurring to the feet results in slower healing and continuous using of the injured foot would cause more damage at the site and the complete lower limb [2].

Platelet rich plasma is a part of the plasma fraction of autologous blood having platelet concentration above borderline [3]. They are free from communicable pathogens, long lasting, less cost than recombinant human growth factor [4]. It promotes capillary angiogenesis and re-epithelialization thus improving regeneration. Suppression of cytokines helps in reducing inflammation [5]. It has antimicrobial actions towards *Escherichia coli*, Methicillin resistant *Staphylococcus aureus*, *Cryptococcus*, *Candida albicans*, etc. [6], Once amputations are done to the foot chances of re-amputations are increasingly tremendous. Thus, maximum effort should be carried out to avoid its necessity [7].

Case Presentation

A seventy-year-old South-Indian female patient was admitted to the hospital with chief complaints of ulcerations on her left foot which was non-healing for the past two weeks with discharges of foul smelly fish. She had a past medical history of Non-insulin dependent Type-II Diabetes Mellitus and was prescribed with Metformin 500mg+ Voglibose 0.3mg (Sugamet V 0.3mg), Nbut

was on irregular therapy for many years. Poor compliance with medications was observed. The patient initially noticed an abscess on her left foot and sole which later increased in size and ruptured resulting in ulceration of foot. She belonged to low socio-economic class category and did not have any control of her diabetic diet. She had frequent intakes of caffeinated products along with habit of chewing of beetle nuts. She was on menopause, had common habit of self-medication and intake of OTC drugs for her knee pain, fever, cold conditions etc., Lack of awareness for performing routine monitoring of blood sugar levels or urine analysis. On general examination, the patient was conscious, restless, oriented, and afebrile; the patient was examined with fatigue with poor diet. Examination of her lower extremity revealed pitting edema along with gangrene on her diabetic foot. Her laboratorial examinations revealed a wide variation from the normal values (Table 1) her pharmacotherapy was initiated with intravenous administration of Ceftriaxone 1g (Taxim), Metronidazole 500mg (Flagyl), Gentamycin 100 mg (Septopal), B-complex and other supplements. Wound was irrigated with normal saline and the dressing was done from time to time. After few days she was initiated with Platelet rich plasma which was highly rich in growth factors and help in healing process. It is a much better novel and invasive therapy with better results obtained (Figure 1).

Diagnostic parameters	Patient value	Normal values	Inference
White Blood Cells	2230 mg/dl	4000-11000 mg/dl	Decreased
Red Blood Cells	3.31 mill/cc	3.8-4.8 mill/cc	Decreased
Hemoglobin	8.6 g/dl	12-17 g/dl	Decreased
MCV	78.9 fl	76-96 fl	Within limits
MCH	26 pg	27-32 pg	Decreased
MCHC	33	31-35	Within limits
Platelets	4.66 lakhs/cumm	1.5-4 lakhs/cumm	Increased
Lymphocytes	6.7%	20-40%	Decreased
Monocytes	4.5%	2-10%	Within limits
Neutrophils	77%	40-80%	Within limits
Red Blood Sugar	210 mg/dl	80-140 mg/dl	Increased
Urea	18 mg/dl	7-18 mg/dl	Within limits
Creatinine	0.5 mg/dl	0.6-1.3 mg/dl	Decreased
Urine colour	Pale yellow	Pale	
Sugar	Nil	Nil	
Pus cells	10-15	Nil	
Epithelial cells	8-12	Nil	
ESR	25mm/hr	5-20mm/hr	Increased
Temperature	99°F	98.4°F	Increased
Blood pressure	120/80 mm/hg	120/80 mm/hg	
Pulse rate	86/min	71-75/min	Increased
Respiratory rate	22 breaths/min	12-20 breaths/min	Increased

Table 1: Laboratorial examination of the patient.



Figure 1: Diabetic foot condition of the patient with ulceration, gangrene and edema present.

Discussion

Ulcers are skin defects that extend into tissues, muscles, joints and even bones. Treatment is based on health status, reducing the number of amputations, improving quality of life. A control on carbohydrate metabolism and insulin sensitivity could be maintained by physical activity for a period of years [8]. There is a dose association between fibrinolysis and aerobic fitness. Patients with type II DM have an impaired fibrinolytic activity with increased levels of plasminogen activator inhibitor-I (PA-I) [inhibitor of tissue plasminogen activator]

Regular physical activity lowers the triglyceride rich VLDL. Complication of diabetic foot to extremes of amputation could be avoided by early identification of the risk conditions, proper evaluation, empirical therapy with a multidisciplinary team required [9].

Peripheral edema is one of the commonly reported complications of lower limb diabetic foot ulceration. The making use of compression therapy would be more helpful in eradicating the situation but is not followed much. Chronic venous insufficiency is the known common cause due to venous hypertension [10]. It is one among the many reasons in prolonging the healing of wound which reduces capillary blood flow, reducing nutrition and oxygenation for wound healing.

In a chronic non-healing wound there are high levels of Matrix Metalloproteinase (MMP), Neutrophils examined which delays healing. Pre-capillary arterioles in the dermis and vasoconstriction in the arteriovenous anastomoses are directly associated with neuropathy [11]. Peripheral arterial disease almost complicates edema conditions making it difficult to treat. Thus, proper assessment with appropriate therapy is essential for management of condition. Early identification of edematous condition in such situation further reduces complications like cellulitis, ulceration of leg etc., and is an adjunctive therapy for such condition [12].

Non-pharmacological therapy conveyed to her were on the following:

- Having a healthy balanced diet which controls carbohydrate levels in blood, it includes non-fat dairy and lean meats, whole grains, fruits, vegetables, whole grains.
- Avoiding too much of pressure on the affected leg. Active lifestyle helps control diabetes and ease stress.
- Regular reviewing of prescriptions and visiting doctors minimally twice a year especially for eye checkup, foot ulcers and nerve damage.
- Management of stress by engaging in yoga, deep breathing, hobbies bringing relaxation and pleasure.
- Proper hydration through fluids and urinating frequently.

- Washing hands and feet daily with mild soap and lukewarm water, gently drying the feet particularly between toes.
- Making use of clean sock and shoes which does not cause too much of pressure on foot.

Pharmacist counseling to diabetic patients could be on the following concerns in regard to foot complications.

- Complex interplay of primary disease control, lifestyle choices.
- Clinical observations support connections among blood sugar, sole pressure, limb neuropathy which contribute to ulcer manifestations and long-term damage.
- Uncontrolled diabetes sets the body up for underlying damage and poor response to normal foot trauma and pressure.
- Damage by elevated blood sugar in tissue decreases skin thickness, increases skin hardness, increases muscle atrophy, reduces tender and joint mobility, reduces protective pads on feet.
- Changes result from poor weight distribution across soles, friction, skin cracks.
- Blood sugar damage to the ends of nerves and blood vessels in lower limbs also impair sensation and blood flow.
- People with diabetes appear to walk more slowly and have slower reaction times to foot trauma. Overall Poor physical activity habits also increase likelihood of vascular edema or unnoticed nerve or skin changes to encourage a cycle of damage.
- Risk for diabetic foot includes; diabetes for more than 10 years, poor blood sugar control, kidney dysfunction, poor visual activity.
- Poor footwear is one of the most common contributors to initial developing of foot complications.
- In order to maintain foot health, self-checks each day which includes washing, drying, nail clipping and emollient use. Patients are advised against going on barefoot or wearing compression stocking or socks with tight elastic.
- Nail changes that increase the risk of infection and tissue damage are important to note on exams.
- Morbidity of Amputation has a huge quality of life impact and financial impact on patients, families and health care systems.
- Nerve changes inhibit protective sweating that moistens feet to prevent cracks and fissures.
- Pain symptoms include burning, numbness; tingling and limb fatigue which changes over these and worsens at evening. Agents best suited for its treatment are;

- i. First line - Tricyclic Antidepressants
- ii. Second line - Carbamazepine, Gabapentin, Pregabalin.
- iii. Topically- Capsaicin cream on unbroken skin.
- iv. Oral opiates- tramadol or oxycodone
 - Minimize painful sensation as sensory impairment progresses from tingling to full loss of protective sensation, foot injury can go unnoticed. The surrounding muscle structure also weakens and changes gait.
 - Development of diabetic foot ulcer from unnoticed trauma is the primary cause of diabetic foot ulcer.
 - Peripheral neuropathy screening is performed at shorter interval as time with diabetes lengthens.
 - High risk patients include those with a history of foot ulcer, physical deformities, known vascular damage.
 - Examination involves with tuning forks, 10g monofilaments, cotton wool.
 - Large fluctuations of blood sugar or continually high glucose levels impair body's ability to heal skin damage before ulceration occurs and cause vascular or neurologic changes that limit patient awareness of damage.
 - Lifestyle factors which increase ulcer risk include reduced mobility, lack of physical activity, depression, poor nutrition, obesity. Reduced circulation of blood to vessels increase the risk of both ulcers and their infections.
 - Microvascular damage changes blood flow to lower limb skin and reduces oil and sweat gland function in the extremities increasing rates of dry cracks and fissures that trigger ulcers.
 - Poor arterial perfusion mutes local infection. Symptoms like redness and warmth increases propensity of gangrenous spread, it prevents immune cells and antibiotics from reaching infected ulcers to complicate healing and spread infection to surrounding tissue.
 - Foot emergencies in patients with prior ulcers involve new wounds, swelling or discoloration (red, blue or black).
 - Annual foot checkups require nerve and vascular evaluation.

Conclusion

Pharmacist could engage in guiding the diabetic patients on their medications and any other queries raised by the patients regarding the disease which could not be asked to the physicians. Counseling on drugs with their administration, empirical therapy for antibiotics selection by culture sensitivity etc., could be carried out by this group of health care professionals. Patient education is a pharmacist domain that plays a crucial role in disease care. He can play a vital role on health care team in disseminating knowledge to patients about the connections of blood glucose, pressure, numbness and edema to wounds, infections and vascular disease in diabetic foot.

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