



ORIGINAL- ARTICLE



The role of LMWH in fate of diabetic foot infection

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Abstract

Diabetic foot infection holds a big challenge for both the patient and the orthopedic surgeon. This study aimed to explore the possible causes and to evaluate the effectiveness of the treatment diabetic foot infection by use LMWH and antibiotic. Sixty two patients with established diabetic foot infection were registered. All patients with diabetic foot infection underwent immediate or delayed treatment with LMWH (Enoxaparin sodium). Evaluation of diabetic foot infection was done by; careful clinical examination, laboratory investigation, and measurement of percutaneous oxygen tension. According to timing of treatment with LMWH early or late, the patients were divided into three groups early (less than 2 weeks), within 2 weeks, and delayed (more than 2 weeks) treatments. From the total 62 patients, there were 39 females which represent 62.9 % and 23 males represent 37 % of total. Their age range was 28-64 years with the mean age of the patients was 43 years. Majority 42 patients represent (67.7%) of total in the 4rd and 5th decay. The duration between clinical presentation and time of start treatment in less than 2 weeks was 21 patients which represent 33.8% where good prognosis was present, within 2 weeks was 17 patients which represent 27.4% where good prognosis was present and more than 2 weeks was 24 patients which represent 38.75 majority of patients were bad prognosis was present. Good response in 69.3% this group was present within 2 weeks and less and start to get treatment with LMWH (Enoxaparin sodium) and the other group was 30.6% present late more than 2 weeks and start treatment too late and get bad response. In conclusion, the chief causes that stand behind diabetic foot infection which we revealed by our successive clinical, radiological, laboratory and active operative judgments in this study were The most common precipitating factors penetrating wound in planter surface of foot in 38 patients which represent 61.2% followed by trauma 12 which represent 19.3% followed by thermal injury by electrical source and wear tight shoes was 6 respectively which represent 9.6%. Early treatment with LMWH and antibiotic express a good response in all patients present within and less than 2 weeks because LMWH, can improve the capillary circulation in the ulcer margin, which positively influences the healing process of chronic foot ulcers in diabetic patients.

Key words: DM, foot infection, role of LMWH evaluation, treatment

1 | INTRODUCTION

Diabetic foot ulcers (DFUs) are common and disabling, giving rise to significant morbidity and mortality as well as worldwide socioeconomic problems. Despite treatment, DFUs easily become

chronic wounds and may lead to major lower limb amputations. The global number of diabetic patients in year 2000 was 171 million individuals; the number is expected to grow to 366 million in the year 2030⁽¹⁾. Diabetic complications may be disabling or even life threatening⁽²⁾. Diabetic foot is a long-standing diabetes complication in which

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which infection, ulceration, and/or necrosis of tissues of the lower limb occurs, owing to presence of neuropathy and peripheral artery disease as basic etiological factors⁽³⁾. Diabetic foot ulcers can be recognized by a clinical pattern including infection, ulceration, and/or necrosis of tissues of the lower limb. The foot ulcer incidence rate ranges between 2% and 10% among patients with diabetes mellitus⁽⁴⁾. According to various studies, there is 15-46 fold higher Lower Limb Amputation risk in diabetics as compared to general population⁽⁵⁾.

Peripheral Artery Disease (PAD) is a contributing factor to the development of foot ulcers in up to 50% cases and there is increased risk of amputations and hospitalization with increasing severity of infection⁽⁶⁾,⁽⁷⁾.

The etiology of diabetic foot ulcers can be grouped into three major classifications: neuropathic (due to damage of the nerves); ischemic (due to a poor blood supply); or neuroischaemic (due to damage to the nerves and a poor blood supply). The loss of sensation caused by peripheral neuropathy means that injuries to the feet may not be noticed when they happen, and these, potentially, can develop into more serious wounds. If the blood supply is partially or completely blocked, tissue will begin to die, which can result in the development of painful ulcerations on the feet. For healing to occur it is of crucial importance to have intact microcirculation in the skin around the ulcer, and adequate arterial blood supply to the ulcer area.

Hyperglycemia can decrease fibrinolytic activity, which increases blood viscosity and induces a high coagulation state in people with DM⁽¹¹⁾. The high coagulation state can damage vessel walls and lead to vascular dysfunction, coagulation-anticoagulation disorders and hematological disturbances⁽¹²⁾. This high coagulation state contributes to the slow healing of diabetic foot ulcers. heparin has potent anticoagulant properties that are used to treat and prevent clotting disorders where there is excessive or undesirable clotting. Heparins can be separated into two groups

1-unfractionated heparin (UFH) (heparin in a range of molecular sizes).

2- Low molecular weight heparin (LMWH) (smaller heparin molecules).

Both these are potent antithrombotic agents that also enhance fibrinolytic activity and have anti-inflammatory effects. UFH is a naturally-occurring polysaccharide that works as an anticoagulant by inhibiting the activity of

several blood coagulation factors. Laboratory work has shown that heparin-induced precipitation of low-density lipoprotein in the blood causes a reduction in the levels of fibrinogen (a clotting agent). This effect, if transferable to people, could lead to the limiting of necrotic tissue and a reduction in the amputation rate in people with severe diabetic foot syndrome⁽¹⁵⁾.

Studies have claimed that heparin can improve haemorrhological parameters, increase arterial blood supply and enhance healing in patients with diabetic foot ulcers⁽¹⁶⁾.

LMWHs consist of short chains of polysaccharide, obtained from various methods of fractionation or enzymatic depolymerization of UFH⁽¹⁷⁾. LMWH has advantages for the treatment of diabetic foot ulcers compared to UFH. Firstly, LMWH has more favorable bioavailability and pharmacokinetics, so it can be administered subcutaneously without monitoring. Secondly, LMWH may result in fewer bleeding complications due to a less obvious effect on platelet function and vascular permeability⁽¹⁸⁾, which means that it can be used long-term as an out-of-hospital treatment because of its relative safety. Subcutaneous injection of LMWH, can improve the capillary circulation in the ulcer margin, which positively influences the healing process of chronic foot ulcers in diabetic patients⁽¹⁹⁾. They have beneficial effects on local tissue microcirculation and oxygenation through the inhibition of thrombin generation and increases in plasma fibrin gel permeability, which may promote vascular perfusion in the ischemic foot significantly and lead to improvements in its blood supply. They can promote healing of chronic ulcers by stimulating production of basic fibroblast growth factor and transforming growth factor-beta⁽²¹⁾.

Laboratory work has also shown that they have positive effects in vitro, including promotion of the synthesis of heparin sulphate in endothelial cell cultures⁽²²⁾, and the proliferation of fibroblasts obtained from diabetic ulcers⁽⁷⁾. Heparin can promote neo vascularization in ischemic limbs by improving the structure and number of capillaries^{(13),(14)}. All these activities mean that heparin and related substances might act as a scaffold to enhance the activity of growth factors and reduce the inflammatory response in the ulcer bed.

2 | SUBJECTS AND METHODS

This prospective study was carried out in orthopedic wards in Al-mawany teaching Hospital throughout four years (April 2018 – April 2022). Sixty two Patients were hospitalized with clinical signs highly suggestive foot infection in diabetic patient detailed history was obtained from these patients with special emphasis on time of development of infection Patients were examined by different doctors for the signs of diabetic neuropathy and ischemia using the routine physical examination. All patients The routine haematological investigations were carried out in from of Hb%, R BI S, BI Urea and measure O2 tension by used of pulse oximeter

All patients The routine haematological investigations were carried out in for of Hb%, R BI S, BI Urea and measure O2 tension by used of pulse oximeter All patients were subjected to send for x ray, nerve conduction study (Nerve conduction studies are generally considered the criterion standard for diagnosing peripheral neuropathy) and Doppler ultrasound examination for vessel of lower limb. All patient start treatment with Antibiotic, simple wound debridement and heparin like substance for 15 days and follow them every 5 days ,15 days, month and two months searching for singe of responding.

3 | RESULTS

During the period of four years (April 2018 – April 2022). Sixty two patients with foot infection in diabetic patient were studied. There were 39 females which represent 62.9 % and 23 males represent 37 % of total. The mean age of the patients was 43 years. The youngest patient age was (28) year and oldest one was (64). Majority 42 patients represent (67.7%) of total in the 4rd and 5th decay. The evaluation of presenting symptoms revealed foot ulcer was the most common presenting symptom found in 28 patients which represent (45.1%). The least presenting symptoms was paresthesia found in 8 patients which represent (12%). Table (1)

The most common precipitating factors penetrating wound in planter surface of foot in 38 patients which represent 61.2% followed by trauma 12 which

represent 19.3% followed by thermal injury by electrical source and wear tight shoes was 6 respectively which represent 9.6%. The group of patients which present within 2 weeks and less represent 43 patients which represent 69.3% has good response to treatment, while the other 19 patients present after 2 weeks which represent 30.6% has poor response to treatment. table (2) 49 patients which represent 78.8% have got good response to treatment while the rest 13 patients which represent 19.9% have got poor response to treatment. Table (3) The nerve conduction study was performing and the result was peripheral neuropathy for sensory and motor in all patient 62 patients which represent 100%.

The duration between clinical presentation and time of start treatment was less than 2 weeks was 21 patients which represent 33.8% where good prognosis was present, within 2 weeks was 17 patients which represent 27.4% where good prognosis was present and more than 2 weeks was 24 patients which represent 38.75 majority of patients were bad prognosis was present.

4 | DISCUSSION

The global number of diabetic patients in year 2000 was 171 million individuals; the number is expected to grow to 366 million in the year 2030⁽¹⁾. Diabetic complications may be disabling or even life threatening⁽²⁾. Diabetic foot is a long-standing diabetes complication in which infection, ulceration, and/or necrosis of tissues of the lower limb occurs, owing to presence of neuropathy and peripheral artery disease as basic etiological factors⁽³⁾. The gold standard for the assessment of response to the use of LMWH in treatment of Diabetic foot ulcers in our study is the clinical experience. In order to recognize diabetic foot ulcers, the clinician must perform regular neurological examinations of the lower limb and the stat of lower limb vascularity and presence of ischemia of lower limb to assess for neuroischemic compromise. If diabetic foot ulcers are suspected, immediate referral to a hospital and start management. In presenting study females in the fourth and fifth decades of life are more prone to diabetic foot ulcers than male. In our study there was no age tend to be immune against Diabetic foot ulcers, we reported 28 years old as youngest patient, in our series people in the fourth and fifth

decades of life were commonly affected. The most common precipitating factor was penetrating wound and the least cause was thermal injury. By the nerve conduction study the finding was motor and sensory peripheral neuropathy of both lower limb nerve in all patients. By colored Doppler ultrasound examination about 9 patients with atherosclerotic changes in the proximal vessels of lower limb and the rest of patients has not. By pulse oximeter (Arterial oxygen supply can also be measured by transcutaneous oximetry.⁽²⁵⁾ all patients have low oxygen tension at time of examination. The group of patients which present within 2 weeks and less represent 43 patients which represent 69.3% has good response to treatment, while the other 19 patients present after 2 weeks which represent 30.6% has poor response to treatment. Good response in 69.3% this group was present within 2 weeks and less and start to get treatment with LMWH and the other group was 30.6% present late more than 2 weeks and start treatment too late and get bad response.

In our study we found that female patients whom has foot ulcer was response to LMWH (Enoxaparin sodium) in form of 34 females has got responded from complete healing to partial foot amputation and just 5 patient show bad response to treatment and end with major amputation above knee joint all those 5 patients present after 2 weeks, while male patient 20 out of 23 patients has good response to treatment just 3 patients was failed to respond to treatment and end with major amputation above knee joint and those patients was present after 2 weeks and more .

In our observation we found 49 patients which represent 78.8% have good response to our treatment ranging from complete healing, minor amputation and toe amputation 20.9%, 37% and 20.9% respectively as a result of started treatment with LMWH more early. While the rest 13 patients which represent 20.9 % have got poor response to treatment as a result of started treatment to late. By use of Enoxaparin sodium amp 2000 unit twice a day for all patients present to us early less the 2 weeks has got very good response to treatment, patients present to us within 2 weeks has got good response to our treatment, while patients present with more than 2 weeks has got less response. and

change the fate of foot from major amputation to less severity amputation. Rullan indicated that diabetic foot ulcers treated with bemiparin, another LMWH preparation, administered once daily by subcutaneous injection were observed to have better ulcer improvement rates, complete healing rates and few adverse reactions⁽²⁰⁾.

I disagree with Nicolaas C. Schaper found that Pharmacological treatments to improve perfusion have not been proven to be beneficial. I agree with Rietzsch and his collage in their thought that Fibrinogen levels were reduced after LMWH. treatment. No severe complications were noted. I Agree with Bonnie in his believed that evidence is accumulating for LMWH and their potential role in wound healing. Clinical trials have shown efficacy of subcutaneous low-molecular-weight heparin in selected patients with neuroischemic diabetic foot ulcers.

I Agree with Jornekog G in his postulated that the results indicate that LMWH positively influences the healing process of chronic foot ulcers in diabetic patients, possibly by improving the capillary circulation in the ulcer margin, in spite of an unchanged arterial and total skin microcirculation of the region

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