

## Diabetic Foot Infections - Lessons from Evidences and Experiences

Lázaro-Martínez JL\*

Diabetic Foot Unit, Facultad de Medicina, Universidad Complutense de Madrid, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, Spain

Diabetic foot is the leading cause of non-traumatic lower extremity amputation. Every 30 seconds a lower limb is lost to diabetes somewhere in the world, 85% of these being preceded by non-healing ulcer [1]

The main factors affecting healing in diabetic foot ulcers and therefore prognosis include peripheral vascular disease (PVD) and infection. Although the prevalence of peripheral vascular disease has increased among in U.S.A. and UE countries, conversely, an infected foot ulcer precedes approximately 60% of amputations, making infection perhaps the most important proximate cause of this outcome [2].

Diabetic foot infections can be classified as mild, moderate or severe affecting soft tissues and/or bone [2]. Soft tissue infections are more serious as they affect deeper tissues and when are associated with necrosis [3]. Urgent aggressive debridement combined with antibiotic treatment are mandatory in this type of infections to reduce or minimize amputations. A misdiagnosis or therapeutic's delay in this type of infections can limb-threatening and even the lives of these patients [4].

Although necrotizing soft tissue infections are most severe, bone infections are more frequent and in many occasions an early diagnostic is not easy. Sometimes osteomyelitis has not inflammatory signs, pus discharge, bad odour and neither clinical signs have presented. In this situation osteomyelitis offers many diagnostic's doubts.

First of all osteomyelitis is not equal in all cases: clinical presentation, general inflammatory markers and evolution can be different in every patient. Our research group has shown that there are 4 types of bone infection, regarding histopathologic findings [5]: Acute Osteomyelitis (AO), Chronic Osteomyelitis (C=O), Chronic-Acute Osteomyelitis (CAO) and Fibrosis Osteomyelitis(FO). Association between inflammatory clinical signs and CO and FO were very poor, so clinical diagnostic could be more difficult in these cases.

Furthermore sometimes suspected bone infection does not accompanied by a standard diagnostic's protocol. It has been shown that the combination of clinical diagnostic tests such as Probe-To-Bone test and simple plain XR can bring similar diagnostic validation which provides a RMN [6]. However, in many settings patients undergo expensive diagnostic tests subject to delays and waiting, which in many cases prevents early diagnosis of bone infection.

In the other hand osteomyelitis have 4 different classes regarding clinical and pathological features [7]. Osteomyelitis without ischemia and without soft tissue involvement (class 1), osteomyelitis with soft tissue involvement (class 3) and osteomyelitis with ischemia and with soft tissue involvement (class 4). This division into 4 classes showed a statistically significant trend toward increased severity, amputation rate and mortality. An appropriate approach of osteomyelitis can be reach 100% of limb salvage in class 1.

Probably due to osteomyelitis does not have a homogeneous clinical presentation and by the potential deterioration regarding PVD and/or the presence of soft tissue necrosis, there is no a universal agreement about the most appropriate approach.

The optimum approach is currently being debated and the definitive role of surgery and antibiotic treatment is not sufficiently well clarified.

Both alternatives offer advantages and disadvantages. Medical treatment can be applied in any Health Care 's setting (primary care or hospital), does not require surgeons trained in diabetic foot surgery and avoids the financial cost and potential medical/surgical complications of surgical procedures. Surgical procedures contrary offers higher rates of limb salvage, reduced amputation's rates, could also reduce the period of antibiotic therapy, can remove a bone deformity could have a prophylactic effect eliminates the ulcer causing deformity and allows for bone samples for histological and microbiological analysis [8].

The main criticism that has been made in studies on exclusively with antibiotics treating is that most of them diagnostic confirmation bone infection that has been removed is not provided , because the remission of inflammatory signs, 'apparent remission', or limb salvage are not appropriate endpoints for demonstrating that the bone infection has actually been eradicated. However, in some types of osteomyelitis is difficult to assess the patient's improve according clinical signs of infection, simply because they do not exist [9].

Recently a randomized comparative trial has been published evaluating antibiotics versus conservative surgery for treating diabetic foot osteomyelitis [8]. In this study 52 patients with diabetic foot osteomyelitis were randomized to receive antibiotic treatment exclusively (AG) or conservative surgery (SG). Eighteen patients (75%) achieved primary healing in the AG and 19 (86.3%) in the SG (p=0.33). The median time to healing was 7 weeks (Q1 5, Q3 8) in the AG and 6 weeks (Q1 3, Q3 9) in the SG (p=0.72). No difference was found between the two groups regarding minor amputations (p=0.336). The question is what lesson we can take from this study that makes draw in both options' treatment?

Analyzing inclusion and exclusion criteria of patients probably could be defined a patient's profile in which the first option's treatment should be the exclusively antibiotics: patients with neuropathic forefoot ulcers complicated by osteomyelitis without ischemia or necrotizing soft tissue infections. In such patients should be begun with broad-spectrum's antibiotic therapy for 90 days and then evaluating patient's improve. If patient within 90 days with antibiotic therapy suffer from a complication (exposed bone or soft tissue

**\*Corresponding author:** Lázaro-Martínez JL, Diabetic Foot Unit, Facultad de Medicina, Universidad Complutense de Madrid, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, Spain, Tel: +34-91 394 22 03; E-mail: [diabetes@ucm.es](mailto:diabetes@ucm.es)

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necrosis appears) or clinical signs of infection worsen, conservative surgery should be consider.

Conservative surgery consisting of removal of the infected bone without performing amputation of any part of the foot and has provided very good results in patients well vascularized, even when bone infection is accompanied by soft tissue infection, with 100% of limb salvage rates [10].

In my opinion osteomyelitis is debated still today due to various causes: the first and most obvious is the absence of evidence to the best option of treatment: antibiotics versus surgery. The second reason is the heterogeneity of health care settings where the diabetic foot is being treated. In some units lacking of surgeon specialized in diabetic foot surgery or in the other hand, lacking of internal medicine doctors specialised in diabetic foot infections, the first treatment is always the option in which team members are better trained. If patient is being treated by diabetic foot's surgeon probably surgery it will be the first option instead when bone infection is treated in the absence of surgeons, probably it will try to resolve it by antibiotic treatment.

Furthermore, in a non-specialized diabetic foot unit, usually there is a misconception from osteomyelitis. Most professionals understand diabetic foot osteomyelitis infection equal, but it is not. The heterogeneity of clinical presentation, and dissemination of their involvement in bone tissue coupled with the diversity in the inflammatory response of patients with the presence of some degree of peripheral vascular disease, are making hard to treat this complication with just one treatments' option. Not every patient needs to be treated differently, but treating all alike is not the most desirable option.

Definitely stratification or classification of diabetic foot osteomyelitis attending general and local criteria, could establish a standard protocol that could respond to most cases. Meanwhile further research is the only way to improve the care of our patients with diabetic foot.

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