

Choices and Challenges of Antibiotics Therapy in Diabetic Foot Infection

Diabetic foot can be defined as any foot pathology that results directly from diabetes mellitus or its long-term complications.^[1] This is one of the most common complications of diabetes mellitus requiring hospitalization for not only leading to significant morbidity an expensive investigations and costly treatment but also for progression to limb-threatening and life-threatening diabetic foot infection. The two main causes of diabetic foot wounds are neuropathy and ischemia.^[2] Among the diabetic patients, the prevalence of foot ulcer ranged from 12% to 25%.^[3] Diabetic foot wounds are prone to get infected which spread through soft tissue and the bone as a result of impaired defense mechanisms and delayed process of wound healing^[4] advancing the wound age. A study from South India reported the prevalence of infection among patients with diabetic foot up to 11%.^[5] Similar studies are not many from the vast population of patients with diabetes mellitus in our country and the one by Jain and Barman published in the current issue of Indian Journal of Endocrinology and Metabolism is most welcome addition to published data of the region.^[6] Interestingly, the size of the problem of diabetic foot infection is not similar in different geographical regions of India, and the major determinants of data variability are patients' access to or availability of diabetic foot care facilities in the particular region.^[7] The existing health-care facilities in the developing part of the world do not focus diabetic foot care adequately as their resources are drained to detection and control measures of hyperglycemia of diabetic patients.

The challenges are numerous and unique to developing countries for the diabetic foot management. Large number of patients with diabetic foot ulcer has advanced grades of diabetic foot ulcers not amenable to available treatment in resource constraint health-care system. The uniqueness also lies in the presentation of diabetic foot infection in patients from different regions with diabetic foot that has been briefly referred to in the following paragraphs. Microbial infection changes characteristics due to multiple attempts of inappropriate antibiotics therapy (type, doses and duration) initiated by primary care physicians. It is needless to reiterate that diabetic foot care mandates involvement of patients and caregiver together with education and training of their performance as an example of "shared care."

Sporadic information is available regarding the prevalence and characteristics of microbial infection of diabetic foot through some of the published studies conducted in our country.^[8,9] In a prospective study^[8] conducted during 2009, on 62 diabetic patients highlighted some of the characteristics of diabetic foot infection. Among the study participants, 35% patients had polymicrobial infection and 21% had sterile culture by standard techniques. Gram-negative outnumbered Gram-positive isolates

by almost two times. *Escherichia coli* were the most common among the Gram-negative isolates. Methicillin resistant *Staphylococcus aureus* (MRSA) was only 44.7% in this study while it was 100% in a study from Iran.^[10] In the article published by Jain and Barman, in this issue of journal has reported dominance of *Staphylococcus* infection over Gram-negative *E. coli* with MRSA around 41% in diabetic foot ulcer.^[6]

The variability in the characteristics of diabetic foot infection has many issues

- Factors that render it to wound infection such as age of the wound, poor wound hygiene, and host immunity
- Polymicrobial nature of wound infection due to chronicity of the nonhealing ulcer
- Development of MRSA and other microbial resistance to antimicrobial agents
- Pretreatment with antimicrobial agents on empirical basis paving way to emergence of antimicrobial resistance or transforming the wound culture sterile.

These challenges are not amenable to simple measures. Microbial study of diabetic foot wound with identification of sensitivity to antimicrobial agents would help in choosing the appropriate antibiotics but the absence of isolate from the infected wound site or polymicrobial nature of infection remains an insurmountable challenge. The molecular techniques that help identify the isolate from the wound site otherwise sterile on routine evaluation are a sure way but inaccessible to most of the clinics dedicated to diabetic foot care. My group has published a paper using the molecular technique to identify the diversity and colonization of microbial agents undetected by standard culture techniques in the tissue from diabetic foot ulcers.^[11] This would be an ideal measure yet to emerge a tool to strengthen the diabetic foot clinic for the handling of diabetic foot infection in cost-effective manner. Anaerobic infection of diabetic foot infection had been held as a challenge for successful eradication of infection but surprisingly enough our own study showed that anaerobic infection of diabetic foot did not require specific intervention.^[12] Anaerobes do not pose risk with the healing stages of the wound given that aerobic infection has been eradicated in an efficient manner.

In the paper published by Jain and Barman,^[6] in the current issue of this journal has also covered points of selection of antibiotics for diabetic foot infection and this has been in the line of the earlier studies showing the predominance of Gram-negative *E. coli* infection in diabetic foot infection of longer duration. Piperacillin and tazobactam are a good parenteral antibiotic followed by newer generation cephalosporins. Quinolones, aminoglycosides, and macrolides are the next choices of

antibiotics. Tigecycline, vancomycin, and teicoplanin are to be reserved for the limb- and life-threatening infection as we would not have further choices consequence to early use of these agents. *Pseudomonas* infection is occasional in the diabetic foot wound particularly in those having burn injury of the foot. Aminoglycosides and the tigecycline might eradicate *Pseudomonas* if the newer generation cephalosporins have not shown promise in the containment of the infection. Choice of antibiotics therapy, therefore, depends on the severity of infection, involvement of bone, previous antibiotics therapy, the type of microorganism in wound isolate, patient's comorbid conditions, cost, and safety profile of the agents. It should be reflex phenomena in the mind of the treating physicians to adhere to the above viewpoint which has been very elegantly outlined in the International Working Group on the Diabetic Foot (IWGDF) guidelines for the diabetic foot infection.^[13]

Evaluation of osteomyelitis is essential to decide the duration of antibiotics therapy. Probe to bone test raised erythrocyte sedimentation rate and radiological features are most helpful in decision-making for the presence of diabetic foot osteomyelitis. Magnetic resonance imaging, single-photon emission computed tomography scan, and other emerging techniques have a very weak role in fixing the problem of Diabetic Foot Osteomyelitis^[14] as they have poor cost-effectiveness.^[13,15,16]

IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes covers almost every aspect. It has mapped the steps to be taken for treating diabetic foot infection addressing the need of immediate empirical or rational selection of antibiotics, route of administration, duration, and monitoring of untoward effects. It has also attempted to undermine the measures which have a weak level of evidence in containment of infection such as local antimicrobial agents, hyperbaric oxygen therapy, larval therapy, granulocyte colony stimulating factor therapy, negative pressure wound therapy, and silver dressing.

The issue of particular importance in the developing country has also been mentioned in the guideline. The emphasis on diabetic foot care should aim for preventing infection by wound hygiene, wound assessment, and appropriate measures for good glycemic control supported by improvement in limiting factors for wound healing involving offloading, correction of anemia, and finally wound debridement. The future of management of diabetic foot infection lies in use of the advanced molecular techniques for the identification of microorganisms combining next generation antibiotics therapy with restoration of the blood flow to the ulcer region and enhancement of the immunity of individuals for tissues infections.

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DOI:

10.4103/ijem.IJEM_481_17

How to cite this article: Singh SK, Gupta B. Choices and challenges of antibiotics therapy in diabetic foot infection. *Indian J Endocr Metab* 2017;21:647-8.