Journal of Infectious Diseases & Therapy

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J Infect Dis Ther 2022, 10:5

Short Communication Open Access

Practical and Clinical Aspects of Pseudomonal Diabetic Foot Infections

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Received: 22-Jul-2022, Manuscript No. JIDT-22-69972; **Editor assigned:** 25-Jul-2022, PreQC No. JIDT-22-69972 (PQ); **Reviewed:** 08-Aug-2022, QC No. JIDT-22-69972; **Revised:** 15-Aug-2022, Manuscript No. JIDT-22-69972 (R); **Published:** 22-Aug-2022, DOI: 10.4172/2332-0877.1000512

Citation: Soldevila-Boixader L, Uckay I (2022) Practical and Clinical Aspects of Pseudomonal Diabetic Foot Infections. J Infect Dis Ther 10: 512.

Abstract

In Diabetic Foot Infections (DFI), the (empirical) antibiotic therapy bases on the clinical severity of infection, the local epidemiology of pathogens, and their susceptibility patterns. *Pseudomonas aeruginosa* is a particular microorganism that has a different predominance between the geographical areas. *P. aeruginosa* also reveals several virulence factors and resistance mechanisms that make it necessary for the clinician to identify it early. Characteristics of pseudomonal DFIs (chronic ulcers, possible greenish color, selection by current antibiotic therapy, maceration, calcaneal localization) might be helpful to think on *P. aeruginosa*. The ultimate proof, however, remains the deep microbiological cultures. In terms of therapy, available evidence does not seem to require combined regimens or a prolongation of the targeted systemic therapy.

Keywords: Diabetic foot infection; Ulcer; Management; Diagnosis; *Pseudomonas aeruginosa*

About the Study

The Diabetic Foot Infections (DFIs) are increasing worldwide and are associated to substantial morbidity, costs, failure risks and adverse events related to therapy. Some microorganisms produce more bacterial virulence mechanisms, and biofilms, than others. *Pseudomonas aeruginosa* is optimized to invade into the deeper wound bed tissue impairing the wound healing, surviving in anaerobic conditions and collaborating with cell death [1]. It is naturally resistant to many antibiotics used for mild and moderate DFIs (aminopenicillins, 1st and 2nd generation cephalosporins) and has the capacity of acquiring resistance during therapy [2].

P. aeruginosa DFI is rare in temperate geographic areas (7%-12%) compared to (sub) tropical regions. In South Asia or the Middle East, the presence of *P. aeruginosa* in DFI yields a variability between 5% to 30% [3]. The clinical features of pseudomonal DFIs make it difficult for clinicians to recognize its presence [4] and the optimal antibiotic regimens remain unknown. We discuss frequent unresolved issues regarding pseudomonal DFIs.

We reviewed the most relevant publications regarding the management of pseudomonal DFI in PubMed and the internet, and add practical aspects basing on our own clinical experience. In this communication, we do not pronounce on the antibiotic choices for a targeted treatment of pseudomonal DFI that are highlighted in almost all guidelines on DFI management [4,5].

Diagnosing the presence of Pseudomonas

The two major DFI guidelines (i.e. IWGDF [5] and IDSA [4]) recommend an empirical antibiotic coverage for *P. aeruginosa* only in tropical/subtropical settings (where the prevalence is high), or when *P. aeruginosa* has been already isolated within the last weeks (risk of recurrence), for severe infection (rapidly progressing infection with anticipated tissue loss), or in clearly macerated DFU infections [4,5]. *P. aeruginosa* is ubiquitous in water in the community setting. Several publications link a *P. aeruginosa* infection to hydrotherapy, heated swimming pools and spas [6].

In a prospective trial, we tried to identify the "yellowish-green" wound exudate and the characteristic grapefruit-like smell, as predictive elements for pseudomonal DFI. The sensitivity of these combined visual and olfactory features was too low (32%), even for experienced surgeons, internists, or nurses [7] treating DFI patients for years and decades. Other research groups used a fluorescent light to detect Pseudomonas in contaminated DFUs, which works. However, this tool cannot necessarily predict the need for an anti-Pseudomonas antibiotic therapy; for which further (clinical) studies are needed [7]. Anatomically speaking, a macerated DFU in the calcaneal zone largely increases the chance of pseudomonal involvement [8,9], while prior amputations and iterative wound dressings could be other clues for Pseudomonas, which, again, should be evaluated in prospective studies [10]. Today, the only indication for an anti-Pseudomonas antibiotic therapy in DFI are positive microbiological deep tissue samples, sepsis related to DFI; and maybe a severe infection in a setting with a very high prevalence of *P. aeruginosa*. The use of the Gram stain to tailor an empirical treatment should also be validated. In our regions, most Gram-negative pathogens are fermenters (no Pseudomonas spp.), remaining susceptible to standard antibiotics [4,5].

Antibiotic regimens

Some author groups treat severe pseudomonal infections, such as bacteremia or ventilator-associated pneumonia, with a combination therapy [2]; at least initially and particularly in immune-compromised

patients. Likewise, a combined regimen with beta-lactams agents and colistin is proposed by some researchers for almost all orthopedic, multidrug-resistant pseudomonal infections, especially when they are resistant to quinolones [11]. However, such an approach in DFI is debatable [12], as the diabetic foot is different from the aforementioned infections with a much lower incidence of bacteremia [2]. A Genevian research group retrospectively assessed all their DFIs. Among the 104 pseudomonal cases, there was no association between failure of treatment and the total duration of antibiotic therapy, duration of intravenous therapy, duration of combined antibiotic therapy, or the duration of oral (fluoroquinolone) therapy. Among the 15 cases of pseudomonal recurrence, only 2 (13%) developed resistance to the mono-therapeutic antibiotic agent used for the index episode [13].

Conclusion

The proof of a pseudomonal involvement n DFI relies on microbiological cultures, while the presence of a maceration, the occurrence in a (sub) tropical setting, or a calcaneal infection significantly increases its probability. For pseudomonal DFIs, other than choosing an antibiotic agent that is active against the organism, it does not appear necessary to treat with a different regimen compared with the mono-agent therapy of non-pseudomonal DFIs.

Acknowledgments

LS-B was supported by a grant from the Spanish Ministry of Education (FPU2018-02768) and by a mobility grant provided from the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC).

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