

-Additional material-

Review

Diabetic foot ulcers: current advances in antimicrobial therapies and emerging treatments

Jesus M Ramirez-Acuña^{1†}, Sergio Cardenas^{1†}, Pedro Marquez-Salas^{1,2}, Idalia Garza-Veloz^{1,2*}, Aurelio Perez-Favila^{1,2}, Miguel Cid-Baez¹, Virginia Flores-Morales³, and Margarita L Martinez-Fierro^{1,2*}

¹ Molecular Medicine Laboratory. Unidad Academica de Medicina Humana y Ciencias de la Salud, Universidad Autonoma de Zacatecas. Carretera Zacatecas-Guadalajara Km.6. Ejido la Escondida, C.P. 98160 Zacatecas, Mexico

² Unidad Academica de Ingenieria Electrica, Universidad Autonoma de Zacatecas, Jardín Juárez 147, Centro, 98000 Zacatecas, Mexico

³ Laboratorio de Sintesis Asimetrica y Bioenergetica (LSAyB). PA de Ingeniería Química, UACQ, Universidad Autonoma de Zacatecas. Carretera Zacatecas-Guadalajara Km.6. Ejido la Escondida, C.P. 98160 Zacatecas, Mexico.

[†] Equal contributors

* Correspondence: idaliaqv@uaz.edu.mx (I.G-V); margaritamf@uaz.edu.mx (M.L.M-F)

Additional Table S1. Conventional antibiotic therapies according to the DFU infection degree.

Infection severity (IDSA)	Recommended antibiotic/therapy regimen	Bacteria coverage	Monitoring	Reference
Uninfected	N/A	N/A	N/A	N/A
Mild	Topical antiseptics + oral antibiotics	Broad-spectrum activity, antifungal and antiviral properties.	Thyroid dysfunction (povidone iodine 10%)	[1]
	- Povidone iodine 10% solution - Chlorhexidine - Acetic acid 5% - Silver compounds		Ear toxicity (chlorhexidine)	
Moderate	Topical antiseptics + oral antibiotics	Activity against Gram +, Gram -, <i>S. aureus</i> MSSA, anaerobes.	Allergic reactions	[2–4]
	- B-lactams (Amoxicillin-clavulanate, Ampicillin) - Dicloxacilline - Cephalosporin's (Cephalexin, Cefoxitin, Ceftriaxone, Ceftazidime). - Quinolones (Ciprofloxacin, Levofloxacin). - Metronidazole - Clindamycin		QT prolonging (Quinolones, clindamycin) Nephrotoxicity (Vancomycin)	
Severe	Combination of Intravenous	Broad	Allergic	[2–7]



	antibiotics	spectrum	reactions
	- Piperacillin/tazobactam + Clindamycin	(Gram +, Gram -),	QT prolonging (Quinolones, clindamycin)
	- Carbapenems (meropenem, imipenem, ertapenem)	MRSA, <i>P. aeruginosa</i> , anaerobes.	Nephrotoxicity (Vancomycin)
	- Ampicillin/Sulbactam		
	MRSA		
	- Vancomycin		
	- Linezolid		
	- Daptomycin		
	<i>P. aeruginosa</i>		
	- Cefepime		
	- Ceftazidime		
	- Meropenem		
	- Piperacillin/tazobactam		
	Anaerobes		
	- Metronidazole		
	- Clindamycin		
	Osteomyelitis		
	- Quinolones		
	- Linezolid		
Term of treatment (IDSA)	<i>Mild infections:</i> 1–2 weeks' treatment. <i>Moderate-Severe infections:</i> 2–3 weeks' treatment.		
Assessment of wound treatment	Every 2 weeks and at every dressing change.		

References

1. Alavi, A., et al., *Diabetic foot ulcers: Part II. Management*. Journal of the American Academy of Dermatology, 2014. **70**(1): p. 21.e1-21.e24.
2. Tayeb, K.A., et al., *Managing infection: a holistic approach*. J Wound Care, 2015. **24**(Sup5b): p. 20-30.
3. Smith, K., et al., *One step closer to understanding the role of bacteria in diabetic foot ulcers: characterising the microbiome of ulcers*. BMC Microbiology, 2016. **16**: p. 54.
4. Aumiller, W.D. and H.A. Dollahite, *Pathogenesis and management of diabetic foot ulcers*. Journal of the American Academy of PAs, 2015. **28**(5): p. 28-34.
5. Saseedharan, S., et al., *Epidemiology of diabetic foot infections in a reference tertiary hospital in India*. Brazilian Journal of Microbiology, 2018. **49**(2): p. 401-406.
6. Roberts, A.D. and G.L. Simon, *Diabetic foot infections: the role of microbiology and antibiotic treatment*. Semin Vasc Surg, 2012. **25**(2): p. 75-81.
7. Karri, V.V.S.R., et al., *Current and emerging therapies in the management of diabetic foot ulcers*. Current Medical Research and Opinion, 2016. **32**(3): p. 519-542.
8. Everett, E. and N. Mathioudakis, *Update on management of diabetic foot ulcers*. Annals of the New York Academy of Sciences, 2018. **1411**(1): p. 153-165.