Minocycline: An Old Drug for a New Bug: Multidrug-Resistant \textit{Acinetobacter baumannii}

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\textit{Acinetobacter baumannii} is listed in the Centers for Disease Control and Prevention’s (CDC) report “Antibiotic Resistance Threats in the United States, 2013” as 1 of 18 microorganisms whose threat level is “urgent,” “serious,” or “concerning” according to their current and projected health and economic impacts [1]. The \textit{A. baumannii} threat level is ranked as “serious” and carries a warning that this organism requires prompt and sustained action by healthcare providers to ensure that this problem pathogen does not continue to become more resistant to antimicrobials and spread. The CDC estimates that nearly 7000 of 12,000 (63\%) healthcare-associated \textit{Acinetobacter} infections are multidrug resistant (MDR), defined as resistance to $\geq 3$ different classes of antimicrobials. Hospitals around the world are witnessing the loss of antibiotics for the treatment of MDR-\textit{A. baumannii} (MDR-AB) infections [2]. The lack of clinically effective antimicrobials to treat \textit{A. baumannii} infections has led clinicians to reevaluate other “older” agents for the treatment of MDR-AB.

Minocycline is an "old drug" that was first introduced in the 1960s. It is available both intravenously and orally with United States Food and Drug Administration approval for the treatment of infections caused by \textit{A. baumannii} [3]. The intravenous formulation was voluntarily withdrawn from the US market in 2005 and, due in part to the continued emergence and spread of MDR-AB, was reintroduced to the US market in 2009. The reintroduction of intravenous minocycline provides an additional agent in the limited armamentarium for treating MDR-AB. Minocycline represents an option in the treatment of MDR-AB infection, as susceptibilities to \textit{A. baumannii} remain high, conversion from intravenous to oral therapy is available, and toxicity is relatively limited. However clinical experience with intravenous minocycline for the treatment of MDR-AB infections is limited to in vitro evaluations, case reports, or small case series.

The first article in this supplement, by Mariana Castanheira and colleagues, summarizes some of the characteristics of the tetracycline class of antimicrobials and directly compares the in vitro activity of minocycline to doxycycline, tetracycline, colistin, carbapenems, and other agents against select gram-negative organisms including \textit{A. baumannii} collected between 2007 and 2011 from medical centers located worldwide. Minocycline and colistin were the only 2 antimicrobials that exceeded 50\% susceptibility rates (79.1\% and 98.8\%, respectively). Importantly, they note that microbiology laboratories should not use tetracycline hydrochloride susceptibility testing as a surrogate for other tetracyclines, as minocycline is sometimes active against \textit{A. baumannii} when tetracycline is not.

David J. Ritchie and Alexandria Garavaglia-Wilson provide a thorough review of the literature that reports successful use of intravenous minocycline for the treatment of serious MDR-AB infections, particularly for nosocomial pneumonia. After reviewing the pharmacokinetics and pharmacodynamics of minocycline, the authors describe the clinical experience observed with intravenous minocycline from reported observational
data in the form of case reports and series. Although the data are limited, the findings are generally favorable and encouraging. Minocycline’s rapid and substantial penetration into lung tissues, along with its favorable safety profile and intravenous to oral step-down therapy, supports its use as an option for treatment of MDR-AB infections.

Debra A. Goff and colleagues describe the clinical experience from The Ohio State University Medical Center with intravenous minocycline for critically ill patients with MDR-AB infections. The observed decline in susceptibility of *A. baumannii* to carbapenems and ampicillin-sulbactam required the antimicrobial stewardship program to evaluate minocycline. The observed clinical and microbiologic success rate of 73% and 78%, respectively, suggests that intravenous minocycline in combination with a second active agent, primarily intravenous colistin, warrants consideration for the treatment of MDR-AB infections, as options are exceedingly limited.

Jason Pogue et al describe the processes by which the antimicrobial stewardship committee and pharmacy and therapeutics committee at Detroit Medical Center (DMC) evaluated the utility of minocycline in the management of MDR gram-negative bacilli, brought minocycline onto formulary, and integrated it into treatment algorithms. They describe the emerging role of intravenous minocycline in management of infections due to these pathogens and the experience at DMC in treating carbapenem-resistant Enterobacteriaceae and MDR-AB infections.

**Notes**

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**References**