

Pan-resistant *Acinetobacter baumannii*: Is there any available alternative therapy?

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The *Acinetobacter baumannii* (*A. baumannii*) is frequently found in the hospital environment, particularly in moist areas, such as in humidifiers, water sinks and ventilators [1]. Although the prevalence of species of the genus *Acinetobacter* other than *A. baumannii* has seemingly increased as a cause of nosocomial infections in different geographical areas, the latter species continues to be the most prevalent in hospital settings [2]. More recently, *Acinetobacter* emerged as a particularly important pathogen in unusual situations such as earthquakes and war zones [3]. This prevalence was illustrated by reports of outbreaks of multi-drug resistant *Acinetobacter* infection associated with the U.S.-Iraq conflict [4]. Recently, isolation of multi-drug resistant *A. baumannii* as an emerging nosocomial pathogen has been reported from respiratory tract, wounds, blood and urine in Iran [5]. Several characteristics of this microorganism such as the intrinsic resistance associated with the interplay between decreased outer membrane permeability and constitutive expression of some efflux pumps, the acquisition of genetic elements and the ability to survive in the environment [6] should be highlighted because they can result in development of multi-drug resistant, extended-drug resistant and pan-drug resistant *A. baumannii* strains. Therefore, not many alternatives are available for treatment of pan-resistant *A. baumannii* strains infections. The currently available drugs which show a lower percentage of resistant clinical isolates are colistin and tigecycline. Colistin has been used in several studies to treat infections caused by multi-drug resistant *A. baumannii*, with suboptimal results. To improve its efficacy, recent pharmacokinetic/pharmacodynamic assessment suggested that colistin dosage should be optimized with an initial loading dose in order to reach therapeutic concentrations more rapidly [7]. Tigecycline has shown good in vitro activity against *A. baumannii*, however, few studies have been reported from non-comparative studies concerning its efficacy in *A. baumannii* infections ???. Moreover, rapid appearance of resistance has occurred during the treatment which was most likely associated with the overexpression of AdeABC and/or other efflux pumps. Among the possible combination therapies for treatment of multi-drug resistant *A. baumannii* infections, rifampin plus colistin has been evaluated in ventilator-associated pneumonia and bacteremia ????. Once more, the results were discordant and it may stress that a high dose of rifampin must be used. Furthermore, to avoid the appearance of rifampin resistance during the treatment, it is necessary to ensure, in case of empirical therapy, that the drug combined with rifampin is active against the *A.*

baumannii strains that are etiology of infections in that particular setting.

The problematic situations posed by *A. baumannii* have not been reflected in the development of new antibacterial agents against this microorganism. The latest drugs developed, such as doripenem, ceftobiprole and ceftalorine, did not show activity against *A. baumannii* resistant to carbapenems or cephalosporins ???.

We need new antibacterial agents to control *Acinetobacter baumannii* infections. Targeting antibiotic resistance is an attractive approach because it would help to reduce antibiotic resistance itself, and it would allow the recovery of antibiotics to which bacteria have already become resistant [2]. Antimicrobial peptides have attracted increasing interests as potential new antimicrobial agents. Some of these antimicrobial agents show good in vitro activity even against colistin-resistant *A. baumannii*. Additionally, non-antimicrobial approaches need to be addressed as well since recently, in a murine model of disseminated sepsis, active and passive immunization with an inactivated whole cell vaccine was effective in preventing infection by *A. baumannii* [8]. Finally, it must be stressed that there is an urgent need to reinforce researches on epidemiology of resistance, surveillance and the proven measures to control hospital infections.

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