Minocycline: The second important antimicrobial in multidrug-resistant *Acinetobacter baumanii* infections

Multidrug resistant (MDR) *Acinetobacter baumanii* infections have the propensity to increase the hospital stay, cost of treatment, morbidity, mortality, and above all remain very difficult to treat.[1] Independent risk factors for colonization or infection with resistant strains of *Acinetobacter* are prior methicillin-resistant *Staphylococcus aureus* colonies, previous use of carbapenem and fluoroquinolone, immobilization, previous admission in intensive care unit for major surgery or mechanical ventilation, having a central venous catheter *in situ*, hemodialysis, or malignancy.

A. baumanii are member of the ESKAPE group of pathogens which also includes *Enterococcus faecium*, *S.aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterobacter spp*.[2] At present, the recommendations are to treat MDR *A. baumanii* infection with two antimicrobials one of which should essentially be colistin. The purpose of using combination antimicrobials is to reduce drug resistance by effectively treating the infection, and to have better outcomes.[3] Colistin resistance is also emerging possibly due to mutation in genes encoding Pmr A and B proteins. In *A. baumanii* sensitive only to colistin, antimicrobials such as carbapenems, quinolones, aminoglycosides, and tigecycline have been used with variable efficacy.

Minocycline is a semi-synthetic, second-generation drug belonging to the tetracycline family. It is effective against gram positive, gram negative, and many atypical bacteria including *Mycobacterium* species *Bacillus anthracis*. Earlier it was used for treating sexually transmitted diseases and acne vulgaris.[4] It is a bacteriostatic and acts by inhibiting protein synthesis. US-FDA has recently approved the use of intravenous (IV) minocycline in hospitalized patients who have positive cultures for MDR *Acinetobacter* species. This approval is a Qualified Infectious Disease Product (QIDP) designation under the GAIN act i.e., Generating Antibiotic Incentives Now Act. When used in *A. baumanii* infections, IV minocycline exhibits bactericidal activity and synergistic bactericidal effects when combined with colistin or other susceptible antimicrobials.[5] The recommended dose is 100–200 mg twice daily for IV use.

Castanheira *et al*. found that minocycline was highly susceptible to *A.baumanii* strains along with colistin when compared to doxycycline, tetracycline, and other broad-spectrum antimicrobials (minocycline 79.1% and colistin 98.8%). The authors tested the efficacy of minocycline against 5477 *A. baumanii* and other gram-negative pathogens to arrive at the above conclusion.

Minocycline works effectively when used for *Acinetobacter* colonies in lung, meninges, soft tissue, and blood. However, due

to its limited solubility in urine, it might not be effective in urinary pathogens. The most common adverse events with minocycline are nausea, anorexia, diarrhoea, dizziness, light headedness, vertigo, tinnitus, and reducedhearing. It should be used with caution in patients with hepatic dysfunction. Dose adjustment is suggested in patients with azotemia, renal dysfunction, and hyperphosphatemia. Monitoring of blood urea nitrogen and creatinine is required in these patients.

In the present scenario MDR *A. baumanii* infections are very difficult to treat. With colistin-resistant strains also emerging from several units, options are limited. Minocycline appears promising but should be used judiciously by clinicians for treating *A. Baumanii infections*.

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