A review on multidrug - resistant Acinetobacter baumannii

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ABSTRACT

Multidrug-resistant Acinetobacter baumannii (MDR-Ab) is an emerging pathogen in health care settings. Male sex, ischemic heart disease, mechanical ventilation and antibacterial drug treatment, ICU admission are individual risk factors for MDR-Ab infections. Dealing with multidrug-resistant Acinetobacter baumannii is to a great challenge for physicians and clinical microbiologists not only due to its ability to survive in a hospital milieu but also because of the increasing mortality and morbidity associated with this pathogen. Moreover there is a reduction in the number of clinically available antibiotics active against this pathogen. Tigecycline usage in MDR A. baumannii infections demonstrated good microbiological and clinical activity but extensive use could lead to resistance developing during and after treatment. Colistin and intravenous colistimethate sodium are used as a “last-resort” treatment of infections caused by MDR A. baumannii.

Keywords
Multidrug-resistant Acinetobacter baumannii; Risk factors; Tigecycline; Colistin.

Introduction

MDR Acinetobacter is defined as Acinetobacter isolate resistant to at least three classes of antimicrobial agents - all penicillins and cephalosporins including inhibitor combinations, fluoroquinolones, and aminoglycosides. Management of multidrug-resistant Acinetobacter spp. infections is a great challenge for physicians and clinical microbiologists. Its ability to survive in a hospital milieu and its ability to persist for extended periods of time on surfaces makes it a frequent cause for healthcare-associated infections (Fournier et al., 2006). MDR A. baumannii has recently been established as a leading nosocomial pathogen. The organism can survive on environmental surfaces for months, making nosocomial transmission extremely difficult to prevent and control. (Hawkey et al, 1996). The incidence of MDR A. baumannii isolation had doubled compared to the previous years, and the organism became endemic in many wards (Aharon et al., 2005). The increasing recovery of multidrug-resistant Acinetobacter baumannii is a frightening reality [Livermore et al., 2003]. These MDR strains often spread to cause outbreaks in cities, countries, and continents (Bergogne et al., 1996). MDR-
Ab has emerged worldwide as an important health care-associated pathogen, causing infections such as ventilator-associated pneumonia, bloodstream infections, and wound infections (Villegas et al., 2003). MDR – Ab infections have an extremely high crude mortality rate and occur most frequently in severely ill patients (Maragakis et al, 2008). MDR-Ab is an emerging pathogen in health care settings, especially in the intensive care setting (Fedrerico et al., 2007) and lead to multiple outbreaks (Jawad et al, 1996).

Epidemic outbreaks of multi-drug resistant *Acinetobacter baumannii* in intensive care units (ICUs) are increasing (Ji Ye et al., 2010). The global emergence of multidrug resistant *Acinetobacter baumannii* has reduced the number of clinically available antibiotics that retain activity against this pathogen. For this reason, the development of novel treatment strategies for infections caused by *A. baumannii* is necessary (Mexitxell et al., 2013).

**Risk factors for MDR-Ab**

Risk factors for colonization or infection with multidrug-resistant Acinetobacter species are prolonged length of hospital stay, exposure to an intensive care unit (ICU), receipt of mechanical ventilation, colonization pressure, exposure to antimicrobial agents esp., carbapenems, colistin, recent surgery, invasive procedures, underlying severity of illness.(Cisneros et al., 2002). The individual risk factors for isolation of MDR *A. baumannii* that were identified by multivariate analysis were male sex, underlying comorbidity of ischemic heart disease, mechanical ventilation, and antimicrobial drug treatment. Two agents used in the hospital were associated with MDR *A. baumannii*: metronidazole was identified as a risk factor and the penicillin group was identified as having a protective effect (Aharon et al., 2005). The risk factor analysis of MDR-Ab infections done by Huang et al., 2013, revealed more prevalence of MDR-Ab in male patients who belonged to above 65 yrs age group and in respiratory samples. This study also suggested ICU admission of the patient as an independent risk factor for MDR-Ab infection. Outbreaks of MDR-Ab infection have been traced to respiratory care equipment, wound care procedures, humidifiers, and patient care items (Bernades et al., 2004). Medical equipment has been implicated, emphasizing the need for special attention to disinfection of shared items and extra caution with respiratory care and wound care procedures (Villegas et al., 2003).

Wilks et al., 2006, reported a recent outbreak of multidrug-resistant Acinetobacter infection, with environmental contamination found on curtains, laryngoscope blades, patient lifting equipment, door handles, mops, and keyboards.

**Clinical implications of MDRAB**

The incidence of severe infection caused by MDR *A. baumannii* has been increasing worldwide. Crude mortality rates of 30 – 75% have been reported for nosocomial pneumonia caused by *A. baumannii* (Vikas et al., 2010). *Acinetobacter* pneumonia increases the ICU stay by several days. The median length of stay with such an infection is reported to be 21 days as compared to 14 days for controls. Such an event in addition to causing inconvenience to patients puts extra financial burden on the healthcare system (Fagon et al., 1993).
MDR A. baumannii infections tend to occur in immunosuppressed patients, in patients with serious underlying diseases, and in those subjected to invasive procedures and treated with broad-spectrum antibiotics (Garcia et al., 2001). They are implicated as the cause of ventilator-associated pneumonia (VAP), urinary tract infections, and bacteremia. A. baumannii also causes, albeit less frequently, complicated skin and soft tissue, abdominal, and central nervous system infections (Fournier et al., 2006). Of recent importance is that A. baumannii has become a major pathogen found in combat-associated wounds (Aronson et al., 2006). The factors contributing to colonization, virulence, and invasion are being defined (Smith et al., 2007). It is often difficult to distinguish between infection and colonization with A. baumannii (Joly et al., 2005). There is considerable controversy over whether infections caused by this organism lead to unfavorable outcomes (Blot et al., 2003). However, various studies revealed that the recovery of A. baumannii in the hospitalized patient is an indicator of severe illness, with an associated mortality of approximately 30% (Wilson et al., 2004).

**Treatment**

Historically, carbapenems have resulted in the best therapeutic response for infections caused by MDR A baumannii. But if the isolates are resistant to the carbapenems, antimicrobial resistance poses great limits for therapeutic options in infected patients. Doripenem is active against Carbapenemase-negative A. baumannii isolates, but is inactive against A. baumannii isolates expressing plasmid-mediated carbapenemases. For Carbapenem - resistant A baumannii, tigecycline and colistimethate are two of the most frequently used alternative agents (Vikas et al., 2010). Tigecycline has been studied against MDR A. baumannii infections and demonstrated good microbiological and clinical activity. But in the coming few years’ extensive use could affect its activity, owing to resistance being developed during and after treatment with this drug. For the treatment of MDR A. baumannii infections, Tigecycline can be used in combination with levofloxacin, amikacin, imipenem, and colistin but tigecycline / piperacillin-tazobactam combination is antagonistic and should not be considered. Colistin and intravenous colistimethate sodium are peptide antibiotics that have been increasingly used as a “last-resort” treatment of infections caused by MDR A. baumannii. Unfortunately, there have been few reports of resistance to colistin in A. baumannii. (Gales et al., 2001). Among severely ill patients with MDR Acinetobacter species infections, including bacteremia, pneumonia, sepsis, CNS infection, and intra-abdominal infection, improvement with colistin of about 80 % was observed (Markagakis et al., 2008). But colistin is reported to have relatively poor lung and CSF distribution and the clinical outcomes vary for different types of infections (Levin et al, 1999). Various studies have reported higher clinical response rates for parenteral colistin treatment of MDR Acinetobacter species infections in ventilator-associated pneumonia. (Markagakis et al., 2008). Hetero resistance i.e subpopulations of genetically identical subclones that are more resistant than the original parent clone is a particularly frightening development that has been recently described for A. baumannii (Li et al, 2006). The impact of heteroresistance will need to be evaluated
and monitored in a prospective manner as clinicians begin to study outcomes in patients undergoing treatment with colistin.[30]. But, presently there are no better available options except colistin and tigecycline for treatment of multidrug resistant Acinetobacter baumannii infections.

MDR A. baumannii has recently been established as a leading nosocomial pathogen. MDR-Ab is an emerging pathogen in health care settings, especially in the intensive care setting. There is an increased prevalence of MDR-Ab in elderly male patients and in respiratory samples. ICU admission is as an independent risk factor for MDR -Ab infection. At present colistin and tigecycline remain drugs of choice for MDRAB infections. Tigecycline should not be used in combination with piperacillin-tazobactam for MDR-Ab infections. Keeping in view reports of resistance to tigecycline as well as colistin, though few, there is a need for newer drugs for these infections in the coming years.

References


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