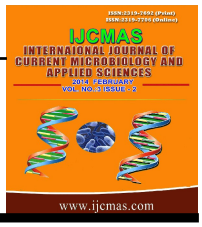
International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 3 Number 2 (2014) pp. 9-13**
http://www.ijcmas.com



Review Article

A review on multidrug - resistant Acinetobacter baumannii

Pavani Gandham*

Department of Microbiology, Apollo Institute of Medical Sciences and Research, Hyderabad, India
**Corresponding author*

A B S T R A C T

Multidrug-resistant *Acinetobacter baumannii* (M DR-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 com binations, fluroquinolones, and aminoglycosides. Management of multidrug-resistant *Acinetobacter* **s**pp. 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 heartdisease, 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 Carbapenemasenegative *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 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

Aharon A , Shiri Navon V, Orly H. 2005 . Multiresistant Acinetobacter baumannii Emerging Infectious Diseases 11(1) :22-29

Aronson, N. E., J. W. Sanders, and K. A. Moran. 2006. In harm's way: infections in deployed American military forces. Clin. Infect. Dis. 43:1045-*1051*.

Bergogne-Berezin, E., and K. J. Towner. 1996. Acinetobacter spp. as nosocomial pathogens: microbiological, clinical, and epidemiological features. Clin. Microbiol. Rev. 9:148-165.

Bernards AT, Harinck HI, Dijkshoorn L, van der Reijden TJ, van den Broek PJ. 2004. Persistent A*cinetobacter baumannii?* Look inside your medical equipment. Infect Control Hosp Epidemiol. 25:1002–4.

Blot, S., K. Vandewoude, and F. Colardyn. 2003. Nosocomial bacteremia involving *Acinetobacter baumannii* in critically ill patients: a matched cohort study. Intensive Care Med. *29:471-475*.

Cisneros JM, Rodríguez-Baño J. . 2002. Nosocomial bacteremia due to *Acinetobacter baumannii*: epidemiology, clinical features and treatment. Clin Microbiol Infect11:687–93

Fagon JY, Chastre J, Hance AJ, Montravers P, Novara A, Gibert C. 1993.Nosocomial pneumonia in ventilated patients: a cohort study evaluating attributable mortality and hospital stay. Am J Med. 94:281–8.

Federico P, Andrea M, Kristine M . 2007. Global Challenge of Multidrug-Resistant *Acinetobacter baumannii*. Antimicrob Agents Chemother. 51(10): 3471-3484.

Fournier PE, Richet H. 2006. The epidemiology and control of *Acinetobacter baumannii* in health care facilities. Clin Infect Dis. 42:692–9.

Gales, A. C., A. O. Reis, and R. N. Jones. 2001. Contemporary assessment of antimicrobial susceptibility testing methods for polymyxin B and colistin: review of available interpretative criteria and quality control guidelines. J. Clin. Microbiol. 39:183-*190*.

Garcia-Garmendia, J. L., C. Ortiz-Leyba, J. Garnacho-Montero, F. J. Jimenez-Jimenez, C. Perez-Paredes, A. E. Barrero-Almodovar, and M. Gili-Miner. 2001. Risk factors for *Acinetobacter baumannii* nosocomial bacteremia in critically ill patients: a cohort study. *Clin. Infect. Dis. 33:939-946.*

Hawkey PM. 1996. Influence of relative humidity and suspending menstrua on survival of *Acinetobacter* spp on dry surfaces. J Clin Microbiol. 34: 2881-2887.

Huang J, Chen E, QU Hong-ping. *2013*.Sources of multidrug-resistant *Acinetobacter baumannii* and its role in respiratory tract colonization and nosocomial pneumonia in intensive care unit patients . *Chin Med J 126 (10):1826-1831*

Jawad A, Heritage J, Snelling AM, Gascoyne-Binzi DM, Hawkey PM. 1996. Influence of relative humidity and suspending menstrua on survival of *Acinetobacter* spp. on dry surfaces. J Clin Microbiol. 34:2881–7.

Ji Ye J, Moo S P, Song E K. 2010.Risk factors for multi-drug resistant *Acinetobacter baumannii* bacteremia in patients with colonization in the intensive care unit. BMC Infectious Diseases 10:228

Joly-Guillou, M. L. 2005. Clinical impact and pathogenicity of *Acinetobacter*. Clin. Microbiol. Infect. 11:868-*873.*

Levin AS, Barone AA, Penço J, Santos MV, Marinho IS, Arruda EA, et al. Intravenous colistin as therapy for nosocomial infections caused by multidrug-resistant Pseudomonas aeruginosa and *Acinetobacter baumannii*. Clin Infect Dis. 1999;28:1008–11.

Li, J., C. R. Rayner, R. L. Nation, R. J. Owen, D. Spelman, K. E. Tan, and L. Liolios. 2006. *Heteroresistance to colistin in multidrug-resistant Acinetobacter baumannii.* Antimicrob. Agents Chemother. 50:2946-*2950.*

Livermore, D. M. 2003. *The threat from the pink corner.* Ann. Med. 35:226-*234.*

Maragakis LL, Perl TM. 2008 . *Acinetobacter baumannii*: epidemiology, antimicrobial resistance, and treatment options. Clin Infect Dis. 46(8):1254-6

Meritxell G, Marina R, Rafael L .2013 ..Emerging therapies for multidrug resistant *Acinetobacter baumannii.* Trends in Microbiology .*21(3):157-163.*

Pournaras, S., A. Markogiannakis, A. Ikonomidis, L. Kondyli, K. Bethimouti, A. N. Maniatis, N. J. Legakis, and A. Tsakris. 2006. Outbreak of multiple clones of imipenem-resistant *Acinetobacter baumannii* isolates expressing OXA-58 carbapenemase in an intensive care unit. J. Antimicrob. Chemother. 57:557-*561.*

Smith, M. G., T. A. Gianoulis, S. Pukatzki, J. J. Mekalanos, L. N. Ornston, M. Gerstein, and M. Snyder. 2007. New insights into Acinetobacter baumannii pathogenesis revealed by high-density pyrosequencing and transposon mutagenesis. Genes Dev. 21:601-614.

Vikas M , Sinha S , NP Singh. . 2010 . Multidrug Resistant *Acinetobacter*. J Glob Infect Dis. 2(3): 291–304.

Villegas MV, Hartstein AI. 2003. *Acinetobacter* outbreaks,1977-2000. Infect Control Hosp Epidemiol.24:284-295.

Wilks M, Wilson A, Warwick S, et al. .2006. Control of an outbreak of multidrug-resistant *Acinetobacter baumannii*—calcoaceticus olonization and infection in an intensive care unit (ICU) without closing the ICU or placing patients in isolation. Infect Control Hosp Epidemiol. 27:654–8.

Wilson, S. J., C. J. Knipe, M. J. Zieger, K. M. Gabehart, J. E. Goodman, H. M. Volk, and R. Sood. 2004. Direct costs of multidrug-resistant *Acinetobacter baumannii* in the burn unit of a public teaching hospital. *Am. J. Infect. Control 32:342*-344.