REVIEW

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Acinetobacter baumannii is an opportunistic pathogen as an MDRO in ICU

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INTRODUCTION

The genus that we know as Acinetobacter has undergone significant modifications over the past 30 years. Acinetobacter baumannii has become one of the most troublesome pathogens for health care institutions globally. Clinically, especially over the past 15 years, due to its extraordinary ability to increase or become a bacterium that is resistant to antibiotics, making it one of the threatening organisms in the health sector today.

A. baumannii strains resistant to all known antibiotics have now been reported, signifying a sentinel event that should be acted on promptly by the international health care community. Acting in synergy with this emerging resistance profile is the uncanny ability of A. baumannii to survive for prolonged periods throughout a hospital environment, thus potentiating its ability for nosocomial spread. However, in the present time, the infection caused can involve the central nervous system, skin and soft tissue, and bone has been monitored as a major problem for certain institutions.[3]

Interest in Acinetobacter, from both the scientific and public community, has risen sharply over recent years. This level of significant progress in our understanding of interesting about these organisms have attracted more attention since it was last reviewed in this journal in 1996. In this review, we describe the progress of this understanding and also provide a comprehensive assessment of the microbiological, clinical and epidemiological characteristics of A. baumannii, the most clinically relevant species.[4]

Taxonomy and Species Characteristic

The genus Acinetobacter, as currently defined, is a gram-negative, aerobic, nonfermenting, nonfastidious, nonmotile, catalase-positive, oxidase-negative bacterium. Naming these species have undergone substantial taxonomic changes for years due to advanced understanding of the molecular structure of the genetic group of these microorganisms.[5] This new classification, which seems to have been widely accepted among taxonomists, is classified as a Gamma Proteobacteria which is included in the Pseudomonadales group and the Moraxellaceae family. Therefore, according to the specified taxonomic classification; Domain: Bacteria, Phylum: Proteobacteria, Class: Gamma Proteobacteria, Sequence: Pseudomonadales, Family: Moraxellaceae, Genus: Acinetobacter. Species A. baumannii, Acinetobacter haemolyticus and A. calcoaceticus have clinical significance.[1]

Acinetobacter species originating from humans grow well on agar media that are routinely used in clinical microbiology laboratories, such as sheep blood agar or tryptic soy agar, at an incubation temperature of 37 °C. These organisms form fine grayish, sometimes slimy colonies; similar to colonies A. calcoaceticus type A. baumannii is similar to Enterobacteriaceae, with colony diameters of 1.5 to 3 mm after overnight culture process, while most other Acinetobacter species produce smaller and more transparent colonies. Unlike the other case with Enterobacteriaceae, the Acinetobacter species is outside A. calcoaceticus type A. baumannii may not grow on McConkey's agar.[2]

Natural habitat

Organisms that including to the genus Acinetobacter are often thought to be everywhere in nature given that they can be found from almost all soil and surface water samples.[6] This understanding has contributed to the common misconception that A. baumannii is everywhere. Although not all Acinetobacter is in their habitat in natural environments, thorough and systematic research to investigate the natural habitat of various species of Acinetobacter in the environment has not been done. [7]

As a pathogenic germ, A. baumannii specifically likes moist tissue such as mucous membranes or exposed skin areas, either due to accidents or injuries. The skin and soft tissue infected with A. baumannii begins with the appearance of *peau d'orange* (similar to orange peel) followed by changes in the rough surface of the skin like sandpaper which eventually changes to vesicles on the skin. In areas of skin disruption hemorrhagic bullae can be seen, with a visible necrotizing process followed by bacteremia.[8] If left untreated, this infection can lead to septicemia and death.

Pathogenesis and Virulence Potential

While it is believed that there are factors that can contribute to the virulence of A. baumannii,

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one of the special factors is OmpA, which is an outer membrane protein (OMPs), with absolutely contributing significantly to diseases that cause potential pathogens.[9] A.baumannii OmpA binds to the host cell epithelium and mitochondria, which are bound to the mitochondria. OmpA causes mitochondrial malfunction and causes the mitochondria to become swollen, followed by the release of cytochrome C, heme protein, which in turn causes the formation of apoptosomes called cell apoptotic reactions, which is the most surface protein in pathogens, also plays a role in resistance to complement and biofilm formation.[10,11] Two key strategies for surviving stress and potentially related virulence factors are important, helps improve bacterial survival both inside and outside the host cell.

The ability of A. baumannii to form biofilms that enable it to survive and grow continuously in unfavourable conditions and environments. A. baumannii has indeed been shown to form biofilms on abiotic surfaces, including those on glass and equipment used in intensive care units, or on biotic surfaces such as epithelial cells.[10] The most common factors that can control biofilm formation include patient nutritional conditions, Pili assembly and production of biofilm-associated protein (BAP) both contribute to the initiation of biofilm production and maturation after A. baumannii attach to particular.[10]

When piles attach to the abiotic surface, they will initiate microcolony formation, followed by full development of the biofilm structures. BAP appears on the surface of bacterial cells and contributes to the development and maturation of biofilms by stabilizing mature biofilms on abiotic or biotic surfaces.[10] Other key proteins that have been shown to contribute to the virulence of A. baumannii are phospholipase D and C. While phospholipase D is important for resistance to human serum, pathogenesis and epithelial cell evasion,[12] phospholipase C increases toxicity to epithelial cells. Along with OmpA, fimbria, also contribute to the surface of bacterial cells.[13]

Antibiotic Resistance

The rapid emergence of a multi-resistant Acinetobacter strain in the organism's ability to quickly adapt to environmental changes. The ability of the mechanism of resistance of organisms coupled with comorbid factors of patients is an important role in the route of development of organisms to become pathogens that are resistant to various drugs.[14]All genomic variants of A. baumannii contain a non-inducible chromosomal AmpC cephalosporinase, also known as Acinetobacter-derived cephalosporinases (ADCs).[15]

The presence of an upstream IS element known as ISAba1 determines the regulation of the AmpC gene. Overexpression of AmpC cephalosporinase and resistance to extended-spectrum cephalosporin is intrinsically linked to the presence of ISAba1.[16] Cefepime and carbapenems, however, appear to be stable in response to these enzymes.[15]

Clinical Symptoms

A. baumannii infection has reached in various anatomical regions with varying degrees of illness and patient outcomes. There is considerable debate regarding the actual impact of clinical infections and their relation to the mortality rate of patients. While a number of studies have concluded that infection with Acinetobacter has a detrimental impact on patient outcomes.[17] Other similar studies imply little or no effect on patient outcomes as a result of infection.[18]

Hospital-acquired pneumonia

Ventilator-associated pneumonia (VAP) is generally associated with infection. Longer hospital stays, longer use of mechanical ventilation and previous antibiotic use are factors that are known to increase the risk of VAP due to Acinetobacter. These individuals can act as opportunistic carriers of epidemic stains. Contaminated ventilators or respiratory care equipment and intrahospital transmissions can also contribute at the outset of the outbreak.[19]

Community-acquired pneumonia

Pneumonia obtained from outside the hospital and caused by Acinetobacter has been noted in Australia and Asia. The source of infection may originate from the trachea, which occurs in up to 10% of the population with excessive alcohol consumption. This is characterized by a sudden onset and secondary infection bloodstream and has a mortality rate between 40% and 60%.[20]

Bloodstream infections

In a seven-year review (1995–2002) of nosocomial bloodstream infections in the United States, Acinetobacter accounted for 1.3% of all monomicrobial blood-stream infections. Acinetobacter was a more common cause of ICU acquired bloodstream infection than of non ICU ward infection. Acinetobacter bloodstream infection had the third-highest crude mortality rate in the ICU, exceeded only by P. aeruginosa and Candida spp infections.[21]

Meningitis

Post-neurosurgery, Acinetobacter nosocomial in meningitis is becoming increasingly common with many other Gram-negative bacteria also being a problem in postoperative care. Installation of an external ventricular drain becomes a place of

opportunistic infection. The mortality rate may be as high as 70%, but this is not possible to discern the definitive cause of mortality.[22]

Treatment

As resistance has increased, some antimicrobials can be used reliably for the treatment of effective Acinetobacter MDR infections. Because some antimicrobials remain effective effectively in the treatment of nosocomial Acinetobacter infections, the search for new drugs and reevaluation of older agents have become a priority.[23]

Carbapenems

Carbapenems (imipenem and meropenem) resistance Acinetobacter is increasingly reported, making MDR Acinetobacter infections difficult to treat. However, carbapenems continue to be the treatment of choice in cases where isolates are still susceptible to this antimicrobial class.[24]

Sulbactam

Sulbactam, an inhibitor of B-lactamase, demonstrates in vitro bactericidal activity against Acinetobacter spp. and it is suitable for mild infections. Several studies illustrate the use of several single agents in MDR A. baumannii infection therapy. The adequate performance (up to 67.5% healing rate) of sulbactam in treating various types of infections such as meningitis, pneumonia, peritonitis, surgical site and urinary tract infections, caused by MDR A. baumannii which also showed resistance to imipenem was further verified by prospective and retrospective set of patients.[25]

Tigecycline

Tigecycline derivative of minocycline and has bacteriostatic activity against MDR A. baumannii.[25] High-level resistance to tigecycline has been reported for some multidrug-resistant A. baumannii isolates, with a concern that this organism can quickly escape this antimicrobial mediated efflux pumps. Overexpression of a multidrug efflux pump in A. baumannii isolates with reduced susceptibility to tigecycline has been described.[26]

Aminoglycosides

Tobramycin and amikacin are some of the aminoglycoside agents used as therapeutic options in cases of infection with multidrug-resistant A. baumannii isolates that retain susceptibility. These options are typically used in combination with another active antimicrobial agent. Many multidrug-resistant A. baumannii isolates maintain an intermediate susceptibility to amikacin or tobramycin to which resistance is highly correlated with aminoglycoside modifying enzymes or efflux pump mechanisms.[27]

Colistin

Colistin, a cationic polypeptide, is part of the polymyxin family (colistimethate or colistin-sulfomethate or polymyxin E) and is a potent broad-spectrum antimicrobial agent. This agent was initially used in the 1960s and 1970s but was not prescribed frequently because of concerns with nephrotoxicity and neurotoxicity. Clinicians are going back to the use of polymyxin B or polymyxin E (colistin) for highly drug-resistant A. baumannii infections. Observational studies have shown a rate of 57–77% of cure or improvement among severely ill patients with multidrug-resistant A. baumannii infections treated with colistin. These infections included pneumonia, bacteremia, sepsis, intra-abdominal, and central nervous system infection.[28]

CONCLUSIONS

In conclusion, A. baumannii is an important opportunistic and emerging pathogen that can lead to serious nosocomial infections. Its pathogenic potential includes the ability to adhere to surfaces, form biofilms, display antimicrobial resistance and acquire genetic material from unrelated genera, making it a versatile and difficult adversary to control and eliminate. The optimal treatment for A. baumannii, especially nosocomial infections resulting from multiple resistant strains, remains to be established. It is thus a clinical imperative that well-designed procedures are put in place to help guide clinicians on decisions regarding the current best therapeutic practice. Furthermore, new experimental approaches are warranted to develop and evaluate novel therapeutic strategies for dealing with A. baumannii infections.

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