Acinetobacter Infections and Treatment

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Abstract

Acinetobacter baumannii have been a leading cause of nosocomial infections, causing significant morbidity and mortality. It is the most commonly isolated microorganism from clinical specimens. A. baumannii has low virulence and causes opportunistic nosocomial infections. The most important features of A. baumannii are the ability to persist in the hospital environment and the increased multidrug antibiotic resistance it may present, which compromises the treatment of infections caused by this microorganism. In recent years, there have been reports of multidrug resistant A. baumannii outbreaks. (J Pediatr Inf 2014; 8: 28-32)

Keywords: Acinetobacter baumannii, nosocomial infections, antimicrobial resistance, treatment

Introduction

Acinetobacter spp. increasingly causes nosocomial infections in our country as well, just like over the world. It causes ventilator-related pneumonia especially in patients staying in the intensive care unit, bacteraemia, urinary system infections, meningitis and skin and soft tissue infections (1). Antibiotic resistance of the bacteria hospital-acquired Acinetobacter infections is a serious problem in the treatment. The prevalent use of broad spectrum antibiotics such as aminoglycosides, ureidopenicillins, fluoroquinolones and third generation cephalosporins has caused the development of antibiotic resistance in the Acinetobacter types. A. baumannii have natural resistance to the antibiotics such as ampicillin, amoxicillin and first generation cephalosporins (2, 3).

Microbiologic features

Acinetobacter spp are gram-negative cocco-bacillus that likes to reproduce at 35-37°C, without flagellums and immobile, oxidase negative, catalase positive and involuntary aerobe. On the bacteriae cell wall, there are polysaccharides with antigenic features, glikokaliks proteins, fimbrae proteins responsible for adhesion to sensitive cells. Acinetobacter-spp bacteria easily reproduce in many mediums such as eosin methylene blue, commonly used in laboratories and blood agar (4).

More than 30 species of Acinetobacter-spp bacteria have been identified. Most of the species are available in the environment and they do not generate illnesses in human beings. Since it is difficult to differentiate the bacteria types according to their phenotypic features, sometimes the term Acinetobacter calcoaceticus-Acinetobacter baumannii complex is used. Acinetobacter baumannii, Acinetobacter calcoaceticus and Acinetobacter lwoffii are the most commonly reported Acinetobacter-spp in the clinic literature. Among these types, the most common and important types causing clinic pictures are A. baumannii (5, 6).

Epidemiology

Since Acinetobacter-spp bacteria are able to use a great variety of metabolites and carbon sources for their metabolisms and energy needs, are dry-resistant and able to survive in different heat and pH environments, they can freely live in nature as saprophyte and survive on inanimate surfaces (1).

Acinetobacter-spp can colonize as contaminant- saprophyte bacteria on skin and mucous membranes. While Acinetobacter colonization has been detected on skins of 25% of healthy adults, temporary pharyngeal Acinetobacter has
been found on the skins of 7% of children and adults. Acinetobacter-spp are the most common gram-negative bacteria that hospital personnel carry on their skins. The multiple-resistant Acinetobacter in the stool of intensive care unit patients has been isolated and colonization was detected in the 45% of tracheostomy patients (4, 6).

Even though Acinetobacter prevalence varies according to the type of clinic samples and from country to country, it has noticeably increased in the last 20 years. According to the data of Centers for Disease Control and Prevention and National Nosocomial Infection Surveillance, it was reported that Acinetobacter-spp were responsible agents in the 2.4% of nosocomial sepsis, 2.1% of surgical wound infections, 1.6% of nosocomial urinary system infections and 6.9% of nosocomial pneumonia (7, 8).

Risk factors

While alcoholism, smoking, chronic lung disease, diabetes mellitus and living in tropical climates are the risk factors in community-acquired Acinetobacter infections; elongated hospital stays, surgical intervention, presence of lesions on the body, previously acquired infections, the use of broad spectrum antibiotics, central venous or the presence of urinary system catheter, hospitalization in intensive care unit or burn unit, parenteral nutrition, mechanic ventilation and more importantly deficiencies in the infection control programs implemented at hospitals are the factors increasing the risks in nosocomial infections (9, 10).

Pathogenesis and virulence factors

The fact that Acinetobacter types are able to survive on dry and lifeless surfaces and their ability to adopt to changing environmental conditions is an important factor in pathogenesis. Other factors effective in the virulence Acinetobacter types are as follow (11-14):

Polysaccharide capsule
It is composed of L-rhamnose D-glucose, D-mannose and D-glucuronic acid. It enables the surface of the bacteria to be hydrophilic and helps the bacteria to be protected from phagocytose. Additionally, it also allows the bacteria colonies to cling onto surfaces of invasive instruments such as intravenous catheter and tracheal cannula, and penetrate into deeper tissues.

Sticking to the cells
Surface components in polysaccharide structure, fimbrias in glycoprotein structure and membrane components enable the bacteria to stick to the cell surfaces. OmpA (AbOmpA), which is a surface protein with 38 kDa molecular weight present on the A.baumannii cell wall also plays a role in allowing the bacteria to stick to the epithelial surfaces. AbOmpA causes apoptosis of epithelial cells as the reason for the emission of proapoptotic molecules.

Lipopolysaccharide and enzyme production
On the baumannii cell wall, there exist various lipopolysaccharides (LPS) whose structures and antigenic features are known. Another factor in the virulence is the enzymes that Acinetobacter produces in great amounts and secretas out of the cell. It was demonstrated in in-vivo and in-vitro studies that this caused lipid destruction of the enzymes and had a negative impact on the neutrophils.

Biofilm formation
A. baumannii; formation on surfaces such as steel, polystyrene and glass together with biotic surfaces such as epithelial cells may constitute biofilm. It is thought that important cellular components regarding biofilm formation in Acinetobacter spp are the pili formation systems and OmpA protein released out of the cell.

Other factors effective in pathogenesis
A. baumannii strains have the ability to use different iron resources and an independent iron recovery system enabling the host to colonize. The requirement to be able to use the iron in the environment for the bacteria to reproduce plays a crucial role in the pathogenesis of the infection.

Infections caused by Acinetobacter

Respiratory tract infections
It was reported that Acinetobacter spp cause community-acquired bronchiolitis and tracheobronchitis in children, and tracheobronchitis in healthy adults (1, 15).

The most common infection caused by Acinetobacter spp is pneumonia and Acinetobacter causes both community-acquired and nosocomial pneumonia. Community-acquired pneumonia develops in conditions such as alcoholism and smoking in adults, diabetes mellitus, renal failure and underlying lung disease that weaken host immunity. It reaches greater levels of prevalence in regions with tropical climate. Community-acquired pneumonia caused by Acinetobacter spp is usually sudden-onset and have fulminant progression. Septic shock is seen in 1/3 of the patients. There are many publications in the literature reporting that mortality rate in community-acquired pneumonia varies between 40-60% (16-18).

In the US in 2008, the National Healthcare Safety Network (NHSN) reported that the most important agent in gram negative nosocomial infections was Acinetobacter spp and this bacteria was responsible for the infection in...
8.4% of ventilator-related pneumonias (19). In the nosocomial Acinetobacter pneumonia, multilobar involvement, cavitation, pleural effusion and bronchopulmonary fistula formation were observed. In the nosocomial Acinetobacter pneumonia, mortality is reported to between 35-70%. The existence of bacteremia or sepsis symptoms and presence of previous colonization is a negative is a sign of poor prognosis in nosocomial Acinetobacter pneumonia (1, 17).

**Bacteremia**

Acinetobacter spp cause 1.5% to 2.5% of the nosocomial bacteremia. Nosocomial Acinetobacter bacteremia is frequently associated with respiratory tract infections and intravenous catheter use and is less frequently associated with urinary tract, lesions, skin and abdomen infections (7, 20, 21). In about 1/3 of the patients with Acinetobacter bacteremia, septic shock develops. Mortality rate in Acinetobacter bacteremia is between 20 to 60%. Mortality of Acinetobacter pneumonia-caused bacteremia is higher than mortality of intravenous catheter-caused bacteremia (39% vs. 4%) (21-23).

**Endocarditis**

Acinetobacter-caused endocarditis might rarely develop on the natural and prosthetic cardiac valves. Acinetobacter-caused endocarditis has an acute onset and serious progression. Endocarditis developing on the natural cardiac valves may have greater mortality than prosthetic cardiac valves (24, 25).

**Central nervous system infections**

Nosocomial Acinetobacter meningitis is rare. Neurosurgery interventions, cerebrospinal fluid leakage, intracranial haemorrhage and prior antibiotic use are risks factor in the development of Acinetobacter-caused meningitis. However, Acinetobacter meningitis has a high mortality (20-30%) and leaves serious neurological sequel in the patients (26-28).

Nosocomial Acinetobacter spp meningitis is rare and is generally seen in hot climates. In nosocomial meningitis, the bacteria are generally not highly resistant (29).

In nosocomial meningitis, most of the patients have the symptoms of fever and meningeal irritation, and these symptoms may be accompanied by seizure. Pleocytosis dominated by neutrophil is present in the cerebrospinal fluid. Cerebrospinal fluid has low level of glucose and high level of protein (27). In gram staining, Acinetobacter spp may morphologically be confused with N. meningitidis (1).

**Skin-Soft tissue and bone infections**

Acinetobacter types may colonize in surgical and traumatic lesions, and may cause serious soft tissue infections, and develop into osteomyelitis. Acinetobacter-caused soft tissue infections may be related to prosthetic material and may develop into infections requiring broadly spectrum debridement. Acinetobacter may also cause skin infections such as community-acquired and nosocomial cellulite and furuncle. It may cause cellulite formation at the catheter insertion site and may only heal by the removal of catheter (1, 30).

**Urinary tract infection**

Acinetobacter-caused urinary tract infections are not frequent; however, Acinetobacter may frequently colonize in the urinary system, especially in the presence of catheter. Prevalence of catheter-caused urinary system infections is reported to be 1.2% (19).

**Other infections**

Acinetobacter spp may colonize in the eyes as well. It may cause corneal ulcerations, endophthalmitis and peri-orbital cellulite. It may cause infection in the eye after surgery or trauma (31, 32).

Acinetobacter spp may cause nosocomial sinusitis. This picture has been linked to the development of nosocomial pneumonia. Mechanical ventilation is a risk factor for nosocomial sinusitis (33).

Acinetobacter spp may cause septic arthritis, pancreatitis, hepatic abscess and peritonitis (1, 34).

**Treatment of acinetobacter infections**

It is important to be able to differentiate between colonization and infection before the treatment. In the infections caused by antibiotic-resistant Acinetobacter, broad spectrum cephalosporins, beta-lactam/beta-lactamase inhibitors, carbapenems may be used on their own or combined with antipseudomonal florokinolons or aminoglycosides. Duration of treatment may vary depending on the location of the infection and its severity (1).

It was demonstrated that sulbactam, a beta-lactam inhibitor, the carbapenem-resistant A. baumannii, had over 90% in-vitro efficiency and was comparable with imipenem. However, in Acinetobacter infections, the use of antibiotics with sulbactam on their own are not recommended due quick-developing resistance (35, 36).

The antibiotics likely to be used for multiple-drug resistant Acinetobacters are limited. The Polymyxin group antibiotics (Polymyxin B and Polymyxin E) with in-vitro efficacy, and tigesiklin and combined antibiotics may be an option in the treatment of multiple-drug resistant Acinetobacter infections. Quick resistance may develop against tigesiklin and the clinical experience of this drug for the treatment of A. baumannii is rare (37).

If there is a carbapenem-sensitivity for Acinetobacter-caused meningitis, carbapenem may be used on its own
or may be given intrathecally or interventricularly together with aminoglycoside. If there is carbapenem resistance, intravenous colistin may be used on its own or may be given intrathecally or interventricularly together with colistin or aminoglycoside. Colistin may also be used combined together with intravenous rifampicin (38). In antibiotic-resistant Acinetobacter meningitis, tigecycline is not recommended due to its pharmacodynamic characteristics (39).

Another issue that has been under discussion recently is that beta-lactam antibiotics, especially those such as cefepime, piperacillin-tazobactam and carbapenems (meropenem, imipenem, and doripenem) are to be given with long-term infusion. The serum concentrations of drugs given with long-term infusion stay longer above the minimum inhibitor concentration (MIC) value and ensures more bactericidal effect over the sensitivity-reduced bacteria. While imipenem and meropenem serum are half-life less than four hours and the benefit of infusions longer than three hours are limited, the long-term infusion of doripenem increases drug effectiveness since serum's half-life is long (37, 40).

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**References**


37. Fishbain J, Peleg AY. Treatment of Acinetobacter Infections. Clinical Infectious Diseases 2010; 51: 79-84. [CrossRef]

