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Lettera all'Editore

Letter to the Editor

Rapida diffusione di isolati di *Acinetobacter baumannii* multiresistenti in Unità di Terapia Intensiva e attività *in vitro* di colistina e tigeciclina

Rapid spread of multiresistant Acinetobacter baumannii isolates in intensive care units (ICUs) and in vitro activity of colistin and tigecycline

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Acinetobacter baumannii is a pleomorphic aerobic gram-negative bacillus, which is widespread in nature and frequently isolated from the hospital environment and hospitalized patients.

The organism is particularly common in patients who are intubated and in those who carry multiple intravenous lines or monitoring devices, surgical drains, or indwelling urinary catheters, and usually causes a large number of clinical conditions, including pneumonia, bacteraemia, urinary tract infections, wound infections, endocarditis and meningitis.

A. baumannii is susceptible to relatively few antibiotics including meropenem, colistin, amikacin, rifampicin, minocycline and tigecycline [1]. Multidrug-resistant *A. baumannii* is not a new or emerging phenomenon, as it is inherently resistant to multiple antibiotics. Therefore, the treatment of severe *A. baumannii* infections is often difficult [2, 3].

In recent years *A. baumannii* has emerged as an important nosocomial pathogen, particularly in intensive care units (ICUs) where several outbreaks have been described. More recently, microbiological surveillance data showed an increased prevalence of up to 4% of *A. baumannii* isolates in ICUs of Italian hospitals [4-7].

In 2011 a significant increase in *A. baumannii* isolates (Vitek II system, bioMérieux, Marcy l'Etoile, France) was observed in the ICU of the SS Annunziata Hospital of Taranto in southern Italy. In the same year, 81 strains were isolated, compared to 11 and 10 isolates in 2009 and 2010. Therefore, at present *A. baumannii* is the prevalent strain among the bacterial isolates in our ICU with an incidence rate of 15% (2.7% in 2009 and 1.9% in 2010) versus *Pseudomonas aeruginosa* (11.8%) and *Klebsiella pneumoniae* (11.3%). In most cases (79%), *A. baumannii* was isolated from the respiratory tract and in 12.3% from the bloodstream, while in the remaining cases from liquor and cutaneous wounds.

Our data show that the most common phenotype (99% of the isolates) was resistant to piperacillin, piperacillin/tazobactam, cefepime, ceftazidime, aztreonam, ciprofloxacin, levofloxacin, minocycline and imipenem. Resistance to gentamicin and isepamicin was observed in 3.7% and 10.3% of the isolates.

No resistance to colistin or tigecycline was observed in any *A. baumannii* strain isolates. In vitro activity of antimicrobial agents against *A.*

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Table 1 - Distribution of antibiotic susceptibilities for 81 *Acinetobacter baumannii* isolates in the ICU of the SS Annunziata Hospital of Taranto in 2011.

Antibiotics	*Susceptible breakpoint of antimicrobial (μg/ml)*	*No. (%) susceptible*
Aztreonam	≤1	1 (1.2)
Cefepime	≤1	0
Cefotaxime	≤1	0
Ceftazidime	≤1	4 (4.9)
Ciprofloxacin	≤0.25	1 (1.2)
Colistin	≤0.5	81 (100)
Gentamicin	≤1	3 (3.7)
Imipenem	≤1	1 (1.2)
Isepamicin	≤1	7 (8.6)
Levofloxacin	≤0.25	0
Minocycline	≤1	1 (1.2)
Piperacillin	≤4	1 (1.2)
Piperacillin/tazobactam	≤4	1 (1.2)
Rifampicin	≤2	2 (2.4)
Ticarcillin	≤8	1 (1.2)
Tigecycline	≤2	81 (100)
Tobramycin	≤1	2 (2.4)
Trimethoprim/ sulfamethoxazole	1/19	0

baumannii clinical isolates is summarized in table 1.

The high prevalence isolation rate observed in our ICU during 2011 gives cause for concern. Indeed, recent studies and systematic review show that acinetobacter infection or colonization is associated with increased mortality up to 41% versus 21% of controls and prolonged length of ICU hospital stay [8-10].

However, it is difficult to determine the attributable mortality of these infections regardless of the patient's severe underlying illnesses. Some parameters such as antimicrobial resistance, poor availability of therapeutic options and an empirical therapy may affect the mortality rate, which is twice as high in patients receiving an inappropriate versus appropriate antibiotic therapy [11].

Antimicrobial resistance among acinetobacter strains has increased in the past decade. Often, strains isolated in ICU are highly resistant to beta-lactams, aminoglycosides, fluoroquinolones and carbapenems, and are susceptible only to colistin. Colistin is an old antimicrobial which is widely considered for the management of infections caused by multidrug-resistant gram-negative pathogens including *A. baumannii,* in particular for critically ill patients in ICUs [12]. However, the emergence was reported of *A. baumannii* strains which are resistant to colistin with a rate of 25.8% [7]. In vitro activity of colistin is increased significantly by the presence of rifampicin and the combination is effective and safe for severe infections due to multidrug-resistant *A. baumannii*, with a clinical and microbiological response in 76% of cases and a 21% reduction in infection-related mortality [13]. Another antibiotic, tigecycline has provided hope for the treatment of these infections with its activity against multidrug-resistant acinetobacter strains, but isolates showing reduced susceptibility have emerged in many countries such as Israel, Spain, USA, China and Italy [14-16]. However, some studies showed in vitro synergistic activity of tigecycline in combination with various antimicrobials such as colistin, amikacin, levofloxacin and imipenem against tigecycline non-susceptible strains in a percentage of 8-16% [17]. In conclusion our data show a worrying rapid spread of multidrug resistant *A. baumannii* strains in ICUs and confirm that treatment options against these infections are very limited [18-21].

It is necessary to apply various methods for control and prevention of multiresistant *A. baumannii* infection based on standard precautions such as hand hygiene, barrier precautions, environmental cleaning and disinfection, and surveillance to identify infected or colonized patients.

However, it is also very important to promote judicious antimicrobial use as well as to begin empiric antibiotic therapy based on local surveillance data. Normally, carbapenem drugs should not be used for empiric therapy but reserved for targeted therapy. Hence sounder clinical assessment based on the employment of new combination therapies including tigecycline and colistin needs to be considered and adopted.

Keywords: *Acinetobacter baumannii*, ICU, antibiotic resistance.

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