



NOSOCOMIAL INFECTIONS CAUSED BY ACINETOBACTER BAUMANII – THE DIFFICULTY OF THE THERAPY CONCERNING MULTIDRUG RESISTANCE

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Abstract. Nosocomial infections are known for the severity of the clinical symptoms and the reserved prognosis due to the involvement of multidrugresistant germs, most of which are frequently identified as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *E coli*, *Klebsiella pneumoniae* extended-spectrum β -lactamase production (ESBL +); during the past two decades we have witnessed an alarming increase in the occurrence of the *Acinetobacter baumannii* multiresistant infections in the intensive care units (ICU), surgical units, thus turning into a fearful emergent pathogen agent. We decided to describe the clinical aspects associated to *Acinetobacter baumannii* nosocomial infections in the County Emergency Clinical Hospital in Sibiu and also their present susceptibility to antibiotherapy, evolution and prognosis. Nosocomial infections were generated by *Acinetobacter* in 95 cases out of 258, in tumoral diseases in 23 cases, politrauma or abdominal surgical interventions – 9 cases each, fractures – 13 cases with an unfavorable evolution in 7 cases. The sensitivity of the isolated stems is preserved in the cases of colistin – 98.15%, meropenem – 93.75% and imipenem – 86.02%.

Keywords: *Acinetobacter*, nosocomial infections, resistance

Theoretical considerations

From a taxonomic point of view, the *Acinetobacter* kind represent gram-negative bacteria which are aerobic, nonmotile, non-fermentative, catalase-positive, oxydase-negative, detached from *Moraxella*, 32 ubiquitous species having been identified up to now. The main species encountered in practice is *Acinetobacter baumannii* included in the complex *A. calcoaceticus* – *A. baumannii*, along with species 3 and 13 TU [1]. *A. baumannii* can resist over five months in the hospital environment on surfaces, equipment or through contamination of the medical-care personnel – it is frequently pres-

ent on eyebrows and armpits in 50% of the ICU personnel; it can contaminate the air-conditioning system, the IV and urinary catheters, the drinking water and humidifiers etc. The tegumental colonization seems to be the most frequently incriminated factor for the occurrence of nosocomial infections – wound over-infections, respiratory and urinary infections, sepsis, meningitis etc.

Among the virulent factors of *A. baumannii* we can mention: the exopolysaccharide synthesis, the membraned protein Omp 38 (responsible for cellular apoptosis), the biofilm formation (favored by the presence of the pili, which play a certain role in the cellular adhesion) and the unique system of iron usage. The neutrophils are known to play a major role in the defense of the host as far as the *A. baumannii* respiratory infections are concerned. Their recruitment at the infection site is quick, up to 4 hours, which explains the severity of the evolution in neutropenic patients and suggests a possible therapeutic approach for immune-compromised

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patients.

If prior to 1970 the *Acinetobacter* species showed no resistance and were susceptible to betalactams, aminoglycosides and chinolones, we presently witness the acquisition of an alarming resistance, sometimes without any efficient therapeutic resources on immune-depressive ground or depending on the infection's sites, this inefficiency being due to the limited penetrability of antibiotics, such as colistin. Different papers speak about the presence of pan-resistant strains [2] as being associated with the resistance to anti-pseudomonas penicillin, carbapenems, aminoglycosides, cephalosporines and fluoroquinolones through the reduction of membrane permeability, synthesis of β -lactamases, efflux systems, porine deletion, acquisition of OXA-carbapenemase (OXA -23, -24,-58), genic mutations *gyrA*, *parC*, acquisition of genic elements – integrons resistance class I, II, transposons, plasmids and other species such as *Proteus mirabilis*, *Klebsiella pneumonia*, *Enterobacter cloacae*, *Serratia marcescens*, which code for acetyltransferases, phosphotransferases, nucleothyltransferases involved in the resistance to aminoglycosides; they preserve their sensitivity to polymixine B, colistin and tigecycline.

The possible involvement of *Acinetobacter* in the etiology of community infections, for instance in community pneumonia, skin and soft tissue infections or sepsis appears on particular grounds: diabetes mellitus, obstructive chronic bronchopneumopathy, ethylism etc.; although the community strains are susceptible to most antibiotics, the mortality rate is still high: 40-64 %. The use of antibiotics leads to selection pressure which may result in the appearance of multidrug-resistant *A. baumannii* (MDR), particularly in ICUs associated with severe infections in critical state patients, sub-

sequent to using large spectrum antibiotics, most frequently carbapenems - meropenem, and also to prolonged hospitalization, mechanical ventilation or IV and urinary catheters. In Europe, during 2001-2004, the SENTRY surveillance system proved the preservation of the susceptibility of colistin in 97.3% of the cases, imipenem – 73.7% and meropenem 70.4%, respectively but below 50% in the case of cephalosporin and ciprofloxacin. *Acinetobacter* is responsible for 2 – 10% of the Gram negative bacteria infections in the ICU in the USA and Europe, 7.8-23% of intra-hospital mortality and 10-43 % of deceases in the ICUs. [4]

The therapeutic approaches are presently limited: carbapenems, doripenem being more efficient in the ventilation pneumonia therapy, the association of polymixine B with carbapenems, rifampin or azithromycin (synergic in vitro), aminoglycosides, fluoroquinolones, tygecycline (associated with the risk of appearance of the efflux pump resistance), colistin and sulbactam [5].

Material and methods

We have performed a prospective study of the nosocomial infections diagnosed at the County Emergency Clinical Hospital in Sibiu between January – December 2008, focusing on the cases in which *Acinetobacter* was isolated, in reference to the grounds where the nosocomial infection appeared, the identification site, coinfections, evolution or sensitivity to isolated stems.

Results and discussions

Acinetobacter was isolated in 95 cases (28.02% of the isolated strains), from a total of 258 cases of nosocomial infections (339 isolated) that were diagnosed in our hospital in 2008 (see Table I).

Etiology	No. of isolated strains
Gram negative bacteria	253
• <i>Acinetobacter</i>	95
• <i>E. coli</i>	44
• <i>Enterobacter</i>	41
• <i>Klebsiella</i>	29
• <i>Pseudomonas</i>	26
• <i>Proteus</i>	11
• <i>Serratia</i>	5
• <i>Citrobacter</i>	1
• <i>Pantoea</i>	1
Gram positive Cocci	86
• <i>Staph aureus</i>	34
• <i>Enterococ faecalis</i>	26
• <i>Enterococ faecium</i>	10
• <i>Enterococ spp</i>	9
• <i>Str pneumoniae</i>	1
• <i>Fungi</i>	7

Table I. Etiology of nosocomial infections

As to **the nosocomial infection site**, Acinetobacter was isolated in 55 cases out of 178 wound infections (30.90%), in 28 cases out of 57 of ventilation pneumonia (49.12%), in 2 cases of systemic infections associated with central venous catheter, 3 associated with urinary infections (7.32%) and one stem of Cerebrospinal fluid -CSF

Acinetobacter was the only identified etiologic agent in 52 cases (54.74%), while in other 42 cases it was associated with at least another etiologic agent (see Table II).

- strokes = 5 patients
- abdominal surgical interventions = 9 patients
- surgically operated fractures = 13 patients
- acute pancreatitis = 3 cases
- hematologic diseases = 2 cases
- post-delivery state = 2 patients
- one case of sepsis shock, pneumococcal acute meningitis, chronic renal failure.

The evolution was unfavorable, leading to decease in 7 cases attributed to Acinetobacter nosocomial infections (7.37%).

No. of isolated strains	Etiology
17	Escherichia coli ESBL+
6	Klebsiella pneumoniae ESBL+
1	Serratia marcescens ESBL+
4	Proteus
4	Pseudomonas aeruginosa
5	Enterobacter
1	Citrobacter freundii
9	Enterococcus spp
1	Staphilococi coagulasoneg
9	Staphylococcus aureus
3	Candida spp
1	Aspergillus

Table II. Other etiologies associated with Acinetobacter

The most frequent association we could diagnose was Acinetobacter-*Escherichia coli*, in 17 cases (see Table III), followed by the association with *Staphylococcus aureus* and Enterococcus, respectively, each of them in 9 cases.

The sensitivity of Acinetobacter strains is preserved with colistin (98.15%), meropenem (93.75%) and imipenem (86.02%). Their susceptibility to aminoglycosides cannot recommend the latter as first line therapy; tobramycin

Esch coli + Acineobacter isolation sites	Plague secretion	Tracheal secretion	Central venous catheter	Escara	Sputum
No. of izolated strains	10	3	2	1	1

Table III. Acinetobacter-E coli isolation sites

Associated pathology

The grounds where Acinetobacter nosocomial infections appeared were mainly immuno-depressed by different diseases for which the patients were hospitalized:

- neoplastic pathology = 23 patients
- cardio-vascular diseases = 10 patients
- diabetes = 6 patients
- extended burnings = 2 patients
- politrauma = 9 patients

68.97%, netilmicin 66.66%, amikacin 29.17%, isepamicin 22.22% and gentamicin 13.33%. The resistance to fluoroquinolones does not recommend them as first line therapy; as for ciprofloxacin, only 8 out of 91 isolated strains were sensitive to it; levofloxacin 4 out of 53, norfloxacin 4 out of 54 and pefloxacin 4 out of 65.

The tests on ceftazidim, cefepime, ticarcillin, ticarcillin-clavulanate have also revealed a very

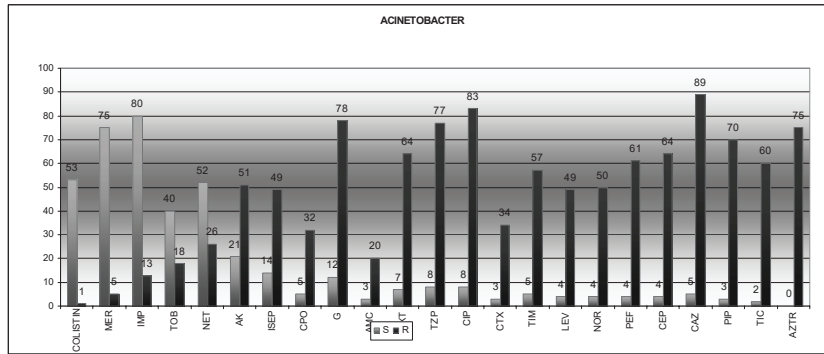


Figure 1. The sensitivity of *Acinetobacter* strains

strong resistance, which led to disregarding these antibiotics as therapeutic options (see figure 1).

Conclusions

Acinetobacter was the most frequent pathogen agent involved in nosocomial infections confirmed in 2008, most frequently isolated in wound infections and ventilation pneumonias. We have also noticed its association on an immune-depressed ground through tumoral pathology, abdominal surgery, orthopedic surgery and politrauma. The sensitivity to antibiotics is preserved for colistin, meropenem and imipenem.

References

1. Dijkshoorn L, Nemec A, Seifert H. An increasing threat in hospitals: multidrug-resistant *Acinetobacter baumannii*. 2007, *Nat. Rev. Microbiol.* 5(12), 939-951
2. Mahgoub S, Ahmed J, Glatt AE. Completely resistant *Acinetobacter baumannii* strains. 2002, *Infect. Control Hosp. Epidemiol.* 23, 477-479
3. Thomas D Gootz, Andrea Marra *Acinetobacter baumannii*: An Emerging Multidrug-resistant Threat *Expert Rev Infect Ther.* 2008; 6(3):309-325
4. Falagas ME, Bliziotis IA, Siempos II. Attributable mortality of *Acinetobacter baumannii* infections in critically ill patients: a systematic review of matched cohort and case-control studies. 2006, *Crit. Care* 10(2), R48
5. Fournier PE, Richet H. The epidemiology and control of *Acinetobacter baumannii* in health care facilities. 2006, *Clin. Infect. Dis.* 42, 692-699