Acinetobacter baumannii: Factors Involved in its High Adaptability to Adverse Environmental Conditions

Abstract

Acinetobacter baumannii has emerged as one of the WHO most dangerous pathogens hit-list and considered a priority of the Public Health Services worldwide. It can cause a wide range of opportunistic infections, typically involving ventilator-associated pneumonia, septicaemia and surgical wound infections mainly in immunocompromised patients. Two main features contribute to the great interest of *A. baumannii* over the other related species: first, the ability of clinical isolates to develop multidrug-resistance acquired by either mutations or genetic elements such as plasmids, transposons, or resistant islands and second, the ability to colonize almost any surface and survive in the environment making it very difficult to eradicate from clinical settings. The emergence of nosocomial and community-acquired infections due to *Acinetobacter* are mainly a result of high adaptability to adverse environmental conditions and the ability to persist for months in dry and harsh environments. They are able to survive exposure to commonly used disinfectants such as chlorhexidine, gluconate and phenols and is able to survive much better, compared with other gram-negatives, on fingertips or on dry surfaces thus facilitating its spread via hospital personnel, infrastructure, and medical devices. To add to this, the detection of MDR isolates is on the increase and although the search for novel antibiotics remains a major concern, a more urgent priority must be to investigate novel targets such as inhibitors of mechanisms of persistance in order to erradicate *A. baumannii* from the nosocomial environment.

Editorial

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Introduction

Acinetobacter baumannii has emerged as one of the WHO most dangerous pathogens hit-list and considered a priority of the Public Health Services worldwide. It can cause a wide range of opportunistic infections, typically involving ventilator-associated pneumonia, septicaemia and surgical wound infections mainly in immunocompromised patients [1]. The general morbidity and mortality rates of infections caused by *Acinetobacter baumannii* are similar to those of MRSA and that's why it has been termed the gram-negative MRSA.

During the last years, other members of the group, such as *A. pittii* and *A. nosocomialis* are also emerging as nosocomial pathogens, but *A. baumannii* is undoubtedly the species showing the highest clinical relevance as causes nosocomial pneumonia that affects patients in intensive care units with a rate of mortality of 30 to 75% [2,3]. Two main features contribute to the great interest of *A. baumannii* over the other related species: first, the ability of clinical isolates to develop multidrug-resistance acquired by either mutations or genetic elements such as plasmids, transposons, or resistant islands and second, the ability to colonize almost any surface and survive in the environment making it very difficult to eradicate from clinical settings [4].

The A. baumannii infections are mainly associated with nosocomial infections, but community acquired infections such as diarrhea outbreaks and pneumonia have been reported in tropical regions of the world especially during warm and humid months. Despite the increasing significance of these infections in many parts of the world, there are no many epidemiological reports on their incidence particularly in developing countries [5].

The success of *A. baumannii* as a nosocomial pathogen is a result of different factors:

a) A successful adaptation to adverse environmental conditions;

b) The long persistence on dry surfaces;

c) The resistance to antibiotics;

d) Plasticity of their genome and

e) The increase of immunocompromised patients.

To add to this, the frequent detection of MDR isolates, and although the search for novel antibiotics remains a major concern, it is a more urgent priority to investigate novel targets such as inhibitors of mechanisms of persistence in order to eradicate *A. baumannii* from the nosocomial environment. Moreover, extreme pH as well as the pH shift as the pathogen moves from its environmental niche to the patients body represents a great physiological stress on the pathogen that can be a key factor to use as target for new interventions [6].

Ecology of *Acinetobacter baumannii*

Acinetobacter spp. are mostly free living saprophytes and, although there have been found ubiquitously in nature, the precise environmental reservoirs are unknown. *A. baumannii*, *A. pittii*, and *A. calcoaceticus*, have been reported to inhabit soil and aquatic environments. The organisms have also been isolated from freshwater ecosystems; raw sewage and wastewater treatment plants and activated sludge. *A. baumannii* has also demonstrate its ability to grow on crude oil [1,7].

Generally considered part of the normal flora of the skin and mucosa of the pharynx, human respiratory secretions, urine, rectum and other clinical samples. They are the only group of gram-negative bacteria that may be natural residents of the human skin with carriage rates of 42,5% in healthy individuals and as high as 75% in hospitalized patients [1]. This asymptomatic colonization enables its spread both within and between hospitals.

In the hospital environment, it has been isolated from ventilator tubings, arterial pressure monitoring devices, humidifiers, washbasins and also from the skin of healthcare personnel, mattresses, pillows and in all types of ventilator equipment and moist situations such as sinks and tap water. Hospital food could also be a potential source of *A. baumannii* as different *Acinetobacter* spp. have been recovered from vegetables and fruits and they have been implicated in the spoilage of chicken, meat, fish and eggs, even when stored under refrigeration or after adequate gamma irradiation [1].

Acinetobacter baumannii has also been isolated from different animal sources, including birds and fish and is among the species implicated in animal diseases. They have also been isolated from lice collected from homeless people [1,2].

Survival of *A. baumannii* under stress conditions

The emergence of nosocomial and community-acquired infections due to *Acinetobacter* are mainly a result of high adaptability to adverse environmental conditions and the ability to persist for months in dry and harsh environments. They are able to survive exposure to commonly used disinfectants such as chlorhexidine, gluconate and phenols and is able to survive much better, compared with other gram-negatives, on fingertips or on dry surfaces. The resistance to desiccation has contributed to the emergence of *A. baumannii* as a significant nosocomial pathogen as enables it to withstand dry environments for months, thus facilitating its spread via hospital personnel, infrastructure, and medical devices [1,2].

In general three strategies have been described to survive on surfaces for long periods of time when changing environments or periods when basic requirements for growth are missing being a continuous source of transmission:

a) Bust and boom where a few surviving cells resume growth and replicate rapidly when the environmental conditions are suitable;

b) Cellular quiescence where the bacterial population persist in a viable nonreplicating state displaying metabolic capacity and;

c) True dormancy in which proper sporulation takes place. Although there are reports of some experiments that lead to think that biofilm producing *A. baumannii* could show a dormant phenotype more studies are needed. Considering *A. baumannii* is not a spore-forming bacteria the bust and boom strategy could explain its behavior. Moreover, although *A. baumannii* is generally viewed as an extracellular pathogen, but more evidence is being discovered that an intracellular lifestyle can be supported [8].

Bacterial tolerance to antibiotics has been linked with the emergence of persister cells, the phenotypic variants that are multidrug tolerant and are responsible for the chronicity of infections. Some reports indicate that the persistence is a phenomenon widely distributed among clinical isolates of *A. baumannii*, probably due to the antibiotic stress prevalent in the hospital environment also responsible for the selection of genetic virulence determinants [9]. However the genes involved in the persistence phenotype in this species are yet to be decoded.

Recent reports of the genetic requirements for *A. baumannii* persistence identify virulence factors as zinc and iron acquisition systems, capsule and LPS biosynthesis genes, amino acid metabolism and acquisition genes, and the *bfmRS* TCS but more studies are needed to increase knowledge in these aspects [10].

Biofilm formation on abiotic surfaces enhances *A. baumannii* capacity of survival in the environment (on fingertips and inanimate objects such as glass, plastic, and other environmental surfaces) even after exposure to dry conditions and nutrient starvation during extended periods of time. *A. baumannii* has been reported to have one paired Quorum Sensing system named AbaR-AbaI related to biofilm formation which is well known to be one of the principal factors conferring the ability of this species to survive on biotic and abiotic surfaces in nosocomial environments [11]. Quorum sensing is a bacterial communication method for recognizing cell population density with signal molecules. When the concentration of a quorum signal reaches the threshold, physiological properties and expression of diverse genes are altered, often resulting in a multi-cellular phenotype of unicellular species. QS regulates virulence, motility, antibiotic production, biofilm and expression of many other genes such as a type IV pilus system, oxidative stress defense and multi-drug resistance efflux (MDF)-, ABC- and RND-type pumps among others [12].

ROS stress causes macromolecular damage, and bacteria respond to it by producing enzymatic scavengers, such as catalase and superoxide dismutase, antioxidant enzymes widely distributed in nature. In *P. aeruginosa* both enzymes have been demonstrated to be controlled by quorum-senning mediated systems. In *A. baumannii* one quorum sensing has been identified involving the etranscriptional regulator AbaR but no links between quorum sensing and oxidative stress has been reported [9].

The A. baumanii has also been shown to coexist with *P. aeruginosa*, with evidence of interspecies interactions between them that may affect virulence and antibiotic sensitivities in both pathogens [13]. Several processes demonstrate unique cross-kingdom extracellular signalling between *A. baumannii* and *P. aeruginosa*, probably to control the microbial composition in

niches containing both organisms, and modulate the virulence of the mixed species community [8]. Such antagonistic interactions also suggest the potential for novel therapeutic agents to combat diseases that are challenging to treat due to antibiotic resistance.

Selection for increased survival of environmental stresses, such as clinical disinfectant strategies, antimicrobial compounds, etc. selects for strains displaying a hypervirulence phenotype such as MDR in clinical settings. It demonstrated the high prevalence of hypermutators among clinical *Acinetobacter baumannii* isolates [14]. Many mutators are found from an environment of high selective antibiotic pressure. Studies of clinical isolates have revealed that weak mutators can be present at earlier stages of infection, and a modestly elevated mutation rate can give them an adaptive advantage. Mutators can exhibit increased frequency of recombination, interspecies recombination and transformation. This events might explain in part the ability of *A. baumannii* to adapt in clinical settings [13].

Conclusion

Despite the huge increase in the frequency of infections caused by multidrug resistant *A. baumannii*, there is still a lack of awareness of the importance of environmental control of these microorganism. It is well known that resistant bacteria spread among animals and the local environment (soil, air and water) through long-term survival and transfer of genes to the resident flora, direct contact between farm animals and humans and through contaminated food. *A. baumannii* could represent a good example, due to its adaptation to different habitats and high ability to subsist on different substrats.

The escalating emergence of MDR strains of *A. baumannii* represents an alarming situation to the health services worldwide. It is a crisis which needs global responses and interventions to identify new drug targets and strategies. Threats to the current antibiotic treatment strategies and the rapid emergence of resistant isolates highlight the urgent need for developing novel and unconventional therapeutics [6]. Targets related or involved in mechanisms of persistence and stress responses must be kept in mind.

It is well demonstrated that one of the most important causes of antibiotic resistance is the intensive overuse across all ecosystems over the past decades, including humans, animals, aquaculture and agriculture. An effective international program should focused on the decrease of the antibiotic consumption in every sector (human, animal, aquaculture and agriculture). Moreover, as most reports on *A. baumannii* are from clinical samples but other samples, including environmental and food samples should be investigated to increase knowledge of their implications on human health and about the conditions of survival in the environment where they can persist under stress conditions during long periods of time [13,14].

There are many factors that make *A. baumannii* a dangerous organism, and many more likely to be discovered. Pathogenicity involves several virulence factors in combination with with metabolic capabilities and resistance to environmental stresses. Adaptation to stress involves intricate and interconnected regulatory pathways that integrate environmental signals with growth and survival decisions that in turn impact pathogenic potential [8-11].

There is a need for microbiologist to further investigate the virulence mechanisms presents in *A. baumannii* that produces its high persistence and adaptability to adverse environmental conditions and survival under environmental stress conditions for possible discovery of more effective control measures [9,12].

In conclusion, an ecological approach could be the key factor for the success of new points of view and future trends to control *A. baumannii* infections.

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