Control of an outbreak of *Acinetobacter baumannii* infections using vaporized hydrogen peroxide

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**SUMMARY**

**Background:** Multidrug-resistant *Acinetobacter baumannii* (MRAB) is a serious nosocomial pathogen characterized by its survival on inanimate surfaces for long periods, making control of outbreaks difficult.

**Aim:** To analyse two hospital outbreaks caused by MRAB, determine their epidemiology, carbapenem-resistance mechanisms and assess the effectiveness of surface disinfection by vaporized hydrogen peroxide (VHP).

**Methods:** MRAB strains were isolated from patients in two intensive care units (ICUs). Antimicrobial susceptibility testing was performed by E-test. Polymerase chain reaction (PCR) was used to detect the presence of the most common *A. baumannii* carbapenemases. Epidemiological typing was performed by rep-PCR (DiversiLab) and pulsed-field gel electrophoresis. VHP was used to decontaminate the affected ICUs.

**Findings:** MRAB was isolated from 28 patients between January 2009 and September 2010. All isolates were resistant to ciprofloxacin and gentamicin. Twenty-one were also resistant to carbapenems. Carbapenem resistance was associated primarily with the acquired OXA-23-like enzyme. Genotyping revealed three clones; the predominant clone corresponded to the international clone (IC) 2. Typing of the isolates pointed to a multifocal outbreak without a single source of infection, with horizontal spread of the dominating clone among ICU patients. A combination of rigorous infection control measures including strict isolation, education of staff, hand hygiene and surface decontamination using VHP halted the outbreak.

**Conclusion:** The results of this study confirm the importance of rigorous infection prevention and control measures, combined with VHP decontamination in controlling an outbreak of MRAB.

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**Introduction**

The genus *Acinetobacter* are aerobic, non-fermenting Gram-negative rods, some of which are widespread in the natural environment. *Acinetobacter baumannii* is clinically the...
most relevant member of this genus. It has a remarkable capacity for extended survival on environmental surfaces, but its natural reservoir remains unknown.\textsuperscript{1,2} A. baumannii is an important opportunistic pathogen among hospitalized patients, and contributes to increased mortality of these patients especially in intensive care units (ICUs).\textsuperscript{2,3} A. baumannii infections include ventilator-associated pneumonia, bloodstream infections and postoperative wound infections.\textsuperscript{4} Multidrug-resistant A. baumannii (MRAB) has emerged as an important cause of endemic polyclonal nosocomial infections, and hospital outbreaks of infections result in significant morbidity and cost of therapy.\textsuperscript{5}

Data concerning MRAB infections in Poland are still scarce. Control of infections caused by A. baumannii is difficult due to their wide distribution in the hospital environment, the ease of transmission from person to person and the difficulties in identifying the original reservoir. Reducing the incidence of MRAB nosocomial infection involves implementation of strict hand hygiene guidelines, proper decontamination of equipment and also the hospital environment.\textsuperscript{6} The role of cleaning the hospital environment in preventing transmission of nosocomial pathogens has been less well studied. No-touch decontamination technologies, including vaporized hydrogen peroxide (VHP), are being used increasingly in acute healthcare settings.\textsuperscript{7} VHP is a broad-spectrum disinfectant which appears to have low toxicity, does not damage inanimate materials, and degrades into oxygen and water. Specific monitors can estimate the residual concentration of hydrogen peroxide so that toxicity of this agent can be avoided. Achieving adequate contact time between the disinfectant and hospital environment sites and application of correct concentration of the disinfectant can be programmed.

The aim of this study was to analyse two hospital outbreaks caused by MRAB among patients hospitalized in two cardiac surgery ICUs of a highly specialized hospital in Southern Poland in 2009–2010, and to assess the effectiveness of surface disinfection by a VHP decontamination system for control of the outbreak.

Methods

Outbreak setting

The John Paul II Memorial Hospital is a 526-bed teaching hospital located in Krakow, and is the main tertiary referral centre serving southern Poland for invasive cardiology and cardiac and thoracic surgery. The two large cardiothoracic surgery intensive care units admit ~3000 patients annually. In 2009, there was a total of 85 beds in these two units. There were two physicians present in the first ICU per working day and one on each night shift, and five nurses on each working day and night shifts. In the second unit were two physicians (24 h) and 11 nurses per working day, and 10 nurses at night. Prospective active surveillance of infections is carried out using National Healthcare Safety Network definitions.\textsuperscript{8}

In 2009, a total of 20 MRAB-positive patients were investigated; in September 2010, eight new MRAB infections were reported. Clinical samples were obtained for microbiological culture as clinically indicated for each patient. Surveillance cultures from patients for contact tracing were not obtained. Environmental samples in both ICUs were collected during the course of the MRAB outbreaks; twice in 2009 (13 August 2009, 7 September 2009) and once in 2010 (21 October 2010). These samples were collected from monitoring equipment, respirator tubes, resuscitation trolleys, several computer keyboards and screens, nurses’ station desk, sinks, liquid soap, and dispensers of hand disinfectant. No swabs were collected from the hands of staff.

Environmental decontamination

Prior to the outbreak, routine decontamination of the environment was performed using the following disinfectants: (i) preparations containing hydrogen peroxide, chlorides and quaternary ammonium compounds for large surfaces; (ii) preparations containing chlorides and cyanuric acid or sodium bisulphate and sodium tetraborate for sinks, toilets and fluid spills; and (iii) an alcohol-based preparation for rapid disinfection of small surfaces.

When the conventional methods described above failed to terminate the outbreak, environmental decontamination with VHP (Steris Ltd, Basingstoke, UK) was introduced for decontaminating operating theatres and patients’ rooms. VHP is a mobile system for disinfection and sterilization of rooms at low temperatures (20–45 °C). A prevalidated cycle was performed in both ICUs, with an application of 250 ppm for 90 min followed by 400 ppm for 30 min.

Bacterial samples

Clinical samples for microbiological culture included bronchial aspirates, wound swabs, blood cultures, peritoneal fluid, urine and catheter tips. Cultures were processed using standard microbiological methods. Isolates were initially identified as A. baumannii by the Vitek 2 system (bioMérieux, Warsaw, Poland). Species identification was confirmed by gyrB multiplex PCR.\textsuperscript{9} Antimicrobial susceptibility

Antimicrobial susceptibility testing for ampicillin/sulbactam, imipenem, meropenem, ciprofloxacin, amikacin, gentamicin, tobramycin, tigecycline, polymyxin B was performed using E-test strips (AB bioMérieux, Solna, Sweden).\textsuperscript{10} Imipenem and meropenem minimum inhibitory concentrations (MICs) of ≤2 and >8 mg/L were interpreted as susceptible and resistant, respectively, according to the current EUCAST guidelines.\textsuperscript{10} Ampicillin/sulbactam susceptibility was interpreted according to the CLSI guidelines.\textsuperscript{11} Because there is no approved standard for considering A. baumannii susceptible or resistant to tigecycline, provisional MIC breakpoints used for this agent were ≤2, 4, and >8 μg/mL to designate susceptible, intermediate, and resistant isolates, respectively.\textsuperscript{12}

Detection of carbapenemases

To detect the presence of the most common A. baumannii carbapenemases, multiplex PCR was performed as previously described.\textsuperscript{13} The presence of the insertion element IS4ab1 upstream of bla\textsubscript{OXA-51-like} and bla\textsubscript{OXA-23-like} was investigated by PCR.\textsuperscript{14}
Molecular typing

Epidemiological typing of isolates was performed by rep-PCR (DiversiLab System; bioMérieux, Nürtingen, Germany) as previously described.\textsuperscript{15} Isolates that clustered $\geq 95\%$ were considered related. Clusters were compared to our in-house library of worldwide carbapenem-resistant isolates to determine their epidemiological background.\textsuperscript{14} Pulsed-field gel electrophoresis (PFGE) was used as an additional method of typing as described previously.\textsuperscript{16} PFGE banding patterns were analysed with the Molecular Analyst software (BioRad) using Dice coefficient and the UPGMA (unweighted pair group method with arithmetic averages) algorithm.

Results

The index patient was a 67-year-old man with a perforated oesophagus, who developed nosocomial pneumonia with MRAB, subsequently recovered from a bronchial aspirate, in January 2009. By June 2009, when another three patients were found to be colonized or infected with MRAB, an outbreak was declared. From January to December 2009, MRAB infections were reported in a total of 20 patients from the two ICUs.

Sixteen infections occurred in patients following cardiovascular or cardiothoracic surgery. Eleven patients had pneumonia, three had surgical site infections (SSIs), three had bloodstream infections (BSIs), one had urinary tract infection (UTI) and two strains were isolated from catheter tips from patients without bloodstream infections (Table I).

No specific type of care or procedure common to all infected patients could be identified.

MRAB was not recovered from any of the environmental samples obtained in August and September 2009. Routine decontamination of the hospital environment was performed, but this did not result in termination of the outbreak. In December 2009, after standard methods had failed, it was decided to close the affected ICUs temporarily. The patients were transferred to other departments following isolation guidelines. A series of educational training sessions was held for staff. The environmental cleaning and decontaminating procedures were also changed to include daily cleaning of all equipment with a hypochlorite-based agent. Both ICUs were decontaminated using the Steris VHP system on 20 December 2009.

After closure of the units, standardized infection prevention procedures, as recommended by CDC, were implemented in both units including hand hygiene, suctioning procedures, skin preparation, frequency and aseptic technique for intravenous line changes. Contact precautions included the use of gowns, gloves, hand hygiene before and after glove removal, gown and glove removal before leaving the room. Face masks were used if contact with body secretions or respiratory care was likely.\textsuperscript{17–20} In addition, mandatory screening of patients and staff for MRAB carriage was introduced. Surgical units restarted operating and patients were readmitted to ICUs from 1 January 2010 onwards. Between January and August 2010, no there were no further MRAB infections on the units.

The second outbreak occurred in September 2010 in eight ICU patients. New MRAB infections included six cases of pneumonia, and one patient each with UTI and SSI, respectively. Overall, 60\% of pneumonia cases were associated with mechanical ventilation (MV), with a mean length of MV before onset of 15 days. After recognizing the second outbreak in September 2010, the aforementioned decontamination procedures were repeated (17 October 2010). From October 2010 to October 2011 no MRAB were isolated from clinical samples (Figure 1).

None of the patients who had been hospitalized in one of the ICUs in the previous year was re-hospitalized, and patients in 2010 had no reported contact with patients from the previous year. The two units studied were located in separate parts of the hospital and patients were not transferred between them. However, physicians, anaesthetists, nurses, support staff and physiotherapists were working in both ICUs.

Total cumulative incidence of all infections was 6.5 per 100 admissions and the total incidence density was 23.9 per 1000 patient-days in the study period (in 2009/2010). The mean length of ICU stay was 2.7 days. The incidence of MRAB pneumonia in 2009/2010 was 3.6 per 1000 admissions (epidemic level) as compared with the baseline of 1.3 pneumonias per 1000 admissions (risk ratio: 2.8) in 2008 (endemic level). BSI incidence reached 0.6 per 1000 admissions whereas in 2008 there were no such cases reported. Altogether eight patients died, giving a crude mortality rate of 27.6\%. The mean age of patients with MRAB infection was 66 years and was equal to the median age. The mean number of days between admission to the ICU and the first MRAB-positive culture was 23 days (median: 18). The proportion of female patients was 25.8\%. Out of 28 isolates collected in 2009 and 2010 from 28 patients, 26 were from symptomatic infections and two represented colonization (Table I). A. baumannii was not cultured from the environment.

All A. baumannii isolates investigated were resistant to ciprofloxacin and gentamicin but remained susceptible or intermediate to tigecycline. Only one isolate was susceptible to amikacin. The percentages of isolates susceptible and/or intermediate to amoxicillin–sulbactam and tobramycin were 50\% (14 isolates) and 32.1\% (9 isolates), respectively. Twenty-one of 28 isolates (75\%) were resistant to carbapenems, whereas seven isolates were susceptible or intermediate to imipenem (25\%) and six isolates to meropenem (21.4\%) (Table I).

All isolates possessed bla\textsubscript{OXA-51-like} and bla\textsubscript{OXA-23-like}. IS\textit{Abal} was found upstream of all \textit{bla\textsubscript{OXA-23-like}} genes, and these isolates were resistant to carbapenems. Three isolates possessed the acquired \textit{bla\textsubscript{OXA-58-like}}, and one isolate had \textit{bla\textsubscript{OXA-40-like}}. Eight isolates had only the gene encoding OXA-51 and in six of them the \textit{IS\textit{Abal}} element was upstream of \textit{bla\textsubscript{OXA-51-like}} but only one was resistant to both carbapenems (Table I).

PFGE demonstrated the presence of three different clones. Pulsotype 1 included 13 isolates that were emerging in the hospital from February 2009 until December 2009, eight of which were derived from respiratory tract infections. The same clone included seven isolates from the second outbreak episode in September 2010, five of them were from respiratory tract infections. Pulsotype 2 comprised six isolates including two from patients with SSI and three from patients with pneumonia (one from the second outbreak). Pulsotype 3 consisted of two isolates recovered in May 2009 from patients with pneumonia.

Diversilab also revealed three clones (designated A, B and C). Type A corresponded to pulsortypes 2 and 3 identified by PFGE; PFGE pulsortype 1 was further divided into the rep-PCR subtypes B and C. Type B included eight strains (six from the
<table>
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<tr>
<th>Episode of outbreak/laboratory no.</th>
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<th>Minimum inhibitory concentration (mg/L)</th>
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<td></td>
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SAM, ampicillin/sulbactam; CIP, ciprofloxacin; GEN, gentamicin; AMK, amikacin; TOB, tobramicin; TGC, tigecycline; IPM, imipenem; MEM, meropenem; BAL, bronchoalveolar lavage; OXA, oxacillinase type; PFGE, pulsed-field gel electrophoresis.
second outbreak). Type C included 12 isolates (one from September 2010). Clusters identified by the DiversiLab method were compared with our in-house library of worldwide carbapenem-resistant isolates to determine their epidemiological background. The predominant clone (PFGE pulsotype 1, rep-PCR types B and C) corresponded to the international clone (IC) 2. Isolates representing pulsotypes 2 and 3 (rep-PCR type A) were assigned to IC 1 (Figure 2).

Discussion

A. baumannii often colonizes the respiratory tract of patients hospitalized in the ICU and consequently this organism is an important aetiological agent of ventilator-associated pneumonia. Due to possible colonization of wounds and vascular catheters, these organisms also play a role in BSIs, UTIs and soft tissue infections. The attributable mortality caused by A. baumannii infections in the ICUs ranges between 7.8% and 23%, which is similar to what we observed in our study.

A. baumannii has become increasingly multidrug resistant during the last few decades. In the late 1980s, resistance to carbapenems was first described and today many of the isolates from hospitalized patients are susceptible only to tigecycline and polymyxins. In Poland, carbapenem resistance rates have increased for isolates from ICU patients since 2000. Wróblewska et al. reported that A. baumannii BSI accounted for 18.2% of all BSIs and the incidence of imipenem resistance was as high as 40% in two ICUs in Warsaw.

In A. baumannii, resistance to carbapenems is commonly mediated through OXA-type class D enzymes. The genes encoding OXAs may be passed on by chromosomal fragments, plasmids and transposons and are often regulated by insertion sequences such as ISAba1. Presence of OXA-23-like, OXA-40-like, OXA-58-like and OXA-143 is often related to carbapenem resistance. These acquired enzymes are found integrated in the chromosome or on plasmids and the strains which produce them may spread epidemically and exchange resistance genes between them. The majority of strains tested in this study had the acquired OXA-23-like enzyme.

Molecular typing of A. baumannii isolates was performed to assess the epidemiological situation in the ICUs and the use of two complementary methods allowed for a more precise determination of the spread of these strains among ICU patients. Both typing methods showed similar results. Using the commercial DiversiLab system allowed us to compare the examined clones with strains resistant to carbapenems found worldwide. Typing of the hospital isolates pointed to a multifocal outbreak, not to a single source of infection, with horizontal spread of the predominating clone among ICU patients.

The two units where the outbreak investigation was performed took necessary action with regards to updating written procedures, training of personnel and surface decontamination. However, one of the reasons for this prolonged outbreak could be that surveillance cultures of patients and staff were not introduced before ward closure, and patients with undetected MRAB colonization could have served as a reservoir. Lack of screening samples from staff and patients was a limitation of our study. Only after temporary closure of wards had been instituted, and full decontamination of the departments using VHP performed, was the outbreak controlled. Unfortunately, a second outbreak occurred eight months after the first. We do not know the source of the second outbreak. Both

Figure 1. Monthly report of new cases of multidrug-resistant A. baumannii (MRAB) infections. Arrow 1: closure units and Steris VHP intervention (20 December 2009); arrow 2: Steris VHP intervention (17 October 2010).
**Figure 2.** Results of two different typing methods of *A. baumannii* isolates. PFGE, pulsed-field gel electrophoresis.

de novo introduction of the epidemic strain through transfer of a colonized patient and undetected persistence of the epidemic strain in the hospital environment are possible although none of the multiple environmental samples had yielded a positive result. On the other hand, the control measures had at least some effect since no MRAB was isolated from patients’ blood during the second outbreak. It is therefore reasonable to think that some procedural errors were eliminated by strengthening intravascular catheter care and contact isolation, especially hand hygiene, including the implementation the World Health Organization’s ‘My five moments for hand hygiene’.

Hardy *et al.* observed a rapid re-contamination of the environment by MRSA after VHP decontamination, but this was associated with the re-introduction of patients into the hospital ward. Decontamination of the hospital environment using VHP can have important advantages. Hydrogen peroxide is a broad-spectrum disinfectant, considered active against a wide range of nosocomial pathogens. It seems to be particularly effective in the decontamination of large hospital wards and should be used in order to better attain infection control goals.

VHP decontamination was successfully used recently to control nosocomial acquisition of MRAB in a long-term acute care hospital. The results of this study demonstrate that rigorous infection prevention and control measures including strict isolation, environmental cleaning, staff education and proper hand hygiene, along with VHP decontamination were successful in controlling MRAB in an intensive therapy unit setting.
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Conflict of interest statement
None declared.

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References

12. AB bioMérieux. Summary of Etest performance, interpretative criteria and quality control ranges — Table 1. AB bioMérieux Document 2009;05, Solna.