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Major Article

Nosocomial outbreaks caused by *Acinetobacter baumannii* and *Pseudomonas aeruginosa*: Results of a systematic review

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Background: Large outbreaks of infection by *Acinetobacter baumannii* and *Pseudomonas aeruginosa* have been reported. This research compares characteristics of such outbreaks.
Objectives: Determination of risk factors for the occurrence and appropriate infection control measures.
Data Sources: The Outbreak Database, PubMed, and reference lists of identified articles were used. Key words included *nosocomial* and (*outbreak* or *epidemic*) and (*aeruginosa* or *baumannii*).
Study Eligibility Criteria: Articles were included if they describe distinct outbreak(s) caused by *A baumannii* or *P aeruginosa* and were published between 2000 and 2015. There were no further restrictions with respect to language or type of article.
Results: One hundred fifty outbreaks by *A baumannii* and 131 outbreaks by *P aeruginosa* were included, including multidrug-resistant strains in 113 *Acinetobacter* and 49 *Pseudomonas* outbreaks. *Acinetobacter* outbreaks were mainly reported from intensive care units, after use of antibiotics, during mechanical ventilation, and presented with a mortality rate of 47% compared with 23% by *Pseudomonas*. Resistance did not alter mortality by either species. Most infection control measures were implemented or enforced more often in *Acinetobacter* outbreaks.
Conclusions: These findings should support staff in infection control departments and on wards if an outbreak is suspected. Better adherence to the Outbreak Reports and Intervention Studies of Nosocomial Infection guidelines in outbreak reporting is necessary. A precise definition of multidrug resistance for *Acinetobacter* and *Pseudomonas* is lacking.

In the case of a nosocomial outbreak, knowledge about typical sources of a particular pathogen, its most frequent modes of transmission, and appropriate infection control measures is crucial to terminate the event at the earliest time point.[1,2] That is why several systematic reviews on various kinds of nosocomial outbreaks have been carried out already.[3-7]

There are also many reports of nosocomial outbreaks in the medical literature caused by *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. These outbreaks affected many patients, there were severe infections, and numerous fatalities occurred. Furthermore, a dramatic increase was observed with respect to the frequency of multidrug-resistant (MDR) strains among those nonfermenting gram-negative aerobic rods in past decades.[8,9]

Despite this enormous clinical influence, little is known about the characteristics of those events. This systematic review on nosocomial outbreaks by *A baumannii* und *P aeruginosa* is supposed to close this gap of information by providing outbreak data on both species and comparing those findings.

MATERIALS AND METHODS

Retrieval strategy

The Worldwide Outbreak Database (www.outbreak-database.com) represents the largest collection of all kinds of nosocomial outbreaks.[10] Outbreak reports from the medical literature are filed in this database in a standardized manner. This way, users may check for—or even combine—parameters of nosocomial outbreaks (eg, pathogens, pathogen reservoirs, colonizations, and infections) in their

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search as it matches their particular interest. This database was accessed on February 16, 2016, for all outbreaks caused by the 2 abovementioned species.

PubMed was searched on March 10, 2016, to check for any articles that may not yet have been included in the Worldwide Outbreak Database. A search strategy was applied using the following key words and medical subject headings terms: *nosocomial* and (*outbreak* or *epidemic*) and (*aeruginosa* or *baumannii*).

Finally, reference lists of all retrieved articles were checked for any further relevant literature on this topic.

Criteria for inclusion or exclusion of literature

Reports were included only if they were original articles describing a distinct outbreak caused by either *P aeruginosa* and/or *A baumannii*. Reviews may also serve as a source for further original outbreak reports, but results from previous reviews were discarded to avoid bias by preselected metadata.

Articles describing more than 1 outbreak were included only if data analysis was possible for each single outbreak event separately. The same applied if multiple clones were involved that could be clearly distinguished from each other by genotyping.[11] Those events were considered multiple outbreaks occurring at the same time in the same location.

Reports were included only if they were published between 2000 and 2015. This was done to minimize the risk of relying on data from out-of-date settings (eg, sensitivity and specificity of microbiologic diagnostic methods, availability of methods for genotyping, or proportion of single-bed rooms in intensive care units [ICUs] or peripheral wards).

There were no restrictions with respect to the language of the publication. Articles written in English, French, German, and Spanish were always read in full text. In all other cases, especially if the report was written in a language of Asian origin, the extraction of data focused on its English abstract.

Extraction of data

Data on all parameters that are potentially relevant for the evaluation of nosocomial outbreaks[12] was collected. This included data on the general setting of the outbreak, characteristics of patients, environmental findings, and consequences drawn from the outbreak investigation. If provided by the authors, the following information of the nosocomial outbreak got collected as reported in the original articles: year, duration of the outbreak, country, type of medical department, type of ward (peripheral unit vs ICU), number of patients influenced, number of infected patients, number of deceased patients, type of nosocomial infections, any potential or proven risk factors that may facilitate the acquisition of a nosocomial pathogen (eg, length of stay in the hospital or on the ward, immunosuppression, invasive procedures, or mechanical ventilation), sources and reservoirs of the pathogen, occurrence of MDR if named as such in the original article, route of transmission, typing methods for the confirmation of the outbreak (genotyping vs phenotyping only), costs of the outbreak, infection control measures enforced or newly applied (eg, screening of patients, screening of personnel, isolation and/or cohorting, hand hygiene, disinfection, use of protective clothing, changes in the use of medical devices, education of staff, closure of the ward, improvement in the staff-to-patient ratio, air sampling, water sampling, or sampling of other environmental sources).

Data were extracted primary by 1 author (KW) and the findings were then discussed with a second author (RPV) for an independent evaluation of results. Disagreement were solved by discussion among all 3 authors (KW, PC, and RPV).

Statistical analysis

Differences in the frequency of parameters were determined using the EpiInfo database and statistics software for public health professionals as provided on the homepage of the Centers for Disease Control and Prevention (www.cdc.gov/epiinfo/index.html). *P* values < .05 were considered significant; *P* values < .01 were considered highly significant.

RESULTS

Included articles

A total of 150 nosocomial outbreaks caused by *A baumannii* and published in 122 articles and further 131 outbreaks caused by *P aeruginosa* and published in 116 articles were included in this systematic review. The selection process of articles is shown in detail in Figure 1. The corresponding references in total are provided separately for both species as supplemental material to this article.

Outbreaks were reported from 22 different countries all over the world. The most reports of the 150 *Acinetobacter* outbreaks came from the United States and Italy (n = 16 outbreaks each), Spain (n = 13), France and Turkey (n = 11 each), Taiwan (n = 10), and Greece and South Korea (n = 9 each). Publications of *Pseudomonas* outbreaks were mostly available from the United States (n = 23), Japan and Italy (n = 13 each), Brazil (n = 11), the United Kingdom and France (n = 8 each), and India and Spain (n = 7 each).

The cumulative number of outbreaks of over time stratified by pathogen and type of ward (peripheral vs ICU) is shown in Figure 2. The outbreaks caused by *P aeruginosa* were rather evenly distributed. In contrast, outbreaks caused by *A baumannii* were much more often observed in ICUs than on peripheral wards.

Outbreak characteristics

Exact data on mortality was available for 66 *Acinetobacter* outbreaks (686 infections and 323 fatal cases) and 55 *Pseudomonas* outbreaks (619 infections and 144 fatal cases). Thus, mortality rates were significantly higher ($P < .01$) in infections caused by *A baumannii* (47.1%) compared with *P aeruginosa* (23.3%). Among the *Acinetobacter* outbreaks, there were 113 (75.3%) described as MDR by the authors of the articles compared with 49 (37.4%) MDR *Pseudomonas* strains. However, mortality rates did not depend on the resistance profile of the species (mortality of MDR *Acinetobacter*: 48.0% vs non-MDR *Acinetobacter*: 44.6% [$P = .50$]; mortality of MDR *Pseudomonas*: 25.0% vs non-MDR *Pseudomonas*: 24.7% [$P = .91$]). There was no consistent definition of MDR. Table 1 provides an overview on the baseline characteristics of the nosocomial outbreaks caused by *A baumannii* and *P aeruginosa,* respectively.

Confirmation of genetic relatedness by genotyping was done in 130 of 150 *Acinetobacter* outbreaks, resulting in 37 outbreaks with genotyping for some of the isolates and 93 outbreaks with genotyping for all isolates. Genotyping was also performed in 111 of 131 *Pseudomonas* outbreaks, resulting in 38 outbreaks with genotyping for some and 73 outbreaks for all isolates.

Table 2 shows the distribution of medical departments that were affected by nosocomial outbreaks. Data on the type of medical discipline was available only for 98 of 150 *Acinetobacter* outbreaks and 102 of 131 *Pseudomonas* outbreaks. Most outbreaks were reported from surgical units and internal medicine wards. Depending on its source and the route of transmission, an outbreak may take place in more than 1 type of department.