Variability of treatment duration for bacteraemia in the critically ill: a multinational survey

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Objectives: No definitive evidence is available to inform ‘best’ antibiotic practice for treating bacteraemia in the critically ill patient, either in terms of duration of therapy, or the use of mono- versus combination therapy. We therefore undertook a large-scale international survey to assess the variability of current practice.

Methods: A questionnaire was sent to membership lists of national and international intensive care societies.

Results: Responses from 254 intensive care units in 34 countries revealed a wide variation in antibiotic strategy for all types of bacteraemia, ranging from short course (≤5 days) therapy with restricted-spectrum antibiotics, to long course (≥10 days) use of broad-spectrum combinations. Two factors were significantly associated with antibiotic prescribing practice, namely the country of origin (in those with ≥10 responders) and the level of microbiologist and/or infectious diseases specialist input. The greater the specialist input, the shorter the duration of therapy (P < 0.0001).

Conclusions: The wide variability in antibiotic prescribing patterns suggests an urgent need to produce high-quality evidence to identify optimal antibiotic prescribing policies for bacteraemia in the critically ill patient.

Keywords: intensive care, antibiotics, sepsis, infections

Introduction

Critically ill patients are at increased risk of developing bacteraemia owing to alterations in their host defence mechanisms caused by the precipitating disease/illness, the extensive use of invasive procedures, and coexisting endogenous or exogenous immunosuppression.¹ Severely infected patients are associated with a prolonged intensive care unit (ICU) and hospital stay, and carries a high mortality (21–56%).¹–⁴ However, no randomized, prospective clinical trials exist to guide prescribing practice, and the few available observational studies do not offer clear advice.¹ To provide some new insights into this important topic, we have launched an international, multi-stage research project, BASIC (BActeraemia Study in Intensive Care), the first step of which was a survey of intensive care clinicians determining their current antibiotic policy for different types of bacteraemia and fungaemia.

Materials and methods

Data collection

In January 2001, a detailed questionnaire (the full questionnaire is available as Supplementary data at www.jac.oupjournals.org) was posted on critical care websites and sent to membership lists of different ICU networks or societies including the European Society of Intensive Care Medicine (ESICM), Australian & New Zealand Intensive Care Society (ANZICS), Gruppo italiano per la Valutazione degli interventi in Terapia Intensiva (GiViTI) and the UK Intensive Care Society (ICS) (see Acknowledgements). Apart from ICU characteristics (type of ICU, number of beds, patient admission source, annual throughput, etc.), the questionnaire requested details on the perceived incidence of bacteraemia and fungaemia, resistance patterns, type and duration of treatment for specific types of bacteraemia and fungaemia (e.g. peritonitis-related, methicillin-resistant...
**Statistical analysis**

Proportion was used as a descriptive statistic for categorical variables; mean and standard deviations (S.D.) were used for quantitative variables. The variability in responses among ICUs was reported by the use of median, overall range and interquartile range (IQR), the latter being less influenced by outliers. The relationship between microbiologist and/or infectious disease specialist input and the duration of antibiotic therapy was assessed with the Spearman correlation coefficient. A two-tailed \( P \) value less than 0.05 was considered statistically significant. For analyses that were stratified by country, we restricted the sample to countries with at least 10 ICUs responding. Data were analysed using the SAS System (Version 8.02).

**Results**

A total of 254 ICUs from 34 countries responded; 214 (84%) were European, 21 Australasian, and 10 Latin-American (Table 1). These ICUs were mainly general (77.5%), with a mean number of 11.0 beds (S.D. 6.1) and a median of 455 admissions per year (IQR 280–750). Most of the ICUs (77%) had an agreed antibiotic prescribing policy, mainly restriction of use (74% of the total). Sixty percent had an infection control programme, whereas only 28% had infection control nurses associated with the unit.

The median number of patients having bacteraemia and fungaemia (either community, hospital or ICU-acquired) as a proportion of the total number of admitted patients was 6.1% (IQR 3.3–11.8%) and 0.6% (IQR 0.3–1.6%), respectively. MRSA accounted for 25% (IQR 3–60%) of all Gram-positive organisms, whereas 10% (IQR 3–27%) of Gram-negative organisms were multidrug-resistant strains.

For all countries with at least 10 participating centres, a wide variation in the percentage of ICUs using long courses \((\geq 10\) days\) of antibiotics was recorded. This ranged from 3.5% to 75% for primary bacteraemia; from 16.7% to 87.5% for nosocomial pneumonia-related bacteraemia; and from 20.0% to 93.8% for peritonitis-related bacteraemia. Large differences were found in the percentage of ICUs using broad-spectrum antibiotics as first-line therapy. This ranged from 22.2% to 73.3% for community-acquired Gram-positive bacteraemias; from 60.0% to 94.4% for nosocomial Gram-positive bacteraemias; and from 60.0% to 93.8% for community-acquired Gram-negative bacteraemias. Conversely, nosocomial Gram-negative bacteraemias were generally treated with broad-spectrum antibiotics in almost all ICUs (range 93.6–100%).

Decisions to start and stop antibiotic therapy were usually taken by intensive care clinicians alone in over 80% of cases. The overall level of direct input from microbiologist or infectious diseases specialists was low (median 1 visit per week; IQR 0–3). However, this varied widely among countries, being high in the Netherlands (median 5; IQR 3–6) and the UK (median 5; IQR 2–5); medium in Australasia (median 2; IQR 1–5); and low in Italy (median 0; IQR 0–0; range: 0–5) and Spain (median 0; IQR 0–0) (Figure 1). A statistically significant *inverse* association was found between specialist input and the duration of antibiotic therapy. This effect was observed for all types of bacteraemia except for *S. aureus* line-related bacteraemia \((P = 0.10)\) which did not quite reach statistical significance (Figure 2).

As Italy was the country most represented in the survey, and its overall practice was the most extreme, we carried out a sensitivity analysis by removing Italian ICUs to test the hypothesis that this country acted as a confounder. Despite omitting Italian ICUs, statistical significance \((P < 0.05)\) was still reached in five of the seven bacter-
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Discussion

As no high-level evidence is available to inform practice on optimal antibiotic prescribing policies for bacteraemia in the critically ill patient, individual ICUs have developed their own strategies, using either restricted or broad-spectrum antibiotics, for variable periods of time. This survey is the first to document and confirm our impression that large variability in prescribing practice does indeed exist.

Although based on reported prescribing strategy rather than direct observation of actual practice, this study has the advantages of being truly multi-national, and involving a large number of ICUs. Considering the limitations of a questionnaire-based survey, and acknowledging the variable response rate from different countries, the purpose of our survey was to identify variability in overall practice rather than a specific between-country comparison. We indeed documented a wide variation in antibiotic prescribing practice for bacteraemia in ICU patients that is too wide to fit the hypothesis that all observed approaches are appropriate. On the one hand, short courses may potentially fail to eradicate the infecting microorganism with an increased likelihood of relapses, whereas long courses may predispose to drug toxicity and, possibly, fungaemia. Ironically, both policies are considered major determinants for antimicrobial resistance.1,5

What does influence antibiotic prescribing practice, at least for bacteraemia, within the ICU? Obviously, numerous factors can be postulated including financial, educational and cultural considerations. We were interested to find a strong effect relating to country and specialist input, though these two were strongly interconnected with high-level specialist input in the Netherlands and the UK contrasted by negligible direct involvement in Italy. We did not examine whether specialist resource availability or philosophical acceptance of a joint management approach predicated a greater or lesser involvement by microbiology and/or infectious diseases specialists. Certainly, their input gave shorter course duration though we should stress that this is not based on any strong evidence of equal (or better) efficacy. Greater experience and/or confidence and/or interest in continually reviewing antibiotic prescriptions may lead to faster termination of antibiotic regimens though, again, these factors were not directly addressed.

Our findings urge the production of high-quality multi-centre evidence to inform best practice, both in terms of microorganism eradication and prevention of long-term resistance and other complications.

Supplementary data

The questionnaire relating to this article is available as Supplementary data at www.jac.oupjournals.org
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