Decline of EMRSA-16 amongst methicillin-resistant Staphylococcus aureus causing bacteraemias in the UK between 2001 and 2007

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Objectives: Between 1998 and 2000, 95.6% of methicillin-resistant Staphylococcus aureus (MRSA) bacteraemias in the UK were due to two epidemic strains, namely EMRSA-15 or EMRSA-16 (60.2% and 35.4%, respectively). We sought to determine the proportions of these strains before and after the general decline in MRSA bacteraemia that began around 2004.

Methods: Consecutive MRSA isolates collected in 2001, 2003, 2005 and 2007 by the BSAC Bacteraemia Surveillance Programme were categorized to multilocus sequence typing (MLST) clonal complex and to SCCmec type by PCR. MICs were determined by the BSAC method. Data trends were tested for significance using a generalized linear regression model.

Results: Collectively, EMRSA-15 and EMRSA-16 consistently accounted for ~95% of MRSA studied between 2001 and 2007, but the proportions of EMRSA-16 declined from 21.4% in 2001 to 9% in 2007 (P < 0.05), whilst the proportion of EMRSA-15 rose commensurately, accounting for 85% of MRSA in 2007. Ciprofloxacin and erythromycin resistance were common amongst both EMRSA-15 and EMRSA-16.

Conclusions: EMRSA-15 and EMRSA-16 remain the main MRSA strains in bacteraemia in the UK, but the proportion of EMRSA-16 declined from the late 1990s, thus preceding the general decline in MRSA bacteraemias that began in the middle of the present decade.

Keywords: MRSA, surveillance, bloodstream infections

Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) emerged in 1961 and become dramatically more prevalent as agents of bacteraemia in the UK in the mid-1990s in England, Wales and Northern Ireland. By the end of the 1990s, >40% of all S. aureus bacteraemias were due to MRSA, though this proportion (and the total number) of MRSA bacteraemias has since declined and stood at ~20% in 2008.¹ The rise of MRSA in the 1990s and early 2000s correlated with the emergence and spread of two epidemic strains, designated EMRSA-15 and EMRSA-16, which, in 1999–2000, accounted for 95.6% of all UK MRSA bacteraemias; with 60.2% due to EMRSA-15 and 35.4% to EMRSA-16.² EMRSA-15 and EMRSA-16 differ genetically, belonging to distinct multilocus sequence type (MLST) clonal complexes (CCs), namely CC22 (ST22) for EMRSA-15 and CC30 (ST36) for EMRSA-16.³ They also differ in their staphylococcal cassette chromosome mec (SCCmec) types, with EMRSA-15 typically harbouring SCCmecIV whereas EMRSA-16 typically has SCCmecI.⁴ They may differ in resistance profile too, but both lineages are usually resistant to fluoroquinolones and macrolides, and the use of these antibiotics has been described as a risk factor for colonization or infection.⁵ Since its first emergence in the UK, EMRSA-15 has become disseminated in Europe,⁶ Australia,⁷ the Middle East⁸ and the Far East;⁹ EMRSA-16 has been reported widely, in- and outside of the UK, but it is not perceived to be as successful as EMRSA-15.

Here, we report trends for EMRSA-15 and EMRSA-16 among MRSA isolated as part of the BSAC Bacteraemia Surveillance Programme between 2001 and 2007.

Materials and methods

Bacterial isolates and collecting centres

The methods for the BSAC Bacteraemia Surveillance Programme (http://www.bsacsurv.org) have been described previously.¹⁰ In brief, 25 clinical
A total of 374 MRSA were analysed, and throughout the years 2001, 2003, 2005 and 2007, ~95% of the isolates were found to be either EMRSA-15 or EMRSA-16. Among the 29 centres that submitted isolates, all submitted EMRSA-15, whilst 22/29 submitted EMRSA-16, illustrating geographic dissemination of both strains. Nevertheless, the proportion of EMRSA-16 declined from 21.4% in 2001 to 9% in 2007, whilst an increase occurred in the proportion of EMRSA-15, from 75.7% in 2001 to 85.4% in 2007 ($P=0.014$) (Table 1). These data corroborate previous local and national observations of a general decline in EMRSA-16, but do not preclude the possibility of localized variance from this trend. Consideration of previous (phage-type based) data for isolates collected between 1998 and 2000 under the aegis of the European Antimicrobial Resistance Surveillance Study indicated a 14% decline in EMRSA-16, from 35.4% seen in 1998–2000 to the present start point of 21.4% in 2001, and a subsequent decline to 9% in 2007. Whilst these data span different collections and methods, they support the view that the relative and absolute decline of EMRSA-16 began before the plateau and decline in total MRSA bacteraemias seen through the results of the mandatory surveillance system.

As noted previously, the majority of both EMRSA-15 and EMRSA-16 isolates were resistant to macrolides (74% and 85%, respectively) and fluoroquinolones (97% and 95%, respectively), whilst gentamicin resistance was noted in 3% and 24%, respectively. Resistance to tetracyclines was rarer (3% in both strains). Susceptibility to mupirocin was determined only from 2007. Among subsequent isolates, we found 1/8 (13%) EMRSA-16 isolates to be highly resistant (MICs $>256$ mg/L).

In summary, the trends observed here suggest that EMRSA-15 and EMRSA-16 have followed different epidemic curves, with EMRSA-16 having peaked and declined earlier than EMRSA-15, and with each then contributing differentially to the total MRSA bacteraemia rate, which peaked in 2004 and declined thereafter. Whilst the reason(s) for the selective decline of EMRSA-16 are not known, various factors, and possible combinations, warrant consideration, including antibiotic prescribing patterns, infection control measures and various possible biological drivers, such as bacteriophage epidemics. It remains to be seen whether the downward trajectory of EMRSA-16 will continue and if EMRSA-15 will remain the dominant MRSA lineage associated with invasive disease in hospitals in the UK.

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### Table 1. EMRSA-15, EMRSA-16 and other strains amongst BSAC MRSA Bacteraemia Surveillance Programme isolates collected in 2001, 2003, 2005 and 2007

| Survey year | EMRSA-15 | | EMRSA-16 | | Other strain(s) | | Total |
|-------------|----------|----------|----------|----------|----------------|----------|
|             | n | proportion of all MRSA (%) | n | proportion of all MRSA (%) | n | proportion of all MRSA (%) | n |
| 2001        | 78 | 75.7 | 22 | 21.4 | 3 | 2.9 | 103 |
| 2003        | 70 | 73.7 | 20 | 21.1 | 5 | 5.3 | 95 |
| 2005        | 71 | 81.6 | 12 | 13.8 | 4 | 4.6 | 87 |
| 2007        | 76 | 85.4 | 8 | 9.0 | 5 | 5.6 | 89 |
| Total       | 295 | 62 | 17 | 374 |
Transparency declarations

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References


