Has the publication of methicillin-resistant *Staphylococcus aureus* (MRSA) treatment guidelines increased the survival associated with MRSA bacteraemia?

Richard Brindle* on behalf of Wessex Microbiologists†

Department of Microbiology, Portsmouth Hospitals, Portsmouth PO6 3LY, UK

Received 10 July 2009; returned 31 July 2009; revised 14 August 2009; accepted 16 August 2009

**Objectives:** To establish whether local practice review and national methicillin-resistant *Staphylococcus aureus* (MRSA) treatment guidelines have increased the survival of patients with MRSA bacteraemia.

**Methods:** A multisite retrospective analysis of survival of patients with MRSA bacteraemia, which included patients from March 1995 to December 2008. Periods before and after the publication of UK guidelines were compared.

**Results:** Data were analysed for 1675 patients with a mean age of 69.8 years. Survival for the period up to and including 2003 was 64.3%, and was 62.8% for both 2004–2005 and 2006–2008.

**Conclusions:** No significant difference in survival in relation to local practice review or the publication of national guidelines was detected.

Keywords: *S. aureus*, mortality, retrospective

**Introduction**

In January 2004 the Wessex Microbiologists undertook a review of practice on the management of methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection (bacteraemia). At the same time survival of patients with MRSA bacteraemia from participating hospitals, which included patients from March 1995 to December 2003, was analysed. This showed a 28 day survival of 64%. Following the practice review, a submission was placed through the National Co-ordinating Centre for Health Technology Assessment for the National Institute for Health and Clinical Excellence (NICE) to produce guidelines for the management of MRSA infections. The Department of Health then commissioned, from the Infection Societies and others, these guidelines as part of a set of guidelines on MRSA. The guidelines were released for consultation in late 2005 and published in hard copy in April 2006.¹ The latest revision of the guidelines was published in March 2009.²

Since the intention of the request for guidelines was that these would lead to better management of MRSA infections, it was decided in January 2009 to re-examine MRSA bacteraemia survival. At the same time microbiologists’ compliance with the UK guidelines was reviewed.

**Methods**

Each hospital within the Wessex Microbiologists audit group was asked to provide an anonymized list of all MRSA bacteraemias since the previous practice review, together with the age of the patient at the time of the bacteraemia and whether or not the patient survived for 28 days. These data were then added to the previous 2003 survival data and pooled for subsequent analysis. Analysis was done using Epi-Info version 3.5.1 (cdc.gov 13 August 2008). Frequencies, means, age-adjusted mortality rates and Kaplan–Meier survival plots were produced from the data.

**Results**

The pooled data contained information on 1679 patients from 7 hospitals within Wessex (West Sussex, Hampshire and Dorset). Four patients were excluded as they had either no date of birth (3 patients) or no date of death but had been recorded as having died (1 patient). The mean age of the 1675 patients was 69.8 years with a range from 0 to 101 years and median age of 75 years. There was insufficient patient information available to tell how many patients had had more than one episode of bacteraemia.
Brindle

The patient data were divided into three groups based upon the year that the blood culture growing MRSA was taken. Group A (up to the first Wessex review) included all patients recruited up to the end of 2003, including 44 patients from 1995 to 2000. Group B (up to the publication of the UK guidelines) included patients from the beginning of 2004 until the end of 2005, and group C (after the publication of the UK guidelines) included patients from the beginning of 2006 up until the end of 2008. The numbers, mean age and crude survival for the three groups are given in Table 1.

As indicated in Figure 1, the Kaplan–Meier survival plots show no significant difference in survival. Although there was variation in survival rates between hospitals and within each individual hospital over time, there was no consistent correlation between patient age and hospital-specific survival rates.

The annual numbers of MRSA bacteraemias dropped from 300 in 2004 to 111 in 2008. Survival was inversely related to the age of the patient; the 28 day survival of patients in their 20s was 93.9% compared with 37.5% for those in their 90s. Overall, 615 out of 1675 patients survived 28 days (63.3%). Adjustment for age distribution showed no significant change in survival over time.

The practice review, conducted in January 2009, showed 96% compliance with the guidelines.

Discussion

It was hoped that the initial local practice review and the subsequent UK guidelines which discussed higher doses of glycopeptide, increased use of echocardiography and minimum durations of therapy would contribute to improvements in survival. However, this retrospective analysis of MRSA bacteraemia survival was not able to detect any significant improvement in survival over the period of observation. The three patient groups were well matched for age, which is significantly associated with mortality, and the study population included patients from a wide range of hospitals; from small district general hospitals to large tertiary referral centres.

Table 1. Characteristics of the three patient groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Years during which data were collected</th>
<th>No. of patients</th>
<th>Mean age (SD)</th>
<th>Deaths within 28 days</th>
<th>28 day survival (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>&lt;2000–2003</td>
<td>535</td>
<td>70.1 (17.8)</td>
<td>191</td>
<td>64.3% (60.1%–68.4%)</td>
</tr>
<tr>
<td>B</td>
<td>2004–2005</td>
<td>589</td>
<td>69.3 (18.6)</td>
<td>219</td>
<td>62.8% (58.8%–66.7%)</td>
</tr>
<tr>
<td>C</td>
<td>2006–2008</td>
<td>551</td>
<td>69.9 (19.3)</td>
<td>205</td>
<td>62.8% (58.6%–66.8%)</td>
</tr>
</tbody>
</table>

Figure 1. Kaplan–Meier survival plot of patients with MRSA bacteraemia up to 28 days. There was no statistically significant difference between the three groups (log-rank P value = 0.7287).
Guidelines and MRSA survival

It is likely that survival of patients with MRSA bacteraemia is partly related to the underlying co-morbidities of the patients. In a local case-controlled study, patients with MRSA bacteraemia had a 28 day survival of 62% compared with 84% in the controls (K. Eldridge, Southampton University Hospitals, personal communication). Controls were 100 patients with blood cultures growing coagulase-negative staphylococci and were matched with 100 patients with MRSA bacteraemia for both month of age and month of positive blood culture. This translated into 22% of the mortality being attributable to MRSA infection and 16% due to other causes. This directly attributable mortality should be amenable to improvements in treatment. The variations in survival between hospitals are thus likely to be a reflection of the variations in case mix between the smaller general hospitals and tertiary referral centres. However, the data from the present study did not contain sufficient individual patient details to clarify the reasons for survival variation.

One possible reason why the publication of guidelines has had no impact on survival is that the management of MRSA bacteraemia, once identified, has been appropriate, but early treatment, before MRSA infection is confirmed, has frequently been inappropriate. A recent multicentre study from Spain showed that only 21% of patients received appropriate antibiotic therapy and that inappropriate therapy was associated with an increased risk of death. If initial appropriate prescribing is the key to improved survival, one would not expect guidelines, which could only have an effect after the infection is recognized, to influence survival in established bacteraemia. However, the guidelines may have had an effect by contributing to the reduction in the numbers of cases of MRSA bacteraemia, with an associated overall improved rate of survival at a local population level, by reducing the numbers of patients developing bacteraemia as a consequence of MRSA infection at other sites.

Acknowledgements

Matthew Dryden, Bill Gransden, Marjory Greig, Sally Groom, Simon Hill and Graeme Jones for providing the anonymized bacteraemia data from their hospitals. Bernie Higgins (Department of Mathematics, University of Portsmouth) for statistical advice.

Funding

This study was carried out as part of our routine work.

Transparency declarations

None to declare.

References