COMMENTARY

Managing methicillin-resistant Staphylococcus aureus in hospital: the balance of risk

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Introduction

UK National guidelines for management of methicillin-resistant Staphylococcus aureus (MRSA) outbreaks in hospital [1], as distinct from those for management in the community [2], consider an isolation unit (IU) to be desirable. If unavailable, side-room isolation and cohorting (IC) is advised, with temporary ward closures as necessary [1]. Both strategies strain hospital resources [3-6], as does the requirement that transfer of patients between wards and between hospitals be subject to the availability of side rooms for MRSA clearance screening.

The problems posed are especially relevant to geriatricians. Elderly patients are prone to MRSA [6, 7]. Epidemics can lead to acute ward closure and prevent timely transfer of patients to rehabilitation wards from acute geriatric, orthopaedic and surgical wards. Side-room isolation can adversely affect older patients, especially with regard to rehabilitation. Although a National Health Service executive letter [8] commends these guidelines, most MRSA carriage is asymptomatic, major infections are relatively rare and antibiotics are available to treat them.

So are the clinical benefits gained by these measures worth it? The answer rests on the virulence of MRSA and on the effectiveness of these radical measures.

Transmission and virulence

MRSA was first reported in 1961, when three out of 5440 Staphylococcus aureus strains were identified as being resistant to methicillin by the Staphylococcus Reference Laboratory [9]. MRSA isolates now constitute 22-29% of Staphylococcus aureus isolates in some hospitals [10-12], a figure inflated by screening for asymptomatic MRSA but not for methicillin-sensitive Staphylococcus aureus (MSSA). The organism is usually sensitive to teicoplanin, vancomycin, rifampicin, fusidic acid and, sometimes, gentamicin [2]. Epidemic strains of MRSA are referred to as EMRSA, the latest of which (EMRSA-16) now affects more than 50 hospitals in the UK a month [2, 7]. The exact community prevalence is unknown but spread within nursing homes is relatively infrequent and infection rare [2]. Antibiotic usage, especially third-generation cephalosporins [13-22] and, possibly, a slacker approach to general antisepsis principles [3, 23] have been important factors in the rising incidence of MRSA.

Transmission is by direct contact, as for other strains of Staphylococcus aureus which, it should be remembered, are carried asymptomatically by 30% of people in the community [24] and over 50% of hospital patients. Staff dressing MRSA-infected wounds have an 80% chance of carrying the organism on their hands for up to 3 h [25]. Immediate washing with soap and water virtually eradicates carriage [14, 17, 25].

MRSA and other Staphylococcus aureus strains have equivalent virulence, as shown by laboratory, animal model, clinical and case-control studies [17, 26-29]. Most patients appear to be colonized (throat, nose, perineum or wounds) rather than infected (pneumonia, cellulitis, sepsicaemia, enterocolitis or wound infection). In the EMRSA-16 epidemic reported from Kettering, for example, 21% of 400 MRSA-positive patients had infections, with seven directly attributable deaths (<2%) [7].

Although elderly patients feature prominently in many epidemics, the only published studies of mortality and morbidity concern long-stay - not acute - patients [30]. A detailed retrospective clinical and microbiological review of the notes of 63 consecutive elderly patients with EMRSA-16 admitted to the acute wards of our department at the Royal Free Hospital yielded results similar to those from Kettering: 11
patients (17%) had cellulitis (usually of small leg ulcers) and three (5%) had pneumonia (all were patients with throat colonization). There were no MRSA-related deaths.

Studies of other epidemics report infection rates of 40% and more [4, 10, 25, 31, 32] and attributable mortality of 1.25% [33] and 11% [10]. However, standard criteria are rarely used to define the infection, infection rates may be derived from sub-groups, many reports give neither infection rates nor attributable mortality, and comparison with MSSA is infrequent. Patients on burns units or intensive care units, those suffering from gastro-intestinal and other malignancies and those immunocompromised by surgery are most at risk [12, 17, 22, 26, 29, 34-36]. Technological advances in medicine have probably increased the number of vulnerable patients, and severity of underlying disease determines outcome [14, 16, 27, 29]. When this is controlled for, directly attributable mortality equals that of other Staph. aureus types, especially when MRSA infection is treated by appropriate antibiotics (teicoplanin, vancomycin).

Management of outbreaks

Protection of the severely ill patient and the wish to avoid selecting out a totally resistant organism by frequent use of antibiotics such as teicoplanin provide the rationale behind radical infection control measures. In addition to IU or I/C management of all infected and asymptomatic carriers, these include the use of gowns and gloves, handwashing, topical eradication with antiseptic shampoo and soaps, and eradicating nasal carriage with mupirocin. Oral rifampicin and Fucidin are used if topical eradication fails. Clinical infections are treated according to sensitivity. Surveillance screening for asymptomatic carriers is carried out in certain circumstances, as routine screening is not cost-effective [1, 6, 7]. These measures eradicate MRSA only in small outbreaks [5, 33, 37, 38]. Large epidemics can only be contained, usually after a year or more, and often remain numerically large [4, 6, 7, 25, 39, 40].

Detailed review of 25 reports of IU or I/C management reveals many problems in interpretation. There are no controlled trials - probably due to ethical and practical difficulties. Outcome measures vary widely. The clinical impact of epidemics and their management is hard to appreciate as infection rates and directly attributable mortality are often unstated, no comparison is made between IU and I/C, antibiotic and handwashing policies [41], or by [6, 31-2, 43-4] but not others [10, 14, 32, 41]. Failure may follow success [39, 43] and vice versa [6, 43]. I/C may succeed where an IU fails [31]. Success has followed stricter [43] or, paradoxically, more relaxed [6, 31] isolation practices, when relaxation was accompanied by antibiotic policies [31] or by intensive ward-based education and feedback to staff on handwashing and basic antisepsis [6]. One review suggests that strictness of isolation did not affect outcome [5]. Indeed one I/C study contained MRSA by isolating only those with uncontrollable secretions and emphasizing handwashing [25]. Antibiotic policies restricting cephalosporin usage have alone resulted in containment in orthopaedic and trauma units [15] and in surgical wards [19, 21].

It is hard to know which element of any strategy has most influence. Could the behaviour of the individual MRSA be the key factor [6]? Its decline in three health districts with specific infection control policies simply mirrored that across the rest of the region [6]. An Australian study reported a large rise in MRSA despite IU, I/C, antibiotic and handwashing policies [41], concluding that the main impact of the epidemic in the hospital was on its infection-control practices, a frequently reported finding [3, 4, 23, 26].

In the absence of any evidence of special virulence, many hospitals adopt less strict policies. Experience in three UK health districts over 6 years [6], in Australian hospitals over 18 years [3, 4, 23] and in a large American hospital over 7 years [26] has led to use of side-room isolation only for patients whose dressings cannot contain the site of infection [4, 25] or for heavily colonized patients in a unit with a history of previous outbreaks (e.g. intensive care unit or orthopaedic ward) [3, 6]. Microbiological input to these policies stresses discouraging selection of MRSA by reducing antibiotic consumption [23]. Many have heeded Bell's summary of the extensive Australian experience:

"Eliminate well proven causes of cross-infection such as overcrowding, understaffing and poor hygiene before embarking on extraordinary measures directed solely at the control of one particular strain of Staph. aureus" [3].

Conclusion

Clinicians would clearly prefer more relaxed policies, which many microbiologists might resist. However, clinicians should not encourage spread of any infectious organism, let alone one with a narrow spectrum of antibiotic sensitivities. What should they do in the face of an MRSA epidemic? Follow national guidelines whatever their consequences or take heed of Bell's words?
The way forward should be evidence-based, the result of collaborative research between microbiologists, clinicians and public health physicians. Adequate national surveys, distinguishing between carriage and infection, are required to achieve accurate MRSA figures. A meta-analysis of reports of IU or I/C management is needed. So too are prospective studies of the clinical and microbiological profile of an outbreak, with case-control studies (including elderly patients), a review of antibiotic usage and observational studies of handwashing, etc.

If the effect of radical control measures appears equivocal and/or the virulence of EMRSA is not sufficient to warrant them, alternatives should be implemented. Policies requiring clinicians to take responsibility should be enforced. These include basic anti-staphylococcal precautions (handwashing), feedback to staff of hospital infection rates (which has known efficacy in reducing surgical infection) [45] and antibiotic policies. Isolation of patients with MRSA infection should be restricted to those with uncontainable secretions. It is possible that one clinical setting (e.g. liver transplantation) may require a strict policy and that others (e.g. rehabilitation wards for older people) merit more relaxed measures. There is a precedent for this in the differences between hospital and community management of MRSA [1, 2].

The microbiological, clinical and economic effects of these strategies should then be evaluated.

References

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