MRSA: total war or tolerance?

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Keywords: MRSA infection; ICU’s; preventive infection

Both methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) can cause potentially severe infections, such as bacteremia, surgical site infections, complicated skin and soft tissue infections (SSTI), and ventilator-associated pneumonia. However, they are also involved in a large number of mainly minor SSTI and are often mere colonizers without leading to clinical infections. Severe MRSA infections are associated with increased length of stay, morbidity, cost (primarily driven by increased length of stay and not by the cost of antimicrobials) and mortality. In a large meta-analysis of 31 studies of *S. aureus* bacteraemia pooled between 1980 and 2000 [1], Cosgrove *et al.* [1] found a doubling of mortality with MRSA bacteraemia (OR 1.93; 95% confidence interval (CI) 1.54–2.42; *P* < 0.001 vs MSSA). In another calculation, MRSA bacteraemia generated an extra cost of 3700 USD/±3.000 Euro (Rubin *et al.*, 1999). In an assessment of mortality attributable to MSSA and MRSA bacteraemia in the ICU of our hospital, two independent matched cohort studies (MRSA bacteraemic patients vs matched controls; MSSA bacteraemic patients vs matched controls; matching in a 1:2 ratio, based on APACHE II, main diagnosis upon admission, age and year of admission) were used, as MSSA and MRSA bacteraemic patients cannot be compared directly due to the differences in total ICU stay, ICU stay before and after onset of bacteraemia, reflecting differences in patient population. No attributable mortality was found in MSSA (1.3%; 95% CI: −15–18) vs a significant attributable mortality in MRSA bacteraemia (23.4%; 95% CI: 7–40) [2]. MRSA colonization can be controlled through the application of a multi-component programme, as shown by Harbarth *et al.* [3]. This programme consists mainly of a systematic and relentless application of standard precautions. The cornerstone of these standard precautions is alcoholic hand disinfection, prior to and after each patient contact. Hence, one should not be tolerant when dealing with an epidemic of MRSA and should apply all measures that are deemed, and preferably proven, to be effective against colonization and subsequent infection in particular patient populations.

One important feature in the discussion on MRSA management policies seems to be the differentiation of measures between different patient populations. Residents in an elderly home with MRSA colonization do not need to be subjected to the same rigorous set of measures as patients admitted to the hospital with an MRSA infected wound and, finally, as a critically ill patient with MRSA colonization or infection, e.g. MRSA pneumonia or bacteraemia. There is evidently more risk of spreading MRSA in a patient with a large open productive wound, or a tracheotomized patient with important sputum production from bronchopneumonia, than in a patient with MRSA-colonized diabetic foot and easy wound coverage. There is more risk for MRSA cross-infection in a patient who is immobilized in bed and/or unable to co-operate due to dementia or neurologic disease than in a normally walking and fully co-operative individual.

Hence, infection control measures, including MRSA infection control, need to be tailored to the patient setting. In a medical ICU, an extensive control programme including barrier nursing has proven to be cost-effective. Chaix *et al.* [4] performed a case control study in a medical ICU with a 4% prevalence of MRSA carriage at ICU admission: 27 patients with ICU-acquired MRSA infection were compared with 27 controls without MRSA infection between 1993 and 1997 in a matched, control design. Costs in the control programme, derived from a time-motion study of nurses and physicians, were compared with costs attributable to MRSA infection, computed from excess therapeutic intensity. This enabled a determination of a threshold of MRSA carriage, rendering the control strategy dominant and furthermore, provided a sensitivity analysis with variation of the rate of MRSA transmission and ratio of infection to transmission. The total costs of the control programme (contact isolation and microbiologic screening) ranged from 340 to 1480 US$ per patient. The mean cost attributable to MRSA infection amounted to 9.275 US$ (median 5.885; interquartile range 1400–16.720).
A 14% reduction of the MRSA infection rate rendered the control programme beneficial. In a sensitivity analysis, the control strategy proved dominant for prevalence of MRSA carriage on ICU admission rates ranging from 1 to 7%, depending on costs of control measures, for infection rates >50% following transmission. It seems logical that excellent nurse staffing, as demonstrated by a nurse-to-patient ratio of 3.3–4.3 per 24h [5], can attenuate or even counterbalance the benefits of contact isolation demonstrated by Chaix et al [4]. Indeed, Cepeda et al. [5] found no increase in MRSA transmission in a prospective two-centre study, comparing three sequential time periods (a first 3 month period with isolation of MRSA carriers in single rooms or cohortation; a second 6 month period, in which MRSA carriers were only isolated if they were colonized with other multiresistant micro-organisms as well or if protective isolation, e.g. in neutropaenia, was required; and, finally, a third 3 month period with the same isolation strategy as in the first period). The MRSA colonization rates were 12% in the first and the third periods vs 10% in the second period without systematic isolation of MRSA carriers. The authors concluded that there is no evidence that moving patients to single rooms or cohorting MRSA carriers was associated with a reduction of cross-infection. However, the reality is that nurse staffing in many European ICUs does not achieve this optimal ratio. Furthermore, in the larger hospital setting, with significantly less ill patients as compared with the ICU setting, hand washing and in particular, alcoholic hand disinfection, may become dominant as a single measure over patient isolation.

Finally, there is little information on the patient population with chronic renal failure and dialysis. There is sufficient evidence that controlling nasal carriage of S. aureus through decontamination with mupirocin reduces the rates of both MSSA and MRSA S. aureus bacteraemia in dialysis patients. The effects of a contact isolation programme for inpatients as well as outpatients against MRSA cross-infection among patients in a haemodialysis unit was assessed by Osono et al. [6] in a comparison of two sequential periods, with and without separation into a designated area. The frequency of MRSA infection was reduced from 4.5%, before starting the protocol, to 2.9% 2 years later. This reflects the methodologic flaws of many studies in this field, as differences in the incidence of MRSA infection may be due to numerous factors influencing epidemic variation. This is one of the key messages from the systematic review of isolation policies in the hospital management of MRSA published by Cooper et al. [7]. In selecting articles reporting MRSA-related outcomes and describing an isolation policy (n = 46, 18 using isolation wards, 9 nurse cohorting and 19 using other isolation policies, including private rooms), no randomized controlled trials were identified. Most studies were indeed interrupted time series, with only four planned formal prospective studies. There were clearly seasonal variations and changes in MRSA strain types, reflecting epidemic variability. In practically all the studies, multiple control measures were applied simultaneously and hence, the relative contribution of individual measures could not be assessed. However, in spite of weak methodology and inadequate reporting, the authors concluded that organized interventions, including an isolation strategy, could substantially reduce MRSA transmission, even in settings with high MRSA endemicity. The balance of evidence tilts towards effectiveness of isolation measures, but not against.

In conclusion, the absence of multiple, conclusive level 1 evidence studies on the value of isolation measures in the strategy against MRSA cross-infection should not lead to a more tolerant attitude towards the MRSA epidemic. However, an individual differential risk assessment, based on the patient profile, allows identification of mainly the patients with a minor clinical problem, in whom standard precautions, focusing on alcoholic hand disinfection, may be sufficient in order to control cross-infection, without warranting patient isolation in the ward.

Conflict of interest statement. None declared.

References

Received for publication: 30.1.06
Accepted in revised form: 31.1.06