Prevalence of MRSA in Emergency and Elective Patients Admitted to a Vascular Surgical Unit: Implications for Antibiotic Prophylaxis

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Objectives.
1. Audit adequacy of admission screening for MRSA in vascular surgery patients.
2. Establish the prevalence of MRSA carriage at the time of admission in emergency/transfer and elective patients.
3. Establish a threshold prevalence of MRSA that should trigger the use of prophylactic antibiotics active against MRSA.
4. Model some of the costs and efficacy of glycopeptides such as vancomycin, compared to aminoglycosides such as gentamicin, for the prevention of MRSA surgical site infections.

Materials and Methods. 200 consecutive emergency/transfer and 150 consecutive elective patients admitted between April 2004 and January 2005, were studied. Data was obtained from departmental Morbidity and Mortality records and the computerised laboratory medicine information system.

Results. 261 (75%) of the 350 patients were screened for MRSA on admission (target 100%). The proportions of emergency/transfer and elective patients screened were similar (78% and 72% respectively). The prevalence of MRSA carriage detected by admission screening in emergency/transfer patients 30/153 (20%), was significantly higher \( (p < 0.0001) \) than in elective patients 2/108 (2%).

A simple decision analysis model suggests that gentamicin should be used when the prevalence of MRSA reaches 10% and vancomycin when the prevalence reaches 50%.

Conclusions. The high prevalence of MRSA colonisation in emergency/transfer patients has important implications for pre-operative antibiotic prophylaxis.

Keywords: MRSA screening; Antibiotic prophylaxis; Vascular surgery.

Introduction

Surgical site infection is a rare but devastating event for the vascular patient. This may involve the wound or a graft or both. Graft infection is particularly serious occurring at a frequency of 1–6%.1,2 Treatment usually requires re-operation, prolonged hospital stay and long term antibiotic therapy. Even with such interventions morbidity and mortality remain high. Approximately 30% of patients with aortic graft infection die and 20% lose a limb.3 Around 17% of patients with femoro-popliteal graft infection die and up to 50% require amputation.3

Methicillin Resistant Staphylococcus aureus (MRSA) has become a major hospital-acquired pathogen in many countries including the UK over the past 15 years.4,5 In addition, it is now recognised as a community pathogen,6,7 with MRSA accounting for 24% of community acquired Staphylococcus aureus bacteraemia in the catchment of our hospital.8 Most surgical site infections after vascular procedures are caused by Staphylococcus aureus, although graft infections may involve Coagulase Negative Staphylococci.9 Recent audits in the UK show that up to 55% of deep wound and graft infections are caused by Staphylococcus aureus and that 70% of isolates from surgical sites are MRSA.9,10 Infection with MRSA is associated with a poor outcome in vascular surgery patients, with higher rates of amputation after arterial reconstruction in the leg as compared with methicillin-sensitive Staphylococcus aureus (MSSA) infection.9 MRSA aortic
graft infection is associated with very high case fatality rates.11

Because of the serious consequences of MRSA infection in vascular surgery patients, screening for the organism prior to or on admission is recommended.11,12 Although results of admission screening only become available 3 days or more following admission, they provide useful information to guide empirical therapy should the patient develop a post operative infection, and to reinforce procedures such as isolation or cohort nursing designed to prevent spread of MRSA to other patients.13 This information can also be used, when aggregated at the population level, to ensure that prophylactic antibiotic regimens are appropriately targeted.11 The cost effectiveness of this strategy has been demonstrated in both the US and European healthcare systems.14 In our unit it is policy to screen all vascular patients for MRSA within 48 hours of admission.

Antibiotic prophylaxis is recommended for all vascular surgical procedures.15 In the UK, β-lactams such as a first or second generation cephalosporin or co-amoxiclav are often used, with aminoglycosides like gentamicin employed as an alternative for patients allergic to β-lactams.9,15 Prophylaxis for the prevention of surgical site infections caused by MRSA, which is inherently resistant to all β-lactams, is not universal, though many specialists advise the use of glycopeptides (vancomycin or teicoplanin) in patients at high risk of MRSA associated complications.9,11,15–17 High risk situations include surgery in patients known to have MRSA; re-operation for graft infection; re-exploration of sites adjacent to prosthetic grafts and units with high baseline rates of MRSA.11,18 The frequency of MRSA carriage in patients admitted for vascular procedures is not well documented, and is likely to change over time and place.13 Recently a prevalence of >10% MRSA carriage in the population receiving prophylaxis has been suggested as a trigger for the use of glycopeptides.19 However the widespread use of glycopeptides has several disadvantages. Excessive use is linked to the emergence of vancomycin-resistant Enterococci and Staphylococcus species for which there are few therapeutic options.19,20 Vancomycin needs to be infused over an hour and hence must be started on the ward prior to theatre. If rapidly infused it may cause hypotension and histamine release which may have adverse effects during anaesthesia.21,22 Teicoplanin is an alternative but is very costly (British National Formulary (BNF) cost £35.62 for 400 mg compared to £17.32 for vancomycin 1 g). These issues have led to calls for a re-examination of the role of aminoglycosides such as gentamicin for MRSA prophylaxis.19 Gentamicin is usually used for its potent activity against Gram negative organisms such as E. coli and Pseudomonas aeruginosa, with typical minimum inhibitory concentrations (MICs) of 1–4 mg/L and 1–8 mg/L respectively. However it is also highly active against most strains of Staphylococcus aureus including common UK strains of MRSA (MIC 0.12–1 mg/L).23 A bolus of 1.5 mg/Kg at induction gives a peak serum concentration of 5–10 mg/L, exceeding the MIC for MRSA and MSSA by 5–10 fold.23,24 Gentamicin resistance in MRSA is a well described but minor problem and currently 91% of MRSA strains in the UK are susceptible.24 Gentamicin can be given by bolus at induction, intra operative top ups are not required because of its longer half-life compared to cefuroxime,25 and it is cheap (BNF cost £4.20 for 120 mg).

We therefore decided: firstly to audit the adequacy of admission screening for MRSA. Secondly to establish the prevalence of MRSA carriage at the time of admission in elective and emergency/transfer patients. Thirdly to establish a threshold prevalence of MRSA which should trigger the use of prophylactic antibiotics active against MRSA, by modelling the expected burden of MRSA surgical site infections when using β-lactam antibiotics such as cefuroxime, which are not active against MRSA, for prophylaxis. Lastly, to model the efficacy of glycopeptides such as vancomycin, compared to aminoglycosides such as gentamicin, for the prevention of MRSA surgical site infections.

Materials and Methods

Records of all vascular patients were obtained retrospectively from departmental Morbidity and Mortality meeting data sheets, which log all vascular patients admitted to the John Radcliffe Hospital. Between April 2004 and January 2005, 150 consecutive elective admissions (admitted from the community for a planned surgical intervention), and 200 emergency/transfer admissions (patients admitted via the Emergency Department or transferred from neighbouring regional hospitals) were included in our study.

Differences in prevalence of MRSA carriage between the two groups of patients were compared using the chi squared test (STATA 8.2 software).

Our departmental policy was to screen all vascular patients admitted to our unit by culturing nose, throat, axillae, perineum and wound swabs for MRSA. Culture included enrichment as recommended by the English Health Protection Agency.26 If the patient was catheterised a urine sample was also
examined. We analysed screening swabs, which were taken within 48 hours of admission. Patients whose admission screen was negative and where MRSA was cultured from any specimen taken to investigate clinical infection after 48 hours of hospital stay were classed as ‘acquisitions’ (i.e. having acquired MRSA in hospital). This 48-hour cut off is widely used by epidemiologists to define hospital-acquired infection.27 The MRSA admission screening status and the results of all subsequent microbiology tests performed was obtained from the computerised laboratory medicine information system.

A simple decision analysis was used to calculate the number of MRSA wound infections expected at a given prevalence of MRSA in the two groups undergoing surgery28:

**Assumptions underlying the decision analysis**

The proportion of vascular wound infections caused by *Staphylococcus aureus* is 75%.1,9
The wound infection rate when no effective antibiotic prophylaxis is given is 15%.16,29
The relative risk reduction in rate of post operative wound infection with effective antibiotic prophylaxis is 66% (15% → 5%)16,29–33
Vancomycin is 100% effective against MRSA in vitro.19
Gentamicin is at least 80% effective against MRSA strains in the UK in vitro.24
Cefuroxime is ineffective against MRSA in vitro.19

**Model of efficacy of antibiotic prophylaxis in prevention of wound infection in vascular surgery**

Let the proportion of wound infections caused by *Staphylococcus aureus* = W
Let risk of wound infection with inappropriate or no antibiotic prophylaxis = I
Let the relative reduction in risk of wound infection with appropriate prophylaxis = R
Let the prevalence of MRSA in the population receiving prophylaxis = P
Let the proportion of MRSA strains susceptible to the prophylaxis = S
Therefore, the reduction in the risk of wound infection caused by MRSA for any antibiotic prophylactic regimen = \( WIRPS \)
Therefore, the number needed to treat (NNT) = \( 1/WIRPS \)
See Appendix for worked example.

The model was used to examine some of the costs and effectiveness of three different prophylactic antibiotic regimens (cefuroxime + vancomycin, cefuroxime + gentamicin, and vancomycin + gentamicin) for the prevention of post-operative wound infection caused by MRSA. Cost of antibiotics was calculated using the British National Formulary (BNF).

**Results**

**Elective admissions**

Of the 150 patients (M:F 2.8:1, median age 67, range 54–83) in this group, 108 (72%) had evidence of appropriate MRSA admission screening. Only 2 (2%) patients of the 108 screened were colonised with MRSA. No elective patients acquired MRSA during their hospital stay.

**Emergency/transfer admissions**

Of 150 emergency patients (M:F 2.2:1, median age 64, range 36–91), 119 (79%) were screened on admission, and of these 26 (22%) were colonised with MRSA. Of 50 patients (M:F 2.3:1, median age 63, range 39–76) transferred from other hospitals, 34 (68%) were screened on admission, and of these 4 (12%) were colonised with MRSA. Because the number of transfer patients was small, their results were combined with the emergency patients. Of the 200 emergency/transfer patients 153 (77%) were screened for MRSA on admission. and 30 (20%) were colonised with MRSA. Seven (6%) of the 123 patients who screened negative for MRSA on admission, acquired the organism during their stay.

The prevalence of MRSA assessed on admission in emergency/transfer patients (30/153 20%) was significantly higher than in elective patients (2/108 2%) (Odds Ratio 12.9 CI 3.1–113.4 \( \chi^2 \) 18.6 \( p < 0.0001 \)).

Using the decision analysis model the number-needed-to-treat (NNT) to prevent a single MRSA surgical site infection for the two groups using a variety of prophylactic antibiotic regimens was calculated (Table 1, Fig. 1).

In the pre MRSA era the prevalence of MSSA carriage in the general population was 10–20%.34 Using cefuroxime (with 100% activity against MSSA) the NNT to prevent a single MSSA wound infection in vascular surgery was therefore in the order of 135 to 67 (Table 1, Fig. 1). This range of NNTs can be regarded as the ‘gold standard’ for prophylaxis in the pre MRSA era.
When using cefuroxime alone, the absolute risk of developing an MRSA surgical site infection in an elective patient in our unit, with carriage rates of 2%, is calculated to be 0.00225 (0.75 \times 0.15 \times 0.02 see Appendix) or 1 infection for every 444 elective patients undergoing surgery. For our emergency/transfer patients with a carriage rate of 20%, the risk is tenfold higher, 0.0225 or 1 in 44. This corresponds to a potential burden of 6 MRSA surgical site infections in the 265 emergency/transfer patients admitted to our unit each year, at a cost of £12,225 assuming a cost of £2,017 per infection.35 The NNT for vancomycin prophylaxis to prevent a single MRSA surgical site infection in the elective group is 673, and in the transfer/emergency group 67 (Table 1 , Fig. 1 ). Since the NNT for cefuroxime used in populations carrying MSSA is in the order of 135 to 67, the use of vancomycin would be justified for our emergency/transfer patients but not those undergoing elective surgery. At a prevalence of 20%, £1,166 (67 \times £17.32) spent on vancomycin in emergency/transfer patients will prevent one MRSA surgical site infection costing £2,017. In elective patients, where the MRSA prevalence is only 2%, the cost of vancomycin would be £11, 656 (673 \times £17.32) for each infection prevented.

Given the ecological and financial costs, and the logistical problems of glycopeptide prophylaxis, we used the model to examine the efficacy of gentamicin in our patients. We assumed gentamicin was active against 80% of MRSA, a conservative estimate given that in our unit over the study period it was active against 94% of MRSA cultured from admission screens. The NNT for gentamicin to prevent a single MRSA surgical site infection in our elective group is 842, and 84 in the transfer/emergency group (see Table 1). Gentamicin is therefore an attractive option for MRSA prophylaxis in emergency/transfer patients, allowing glycopeptides to be targeted to those patients known to be MRSA colonised at the time surgery, where the NNT for vancomycin is 13 (Table 1 MRSA prevalence 100%). In units using gentamicin in this way, the model suggests there is little benefit to using glycopeptide prophylaxis other than for patients known to be colonised with MRSA at surgery. For example, in our emergency/transfer patients, the NNT to prevent an MRSA surgical site infection when adding vancomycin to a prophylactic regimen that includes gentamicin is estimated to be 337, greater than the ‘gold standard’ NNT of the pre MRSA era of 135 for cefuroxime used against MSSA strains. However when the prevalence of MRSA colonisation reaches 50%, using vancomycin for all patients may be beneficial, as the NNT for its use in addition to gentamicin is 135 (Table 1), equivalent to the ‘gold standard’ NNT for routine cefuroxime prophylaxis for MSSA.

### Discussion

Approximately 3 out of 4 patients admitted to our unit are screened for MRSA in accordance with our unit policy. We found no evidence that compliance with admission screening was influenced by staff perception of risk of MRSA carriage in the two populations studied. The proportion screened in each group was similar: elective 108/150 (72%) and emergency/transfer 153/200 (78%), rates similar to those recently reported in two adult intensive care units in the UK.36

The overall prevalence of MRSA carriage in patients admitted to our unit and screened was 32/261 (12%), higher than the 4% documented in patients admitted to the Leicester UK vascular unit in 2002.13

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**Table 1. Table showing number of patients needed to treat (NNT) to prevent a single MRSA wound infection for 3 different prophylactic antibiotic regimens, according to the prevalence of MRSA in the target population. See Appendix for worked example**

<table>
<thead>
<tr>
<th>% MRSA in population</th>
<th>Vancomycin added to Cefuroxime</th>
<th>Gentamicin added to Cefuroxime</th>
<th>Vancomycin added to Gentamicin</th>
</tr>
</thead>
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<tr>
<td>1</td>
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<td>1684</td>
<td>6734</td>
</tr>
<tr>
<td>2</td>
<td>673</td>
<td>842</td>
<td>3367</td>
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<td>2245</td>
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<td>337</td>
<td>1347</td>
</tr>
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<tr>
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</table>

**Fig. 1. Graph showing number of patients needed to treat (NNT) to prevent one MRSA wound infection for 3 different prophylactic antibiotic regimens, according to the prevalence of MRSA in the target population.**
Rates are likely to vary from region to region and with time, since the MRSA epidemic in the UK and Europe is still evolving, so it is important for each unit to collect local data to inform decisions about antibiotic prophylaxis. We found the prevalence of MRSA in emergency/transfer patients (20%) to be significantly higher than elective patients (2%) \( p < 0.0001 \). We did not collect risk factor data but our emergency/transfer vascular patients often have critical ischaemia with skin ulceration and a history of prior hospital admission which are risk factors for MRSA colonisation. The majority of our elective patients do not have these risk factors. Typically they include patients with claudication (not rest pain), abdominal aortic aneurysm and carotid stenosis. It is noteworthy that elective patients, who would be available for pre admission screening, have a low MRSA carriage rate. The emergency/transfer patients, who by dint of their condition are not available for pre admission screening, have a high rate.

Decision analysis has been used to examine the cost and efficacy of antibiotic prophylaxis in a neurosurgical unit where the prevalence of MRSA in patients transferred into the unit was found to be 15%. A combination of cefuroxime and gentamicin was found to be satisfactory for these patients, with vancomycin reserved for patients known to be colonised or infected with MRSA. Our model is not definitive or comprehensive. The number of variables has been kept small, we did not carry out a sensitivity analysis to explore the relative impact of each variable on the outcome (NNT), and we did not look at all possible costs and benefits. However, in practice such sophistication is not needed since the aim is to guide rather than determine policy. Antibiotic prophylactic regimens in our unit were changed on the basis of the data and model presented here. The 10% threshold prevalence of MRSA for modification of prophylaxis to include gentamicin, suggested by our model, is in accordance with the 10% threshold recently advised by a working party of the British Society of Antimicrobial Chemotherapy. When the prevalence of MRSA reaches 50%, vancomycin is likely to be a safer option (NNT 135). However our model is a simple one and needs to be validated by formal cost benefit analysis.

The prevalence of MRSA colonisation in patients admitted to hospitals in the UK is increasing and probably varies geographically. Vascular teams should therefore conduct their own local studies of MRSA prevalence to ensure their prophylactic antibiotic regimens are targeted appropriately. We have shown how decision analysis can be used to achieve this targeting once the prevalence data is known. There is a pressing need to validate such models with randomised controlled trials comparing aminoglycosides and glycopeptides for prophylaxis in vascular patients with high rates of MRSA carriage.

Appendix.

Decision analysis used to determine risk of wound infection and NNTs with different prophylactic antibiotic regimens.

**Worked Example**

NNT calculation for efficacy of Gentamicin prophylaxis to prevent a single MRSA wound infection in a vascular surgery patient population where the MRSA carriage rate is 20%:

- Proportion of wound infections caused by *Staphylococcus aureus*  \( W = 0.75 \)
- Risk of wound infection with inappropriate or no antibiotic prophylaxis  \( I = 0.15 \)
- Relative reduction in risk of wound infection with appropriate prophylaxis  \( R = 0.66 \)
- Prevalence of MRSA in the population receiving prophylaxis  \( P = 0.2 \)
- Proportion of MRSA strains susceptible to the prophylaxis  \( S = 0.8 \)

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NNT = \frac{1}{NIRPS} = 84
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Acknowledgements

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References