Debate—Guidelines for control of glycopeptide-resistant enterococci (GRE) have not yet worked

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Summary Glycopeptide-resistant enterococci (GRE) have become a focus of concern in many countries because options for antimicrobial therapy of GRE infection are limited. Several guidelines for the control and prevention of GRE colonization and infection have been developed for healthcare settings, and occasional journal articles now report "control" (usually relative reduction of incidence or prevalence rate rather than elimination) of GRE infections. Yet, rates of infection and colonization with GRE continue to climb in many parts of the world, showing that true control has not been achieved. Programmes to control GRE will be effective only when they (1) are less expensive to implement; (2) are shown to be cost-effective despite the fact that they merely reduce prevalence levels rather than eradicating the problem; (3) do not require almost perfect implementation to be effective; (4) are shown to be sustainable; (5) are shown to work in acute-care settings other than selected academic centres; and (6) are shown to work in non-acute care settings. Until then, it is clear that guidelines for control of GRE have not worked. New guidelines that truly control GRE must be developed, and this must be done quickly.

Introduction

Several guidelines for the control and prevention of infection and colonization with glycopeptide-resistant enterococci (GRE) have been developed for healthcare settings.1 GRE are also referred to as vancomycin-resistant enterococci (VRE) in areas where vancomycin is the only member of the glycopeptide drug class in widespread clinical use. Occasional journal articles now appear reporting that use of one or more of these guidelines have "controlled" GRE infection or colonization.2 In these cases, control is usually defined as a relative reduction of incidence or prevalence rate, rather than complete elimination.

There are six considerations preventing the assertion that practice guidelines for control of GRE have worked; each will be discussed below.

Rates of GRE infection and colonization continue to climb

Despite the widespread dissemination of guidelines, reports continue of increasing prevalence of GRE. Several of these are from countries where...
guidelines have been disseminated for several years. For example, a report at the ECCMID Conference in Milan in April 2002, summarized a survey of 3499 stool samples from 13 clinical microbiology laboratories in eight countries of the European Union carried out in March–June 2001. Rates varied significantly among the different countries, and several countries were in a relatively low range of 0.3–5% prevalence of VRE in the stool samples. However, prevalence of VRE from stool isolates obtained in Italy was 7.7%, and prevalence in specimens from the United Kingdom was 32.6%. A current report from Turkey describes the first documented outbreak of VRE, with concomitant plasmid spread. In the United States, national guidelines for control of VRE were introduced by the Centers for Disease Control and Prevention (CDC) in 1995. Yet, prevalence rates of VRE continue to climb nationwide—Mayhall notes that ‘VRE have spread throughout the country, and the only places where they have not been found are probably in places where no one has looked.’ These reports are evidence that current guidelines are not working.

Current guidelines are very expensive

At a time of diminished resources for healthcare institutions, current guidelines for control of VRE demand too large an investment of resources to be widely implemented. For example, at a 600-bed academic centre in the USA, the infection control practitioner was given the responsibility of deciding which patients required culture for potential VRE colonization. In 1995–1996, of 54 052 patients admitted to the hospital, 10 400 had perirectal swabs taken. The reported cost in this study for cultures and isolation was estimated at US$253 099. Likewise, Sample and colleagues, describing an outbreak of VRE in a haematology-oncology unit, found that ‘in addition to contact precautions, other measures that were needed to control the outbreak included closure of the unit to new admissions, creation of a cohort of VRE-positive patients and staff, and thorough cleaning of patients’ rooms with 0.5% sodium hypochlorite.’ These observations from settings in the United States are paralleled by comments from an outbreak of VRE in a non-university hospital in the Netherlands. The authors noted that the control measures ‘were expensive and at times stopped new admissions and surgery. It is unclear whether such strict measures are justified.’ In considering actions to prevent spread of VRE in European hospitals, Ridwan et al. note that ‘a rigorous infection control policy will result in extensive patient discomfort, increased workload for healthcare workers, and substantial extra costs for healthcare organizations.’

Current guidelines lead to VRE reduction rather than elimination—is this cost-effective?

Aggressive measures to control VRE have been taken in many institutions. However, ‘enterococci seldom, if ever, have been permanently eliminated from a hospital, nor their reintroduction prevented.’ Recent forecasts from mathematical modelling predict that VRE endemic prevalence of 12% would be reached over time in a haemodialysis unit, regardless of the number of patients originally colonized. The only factors studied that could decrease this endemic prevalence were decreasing the ratio of patients to healthcare workers to a 1:1 ratio, and improving hand hygiene to 100%. These measures are highly impractical in most healthcare institutions, but even they would reduce prevalence only to 3%, rather than eliminating VRE.

The outbreak of VRE at the hospital in Utrecht referred to above was not completely controlled over a four-month period, ‘despite all efforts.’ The question arises, then, whether such efforts should be continued, especially when they result only in a diminution in cases rather than elimination of the problem. Would it be cost-effective in the majority of healthcare settings to spend huge amounts to reduce rather than eliminate VRE? This is far from certain.

Current guidelines require almost perfect implementation to be effective

A presentation at the Annual Meeting of the Society of Hospital Epidemiology of America (SHEA) in Salt Lake City in April 2002 described the success of weekly surveillance cultures and an ‘aggressive approach’ to isolation precautions in dealing with VRE. Yet, ‘this approach controlled VRE only when adherence to weekly culturing was over 97%.’ Even then, a four-month lag existed between successful implementation of control measures and a relative reduction of prevalence of VRE by 17%. Such compliance is unlikely in most healthcare institutions, and show that current guidelines are not practical.

Current guidelines are difficult to sustain beyond the initial period of concern

VRE persists for extended periods in the healthcare environment. This means that control measures likewise must continue for long periods to be
effective. However, programmes to control resistance in the healthcare setting, whether involving enhanced surveillance, isolation or antimicrobial use, have been reported as difficult to sustain over time. For example, a study in Baltimore evaluated the impact of an active surveillance programme on incidence of VRE in high-risk units of a hospital in two different periods, with no special programme conducted between the two periods of active surveillance. The reduction in incidence per 10,000 patient days of new patients with VRE decreased from 5.8 to 3.8% during the first period of surveillance. When this period of active intervention ended, the rate rose again to 11.4, and a second episode of control reduced that but to 7.7%. These data illustrate that current guidelines alone are unlikely to control VRE over a long period. As Ridwan and colleagues note, 'Half-hearted infection control measures are likely to result in further nosocomial spread, which will eventually result in an increase in infections.' Yet, current guidelines are so complicated and so cost-intensive that their maintenance is likely to be ineffective in most healthcare settings.

Current guidelines have been shown to work only in some acute-care settings. Their efficacy otherwise is unproven

VRE guidelines have been shown effective in reducing infection prevalence in a few acute-care settings (and these are primarily in academic centres). Control measures for GRE are unproven in other settings, whether non-academic acute care, long-term care, or clinic. Farr notes that VRE recognition requires a programme of active surveillance cultures to detect colonization as well as infection. However, 'most US health facilities have never tried this, and the problem keeps getting worse year after year.' In the Netherlands, 'a further problem emerged when colonized patients were well enough to be discharged to non-university hospitals or nursing homes closer to home. Some of the institutions refused to accept these patients because they thought they would be unable to implement full infection control measures and they feared a spread of VRE infection in their own units.' Value of current control programmes is not established in these non-university settings.

VRE must now be considered an important problem in extended-care settings as well. For example, a prospective, cohort study examined prevalence of VRE colonization among 100 residents of 20 long-term care facilities at time of transfer for admission to hospital. Of the 100 patients studied, 45 were found positive for VRE—the authors concluded that urban referral hospitals are a 'major reservoir' for VRE. A cross-sectional surveillance study in an ambulatory care clinic detected 3% of subjects who were colonized with VRE, including one person who did not have any exposure to a healthcare setting or antibiotics. There is little evidence that guidelines for control of GRE work in such long-term care settings. This is especially true when one considers that guidelines measuring short-term effects in these institutions ignore the reality that colonization with VRE may persist for years.

VRE colonization also may be a problem outside the healthcare setting. Healthy volunteers recruited from among hospital employees were screened, along with their family members, for presence of VRE. VRE colonization was found in 5.3% of stool specimens from participants, and was more prevalent in the hospital workers who had patient contact. The authors state that 'these findings demonstrate the spread of VRE within the household and implicate occupational risk for its acquisition.' Guidelines for control of GRE have not been shown to address this setting.

Comment

Programmes to control GRE will be effective only when they (1) are less expensive to implement; (2) are shown to be cost-effective despite the fact that they merely reduce prevalence levels rather than eradicating the problem; (3) do not require almost perfect implementation to be effective; (4) are shown to be sustainable; (5) are shown to work in acute-care settings other than selected academic centres; and (6) are shown to work in non-acute care settings. Until then, it is clear that guidelines for control of GRE have not worked. Several years ago, French predicted that 'the enterococci may now be poised to disseminate glycopeptide resistance among other more pathogenic Gram-positive bacteria.' With report of the recovery of a clinically-important strain of Staphylococcus aureus that appears to have acquired a vanA gene identical to that in Enterococcus faecium, it would appear that this prediction has proven to be accurate. New guidelines that truly control GRE must be developed, and this must be done quickly.
References

1. Mayhall CG. Control of vancomycin-resistant enterococci: it is important, it is possible, and it is cost-effective. Infect Control Hosp Epidemiol 2002;23:420–423.