Antibiotic resistance: effect of different criteria for classifying isolates as duplicates on apparent resistance frequencies

K. P. Shannon* and G. L. French

Department of Infection, Guy’s, King’s and St Thomas’ School of Medicine, St Thomas’ Hospital, London SE1 7EH, UK

Objective: To investigate the effect of screening specimens and different criteria for exclusion of duplicate isolates when surveillance of antimicrobial resistances is performed.

Materials and methods: Trends in resistance were analysed for recent isolates of selected organisms from Guy’s and St Thomas’ Hospitals with the use of various criteria for the exclusion of duplicates, including time since the last isolate and antibiogram pattern, and the effect of excluding screening specimens.

Results: There was a significant difference of about 8% in the apparent frequency of methicillin resistance in Staphylococcus aureus in inpatients if the time limit for duplicates was set at 5 rather than 30 days; it was about 10% if a 5 day limit was compared with a 365 day limit. There was also a significant difference, of 6–10%, in apparent resistance frequencies if isolates from screening specimens were excluded. Apparent gentamicin resistance rates in Klebsiella spp. varied between 11% and 28%, and the number of apparent patient isolates of gentamicin-resistant organisms varied by up to 35%, depending on the duplicate exclusion criteria chosen. Effects were smaller, though still significant, for vancomycin resistance in Enterococcus spp. There was little effect for amoxicillin or cefuroxime resistance in Escherichia coli isolates from general practitioners, where the proportion of duplicates was small.

Conclusion: Improved surveillance of antibiotic resistance is needed. However, care needs to be taken in setting the criteria for classifying isolates as duplicates and in comparing results where these criteria may be different or unknown.

Introduction

The importance of surveillance of antimicrobial resistance is now widely recognized.1,2 When this is carried out, it is customary to exclude from the calculations repeat isolates of the same organism from the same patient. However, there is no clear agreement on what time period to regard as the limit for an isolate to be considered a duplicate.

An automated system3 that gathers information from a large number of hospitals in the USA has a limit of 5 days, after which repeat isolates are not considered duplicates. A report on antibiotic resistance in organisms from blood cultures excluded similar organisms isolated within 7 days.4 In the past, we have excluded repeat isolates within a calendar year, but did not state this clearly.5 In many situations it will probably make little difference to resistance frequencies whether or not repeat isolates are excluded and what the definition of a repeat isolate is. However, in some situations substantial effects are possible.

Many resistant organisms, such as methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE) and gentamicin-resistant klebsiellae, often cause colonization rather than infection. Colonization may persist for months or years.6–8 Repeated admissions and screening of colonized patients adds greatly to the likelihood of duplicate isolates of resistant strains in surveys of laboratory results.

Materials and methods

Antibiotic susceptibility results from the Microbiology Computer System at St Thomas’ Hospital were analysed. Duplicate isolates were detected by a computerized system...
Figure 1. Resistance to methicillin in *S. aureus* from inpatients. The frequency of resistance was compared for all specimens, with duplicates within 5 (▲), 30 (■) or 365 (●) days excluded. The error bars show the 95% confidence interval of resistance frequency calculated by the binomial method.9 The open symbols show the total number of patient isolates. The closed symbols show the percentage resistance. The open symbols show the number of isolates.

Results and discussion

Figure 1 shows resistance to methicillin in isolates of *S. aureus* from inpatients at this institution over the past 6 years. There was an increase in resistance rates, regardless of the criteria used to define a duplicate. However, there was a significant difference of about 8% in the apparent frequency if the limit for duplicates was set at 5 days rather than 30 days, and a difference of about 10% when a 5 day limit was compared with a 365 day limit. The differences between results with 30 and 365 day limits were much smaller, and often not statistically significant.

Since screens are performed for colonization with MRSA but not for colonization with methicillin-susceptible *S. aureus*, results for methicillin susceptibility are biased towards resistance. Figure 1 also shows the effect of excluding screens from the calculations for methicillin resistance in *S. aureus* with the time limit for duplicates set at 365 days. There was a significant difference of 6–10% in apparent resistance frequencies and a difference of 200 to >500 (about 10–15%) in the number of patient isolates per year. Thus, unless ‘clinical’ and ‘screening’ specimens are analysed separately, a hospital with good infection control practices but a large screening programme may appear to have a higher frequency of MRSA than a hospital where the true frequency of MRSA infection is the same but there little or no screening is performed.

Figure 2 shows results for gentamicin resistance in *Klebsiella*. There were significant differences in apparent resistance frequencies when results with the upper time limit for duplicates set at 5 days were compared with 30 days. Exclusion of screening specimens resulted in a significant reduction in apparent resistance frequencies. Figure 2 also shows the effect of using antibiograms to help identify duplicates. As has been noted previously,10 MIC breakpoints that fall in troughs of bimodal or polymodal MIC distributions are most likely to yield reproducible classifications as susceptible or resistant. For example, MIC distributions of co-amoxiclav or cefuroxime for isolates of *Klebsiella* with decreased susceptibilities straddle the breakpoint for resistance, and therefore reproducibility of classification of multiple isolates of this type from a single patient is likely to be less than perfect. This prediction is supported by the finding that if antibiograms were ignored, the percentage resistance to gentamicin was often significantly lower than if differences in the results for one or more of the compounds always tested against *Klebsiella* disqualified an isolate from designation as a duplicate.

Vancomycin resistance in enterococci (Table) showed smaller effects, but there was a significant difference in apparent resistance frequencies when time limits for duplicates of 5 (11.6%) and 365 (9.6%) days were compared. This was accompanied by a reduction of 23.5% in the number of patient isolates.

Since most isolates of *Escherichia coli* from general practice are from uncomplicated urinary tract infections, which are unlikely to generate multiple specimens over prolonged periods, we expected that changing the criteria for duplicates would have little effect on antibiotic resistance frequencies to amoxicillin or cefuroxime in *E. coli* isolates from general practice. This was the case, with only about 12% of isolates being considered duplicates even when the time limit was set at 365 days, and negligible effects on the frequency of resistance to amoxicillin or cefuroxime (Table).

Improved surveillance of antibiotic resistance is needed.

K. P. Shannon and G. L. French
Effect of different criteria for duplicates on resistance frequencies

However, care needs to be taken in setting the criteria for classifying isolates as duplicates and in comparing results where these criteria may be different or unknown. Several resistant organisms that are currently recognized as causing problems in hospital patients, including MRSA, glycopeptide-resistant enterococci and multiply resistant klebsiellae, persist in patients for long periods. Furthermore, the patients may remain in hospital for long periods, or require treatments (e.g. renal dialysis) that require frequent (re-)admission to hospital. Therefore, we believe...
that 365 days is the best time period to use when classifying isolates as duplicates.

References


Received 20 July 2001; returned 13 October 2001; revised 19 October 2001; accepted 22 October 2001