Guest editorial: Surveillance of antimicrobial utilisation

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Antibiotic selective pressure in the community and in hospitals remains the primary (initiating) factor in the emergence and spread of antibiotic resistant organisms; the importance of minimising unnecessary exposure to antibiotics amongst humans and animals has been rightly emphasised by many authors. There is increasing evidence that directly associates antibiotic use with the emergence of resistant bacteria such as Vancomycin-resistant Enterococcus (VRE), Methicillin-resistant *Staphylococcus aureus* (MRSA), resistant Gram-negative bacilli and *Clostridium difficile*.

Furthermore, many studies have detected significant reductions in resistance seen after achieving changes in usage patterns, independent of traditional infection control measures [1-4]. The situation is complex as resistance, once selected, may not go away after withdrawal of the selective pressure. Whilst there may be a higher metabolic cost for resistant bacteria to maintain the additional genetic material associated with resistance, many strains are able to compensate for this through further mutational change or deletion of non-essential DNA. Multi-resistant pathogens may also be co-selected by a range of antibiotics due to their multi-resistance. Associations between virulence factors and antibiotic resistance genes may make the pathogen better able to spread, colonise and invade the hospitalised patient.

The first step in managing this problem for health care facilities to measure antibiotic utilisation in a standardised manner. The National Advisory Board of AICA published a draft methodology based around measurement of usage in internationally accepted defined daily dose (DDD) equivalents [5]. The proposed indicators are in line with current practice in Europe and America. It should be noted, however that the American Intensive Care Antimicrobial Resistance Epidemiology (ICARE) system in the USA has chosen to select DDDs for some agents (third generation cephalosporins for instance) that differ from those recommended by the Collaborative WHO DDD Centre [6].

The second step, once antibiotic usage is being measured, is to analyse patterns of use to identify outliers, significant changes to usage and evidence of excessive use. This needs to be coupled with awareness of the epidemiology of resistance within the hospital.

The articles in this issue provide examples of hospital usage in three Australian regions. In hospitals, the association between antibiotic usage and the prevalence of multi-resistant organisms is complex with many interrelated factors. Hence, antimicrobial utilisation data must not be viewed in isolation but interpreted in combination with other issues such as the hospital's patient case mix, the pre-existing level of multi-resistant organisms, antimicrobial availability and restrictions, and infection control policies. Whilst it is possible to benchmark overall and specific usage against figures from European countries and the USA, this should be done with care. The greatest use comes from analysis of temporal trends within each facility. The paper by Drs Morton and Looke in this edition provides an example of the type of analyses that these data need to go through prior to taking action.

The third step is taking action to modify usage through the implementation of an antimicrobial review programme. One must, at the outset, ensure involvement of all stakeholders, including administration at the highest level, facilitate communication between all parties, and be committed (and funded) to provide ongoing review and maintenance of such

a programme. Such a programme must be cost effective and evidence based to ensure full institutional support. The minimum working party driving this should involve representatives from pharmacy, microbiology and clinical infectious diseases, under the auspices of the quality use of medicines committee. Smaller hospitals without local antimicrobial expertise could obtain regular input from one of the larger institutions.

Adequate communication at regular intervals of local susceptibility data (presented in a useful format designed for each clinical group) and antimicrobial use (preferably with benchmarks) to the clinical units is necessary. This can be used to develop local guidelines with the clinicians; the regular feedback becomes part of ongoing education and also encourages ownership of the issue by the clinicians. Regular review of use through DUE (Drug utilisation evaluation - the evaluation of specific indications that have driven the clinical choice to use a certain antibiotic across a number of patients) should be undertaken to monitor appropriateness of prescribing within locally accepted guidelines, with feedback to the prescribers.

Much has been written about the usefulness of, and difficulties inherent in, antimicrobial guidelines [7, 8]. They remain the most effective tool for appropriate prescribing, when implemented and managed well. Formulary controls in some form are generally also of benefit in limiting inappropriate prescribing. Used in isolation however, they are inadequate, and any restricted antimicrobial policy must include education in some form, or it will fail. Liason with infectious diseases and pharmacy representatives is effective, but very labour intensive, and it is difficult to provide 24 hour cover. Clinical decision support systems are popular, but require considerable infrastructure and maintenance. They require a suitable information system, such as widespread availablity of computer terminals, or hand held devices, and still ongoing review and back up by infectious diseases and pharmacy personnel. The advantages of formulary control, education, and prescriber audit all in one are attractive, and have been found to be effective [Grayson et al, in press] in enhancing appropriate prescribing.

Correct diagnosis is a cornerstone of appropriate prescribing. This includes education of clinicians about infectious diseases and provision of an appropriate consultation service (difficult for smaller institutions), obtaining diagnostic material for microbiology before commencement of antimicrobials (which involves support from the radiology, surgical and microbiology services), and discouraging use of empiric antimicrobials when infection is unlikely. Participation in unit presentations, such as Grand Rounds, or through clinical audit meetings is an effective way to educate.

Limiting total use is a major goal of any antimicrobial review programme. Apart from reducing the pressure on antimicrobial resistance, other advantages such as reduced morbidity from intravenous access devices, reduced antibiotic associated diarrhoea and colitis, and reduced other drug toxicities are important benefits. Antimicrobial stop orders, targeted at certain patients, at certain periods such as after 48 hours intravenous therapy or 5 days, are effective ways of forcing review by the treating team and reducing therapy course length. Other aspects include effective infection prevention and control procedures to limit the spread of multiresistant organisms and thereby reduce the need for certain broad spectrum antimicrobials.

The human impact of antibiotic resistance is large and potentially preventable through more careful husbandry of antibiotics. Health institutions have a responsibility to facilitate local programmes in order to promote the responsible use of antimicrobials, and minimise the adverse impact of antimicrobial use.

References

1. Quale J, Landman D, Saurina G *et al.* Manipulation of a hospital antimicrobial formulary to control an outbreak of Vancomycin-resistant Enterococci. Clin Infect Dis 1996; 23:1020-5.
2. Saurina G, Quale JM, Manikal VM *et al.* Antimicrobial resistance in enterobacteriaceae in Brooklyn, NY: epidemiology and relation to antibiotic usage patterns. J Antimicrob Chemotherapy 2000; 45: 895-898.
3. McNulty C, Logan M, Donald IP *et al.* Successful control of *Clostridium difficile* infection in an elderly care unit through use of a restricted antibiotic policy. J Antimicrob Chemotherapy 1997; 40:707-711.
4. Landman D, Chockalingam M & Quale JM. Reduction in the incidence of methicillin-resistant *Staphylococcus aureus* and Ceftazidime-resistant *Klebsiella pneumoniae* following changes in a hospital antibiotic formulary. Clin Infect Dis 1999; 28:1062-6.
5. Draft Surveillance indicator definitions: antimicrobial utilisation. Australian Infection Control Association National Advisory Board. Australian Infection Control Journal 2001; 6:134-135.
6. World Health Organisation (WHO) Collaborating Centre for Drug Statistics Methodology. URL: www.whocc.nmdcc.no/, accessed February 2003.
7. Robertson MB, Korman TM, Dartnell JGA *et al.* Ceftriaxone and cefotaxime use in Victorian Hospitals. Med J Aust 2002;176:521-529.
8. Watson DAR. Antibiotic guidelines: improved implementation is the challenge. Med J Aust 2002:176; 513-4.