Situation critical? Nosocomial infections and antibiotic resistance on intensive care

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Nosocomial infections are very common, occurring in up to 33% of patients admitted to intensive care units (ICU). Diagnosing these infections can be difficult and infecting organisms are now often resistant to first-line empiric antibiotics.

In the United States 60% of hospital-acquired infections are caused by antibiotic-resistant organisms. Among gram-positive bacteria, 55.3% of *Staphylococcus aureus* isolates are resistant to methicillin (MRSA), and strains resistant to vancomycin have been found. Coagulase-negative staphylococci (e.g. *S. epidermidis*) resistant to methicillin, or tolerant to high levels of vancomycin and teicoplanin, have also been identified. In fact, up to 90% of *S. epidermidis* have a resistance pattern comparable with MRSA. Likewise, the proportion of enterococci resistant to vancomycin has increased from 0.5% in 1989 to 22% in 1997.

The situation with gram-negative organisms is no better. Non-fermenting gram-negative organisms, which have high intrinsic resistance, have acquired further sophisticated resistance mechanisms. Multidrug-resistant *Pseudomonas aeruginosa* strains already exist. One study showed 16% of isolates resistant to three or more of amikacin, ceftazidime, ciprofloxacin, gentamicin, imipenem and piperacillin. One per cent of these isolates were resistant to all these antimicrobials. *Stenotrophomonas maltophilia*, an organism resistant to most beta-lactam antimicrobials and intrinsically resistant to carbapenems, has shown high levels of resistance to aminoglycosides, and 45–85% of isolates are resistant to fluoroquinolones. Similarly, strains of *Acinetobacter baumannii* resistant to all antimicrobials have been found.

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Exposure to antimicrobials lies at the heart of the problem. This presents physicians with a dilemma. Evidence suggests that a delay in initiating appropriate antibiotic therapy causes increased mortality, leading to some advocating a liberal antibiotic policy in the hope that the organisms causing the infection will be sensitive to one or more of the administered agents. Contrasting evidence, however, has shown that restricting the use of empiric antimicrobials leads to a reduction in resistance.

CONSEQUENCES OF DELAYING APPROPRIATE ANTIBIOTICS

Kollef et al (1999) investigated 655 patients presumed to be infected. Mortality in the adequately treated group was significantly lower (17.7% *vs* 42%, $P<0.001$). There was, however, a higher rate of infections caused by resistant organisms in the inadequately treated group, making it likely that these infections were acquired on the ICU. Luna and colleagues (1997) also found a lower mortality in adequately treated patients (38% *vs* 91%, $P<0.001$).

EVIDENCE FAVOURING A RESTRICTIVE POLICY

Singh et al (2000) investigated 81 patients with a low suspicion of ventilator-associated pneumonia (VAP) who received either standard or restricted therapy (ciprofloxacin for 48 hours, stopped if cultures were negative). Patients in the restricted group received fewer antimicrobials ($P<0.0001$), showed less signs of superinfections ($P=0.017$), and had a trend towards increased survival. The study was stopped because clinicians felt it unethical to continue using a liberal policy.

Chastre et al (2003), in patients with VAP, compared 8 days' treatment with antibiotics with 15 days' treatment. They found neither excess mortality (difference 1.6%, 90% confidence interval (CI) = -3.7% to 6.9%), nor more recurrent infections (difference 2.9%, 90% CI = -3.2% to 9.1%) in the 8-day group.

Many questions remain. What is clear, however, is that intensive care physicians are facing an antibiotic crisis. Bacterial resistance are increasing at a rate faster than new antimicrobials are becoming available. New methods to combat the problem are urgently needed. HM

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Anaesthetic and critical care dilemmas are coordinated by **Dr Robert Self** and **Dr Pete Bishop**, Research Fellows at the Centre for Anaesthesia, UCL, London

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