Policies, Policies, Policies! What Antibiotic Policies Work?

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Antibiotics should be used rationally in order to improve patient outcome; to contain the cost of treatment and most importantly to prevent the emergence of antibiotic resistance. Unfortunately, inappropriate use of antibiotics appears to be a universal phenomenon and numerous surveys from around the world have shown high rates of inappropriate prescribing.

There is abundant circumstantial evidence linking emergence of antimicrobial resistance to overuse.[1] Changes in usage often parallels prevalence of resistance; the higher the usage of one antibiotic the higher the prevalence of resistance to that antibiotic. The prevalence of resistance is higher in nosocomial settings where more antibiotics are used. During outbreaks resistant organisms are more likely to be encountered in patients who have received prior antibiotics. Areas in hospitals with the highest usage also have the highest prevalence and the combination of intensive use in a small and confined population in intensive care units is often associated with very high rates of antimicrobial resistance. Long durations of exposure to antibiotics in patients also increases the likelihood of colonization by resistant bacteria.

To improve antibiotic usage, many hospitals have put in place antibiotic policies. While most would agree that antibiotic policies are a good thing, it is difficult to ascertain what interventions work and what don't. It has been pointed out that many papers that have been published on interventions to improve antibiotic usage are based on fundamentally flawed experimental designs and inadequate statistical analysis. In an analysis of 306 such papers only 30% met the minimum inclusion criteria for a meta-analysis.[2] It is recommended that such interventional studies should have controlled before and after design, adequate interrupted time series with at least 3 observations before and after the intervention and the use of segmented regression analysis to compare pre- and post-interventional data.

Despite the lack of scientific evidence, most would agree that appropriate antimicrobial stewardship is required. Every institution should have an antibiotic policy which is an integral part of the hospital infection control programme. The policy must be multifaceted involving all levels of staff. Formulation of the policy should involve all stakeholders to ensure ownership and most importantly, the policy must have the full support of the authorities.

An antibiotic policy is more than just a set of guidelines. It includes education and feedback, strategies to improve prescribing, dealing with forces that influence prescribing, audit and research. Education and feedback are perhaps the most important elements of an antibiotic policy. A variety of

educational strategies should be employed and the programme should be targeted at specific issues peculiar to the institution rather than in a general form. When planning an educational programme there should be well defined measurable targets. Interactive workshops has been shown to result in moderately large changes while didactic sessions are usually ineffective. Academic detailing with "face-to-face" interaction is recommended but considerable resources are required. Senior consultants should provide good role models for their junior counterparts. A meta-analysis has shown that the use of opinion leaders resulted in improvements in prescribing behaviour in 6 out of 7 trials.[3]

A strategy that has been employed successfully is that of Immediate Concurrent Feedback (ICF).[4] This strategy was devised to curb unnecessary use of glycopeptides in a Hong Kong hospital. ICF involved review of all relevant prescriptions on the next working day and errant prescribers are issued a memo with appropriate advice. Through this strategy inpatient prescribing of glycopeptides deemed to conform to guidelines increased to 71% with a difference of 54% ($p < 0.0001$, 95% CIs 47-62%). The average monthly usage (DDDs/1000 admissions) decreased from 76 to 45 but mortality from staphylococcal bacteremia remained unchanged. Another paper using a similar intervention but with an interrupted time series design and segmented regression analysis showed significant decreases in total use and cost of alert antibiotics over a two year period.[5]

Numerous strategies have been described to improve prescribing. The issuance of institutional antibiotic usage guidelines is a commonly employed strategy. Again the formulation of such guidelines must involve all stakeholders, the recommendations must be evidence based but tailored to the local situation. The guidelines should take into account local patterns of infections and resistance with an emphasis on major areas of deficiencies. Other factors that should be considered in formulating such guidelines include constraints in supporting facilities, the availability of specific antibiotics and financial considerations. A recent time-series intervention analysis from the Netherlands has shown a significant increase in compliance of +15.5% (95% CI: 8%; 23%) just through active dissemination of the updated antibiotic usage guidelines. A second intervention involving academic detailing did not further improve compliance.[6]

The microbiology laboratory plays an important role in the successful implementation of an antibiotic policy. Antibiotic resistance surveillance data should be disseminated on a regular and timely basis to those who need to know. Many laboratories practice restricted susceptibility reporting to encourage use of narrower-spectrum and cheaper agents. Where possible laboratories should also provide some form of interpretation of culture reports to help clinicians differentiate between true pathogens and colonizers and prevent unnecessary use of antibiotics. In general there should be a good and close working relationship between microbiologists and clinicians.

Various pharmacy strategies have also been described to improve antibiotic usage. They include the use of modified antibiotic prescribing forms, automatic antibiotic stop orders, monitoring antibiotic use and feedback of the information to physicians and the participation of pharmacists on ward rounds. This has led to the evolution of the specialist antibiotic pharmacist.[7] The restriction of antibiotics and formulary changes has been shown to decrease the prevalence of resistance to the restricted agent but an increase in the resistance prevalence of other agents can result.[8] This has been described as the phenomenon of squeezing the balloon. A system of prior authorization before prescribing has been found to reduce antimicrobial expenditures, increase susceptibilities without any adverse effects on patient survival.[9]

Antibiotic cycling is a strategy that has received interest in recent times.[10] It involves a scheduled rotation of one or different classes of antimicrobial agents with comparable spectra of activity in order to mitigate the effects of selective pressure. Unfortunately like other published papers on interventions to improve antibiotic prescribing, many papers on antibiotic cycling are also not based on well designed studies. A recent meta-analysis on the effectiveness of antibiotic cycling found only 4 papers that met the minimal criteria for analysis. Based on this meta-analysis the authors advised against the routine implementation of cycling as a means of reducing antibiotic resistance rates.[11] Not withstanding this, published trials have consistently pointed to benefits in specific areas and more well designed trials are required in this area as many fundamental questions relating to antibiotic cycling remains unanswered. Interestingly a mathematical model has suggested a cycling strategy is inferior to a strategy where at any given time, equal fractions of the population receive different antibiotics. Based on this model the best strategy would be to give all patients a combination of antibiotics.[12]

The use of information and communication technology can facilitate the process of surveillance and access to information. It has been used innovatively to doctors prescribe antibiotics. A computerized antibiotic assistance programme at the LDS Hospital in Salt Lake City, Utah has resulted in significant reductions in orders for drugs with reported allergies, excess drug dosages, antibiotic-susceptibility mismatches, mean days of excessive dosages and adverse events due to antibiotics.[13]

The antibiotic policy should also have provisions for dealing with forces that influence prescribing. The influence of the pharmaceutical industry cannot be underestimated and measures should be taken to promote responsible marketing practices and regulate promotional activities in hospitals. The profession should work with industry in prolonging the useful lives of antibiotics to the mutual benefit of both parties. Patient demand for antibiotics is perhaps not as serious an issue in hospitals as in general practice. In this regard public education on antimicrobial agents is necessary.

Audit is an essential component of an antibiotic policy. The purpose of audit should be carefully explained to the hospital staff and it must be made clear that audit is not a fault-finding exercise. Audit is essential to measure compliance with the policy as well as other previously defined outcomes to assess the overall effectiveness of the policy. The policy may have to be revised based on audit findings and these findings must be fed back to the prescribers.

A workshop organised by the National Foundation of Infectious Diseases and the CDC in the United States had identified 5 strategic goals for the reduction of antimicrobial resistance in hospitals. They are to optimize perioperative surgical prophylaxis, to optimize empirical therapy, to improve prescribing through educational and administrative means, to establish surveillance and feedback of antimicrobial resistance and to establish guidelines for important areas of antibiotic use.[14] The European Study Group on Antibiotic Policies of ESCMID has also established minimum standards for antibiotic stewardship which include standards pertaining to clinical practice, healthcare administration, pharmacies and laboratories, hospital and primary care executives, education, continuous professional development, clinical governance, the pharmaceutical industry and national measures.[15]

What policies work? There is probably insufficient good quality evidence at this moment to give a definite answer. Nevertheless there is an urgent need to improve antibiotic prescribing and we certainly cannot wait for the evidence before we take any action. Common sense would dictate that we require team work and a multi-pronged strategy. Important aspects in improving antibiotic usage

would encompass self regulation by the profession, continuing medical education and professional development, good clinical governance and audits of antibiotic use.

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