A new tool for improved ambulatory care antibiotic stewardship - National Antibiotic Committee prescribing guidelines

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Educational aims

- To highlight the increasing levels of resistance in several key pathogenic bacteria responsible for common ambulatory care infections
- To identify the role of antibiotic use as the major driver of resistance
- To suggest possible corrective practices and tools, including the newly available National Antibiotic Guidelines

Key words
Antibiotic, resistance, prescribing, stewardship, guidelines

There is clear evidence that antimicrobial resistance in local community bacterial strains is increasing with significant patient safety as well as health economic repercussions. This is particularly relevant for Staphylococcus aureus and E. coli. At the same time, surveillance of antibiotic consumption has identified a high level of ambulatory care use compared to other European countries, of which, a considerable proportion seem to be prescribed for tenuous indications. It is therefore critical to improve antibiotic stewardship in community prescribing and dispensing to address this situation. For this reason, the National Antibiotic Committee has just made available, on its website, the first set of National Antibiotic Guidelines for Ambulatory Care Prescribing - formulated on a stringent evidence base and local antimicrobial susceptibility epidemiology.

Introduction

The threat of antimicrobial resistance has been identified as one of the major challenges facing public health by numerous organisations and scientific societies including the World Health Organisation.[1] The challenge of the "Microbial Threat" has also been recognised by the European Union through numerous communications over the past years culminating in the adoption of a community strategy.[2] Indeed, antibiotic resistance has become one of the most pressing challenges in modern health care and has significant repercussions on both the patient as well as the health care system. Since most infections need to be treated empirically, before microbiology culture and sensitivity results are available a few days later, it is critical that the initial choice of antibiotic is correct. If levels of resistance in pathogenic bacteria are high, the risk of incorrect initial treatment becomes significant. In milder infections this may not be too problematic because treatment could be adjusted after laboratory results are known. However this is not the case in potentially life threatening infections, such as sepsis. These must be treated immediately and effectively, if the risk of serious complications as well as mortality is to be reduced.[3] Antibiotic resistance also has a major impact on health care economics, especially in hospitals.[4,5] Patients with resistant health care acquired infections need to stay longer than originally planned and often require second and third line antibiotics for treatment, which invariably come at a much higher cost. Indeed a single MRSA bacteraemia at Mater Dei Hospital can result in more than €10,000 of additional costs.

Antibiotic use as a driver of resistance

Antibiotic use remains one of the most important drivers causing antimicrobial resistance, especially in the community.[6] Therefore intervention needs to be focused on improved antibiotic stewardship. Judicious use of antibiotics has two main cornerstones: in the first instance antibiotics should only be used for bacterial infections. This seems totally obvious but is indeed one of the main reasons why resistance is increasing all over the world. The use of antibiotics for upper respiratory tract infections, which are commonly of a viral aetiology, is reported to some degree or another within every country. However, a recent Eurosurveillance survey identified

Malta as the second highest European antibiotic consumer.[7] Furthermore around 75% of these prescriptions were for colds, flu, and sore throat all of which are primarily viral conditions. Use of antibiotics in such situations will not improve recovery but it will destroy sensitive bacterial commensal flora in the patient. Mutant resistant strains, normally kept under control by commensals, will proliferate to become the predominant organisms. They in turn can either be cross transmitted to other individuals or alternatively cause secondary infections within that same patient. Indeed studies have shown that following exposure to macrolides, macrolide resistant bacteria immediately develop within the upper respiratory tract and can persist for as long as six months after treatment is stopped.[8] Another area of antibiotic misuse relates to topical creams and ointment. It is not uncommon for these formulations to be used for non-infective dermatological conditions, such as eczema or insect bites, or alternatively boils or abscesses where topical antibiotics are unlikely to penetrate sufficiently. The other major driver of resistance is use of wide spectrum antibiotics. The majority of infections in the community can be predicted in terms of the causative organisms. Skin and soft tissue infections are in the main caused by *Staphylococcus aureus*. The major pathogen behind community acquired respiratory infections is predominantly *Streptococcus pneumoniae* whereas *E. coli* causes more than 85% of urinary tract infections. It is therefore possible, through a basic knowledge of resistance patterns, to use narrow spectrum antibiotics for each of these conditions which target these pathogenic bacteria specifically.

Practice points

- Antibiotic resistance in the local community isolates of *Staphylococcus aureus* and *E. coli* has increased to worrying levels
- The main driver of community acquired bacterial resistance is invariably antibiotic use.
- Improved antibiotic stewardship is critical to address this growing Antimicrobial Threat
- Antibiotic prescribing for respiratory tract infections needs to be more judicious and focused by avoiding treating viral conditions and utilising narrower spectrum formulations
- Topical antibiotics should not be use for non-amenable dermatological conditions which are either not infective (e.g. insect bites, simple eczema) or in which penetration is unlikely (boils and abscesses)
- The National Antibiotic Guidelines can be a useful tool to assist all stakeholders in more prudent antibiotic practices

Local antimicrobial resistance epidemiology

The epidemiology of antibiotic resistance in Malta has been identified as a result of several surveillance initiatives as well as participation in European network activities. Resistance in local community infections is reaching worrying levels.[9] Most perturbing are the levels of community MRSA as well as resistant *E. coli*. In the case of community MRSA, carriage rate amongst healthy individuals who have never required hospital treatment has been found to be more than 8% (Scerri J, University of Malta thesis - 2011). It is one of the highest recorded levels in the world. Most of the strains identified in the study were characteristically a single clone. This clone has already been described and dubbed the Malta clone; it is resistant to beta-lactams as well as fusidic acid.[10] Gram negative bacteria, especially *E. coli*, are also showing increasing resistance to beta-lactams as well as ciprofloxacin. The main drivers of these two phenomena are again thought to be antibiotic use. In the case of MRSA, the clonal characteristics suggests a link with misuse and overuse of fusidic acid creams and ointments. *E. coli* resistance has shown association with use of beta-lactam antibiotics in the community, especially second generation cephalosporins.[11]

It is however encouraging that the most important community pathogen, *Streptococcus pneumoniae*, remains relatively sensitive to penicillin. This is very important since it is the main bacterial pathogen causing lower and upper respiratory tract infections of bacterial origin. Since most antibiotics in the community are prescribed for these conditions, there is a great window of opportunity to address our current prescribing habits and reduce the risk of further resistance development. The amount of wide spectrum antibiotics prescribed in the community in Malta is difficult to understand and even less to justify. More than 80% of antibiotics used in ambulatory care fall in one of four groups: wide spectrum penicillins with beta-lactamase inhibitor, second generation cephalosporins, fluoroquinolones and macrolides.[11] This is clearly not in line with the local epidemiological resistance picture.

Antibiotic stewardship

In order to address these issues, the National Antibiotic Committee has published its first set of guidelines for prescribing of antibiotics in ambulatory care. The guidelines are available on the Committee's weblink: www.nacmalta.info. They aim to provide a tool that will allow better prescribing decisions in terms of what patients are given for presumptive infectious conditions. The guidelines include algorithms to assist physicians in recognising upper respiratory infections of likely viral origin where antibiotics are not required. Similarly the dermatological section lists the common skin conditions and identifies those few indications where topical antibiotics are actually effective. The guidelines also introduce the concept of delayed prescription in which a physician post-dates a prescription by 2 or 3 days and counsels the patient to refer to a pharmacy for its dispensing only if the condition is not improving or has deteriorated after that period of time.[12] Above all, the guidelines emphasise the use of narrow spectrum antibiotics, of which the use of amoxicillin for most upper respiratory tract infections is a key feature. This requires a major culture change since our knee-jerk has clearly been to resort to wide spectrum antibiotics for both upper respiratory as well as urinary infections. However, as clearly identified in the extensive list of references and evidence base that accompanies the guidelines, treatment of most ambulatory care infections is equally effective with narrow as it is with the wider spectrum formulations. The only difference is that the former are far less of a driver of resistance. Furthermore nitrofurantoin is actually superior in terms of antimicrobial susceptibility for urinary tract bacteria causing simple cystitis. Finally use of non-antibiotic topical dermatological creams, such as hydrogen peroxide, offers an equivalent therapeutic option for minor skin infections. The guidelines will be updated in line with emerging literature as well as changing local resistance patterns.

Conclusion

We are literally at a cross road. The increase in antibiotic resistance in Malta over the past decade has been extremely worrying and has impacted on the development of resistance in ambulatory care. Nevertheless we have not yet reached a situation where resistance cannot be tackled or even possibly reversed. This, however, requires a change in habits that developed over many decades. Antibiotic guidelines have been shown to be effective in improving prescribing in other countries.[13,14] Hopefully the national guidelines will serve as a useful tool to achieve this goal locally. Our patients, present and future, deserve nothing less.

The National Antibiotic Committee advises the Superintendent of Public Health on matters related to antibiotic use and resistance. Its current members are: Dr Michael Borg, Dr Anthony Azzopardi, Dr Susan Chircop, Prof Paul Cuscheri, Dr Tanya Melillo, Dr Tonio Piscopo, Ms Isabelle Zahra Pulis, Dr Maria Cordina, Dr Gunther Abela and Mr Peter Zarb. The Comittee can be contacted on: nac.mhec@gov.mt

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