

First do no harm: Optimizing antimicrobial prescribing and antimicrobial stewardship

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ABSTRACT

In the current global climate of continuous increase of antimicrobial resistance and multiply-antimicrobial resistant organisms, it is imperative that the use of antimicrobials is optimized by adhering to good antimicrobial stewardship. The research evidence is overwhelming as to what constitutes best practice. Clearly a holistic approach needs to be followed to achieve this aim by addressing both governance and clinical practice in antimicrobial prescribing. To this effect, a number of evidence-based recommendations are described to assist healthcare organisations and prescribers in the prevention and reduction of antimicrobial resistance and incidence of healthcare associated infections due to these highly resistant organisms.

The take home message is that antimicrobial prescribing is a two-edged sword: on the one hand it can save patients' lives but at the same time if inappropriately prescribed it can lead to morbidity and mortality.

Iraqi New Medical Journal January 2018;4(1)

INTRODUCTION

The use of antimicrobials is crucial in the management of infections and sepsis in general. The judicious use of such anti-infective agents makes a difference between life and death when it comes to the management of serious life-threatening sepsis. However, unlike other medicines, antimicrobial agents including antibiotics may lead to the emergence of antimicrobial resistance which in turn may potentially be responsible for the occurrence of future infections which are difficult to treat because of their antimicrobial resistant nature or to other healthcare associated infections such as *Clostridium Difficile* because of their disturbing effect on the normal human microbial flora.¹

The evidence is so overwhelming that with less use, and when the use of antimicrobials is more prudent then there is less emergence of antibiotic resistance and consequent collateral damage.²

Hence, there is a global campaign to reduce and prevent, when possible, antimicrobial resistance and promote antimicrobial stewardship.³ Antimicrobial stewardship is defined as a coordinated programme that promotes the appropriate use of antimicrobials, improves patient outcomes, reduces microbial resistance, and decreases the spread of infections caused by multidrug-resistant organisms.⁴

Tackling antimicrobial stewardship at hospital or indeed national level entails taking a holistic approach by addressing two main domains: the governance aspect and the clinical good practice aspect in antimicrobial prescribing.⁵

THE GOVERNANCE ASPECT

There needs to be a programme of antimicrobial stewardship that encompasses having a structure and system in place with a nominated lead and overseeing committee that is respon-

sible for overseeing all activities in relation to antimicrobial stewardship in the healthcare organisation. Needless to say how important the role of leadership is in order to ensure effectiveness and success of this programme. A joint up approach between primary and secondary care is so important as multi-resistant organisms recognise no geographic boundaries.⁶ The following are pre-requisites in order to achieve this;

Antimicrobial guidelines/policy

It is imperative that this is in place in order to guide prescribers what to use on the basis of local intelligence in terms of epidemiology of infective agents and antimicrobial sensitivities. It is imperative that the guidelines are owned by all prescribers therefore they should be consulted before it is approved.⁷

Monitoring of antimicrobial prescribing

This can be monitored by on-going regular audits on prescribing. The Pharmacists will play an important role in auditing allergy, dosage, administration and documentation and the prescribers would audit the clinical aspect of prescribing whether the antimicrobial was appropriate for the clinical condition and in the light of culture and sensitivity results and whether it is stopped or appropriately changed to another agent.

Another way of monitoring is by measuring the amount of antimicrobials consumed such as total or individual antimicrobials eg. cephalosporins, quinolones, piperacillin/tazobactams and carbapenems. Resorting to defined daily doses (DDD) of antimicrobials is another modality of monitoring.⁶

Providing regular feedback to prescribers

It is important that regular feedback is provided to all prescribers in all clinical areas. This enables them to be aware of the level of prescribing and compared over time. Comparison with other organisations of similar size and case mix of patients would also be helpful to establish a form of benchmark.

Education and training

It is imperative that prescribers receive fit for purpose education and training in antimicrobial prescribing. Furthermore, this should

also be provided at the stage of induction and refresher training in infection control. Other healthcare professionals apart from doctors such as pharmacists and nurses would benefit by receiving appropriate training as they are a valuable asset in assisting in antimicrobial stewardship.

Roles and responsibilities

Ensure that roles and responsibilities are well defined for all professionals involved in antimicrobial stewardship.

Disseminating information on types of organisms and their resistance profiles

The dissemination on a regular basis of the types of isolates from various samples such as urines, blood cultures and wound swabs and their sensitivity patterns to the clinical specialities of the prescribers is very instrumental in assisting clinicians in making them aware of these infective agents and enabling them in the use of the most appropriate antimicrobials.

Microbiology Laboratory

The laboratory and its staff will play a pivotal role in detecting infective agents and establishing their sensitivity patterns including identifying multiply-resistant antimicrobial organisms such as *Methicillin Resistant Staphylococcus Aureus* (MRSA), Extended Spectrum Beta-lactamase (ESBL) Producing Organisms and Carbapenemase Producing *Enterobacteriaceae* (CPE). Furthermore, its reporting system including restricted reporting of sensitivity to antimicrobials and the advice that it provides are all so crucial in assisting clinicians in good antimicrobial prescribing. Finally, the laboratory guides the local antimicrobial guidelines on what to advise.

ANTIMICROBIAL PRESCRIBING ASPECT

The principles of good antimicrobial prescribing are well established and the research evidence underpinning it in terms of preventing or reducing the emergence of antimicrobial resistance and multiply-antimicrobial resistant organisms and subsequent healthcare associated infections is overwhelming.⁷

The following practical recommendations constitute good evidence based practice for op-

timal antimicrobial prescribing;

Be aware of the local antimicrobial guidelines

This document encompasses advice on the basis of local epidemiology and resistance patterns of infective agents. It is available either in paper format or/and electronic version. It should include a list of allergies against agents and potential alternatives in addition to appendices including prophylaxis and renal doses of the various agents.⁷

Clinical assessment and risk assessment

Following clinical evaluation and conduct of risk assessment of the pros and cons of using an antimicrobial agent within the context of the patient in question, a decision is then made of using or not using and which agent to use. This also entails considering the local prevalence of organisms and resistance patterns.

Check previous microbiology results when available

Previous results including types of infective agents and their sensitivity patterns are instrumental in guiding us about the best choice of an anti-infective agent as the current infection may be due to the same organism with the same sensitivity profile.⁸

Check previous evidence of “alert” organisms

Alert organisms such as MRSA, ESBL and CPE can recolonize and even cause an infection in a patient who is exposed to a broad spectrum i.e. high risk antimicrobial. Therefore, the choice of using an anti-infective agent will be influenced by the presence of previous or current evidence of alert organisms.

Send appropriate microbiology samples to the laboratory before starting antimicrobials

It is imperative that the relevant samples are sent for investigation to establish the aetiological agent of the infective disease. So in serious sepsis and septicaemias blood cultures should be sent as for in urinary infections urine samples should be sent etc. Whenever possible these should be sent before an antimicrobial agent is started.

Point of care testing

Dipstick to detect urinary infections or rapid

bed-side tests to detect lower respiratory infections would be very helpful in the decision making of the choice of antimicrobials used.⁹

Not to start antimicrobial therapy may be the best practice.

Initiation of therapy should only be considered if there is substantive evidence of a bacterial infection otherwise withholding from prescribing would be considered to be the best practice.

For non-severe infections

Not starting treatment and waiting for the microbiological evidence may be a more favourable approach in the interest of patients and the community as a whole.

Delayed instead of immediate antimicrobial administration

This would be a better option if the clinical condition does not warrant immediate treatment after clinical evaluation.

Dose of antimicrobial used

The dose should be the most appropriate and in light what is indicated in the guideline but these should be altered in renal or hepatic impairment. Some life threatening infections like necrotizing fasciitis, infective endocarditis and central nervous system infections require the very maximum doses.

Frequency of administration

Some of the life threatening infections such as necrotizing fasciitis and infective endocarditis require more frequent dosing as indicated in the guidelines. Also the dose intervals need to be adjusted in renal impairment.

Switch from intravenous to oral forms

Once intravenous therapy is started there is the opportunity to switch to an oral form 24-48 hours thereafter. Oral administration is preferred when appropriate as it is the natural route of administration.

Regular clinical reviews

Patients should be reviewed at least daily and a decision is made whether antimicrobials should be continued, changed to alternative

ones or stopped altogether if there is no subsequent evidence of infection.

Acting on the microbiological evidence and rationalising antimicrobials

Once an organism is isolated and identified with its sensitivity profile then the already started antimicrobials should be reviewed with the aim of de-escalating to less broad-spectrum agents in order to minimise emergence of resistance and disturbance of the normal flora and eventually prevent collateral damage. If co-amoxiclav and clarithromycin are started to treat community-acquired pneumonia and *Streptococcus pneumoniae* is isolated from the sputum or blood culture then the best practice is to stop both of them and continue with only the mono-spectrum (i.e. less collateral damaging effect) intravenous benzyl-penicillin for the remaining of the course. If cefuroxime is used to treat a urinary infection and an *E. coli* is isolated which sensitive to amoxicillin then this antibiotic should be used and the cefuroxime stopped.

CONCLUSION

Over-use or inappropriate use of antimicrobials will inevitably lead to the emergence of multiply resistant organisms and subsequent infections that are very hard to treat because of their resistance and not infrequently, super-resistance hence the international terminology used of “superbugs”. Apart from this collateral damage there are other forms of damage that may occur because of disturbance of the normal flora i.e. disturbance of colonization resistance leading to other types of infections such as *Clostridium difficile* to emerge.¹⁰ The extent and impacts of these collateral damages are not only confined to the patient being treated but also to other patients within the healthcare organisation and the community as a whole. It follows that antimicrobial prescribing is at the heart of good infection prevention and control practice

The take home message for us as clinicians and as stipulated in the Hippocratic Oath : First do

no harm !

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Abbreviation list: Carbapenemase Producing Enterobacteriaceae (CPE), Defined daily doses (DDD), Extended Spectrum Beta-lactamase (ESBL), Methicillin Resistant Staphylococcus Aureus (MRSA).

Conflict of interest: Authors have nothing to declare.

Funding: Authors received no funds to complete this report a part from self funding.