Promoting the rational use of antibiotics

Kathleen Anne Holloway*

Abstract

Irrational use of antibiotics is a worldwide problem that contributes to dramatically increasing resistance and causes significant mortality, morbidity and increased health-care costs. This article reviews the available evidence on how we are promoting the rational use of antibiotics in the WHO South-East Asia (SEA) Region, using various WHO sources, and makes some suggestions on how to go forward.

Evidence shows that there is very serious antibiotic misuse, for example: (1) serious overuse of antibiotics in viral upper respiratory tract infection but underuse of appropriate antibiotics for pneumonia; and (2) serious overuse of antibiotics in acute cases of diarrhoea but underuse of oral rehydration solution. The few interventions conducted and adequately evaluated in the Region show that targeted multi-component interventions involving educational and managerial interventions are effective and can improve antibiotic use by 20%-30%.

A country’s policy framework greatly influences antibiotic use. In South-East Asia, antibiotics are available over the counter without prescription in all countries and very few countries are monitoring antibiotic use. Many countries still do not have important policies in place to encourage appropriate antibiotic use and most policies are aimed at the public sector, whereas most people get their medicines from the private and informal sectors. Thus, it is not surprising that irrational use of medicines continues.

There are now global and regional recommendations to have a government structure dedicated to monitoring and improving medicines use and to undertake a national situation analysis in order to develop a roadmap for action. The WHO Regional Office for South-East Asia is now undertaking national situational analyses, at country requests, in order to help them develop coordinated plans of action.

Introduction

Irrational use of medicines is a global problem. It has been estimated that less than half of all medicines are prescribed, dispensed or sold inappropriately1,2 and that less than half of all patients take their medicines as prescribed or dispensed3. Irrational use of medicines can harm patients in terms of poor patient outcome, unnecessary adverse reactions and wastage of resources, often out-of-pocket payments by patients. Irrational use of antibiotics is particularly serious because it is contributing to antimicrobial resistance that is increasing rapidly worldwide and is causing significant morbidity and mortality4,5,6 and millions of dollars worth of extra health-care costs annually7,8. The situation is so serious that WHO published a global strategy for containment9, a regional strategy for South-East Asia Region10 and Member States of WHO have adopted three World Health Assembly resolutions to contain antimicrobial resistance – the last one in 2005 (WHA58.27)11 and another resolution in 2007 on promoting rational use of medicines (WHA60.16)12. In South-East Asia, the

*Regional Adviser, Essential drugs and other medicines, World Health Organization, Regional Office for South-East Asia
Regional Committee adopted a resolution in 2010 (SEA/RC63/R4) on the prevention and containment of antimicrobials. Despite global concern, few countries, globally or in South-East Asia, have taken serious measures to contain resistance or promote rational use of antibiotics. Unless serious action is taken we risk a future without effective antibiotics.

**Use of Antibiotics**

Although medicines are one of our most cost-effective health-care interventions and antibiotics are one of our most effective therapeutic classes of medicine, few low-and middle-income countries are monitoring how they are used. Data on medicines use is conspicuously absent in many health management information systems. By contrast, developed rich regions, such as Europe, are now monitoring antibiotic use and taking action to combat irrational antibiotic use.

In order to monitor the progress in developing countries, WHO headquarters developed a database of quantitative information on medicines use in primary care in developing countries that has been systematically extracted from studies published between 1990 and 2007. Studies numbering 679 from 97 countries were identified of which 151 studies came from the SEA Region. Data show that in low-and middle-income countries less than 40% patients in the public sector and less than 30% in the private sector are treated in compliance with clinical guidelines, and that the situation has not improved significantly over the last 20 years. With regard to use of antibiotics in the Region, it was found that:

- 50% of viral upper respiratory tract infection cases are treated unnecessarily with antibiotics, yet only 53% of pneumonia cases receive an appropriate antibiotic;
- 54% of acute diarrhoea cases are treated unnecessarily with antibiotics, yet only 55% receive oral rehydration solution as recommended in the guidelines; and
- 40% of prescribed antibiotics are prescribed in under-dose.

It was further found that the average patient-dispenser interaction time was less than 1 minute, that only about 40% patients were given dosage instructions, very few drugs were adequately labelled, and that only about 60% patients knew how to take their medicines immediately on leaving the facility.

In many countries of the SEA Region, antibiotics are freely available over the counter without prescription even if this is contrary to regulations. In one study, in three Indian cities it was found that the most commonly prescribed antibiotic class in the community was fluoroquinolones, often for coughs and colds, which is entirely inappropriate. In the same study, high levels of resistance of E.Coli to fluoroquinolones were found in the urine of pregnant women (who were not taking any antibiotics) thus showing how fluoroquinolone use in some community members was contributing to the carriage of resistant organisms in other members of the same community.

**Determinants of irrational use**

In order to further promote rational use of antibiotics, it is important to understand the reasons why providers and consumers behave the way they do. Box 1 summarizes some of the reasons why people use antibiotics unnecessarily.
Box 1: Determinants of irrational antibiotic use

- Lack of provider knowledge, particularly with regard to prescribers who are insufficiently qualified, supervised or supported;
- Prescriber habit (it takes time to look up guidelines so prescribing by habit is faster);
- Poor availability of independent medicines information such as clinical guidelines and drug bulletins;
- Lack of unbiased, independent, government-funded continuing medical education and supervision that includes prescribing;
- Excessive pharmaceutical promotion - which often constitutes the only information prescribers receive and may be biased, emphasising use of the medicines and underplaying the negative consequences such as side-effects, antimicrobial resistance and cost to the patient;
- Very short consultation time (one minute) that does not allow sufficient time to make a proper diagnosis;
- Very short patient-dispenser interaction time (seconds) that does not allow sufficient time to explain to patients how to take their medicines;
- Peer pressure, for example, where doctors fear to be seen to be prescribing differently to their colleagues particularly if those colleagues are senior consultants who may set inappropriate prescribing norms;
- Patient demand in reality and as it is perceived by prescribers (who may perceive a greater demand than the real demand);
- Lack of diagnostic support services such as laboratory services;
- Poor infrastructure such as the inability to undertake observation or follow-up of patients;
- Economic incentives where prescribers gain income from dispensing or selling the medicines they prescribe; and
- Inappropriate medicines supply, for example, where inappropriate antibiotics are supplied while available and appropriate ones are not.

Sources: 1, 20, 21, 22

If an intervention is to be successful it must address any of the above factors that are found to be influencing provider and consumer behaviour. For example, in Indonesia investigation into high injection use found that doctors felt that patients asked for injections while patients did not like injections but felt that doctors liked giving them and were too afraid to refuse. The investigators organized a moderated interactional group discussion between doctors and patients, demonstrating their different viewpoints, after which the injection use decreased by 30%. In India, profit motive and fear of losing patients have been found to influence prescribers.

Targeted interventions to improve antibiotic use

The vast majority of evidence concerning what kinds of intervention are effective in improving the use of medicines comes from developed countries, relatively few studies having been conducted in developing countries. The WHO database on medicines use identified 386 interventions (evaluated in
313 studies), but only 121 of these interventions (in 81 studies) had been evaluated using adequate study design (randomized controlled trial, pre-post study with control group or time series). It was found that many of the interventions targeted antibiotic use and that most were educational in nature. Provider education alone or the distribution or printing of materials were found to have little impact on medicines use (<10%), whereas multi-component interventions involving education of prescribers and consumers, together with supervision (i.e. a combination of educational and managerial interventions targeting both providers and consumers) could improve the use by more than 20%-30%.

About half of the intervention studies indentified in the WHO database come from Asia. A brief description of the studies that came from the SEA Region can be found in a regional publication on the role of education in the rational use of medicines18, which also highlights particular strategies that have been used in the Region. Most interventions targeted antibiotic or injection use or the treatment of acute respiratory infection or diarrhoea. The effectiveness of interventions carried out in the SEA Region is similar to that in other regions. Interventions that aim to increase antibiotic use, for example, training community members to diagnose and ensure the treatment of childhood pneumonia cases with antibiotics, generally result in large improvements of 15%-25%25,26 and can reduce mortality27,28. However, interventions that aim to decrease antibiotic use, for example, training private pharmacies not to sell antibiotics for mild viral upper respiratory tract infection or acute diarrhoea, tend to have more modest effects of less than 15%29,30. Such modest effects have also been found in training health professionals31,32,33,34. However, where education is accompanied by peer review, self-monitoring and feedback, then it is possible to achieve large reductions of more than 30% in antibiotic use35,36,37.

The monitoring, training and planning (MTP) intervention developed in Indonesia38 is an innovative problem-solving approach. This involves providers identifying a problem, measuring it, discussing the underlying factors and how to improve the situation, setting the improvement target and monitoring to see if they attain this target. This method has resulted in large decreases in inappropriate antibiotic use in hospitals38 and has been successfully used in Laos and Cambodia18,38. A similar cyclical quality improvement intervention is also being field tested with success in communities in Indonesia39.

National policies to improve use of antibiotics

National policies greatly influence how medicines are used. Without a favourable policy framework, it will be very difficult to achieve and maintain improved antibiotic use. The Second International Conference on Improving the Use of Medicines40 noted that irrational use of medicines continued, that there was a relative lack of implementation of interventions, almost all of which were small scale, and that the problem was multifactorial in nature, involving many stakeholders. Therefore, they recommended that countries implement national programmes to monitor medicines use and to coordinate implementation of interventions, targeting multiple levels of the health care system in both public and private sectors, to improve use. They also recommended that successful small-scale interventions be scaled up and that more interventions be implemented targeting the community, particularly with regard to informal and private sectors and private pharmacy shops, all of which are particularly relevant in the SEA Region. WHO has developed a database on pharmaceutical policy based on a questionnaire that is sent out to countries once every four years for ministries of health (MoH) to fill in14,41. The last surveys were done in 2003 and 2007.
and Table 1 shows the percentage of countries stating that they had various policies in place – both globally and for the Region. Since different countries contributed to the different surveys, results for both surveys (2003 and 2007) are given.

It can be seen that many countries are not implementing many basic policies that WHO recommends to encourage appropriate use of medicines. Although it may appear that the number of countries implementing policies has increased between 2003 and 2007, caution must be used when interpreting the figures, particularly for the SEA Region, since the sample sizes are very small and different countries responded in different years. The situation is probably worse than it appears here since many countries are not implementing fully the policies that are supposedly in place. Globally and in the SEA Region, many countries are using an updated Essential Medicines List for public sector procurement, but few have updated national clinical guidelines or have a drug and therapeutic committee in most health facilities to undertake monitoring and education of staff. Furthermore, it should be noted that most of these policies are aimed at the public and not the private sector, which provides the major chunk of health care in the Region. It is of particular concern that in all countries antibiotics are available over the counter and no regular monitoring of drug use is being undertaken.

Future challenges

There is now ample evidence of rampant irrational use of antibiotics together with under-implementation of effective interventions and policies to promote rational use of antibiotics. This is contributing to antimicrobial resistance and it is now urgent that countries and the international community take action. While we may not know all the ways to tackle irrational use of antibiotics, we have enough evidence to

<table>
<thead>
<tr>
<th>National policies implemented*</th>
<th>Globally</th>
<th>SEA Region N=10 (overall)</th>
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<tbody>
<tr>
<td>Sample size of countries responding to questions in the policy questionnaire</td>
<td>2003 n&gt;90</td>
<td>2007 n&gt;85</td>
</tr>
<tr>
<td>Prescription audit in the last two years</td>
<td>28%</td>
<td>40%</td>
</tr>
<tr>
<td>National strategy to contain AMR</td>
<td>36%</td>
<td>43%</td>
</tr>
<tr>
<td>Antibiotic non-availability over the counter (OTC)</td>
<td>30%</td>
<td>25%</td>
</tr>
<tr>
<td>Public education on antibiotics undertaken</td>
<td>45%</td>
<td>51%</td>
</tr>
<tr>
<td>Drug and Therapeutic Committees (DTCs) in more than half of general hospitals</td>
<td>53%</td>
<td>58%</td>
</tr>
<tr>
<td>National Drug Information Centre for prescribers</td>
<td>40%</td>
<td>52%</td>
</tr>
<tr>
<td>Obligatory continuing medical education for doctors</td>
<td>49%</td>
<td>56%</td>
</tr>
<tr>
<td>Training for medical students on essential medicines list (EML) and standard treatment guidelines (STG)</td>
<td>67%</td>
<td>68%</td>
</tr>
<tr>
<td>National EML used in public sector procurement</td>
<td>56%</td>
<td>84%</td>
</tr>
<tr>
<td>National EML updated in the last two years</td>
<td>46%</td>
<td>58%</td>
</tr>
<tr>
<td>National STGs updated in the last two years</td>
<td>23%</td>
<td>34%</td>
</tr>
</tbody>
</table>

*If a country did not respond to a particular question, it was assumed that the policy did not exist in that country.
know what our first steps should be. However, we are not taking these steps and investment in this area remains low. Why? There are a number of possible reasons for this.

Firstly, promoting rational use of medicines and containing antimicrobial resistance are not institutionalized within the health care systems of many countries. If there is no department in the MoH dedicated to ensuring appropriate use, who will do the necessary monitoring of antibiotic use and coordination of policy and actors? By contrast the industrial rich nations have invested in national monitoring of antibiotic use and nationwide campaigns to promote rational use of antibiotics\textsuperscript{15,16,17,42,43}.

Secondly, a great deal of extra investment will be needed to restructure the health care systems to undertake the necessary activities. While this may result in significant future savings from reduced misuse of medicines, governments may be reluctant to invest initially, particularly in those countries, as in South-East Asia, where most drugs are paid for out of pocket by patients. By contrast, in rich nations, where there is a substantial health-care infrastructure, most medicines are paid for through insurance reimbursement that can be organized to encourage more rational use e.g. reimbursement of antibiotics when they are used in compliance with clinical guidelines\textsuperscript{15,16,17,42,43}.

Thirdly, health systems have become increasingly fragmented due, among other reasons, to increased verticalization and donor demands. Some countries, for example, have more than 50 drug supply systems from various donors and global drug facilities\textsuperscript{44} – making coordination very difficult – despite global initiatives to improve donor coordination such as the Paris Declaration 2005\textsuperscript{45} and the International Health Partnership\textsuperscript{46}.

Fourthly, there is a huge imbalance of information, with the pharmaceutical industry spending huge amounts of money to promote their products to prescribers and dispensers while governments spend virtually nothing on continuing medical education. Most prescribers, globally and especially in the SEA Region, are receiving most of their information about medicines from the pharmaceutical industry and this information is often biased in favour of more use and less caution\textsuperscript{47,48}.

Fifthly, while quite a lot is known about how to improve the use of medicines in a targeted way in the public sector, not much is known about how to promote rational use at a national level, incorporating the private and informal sectors, particularly in countries lacking in resources to fund huge government bureaucracies. Further research is needed into what kind of coordinating structures will be cost-effective in resource-constrained settings. Furthermore, the basic skills needed to monitor and promote rational use of antibiotics are often lacking and not taught in schools of public health, clinical pharmacology and pharmacy. Such courses should include pharmaco-epidemiology for monitoring use, drug evaluation for selection and management of formularies and how to manage drug and therapeutic committees and antibiotic subcommittees.

The way forward

The causes of irrational use of medicines, and in particular antibiotics, are multiple and small-scale interventions will not change behaviour. Rather a system change is needed and this will be very context specific as different countries have widely differing health-care systems. Multiple global recommendations have been made to have national programmes to promote rational use of antibiotics and other medicines\textsuperscript{9,40} including two recent World Health Assembly resolutions\textsuperscript{11,12} and a regional one\textsuperscript{13}. In July 2010, WHO held a regional meeting for South-East Asia on promoting rational use of medicines\textsuperscript{39}, where delegates from nine
countries recommended, among other things, that:

- All countries have a fully resourced unit or department within their ministry of health dedicated to promoting rational use of medicines and supported by a broad-based steering committee involving all stakeholders; and
- All countries undertake a national situational analysis of the health-care system and pharmaceutical sector with the focus on medicines use in order to identify and prioritize the major problems and develop a coordinated roadmap for action.

WHO is now undertaking such a situational analysis in countries of the SEA Region at their request and developing recommendations for them to use in future planning. In addition, WHO is developing a tool for national stakeholders to use to undertake such an analysis and to monitor progress. However, in order to make progress it will be very important that the recommendations made in a national situational analysis are acted upon. This will require resources. Who will pay? If 5% of all the funds spent on medicines were spent on promoting rational use of medicines, much progress could be made and probably the costs would be recovered through reduced misuse and overuse of antibiotics and other medicines. Governments, donors and global drug facilities can contribute to this process by ensuring that a proportion of all donated funds for medicines goes towards building capacity to monitor and coordinate policies to promote rational use of medicines and antibiotics. Professional bodies and academia can build the necessary skills. Political will is crucial. Will we act now to promote rational use of antibiotics and preserve their effectiveness for future generations or will we sit back and wait for a new non-antibiotic era where future generations will die of infections that are easily treatable today?

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