Rational Drug Bulletin

Volume 24 Number 1 January 2015

Editorial

Whenever a drug is prescribed for a patient, we should consider some points:

(i) Does the patient need any drug at all?

(ii) Is the drug being given to relieve symptoms, to treat the underlying condition, or to make the patient feel that something is being done for him?

(iii) Is the drug the most suitable for that patient and that condition?

(iv) Is the drug the cheapest drug of that type? If it is not, could a cheaper drug do the job as well?

(v) What side-effects may the patient suffer?

(vi) Do the possible benefits to the patient outweigh the possible risks of the drug?

(vii) How may the drug interact with the other drugs the patient is receiving?

If these questions are to be answered, we must be expected to have a thorough knowledge of the drugs we are using. Many illnesses result from unwanted effects of drugs. In many cases these effects could have been avoided, either by a more thorough knowledge of the side-effects and interactions of the drug, or by not using a drug where it was likely to produce only minimal benefits.

Rational Drug Bulletin, published by the Community Development Medicinal Unit, strives to provide this knowledge to the care-givers of its member-organizations.

Published by
Community Development Medicinal Unit
86 Dr. Suresh Sarkar Road
Kolkata 700014
Phone: +91-33-22652363
Fax: +91-33-22652363
Email: rationaldrugbulletin@yahoo.com

Web: www.cdmuindia.org

Antibiotic resistance in India

Antimicrobial resistance, a global problem, is particularly pressing in developing countries where the infectious disease burden is high and cost constrains the replacement of older antibiotics with newer, more expensive ones. Management of common and lethal bacterial infections has been critically compromised by the appearance and rapid spread of antibiotic-resistant bacteria. The Global Antibiotic Resistance Partnership (GARP) was established to begin the process of developing actionable policy recommendations relevant to low- and middle-income countries. Multidisciplinary working groups in India, Kenya, South Africa, and Vietnam took up this challenge in 2009 and have surveyed the state of antibiotic use and resistance and related factors. An estimated 17.5% of global antibiotic consumption is in India whereas in US had the third highest consumption of antibiotics with an estimated 9.2% of global consumption in 2010. In light of this evidence, working groups have begun to define a set of broad policy objectives.

The bacterial disease burden in India is among the highest in the world[1]; consequently, antibiotics will play a critical role in limiting morbidity and mortality in the country. As a marker of disease burden, pneumonia causes an estimated 410,000 deaths in India each year[2], and it is the number-one killer of children[3]. Many of these deaths occur because patients do not have access to life-saving antibiotics when and where these are needed.

At the other extreme, antibiotics are used in situations where these cannot be expected to improve the patient's condition, particularly as treatment for the common cold and uncomplicated cases of diarrhea. 'Drug selection pressure' is the single most important factor in the evolution of drug resistance in bacteria. The reasons for drug pressure are multifactorial and involve both human and animal use. Although drug resistance is primarily a medical problem, the factors that influence the spread of resistance are ecological, epidemiological, cultural, social, and economic. Patients, physicians, veterinarians, and healthcare facilities and retailers - from large pharmacies to local drug sellers - have little motivation (economic or otherwise) to acknowledge the consequences of their use of antibiotics on others, especially on future generations.

Every time an antibiotic is used – whether appropriately or not, in human beings or in animals the probability of the development and spread of antibiotic-resistant bacteria is increased[4,5]. Antibiotic effectiveness is a globally shared resource and a shared responsibility. That responsibility is to maintain antibiotic effectiveness as long as possible, while allowing the maximum possible health benefits to accrue to the world's population. The actions needed to achieve this goal cannot be decided globally. Each nation must adopt strategies tailored to its own conditions. The GARP working groups' recommendations are based on an understanding of the underlying issues, and the proposed solutions are designed to work in the 21st century.

Current Situation in India

Rising antibiotic use

Antibiotic use has been increasing steadily in recent years [Fig 1]. Between 2005 and 2009, the units of antibiotics sold increased by about 40 per cent. The table 1 shows the details

Table 1

Year	2005	2006	2007	2008	2009
Antibiotic purchases in crore rupees (INR)	3,763	4,484	5,075	5,886	6,414

Notes: One crore equals 100 lakhs, equals 10 million
Source: Personal communication of IMS Health Information and Consulting Services-India data from Burzin Bharuch (Pfizer) to Ramanan Laxminarayan on July 30, 2009

Increased sales of cephalosporins were particularly striking, with sales (in units sold) increasing by 60 per cent over that five-year period, but some increase was seen in most antibiotic classes. In comparison, a pilot survey conducted at private retail pharmacies in 2004[6] and a survey in the same areas in 2008 found increased use of cephalosporins, but decreased use of macrolides[7].
The fact that antibiotic use is increasing is not, itself, indicative of a problem, but evidence from studies of prescribing patterns suggests that antibiotics are often used in inappropriate ways.

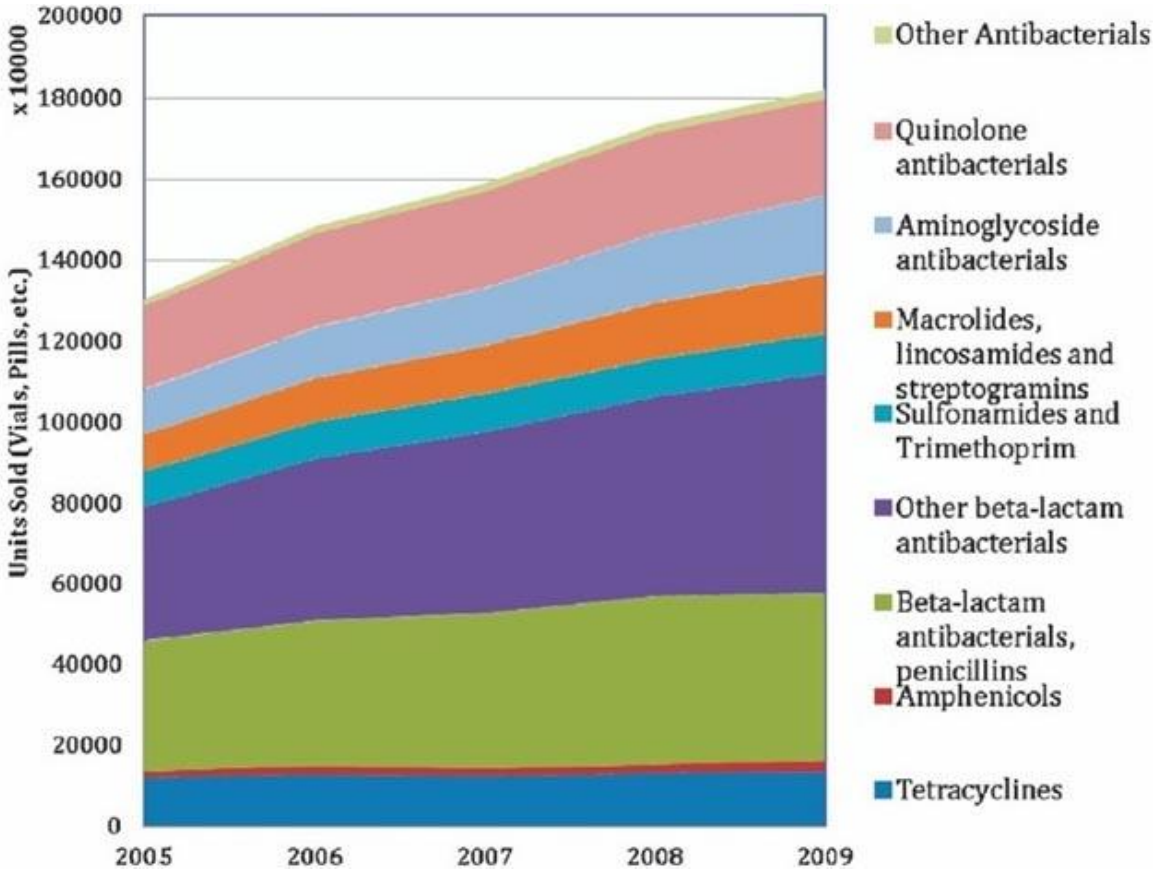

Fig. 1. Units of antibiotics sold in India, by type.

Resistance to antibiotics

Antibiotic resistance has been a low-priority area in most developing and many developed countries. Compared with the immediate challenges of HIV/AIDS, tuberculosis, malaria, pneumonia, and many other infectious diseases, the loss of antibiotics at some future time does not capture the same attention.

Resistance against certain antibiotics is already at high levels in certain places in India (and around the world), but the problem has remained largely unknown because relatively few studies were published and nationwide surveillance was not being carried out. But the issue came to the fore in India when New Delhi metallo- ß-lactamase-1 (NDM-1), first reported in 2009, made front-page news in 2010. Briefly, NDM-1 is an enzyme produced by the gene blaNDM-1; it is named for New Delhi because the Swedish patient in whom it was first identified had undergone surgery in a New Delhi hospital[7] .

The gene was carried on plasmids and could be transferred between different bacterial species, in this case between Klebsiella pneumoniae and Escherichia coli, and most importantly, conferred broad resistance to most antibiotics, including carbapenems. A further study in which NDM-1 was detected in drinking water and seepage water in New Delhi[8] added to the concern and the focus on India - whether deserved or not.

Many are of hospital-acquired Gram-negative infections with Acinetobacter, Pseudomonas, Klebsiella, E. coli, Salmonella, and Neisseria gonorrhoeae. A World Health Organization (WHO) study in which E. coli was used as an indicator organism at four sites found high levels of resistance, especially in pathogenic isolates[9]. The study measured both antibiotic resistance and antibiotic use over the course of at least one year at all sites. Resistance rates were highest to those antibiotics in use the longest.

However, resistance rates to newer antibiotics, such as fluoroquinolones, were particularly high in India[9]. The overall take-home message from studies of resistant infections is that resistance levels have been worryingly high wherever studies have been conducted. Data are not sufficient to clearly delineate trends for specific organisms or specific antibiotics, but clearly outline resistance. This resistance is affecting patients and therapeutic outcomes, with concomitant economic consequences. Antibiotic resistance surveillance has been limited to small-scale efforts by the Indian Council of Medical Research (ICMR) and some private agencies on a pilot basis. The Invasive Bacterial Infection Surveillance (IBIS) project produced valuable information on pneumonia in India, though it was unable to meet its goal of establishing a permanent surveillance system for antibiotic resistance[10]. Evidence that can be pieced together comes from many individual studies, such as studies on methicillin-resistant Staphylococcus aureus

Reference

1. World Health Organization. World Health Statistics. France; 2011.
2. Mathew JL. Pneumococcal vaccination in developing countries: where does science end and commerce begin? Vaccine 2009; 27 : 4247-51.

3. Levine OS, Cherian T. Pneumococcal vaccination for Indian children. Indian Pediatr 2007; 44 : 491-6.
4. Austin DJ, Kristinsson KG, Anderson RM. The relationship between the volume of antimicrobial consumption in human communities and the frequency of resistance. Proceedings of the National Academy of Sciences of the United States of America. 1999; 96 : 1152-6.
5. Laxminarayan R, Malani A, Howard D, Smith D. Extending the Cure. Policy responses to the growing threat of antibiotic resistance. Washington, DC; 2007 [updated 2007; cited]; Available from: http://www.rff.org/Publications/Pages/PublicationDetails.aspx?PublicationID=9575.
6. Kotwani A, Holloway K, Chaudhury RR. Methodology for surveillance of antimicrobials use among out-patients in Delhi. Indian J Med Res 2009; 129 : 555-60.
7. Yong D, Toleman MA, Giske CG, Cho HS, Sundman K, Lee K, et al. Characterization of a new metallo-beta-lactamase gene, bla(NDM-1), and a novel erythromycin esterase gene carried on a unique genetic structure in Klebsiella pneumoniae sequence type 14 from India. Antimicrobial agents Chemotherapy 2009; 53 : 5046-54.
8. Walsh TR, Weeks J, Livermore DM, Toleman MA. Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study. Lancet Infect Dis 2011; 11 : 355-62.
9. Holloway K, Mathai E, Sorensen TL, Gray A. (US Agency for International Development). Community-Based Surveillance of Antimicrobial Use and Resistance in Resource-Constrained Settings. Report on five pilot projects. Geneva: World Health Organization; 2009.
10. Thomas K, Lalitha MK, Arora NK, Das B, Awasthi S, Amita J, et al. Invasive Bacterial Infectious Surveillance II (IBIS 2) Final Report. Vellore; [cited 2011 5 August]. Available from: http://www.inclentrust.org/resources/iphid/iidi/Annex 1-IBISI 2final.pdf.

Information on Pentavalent vaccine

Pentavalent vaccine has been adopted for immunization by most countries in the world and is now being inducted into the National immunization program in India. With this Pentavalent vaccine, the children in India will be immunized not only against Diphtheria, Tetanus (also known as Lockjaw), Pertussis (also known as Whooping Cough), Hepatitis-B (also known as White Jaundice or silent killer) but also Bacterial Meningitis and pneumonia caused by Haemophilus influenzae type b Bacteria (Hib). The doses of pentavalent vaccine is as follows:

Vaccine& its presentation	Protection	Route	Number of doses	Vaccination Schedule
Hib (given as pentavalent containing Hib+DPT+Hep B) Liquid vaccine	Hib Pneumonia and Hib meningitis	Intramuscular	3	6, 10 & 14 week of age

Need for vaccination against HIB

- HIB refers to Bacterial Haemophilus influenza type b which accounts for 40% of Meningitis and more than 20% cases of pneumonia in children.
- HIB contributes to 2% of total mortality in children of under 5 years of age.

- India has annually, 312,000 cases and a death toll of over 72,000 due to HIB in children under 5 years of age

News & views

Drug price watchdog in states?
Jan 04 2015 : The Times of India (Kolkata)

The government plans to spread its regulatory wings to keep medicine prices under stringent check in every nook and corner of the country and save consumers from paying more.
It is working to set up drug price monitoring cells across the country to keep a close watch on real-time price movements, the maximum retail price of medicines and their availability , a senior official said.

The government feels merely bringing drugs under price control will not help consumers unless compliance is ensured. Therefore, it is imperative to have a watchdog in the local market where the trade takes place, the official told TOI.

At present there is National Pharmaceutical Pricing Authority, regulating prices of medicines and also monitoring compliance along with availability .

However, in the absence of adequate field inspectors and physical proximity, the central regulator finds it difficult to keep a routine watch. “We are coordinating with state governments and state drug controllers to set up price monitoring cells with field inspectors in the local market. This will enable routine market inspection and assessment of the market place on a real time basis,“ the official said. NPPA, which will continue to be the central wing and play a pivotal role in co-ordination with state agencies, has started holding meetings with various state officials to kick start the project. According to another official from NPPA, work in the direction has started in states like Rajasthan, Karnataka and Maharashtra.

The government plans to make a start from metropolitan cities and states where the presence of pharmaceutical companies is more. Centre also plans to share the finances for the project.

Infections resistant to `last antibiotic' emerge in India
Dec 29 2014 : The Times of India (Kolkata)

It is the beginning of the end. Hospitals in India are now recording cases of infections resistant to colistin, the last antibiotic available in the world. It was brought back from a 40-year exile in 2005 to treat increasing number of infections resistant to other high-end antibiotics.

For now, colistin is the only cannon left in the medical armoury to treat bacterial infections, mainly those acquired in the hospital that no drug can treat. The number of such cases is rare, but worrisome, say doctors.

The first-ever evidence of pan-drug resistant cases has now been recorded by three Chennai-based doctors.Their paper: `Emergence of pan-drug resistance among gram negative bacteria! The first case series from India' has been published in the latest issue of Journal of Microbiology and Infectious Diseases.

The paper maps 13 cases recorded over 18 months and concluded that pan-drug resistant infections, particularly those in the blood stream, have a higher mortality. Tertiary-care hospitals across the country are recording cases of infections that even colistin can't treat, with the resistance detected at 4 to 5 % in Delhi hospitals, indicative of good infection control mechanism in place, said Ramanan Laxminarayan, vice president for research and policy at the Pub lic Health Foundation of India.

In Pune's state-run Sassoon General Hospital, of the 799 drug-resistant bacteria tested between January and July in 2014, 36 were found to be colistin resistant. Stray cases have been reported at Ruby Hall Clinic in Pune and doctors at Tata Memorial Hospital in Mumbai recall one case in the last three to four years.

“Colistin resistance is still rare. It is carbapenem (the strongest class of antibiotic) resistance that is increasing across the world.Colistin is used to treat cases that are resistant even to carbapenem. It is an emerging problem. Doctors in Greece had published colistin-resistance data in 2006, and the US recorded it two years ago,” said infectious diseases consultant Dr Abdul Ghafur, one of the authors of the paper on the 13 cases.

He is the coordinator of Chennai Declaration that has laid out guidelines for hospitals and doctors on antibiotic use.

Laxminarayan said the use of colistin itself is a concern. and its use was stopped owing to its toxicity four decades ago. “It is not a preferred antibiotic. In Vietnam, it was used only in animals till a few years ago,” he added.

However, India has little choice but to use the drug to treat the rising resistance to carbapenem, a third-generation antibiotic used to treat cases resistant to lower drugs. Most hospitals are still wary of reporting colistin-resistance figures, but doctors admit that it is time to acknowledge the problem so that corrective measures can be taken.

CDMU News

CME program with medical officers of tea gardens in Assam

Community Development Medicinal Unit and Assam Branch Indian Tea Association jointly organized Continuous Medical Education program for Tea Estate in Assam for medical officers in Dibrugarh, Jorhat and Tezpur on November 5, 6 & 7, 2014. A total of 122 medical officers from various tea gardens participated in the program. The topics discussed in the meeting are on rational use of medicines, antimicrobial resistance and medical stores management. The participants felt that such program is necessary in future also.



Training program on Disease Management at Missionaries of Charity – North Bengal

Community Development Medicinal Unit was invited by Missionaries of Charity to organize a training program on disease management for their nurses of 18 centres situated in different areas of northern part of West Bengal, Sikkim, Nepal & Bihar on January 9 & 10, 2015. It is the second sensitization workshop for nurses for individual centres.



Our International Standard Serial Number is ISSN 0972-3064