Editorial

Bacterial resistance in India: Studying plasma antibiotic levels

Akash Pandhare

Access this article online
Website: www.ijccm.org
DOI: 10.4103/0972-5229.167032
Quick Response Code:

Escalating bacterial resistance to modern antibiotics has been posing a great challenge while treating patients with serious infections in hospitals. The dreaded problem is often further compounded by sub-therapeutic dosages and/or indiscriminate overuse of antibiotics in developing as well as developed countries. As per the estimates made available by the Center for Disease Control and Prevention, over 2 million people are sick due to bacterial infections resistant to one or more antibiotics, and that 23,000 individuals die from drug resistance in the United States. Ironically, 40% of the world's antibiotic drugs are produced in India, and that over 58,000 babies succumbed to death in 1 year as a direct result of infection with highly-resistant bacteria transmitted from their mothers.[1] A simulation by the Rand Corporation estimated that resistant micro-organisms could kill about 10 million individuals worldwide in 2050, which is greater than cancer deaths. However, we are yet unaware of the full impact in the absence of an efficient global tracking system overseeing the issue.

Bacterial resistance evolves as a result of mutations in these organisms as well as selection pressure exerted by unrestrained antibiotic use which provides a competitive advantage to such mutated strains; thereby decreasing overall effectiveness of antibiotics in treating even common infections. In addition, suboptimal use of antibiotic agents further allows to foster stepwise selection of resistance. Thus, mutations, in part, herald resistance genes which may now become transmissible via extrachromosomal elements and/or bacterial plasmids, which are DNA structures that mediate the transfer of resistance genes between bacteria. The resultant resistant clones are amenable to rapid worldwide spread which is facilitated by interspecies gene transmission, poor sanitation and hygiene in communities and hospitals, and the ever increasing global travel, trade, and disease transmission.[1] One of the infamous examples of this is the New Delhi matallo-beta-lactamase-1 (NDM-1) resistance gene discovered by Dr. Timothy Walsh and a team of collaborators.[2] It was first discovered in the United Kingdom in patients returning from India, detected in the wastewater of New Delhi, and hence named "NDM-1." NDM-1 has been disseminated to 18 countries including the United States and the European countries over the span of 1 year. Such are the epidemiological consequences of the resistant gene travel in our modern "close-knit" world.

In response to the emerging antibiotic resistance threat, healthcare providers are increasingly being pushed toward the use of newer and higher antibiotics. Not surprisingly, for more than two decades, life-saving broad spectrum antibiotics such as carbapenems are favorably being administered to critically ill patients in

From:
Department of Cell Physiology and Molecular Biophysics, Texas Tech University Health Sciences Center, Lubbock, Texas 79430, USA

Correspondence:
Dr. Akash Pandhare, Department of Cell Physiology and Molecular Biophysics, Texas Tech University Health Sciences Center, Lubbock, Texas 79430, USA.
E-mail: akash.pandhare@ttuhsc.edu

How to cite this article: Pandhare A. Bacterial resistance in India: Studying plasma antibiotic levels. Indian J Crit Care Med 2015;19:574-5.

hospitals. The carbapenems belong to the beta-lactam family of antibiotics with an exceptional activity against a broad spectrum of microbes, and with a long history of safety and efficacy for serious infections.[3] They are beta-lactams of choice for the treatment of infections caused by multi-drug resistant organisms.[3] However, unfortunately, now they also have met with resistant bacteria, for example, the arrival of untreatable strains of carbapenem-resistant *Enterobacteriaceae*. An older carbapenem, imipenem, is degraded by a renal tubular enzyme, dehydropeptidase-1 (DHP-1), and requires co-administration of cilastatin, a DHP-1 inhibitor. However, newer carbapenems such as doripenem, ertapenem, and meropenem are relatively immune to the DHP-1 degradation.[4] Resistant bacteria acquire or develop various strategies to render carbapenems ineffective including structural changes within penicillin-binding proteins, production of metallo-beta-lactamases, and altered membrane permeability due to loss of specific outer membrane proteins, for example, porins.[4]

Toward developing effective interventions to address the emergence of microbial resistance as well as understanding the underlying mechanism (s) of resistance, multi-pronged remedial measures are required to put in place. Of these, a major contributing arm is basic sciences as well as clinical research. In this issue of IJCCM the article by Abhilash *et al*.[6] exemplifies such a contribution to research in India, albeit at a smaller scale, and is a welcome step forward. Here, authors investigate the plasma concentration of imipenem at different loci of infection and conclude that loci variability does not constitute a major factor in affecting the drug plasma concentration within their sample. They further recommend imipenem dosing regimen revisions for the treatment of infection with recalcitrant organisms. Imipenem, indeed, is a tricky antibiotic to use in the case of critically ill patients as compared to that in other patient populations owing to its variable pharmacokinetic activity in the former. Moreover, a very weak correlation exists between its dosage and serum concentration.[5] Importantly, as discussed in the article, a large polymerase chain reaction-based gene screen of isolated bacteria would potentially provide valuable insights into the current/emerging mechanisms of bacterial resistance. Therefore, additional large-scale clinical and microbial gene studies in India are warranted to formulate effective antibiotic dosing regimens, and to deal with the menace of bacterial resistance thereof.

References

1. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, *et al*. Antibiotic resistance-the need for global solutions. Lancet Infect Dis 2013;13:1057-98.
2. 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. Antimicrob Agents Chemother 2009;53:5046-54.
3. Kattan JN, Villegas MV, Quinn JP. New developments in carbapenems. Clin Microbiol Infect 2008;14:1102-11.
4. Zhanel GG, Wiebe R, Dilay L, Thomson K, Rubinstein E, Hoban DJ, *et al*. Comparative review of the carbapenems. Drugs 2007;67:1027-52.
5. Belzberg H, Zhu J, Cornwell EE 3rd, Murray JA, Sava J, Salim A, *et al*. Imipenem levels are not predictable in the critically ill patient. J Trauma 2004;56:111-7.
6. Abhilash B, Tripathi CD, Gogia1 AR, Meshram GG, Kumar M, Suraj B. Pharmacokinetic/pharmacodynamic profiling of imipenem in patients admitted to an intensive care unit in India: A nonrandomized, cross-sectional, analytical, open-labeled study. Indian J of Crit Care Med 2015;19:587-92.