

Pandrug-resistant Infections

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ABSTRACT

Background: Increasing antibiotic resistance, usually from irrational pharmacotherapy, poses a grave challenge to clinicians in managing multidrug-resistance infections.

Aim and objective: To focus attention on the rising incidence of pandrug-resistant infections, related issues and concerns, and their containment.

Materials and methods: The short communication is prompted by the recently reported *in vitro* sensitivity of gram-negative bacteria to a combination of ceftriaxone + sulbactam + EDTA. Appropriate observations from literature are cited to complement the outcome of the said study.

Results: Pandrug resistance (PDR) is defined as a non-susceptibility of the bacteria to all antimicrobial agents in all antimicrobial categories. This is not true that it is restricted to only gram-negative bacteria. *Staphylococcal aureus*, a gram-positive bacteria, may too develop such resistance. The *in vitro* sensitivity observations do not necessarily get reflected in actual clinical effectiveness and efficacy. Therapy is a herculean task. Judicious use of antibiotics and strict infection control measures, preferably as a part of an antibiotic stewardship program, are mandatory to reduce the prevalence of PDR, nay the drug resistance as such.

Conclusion: Pandrug resistance, meaning resistance to all classes of antibiotics, can develop not only in the case of gram-negative bacteria but also gram-positive bacteria, like *S. aureus*. It is best prevented rather than treated.

Clinical significance: Implementation of the antibiotic stewardship program, mainly comprising rational antibiotic therapy, has the potentials to go a long way in safeguarding against PDR, nay antibiotic resistance as such.

Keywords: *Acinetobacter*, Antimicrobial resistance, Antimicrobial stewardship, *Enterococcus*, Extensive-drug resistance, *Klebsiella pneumoniae*, Pandrug resistance, *Proteus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*.

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INTRODUCTION

The research paper by Yadav et al.¹ reporting that pan-resistant infections (PDR) by Enterobacteriaceae and *Proteus* are susceptible to the combination of ceftriaxone + sulbactam + EDTA, makes interesting reading.

In this context, I wish to share the following observations for the benefit of your readers.

First, undoubtedly further *in vitro* studies with special reference to minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) in different centers are warranted to confirm the findings of the aforesaid study. Moreover, *in vivo* studies involving actual patients in healthcare centers too are needed. This is a fact that the *in vitro* sensitivity observations do not necessarily get reflected in actual clinical effectiveness and efficacy. Mercifully, in the recent past, integration of the pharmacodynamic and pharmacokinetic indices has considerably enhanced the correlation between *in vitro* susceptibility testing and *in vivo* clinical effectiveness. As a result, now more realistic breakpoints can be allowed.

Second, pandrug resistance (PDR) to gram-negative bacteria *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Proteus*, *Enterobacteriaceae*, and *Acinetobacter* is on an increase globally. Nonetheless, this is not true that PDR is restricted to only gram-negative bacteria. *Staphylococcus aureus*, a gram-positive bacteria, may too develop PDR.

Third, PDR infections are a huge challenge in pharmaceuticals. Individuals having health issues or compromised immune systems are often at the highest risk for getting such an infection. The two most common types of bacteria that can become resistant to antibiotics are *S. aureus* and *Enterococcus*.

Fourth, there is considerable confusion in the literature about what really constitutes PDR, especially in relation to extensive

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drug resistance (XDR).² As clarified in Table 1, XDR is resistance to all classes of antibiotics except 1 or 2. On the other hand, PDR is resistant to all classes of antibiotics. In other words, there is a non-susceptibility of the bacteria to all antimicrobial agents in all antimicrobial categories. The term, PDR, has also been employed for pathogens that are specifically resistant to seven antimicrobial agents (cefepime, ceftazidime, imipenem, meropenem, piperacillin-tazobactam, ciprofloxacin, and levofloxacin).

While efforts at determining a combination of potential antimicrobials with beta-lactamase inhibitors are in progress, research endeavors need to be boosted for the development and introduction into clinical practice of new antimicrobial agents.

Table 1: Precise definition of three types of antibiotic resistance

Multidrug-resistance (MDR): Resistance to ≥ 3 major classes of antibiotics.

Extensive drug-resistance (XDR): Resistance to all classes of antibiotics except one or two.

Pandrug resistance (PDR): Resistance to all classes of antibiotics.

Finally, prevention of PDR infections, a public health problem,³ needs a special emphasis. Judicious use of antibiotics and strict infection control measures are mandatory to reduce the prevalence of drug resistance. The proactive propagation of antimicrobial stewardship program⁴ in letter and spirit in healthcare facilities may prove a “game changer” in containing the malady.

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