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Mini Review

Tackling MDR Infections in Era of COVID-19 Pandemic

Novy Gupte* and Sapna Pradhan

Department of Pharmacology, Army College of Medical Sciences, New Delhi, India

***Corresponding Author:** Novy Gupte, Department of Pharmacology, Army College of Medical Sciences, Delhi Cantonment, New Delhi, India. **E-mail:** drnovyguptemd@gmail.com

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Abstract

The twin problems of multidrug resistance (MDR) - growing since long - and the ongoing COVID-19 pandemic are matter of grave concern. In 1980-90s MDR infections were treated with carbapenem which lost its shine by the turn of the century. In the first decade of 21st century, colistin, tigecycline and fosfomycin came to our rescue. Later, Ceftazidime*/Avibactam,* Ceftolozane/Tazobactam together with macrolides and quinolones took the command. Once significant resistant strains appear against these agents, we shall exhaust our armamentarium against MDR bugs which are already evincing triggers for extensively drug resistant (XDR) and pandrug resistance (PDR). Along with ongoing fight against COVID-19 pandemic, there is an urgent need to develop new antibiotics from new classes as well as alternative/adjuvant therapies over and above strengthening the infection control measures and antibiotic stewardship programmes.

Keywords: *Antibiotic Resistance; Antibiotic Stewardship; COVID-19; Gram-Negative Bacteria; Multidrug-Resistance (MDR); New Antibiotics*

Introduction

Today, the world is in the midst of unusual times. Ever since its onslaught, the blasted COVID-19 pandemic has been causing huge morbidity and mortality globally with patches of some relief in between. The third wave with predominance of the Delta strain is knocking at the door [1]. Hopefully, it will not be as devastating as the first two waves have been.

Mercilessly, the pandemic has adversely impacted virtually each and every sphere of life. Almost all global public health schemes have suffered considerably. On account of upsurge in the irrational use of antibiotics [2], the existing problem of antibiotic resistance (ABR) stands yet more accelerated the problem. The problem is more pronounced in the low and middle-income populations.

Multidrug-resistant infections

Infectious d The acronym, "ESKAPE", refers to the group of bacteria (both Gram-positive and Gram-negative), namely *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* that are well known to cause ABR infections. These infectious diseases are a major health threat world over, more so in the resource-limited countries [3,4].

Emergence of multidrug-resistant (MDR) strains of Gram-negative bacteria in a bigger way is a matter of grave concern. The Gram-negative bacteria (*Enterobacteriaceae, Klebsiella pneumoniae, Pseudomonas aeruginosa,* etc.) are known to be more resistant to antibiotics than Gram-positive bacteria (methicillin-resistant *Staphylococcus aureus,* vancomycin-resistant *Enterococcus faecium,* drug-resistant *Streptococcus pneumoniae*). The reasons include differences in the cell wall, efflux pumps and antibiotic-destroying enzyme (beta-lactamase, carbapenemase, etc). The development of resistance may be intrinsic (natural) or acquired. In a proportion of cases, this may well be both intrinsic and acquired.

Trends in antibiotic use in MDR infections

Over the past few decades, as a consequence of increasing problem of resistance against the conventional antibiotics, clinicians are left with limited options in pharmacotherapy of serious infections, especially the anaerobic and opportunistic ones in the intensive care unit (ICU). Carbapenem was the antibiotic that ruled the roost until turn of the century in such MDR-Gram-negative infections.

In early years of 21st century, acquired carbapenem resistance that had been noticed in1990s as a result of production of the destructive enzyme, metallo-β-lactamases, spread extensively. At this point of time, colistin (polymyxin), tigecycline, fosfomycin, aminoglycosides : and quinolones as such or in combinations entered the therapeutic regimens for carbapenem-resistant pathogens. To some extent, this approach continued until recently.

In the last decade, on account of reports of development of resistant strains to these agents, their use is on decline. Currently, Ceftazidime/Avibactam, Meropenem/Vaborbactam and Ceftolozane/Tazobactam, etc [5,6] are serving us as our "last hope" against the lethal MDR Gram-negative bacteria.

The fading "last hope"

Now, our "last hope" too is fading. With triggers of extensively drug resistant (XDR) and pan drug resistant (PDR) strains, the currentl practised option of combination therapy too is likely to get exhausted in the years ahead. Once that happens, morbidity from uncontrolled and untreatable lethal infectious disease shall be beyond the beyond. What is worse, there may be reemergence of infectious diseases that had been totally eradicated or controlled to a large extent. Even new infectious disease may come to surface.

Without a shadow of doubt, this is going to be a huge challenge for the humanity, live stock, and the environmental millieu.

The way forward

How about the solution? Obviously, worldwide policies aimed at infection control and judicious use of antibiotics through antibiotic stewardship [7,8] need yet more strengthening. Not just that. additionally, endeavours towards development of new antibiotics need to be boosted. The new antibiotics must come from new classes rather than the existing classes that are already in the loop of antibiotic resistance [9].

Another possible solution is drug repurposing, meaning use of non-antibiotic agents as an alternative or adjuvant to antibiotics. In this behalf, antimicrobial peptides, bacteriophages, immunomodulating agents, probiotics and faecal microbiota are already undergoing research [10]. This approach is supposed to at least augment the efficacy of the antibiotics when used in combination with them.

The sooner these strategies work out, the better. Else, we may well be heading for an uncertain future with morbid infections having a field day and causing limitless deaths and morbidity globally.

Conclusion

The growing problem of MDR bugs has worsened since the onslaught of COVID-19 pandemic on account of further hike in irrational and excessive use of antibiotics. The significant spread of resistant bugs is adversely impacting our "last hope" as far as antibiotics are concerned. Besides controlling COVID-19 pandemic and stepping up infection control measures, there is an urgent need of speeding up development of new antibiotics from new classes and research on alternative therapies such as drug reproposing.

Conflict of Interest

None.

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