Restricting high-end antibiotics usage - challenge accepted!

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ABSTRACT

Objectives: Antimicrobial resistance (AMR) leads to increased morbidity, mortality, and healthcare expenditure. The rate of development of AMR is accelerated by the use and misuse of antimicrobials. Preauthorization and restricted use of high-end antibiotics are the key modalities of antimicrobial stewardship. Hence, choosing the right antibiotics is the key to better clinical outcomes and preventing resistance in hospitals as well as communities. The present study was done to assess the judicious usage of high-end antibiotics among inpatients treated at our hospital. **Materials and Methods:** A prospective observational study was conducted on high-end antibiotic usage using a structured proforma among inpatients treated at our hospital for a 3 month period. Department wise educational intervention was done and feedbacks were provided, after which reassessment was done. **Results and Analysis:** Meropenem was the most commonly used high-end antibiotics. After the feedback and intervention, there was 51.2% reduction in the unjustified antibiotic usage. The appropriateness of the usage increased from 77% observed during preintervention to 88% postintervention. **Conclusion:** The increasing compliance of judicious usage of high-end antibiotics needs to be sustained. Therefore, continuous strengthening of antimicrobial stewardship practices are crucial.

Keywords: Antibiotics, antimicrobial resistance, antimicrobial stewardship, audit, restricted antibiotics usage

Introduction

The emergence of multidrug resistance has become a life threatening challenge in the field of medicine. The advent of antibiotics, dramatically altered the prognosis of patients with bacterial infections. However, excessive and indiscriminate usage of these "miracle drugs" in both human and veterinary practices, has led to the emergence of "superbugs" that endanger their efficiency.[1]

Background of the study

The ability of the microorganisms to become resistant to major therapies used against them has long been recognized.[2-4] The

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emergence of antimicrobial resistance is a complex problem, driven by many interconnected factors, in particular, the use and misuse of antimicrobials. Antimicrobial use, in turn, is influenced by the interplay of knowledge, expectations and interactions of prescribers and patients, economic incentives, characteristics of the health system (s), and the regulatory environment. The intensity of the use of restricted antibiotics is higher in the hospitals although most antimicrobial usage occurs within the community. Hence, it is crucial to develop integrated approaches to improve the judicious usage of these restricted antibiotics and thereby reduce the incidence of spread of resistant bugs in the hospital.[5] Nevertheless, pessimistic viewpoints about the low chances of success to stop the development of antimicrobial resistance have repeatedly been reported.[6] The fundamental predicament is that antimicrobial drugs are a nonrenewable resource and their duration of benefit and availability appears to be limited at the biological level, a constraint not seen with therapies for other disease conditions.[7] Prescriptions issued by

general practitioners (GPs) in the community are a significant contributor to the development of antibiotic resistance. It is quoted that nine out of ten prescriptions generated, reveal the use of antibiotics in the community.[8] High-end antibiotics are increasingly used in the community by the GPs which endanger their efficacy by contributing to the development of bacterial resistance. The other factors responsible include over the counter availability of antimicrobials without professional control, use of drugs with low potency, and efficacy due to poor manufacture or counterfeiting.[9] Moreover, the availability of drugs from persons or quacks who have little or no knowledge of dosage regimens, indications or contraindications as in our country, is an important factor.[10]

AMR is a global problem.[11] Globalization has increased the vulnerability of countries to import diseases.[12,13] The emergence of antimicrobials resistance was mainly attributed to the inappropriate prescribing of antimicrobials and overuse of antimicrobials including self-medication.[14] Although responsibility for health remains predominantly national, to combat AMR, an international collective action is necessary.[15]

Eradication of AMR requires a significant reduction in the use of antimicrobials.[4] Long-time interventions for the containment of AMR would emphasize policies and regulations that encourage more appropriate and rational use of antimicrobials.[16] There are many examples where changes in antimicrobial prescribing practices have had a significant effect on the outbreaks of resistant pathogens.[17] The judicious use of antibiotics is an important strategy for preserving efficacy in the treatment of infectious diseases. Antibiotics used in the community for outpatients represent 90% of the total antimicrobial use. But more than half of these were found to be either inappropriate or unnecessary.[14] Drug use evaluation (DUE) for the higher end antibiotics will not only improve the treatment efficacy but also help in conserving cost and preventing AMR.[18] There are no newer antibiotics in the pipeline especially for organisms such as the colistin-resistant gram-negative organisms. Hence, it is essential to preserve the fewer antibiotics in hand.

Antimicrobial stewardship refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of optimal antimicrobial drug regimen dose, duration of therapy, and route of administration. Preauthorization and restricted use of high-end antibiotics are the key modalities of the antimicrobial stewardship.[19] It should be followed by prospective audit with intervention and feedback. This study was done to assess the usage of high-end antibiotics among patients treated at our hospital as inpatients.

Materials and Methods

This prospective observational study was conducted at P.S.G Hospitals, Coimbatore after obtaining approval from the Institutional Human Ethics Committee (Ethical committee

approval has been obtained. Date of approval- 23/12/2016). The inpatients of the hospital who were prescribed high-end antibiotics during the 3 month period were included in the study. Antimicrobial Stewardship Committee has listed the following antibiotics such as carbapenems, colistin, tigecycline, vancomycin, linezolid, teicoplanin, and caspofungin as high-end antibiotics and their prescriptions were analyzed. The relevant data required for the study were collected from hospital information system (HIS) and medical records of the patients and documented. The data were collected using a well-structured proforma. The National Treatment Guidelines for Antimicrobial Use in Infectious Diseases (2016), India was taken as the standard to assess prescribing practices. Adherence to the antibiotic policy was evaluated and the results were analyzed. The justification of the usage choice was determined based on the hospital antibiotic policy, supporting test reports, and the patient's outcome. The feedback of the audit was conveyed to the clinicians by conducting department specific orientation programs as an educational intervention. The need to rationalize the use of antibiotics was emphasized. We also encouraged the treating clinician to enter online preauthorization form which was available at the hospital to de-escalate the antibiotic or stop it at the earliest. The clinicians discussed the practical challenges faced by them while implementing it. Later, a postintervention study was conducted to study the changes in the prescribing practices following the intervention. The results were analyzed and compared with the preintervention study.

Results and Analysis

The numbers of patients studied in the preaudit were 352, of which 223 were male and 129 were female. In the postaudit, 195 patients were studied of which 125 were male and 70 female. The study showed that age group of 40–59 years and 60–79 years were more prescribed with high-end antibiotics [Figure 1]

The common antibiotics that were prescribed during the study were meropenem followed by vancomycin and colistin [Table 1].

The choice of usage of these antibiotics was analyzed. During both the phases of study, the antibiotics were used more empirically (70%) than therapeutically (30%). In the initial assessment, the high-end antibiotic usage was justified in 77.1% which improved to 88.3% post-intervention [Figure 2]. The rise in justified usage of these antibiotics posts educational intervention was statistically significant with P value <0.001.

Medicine and surgery departments topped the list followed by nephrology and pulmonology. The improvement in compliance after feedback and intervention showed a 51.2% reduction of unjustified antibiotics usage from baseline audit to reaudit which was statistically significant with P value <0.001. The analysis results are shown in Figure 3.

The unjustified usage of the high-end antibiotics was analyzed to find the clinical scenarios causing nonadherence to the antibiotic
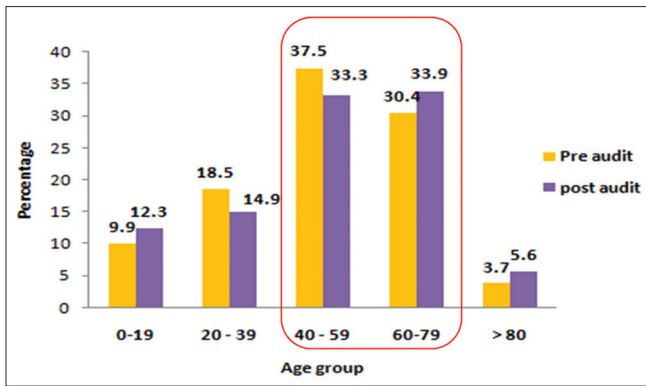
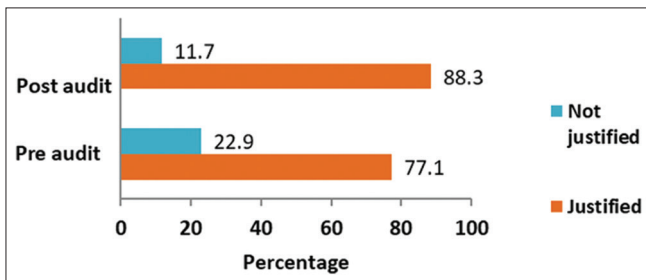**Figure 1:** Most common age groups prescribed with higher-end antibiotics

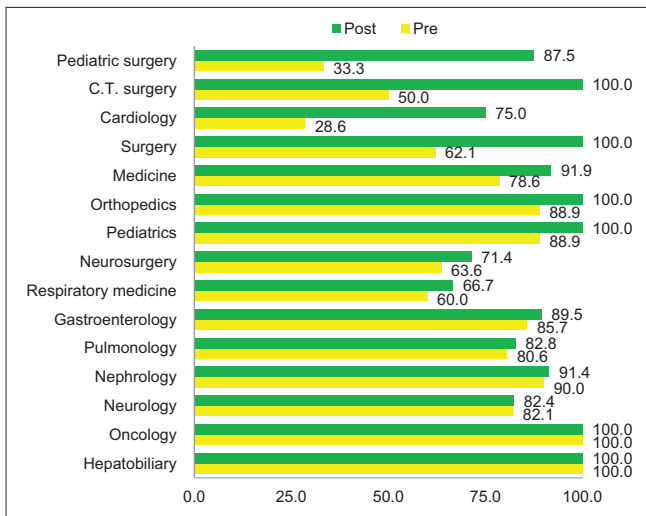**Figure 2:** Comparing the justified usage of high-end antibiotics

Figure 3: Improvement in compliance after feedback and intervention

Table 1: Common high-end antibiotics prescribed during the study		
Antibiotics	Frequency (%)	
	Preaudit	Postaudit
Meropenem	44.82	52.71
Vancomycin	21.45	21.17
Colistin	12.53	11.72
Linezolid	5.54	3.60
Tigecycline	5.54	3.60
Imipenem	5.10	2.25
Ertapenem	3.13	2.25
Doripenem	0.96	-
Teicopanin	0.48	0.45
Caspofungin	0.24	0.90
Total	100	100

antibiotics which were similar to a study done by Singh *et al.*[20] This may be due to the increased comorbidities in the males for which they were hospitalized. The most common age group that were prescribed high-end antibiotics were 40–59 years and 60–79 years, which correlates to the various studies done previously.[20] The prevalence of increased comorbidities in addition to the infectious diseases in these age groups could be the reason behind the increased usage of high-end antibiotics in them. The most common antibiotic prescribed was meropenem which is similar to the study by Singh *et al.*[20] This is because the patients who attend the tertiary care hospitals are usually treated at other centers with the available lower groups of antibiotics. They become resistant to these by the time they are referred to the tertiary hospitals, leaving the treating clinicians with only the higher group as treatment options. Usually the patients present sepsis-like features in the ICUs which is the reason for meropenem and vancomycin being used more frequently. The choice of usage was empirical than therapeutic for the same reason. It takes 48–72 hours to have microbiological evidence to make a perfect choice of antibiotic. Thus empirical usage is justified in most of the cases except where a viral etiology is confirmed by the serological tests which would be available earlier than bacterial culture reports. But it is essential to revisit the usage choice once the culture reports are available and to de-escalate or escalate the antibiotics. Also, the clinical condition of the patient must support this change or continuation of the antibiotic. The reanalysis of the empirical usage has been found low in many centers leading to over-use of these high-end antibiotics. Also extensive surveys of the ICUs have shown that in most situations, decisions regarding the treatment initiation, termination, and choice of antibiotics are made by the clinicians without the involvement of a microbiologist, in nearly 95% of the cases.[21] Under such circumstances, the treatment becomes host-directed instead of being pathogen directed.[22] Host directed treatment also limits the de-escalation in the quest of providing full protection to the patient irrespective of the susceptibility pattern of the causative pathogen.[23] Our results confirm the tendency of physicians to prescribe broad-spectrum therapy empirically.

policy. It showed that though there was no microbiological evidence to continue high-end antibiotics, they were continued for reasons such as relapse of infection, sampling for culture not possible, and clinical suspicion of persistence of infections suggested by other diagnostic parameters.

Discussion

This study analyzed the prescription practices at our hospital and assessed the usage of restricted high-end antibiotics. Our study showed that males were predominantly given these restricted

This study also showed that de-escalation of the empirically started antibiotics was 25%.

Inappropriate or overuse of high-end antibiotics was due to delay in obtaining culture reports, culture not done for reasons such as sampling not possible, or it was reported sterile but clinical signs demanded its use, and so on. The provision for a written explanation for any deviation from the policy could have counted for higher compliance rate and a better assessment of the major hindrances against compliance.[23] Moreover, relapses after treatment with lower group of antibiotics demand the usage of high-end antibiotics. The differences in in-vitro and in-vivo action of the antibiotics are another point to consider in analyzing these antibiotics usage.

In a multicenter study, it was reported that antibiotics given in 25.8% of cases of clinically proven infections and 15.95% cases of microbiologically documented infections, were inappropriate.[24] In another study, rates for unnecessary use and inappropriate use of antibiotics were 27% and 35.8%, respectively.[25] Willemsen et al.[26] reported 37.4% antibiotic use was inappropriate in Netherlands. Similarly, in India, 30%-40% antibiotic use was found inappropriate.[27,28]

In our study, the appropriateness of the usage of high-end antibiotics was around 77% in the preintervention audit which was higher than the reported values. In studies carried out in Israel and Switzerland, appropriateness of antibiotic use has been reported quite high ($80 \pm 9\%$ and 71%, respectively).[29,30] After our educational intervention, there was further improvement in the appropriateness of antibiotic usage after our intervention from 77 to 88% which is similar to that in Switzerland.[29,30]

A study by Thuong et al. in France, showed that implementation of antibiotic order form for restricted antibiotics and follow-up can be associated with a marked reduction in antibiotic consumption and with acceptably appropriate use of such drugs.[31] A combination of both restrictive and educational measures appears to be necessary to improve overall antibiotic usage in hospitals.[32-34] This multifaceted approach should involve clinicians, clinical microbiologists, pharmacists, and infectious disease experts.[31]

Studies also show that audit and feedback strategies can be significantly effective in increasing adherence to policy guidelines. Ours was a small effort to add on to the bigger antimicrobial stewardship program that is active in our hospital and thereby help in reducing the emergence of "superbugs" in the hospital as well as in the community. This can help the patients to have reduced duration of hospital stay, economic burden, and the risk of infections to the healthcare workers from the patients and vice versa.

Conclusion

Antimicrobial stewardship committee has the potential to reduce the misuse of a few high-end antibiotics with us at present. Developing hospital antibiogram based policies, strict implementation, coordinated decisions in the use of high-end antibiotics for the treatment of patients along with hospital infection, control practices are essential components to be developed in every hospital to prevent misuse of these drugs. Strengthening of preauthorization and restriction of the high-end antibiotics are crucial to reduce the development of MDROs in the future. Clinical audits followed by feedback and intervention can improve the rationalized prescription of such last-resort antibiotics. It is high time; we join hands to save the few effective antibiotics for future generations.

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Conflicts of interest

There are no conflicts of interest.

References

1. Wise R, Hart T, Cars O, Streulens M, Helmuth R, Huovinen P, et al. Antimicrobial resistance. Is a major threat to public health. BMJ 1998;317:609-10.
2. Standing Medical Advisory Committee Sub-Group on Antimicrobial Resistance. The path of least resistance. London: Department of Health; 1998.
3. Ashley D, Brindle M. Penicillin resistance in staphylococci isolated in a casualty department. J Clin Pathol 1960;13:336-8.
4. Smith RD, Coast J. Antimicrobial resistance: A global response. Bull World Health Organ 2002;80:126-33.
5. Coast J, Smith R, Miller M. Superbugs: Should antimicrobial resistance be included as a cost in economic evaluation? Health Econ 1996;5:217-26.
6. WHO. Global Strategy for the Containment of Antimicrobial Resistance. Geneva: World Health Organization; 2001.
7. Taylor R, Shakoor O, Behrens R. Drug quality, a contributor to drug resistance? Lancet 1995;346:122.
8. Biezen R, Roberts C, Buising K, Thursky K, Boyle D, Lau P, et al. How do general practitioners access guidelines and utilise electronic medical records to make clinical decisions on antibiotic use? Results from an Australian qualitative study. BMJ Open 2019;9:e028329.
9. McGregor A. Counterfeit drugs flood developing world. Lancet 1997;350:1690.
10. Dua V, Kunin C, White L. The use of antimicrobial drugs in Nagpur, India. A window on medical care in a developing country. Soc Sci Med 1994;38:717-24.
11. Smith R. Antimicrobial resistance: The importance of developing long term policy. Bull World Health Organ 1999;77:862.
12. Yach D, Bettcher D. The globalisation of public health, I: Threats and opportunities. Am J Public Health 1998;88:735-8.
13. Fidler D. The globalisation of public health: Emerging infectious diseases and international relations. Ind J Global Legal Stud 1997;5:11-51.
14. Shaikhan F, Rawaf S, Majeed A, Hassounah S. Knowledge, attitude, perception and practice regarding antimicrobial use in upper respiratory tract infections in Qatar: A systematic review. JRSM Open 2018;9:2054270418774971.

15. Fidler D. Legal issues associated with antimicrobial drug resistance. Emerg Infect Dis 1998;4:169-77.

16. Smith RD, Coast J. Antimicrobial resistance: A global response. Bulletin of the World Health Organization 2002;80:126-33.

17. Gessel H van, Duguid M. Strategies for implementing and sustaining antimicrobial stewardship. Wwwsafetyandqualitygovau.//https://www.safetyandquality.gov.au/wp content/uploads/2012/02/chapter 1_implementing_microbial_stewardship_program.pdf [Last accessed on 2018 Apr 16].

18. Mehdi M, Mirrahimi B, Mousavi S, Moradi M. Drug use evaluation of three widely prescribed antibiotics in a teaching hospital in East of Iran. J Pharm Care 2013;1:100-3.

19. Hulscher ME, Grol RP, Van der Meer JW. Antibiotic prescribing in hospitals: A social and behavioural scientific approach. Lancet Infect Dis 2010;10:167-75.

20. Singh AP, Gupta U, Das S. Monitor the use of antibiotics in intensive care units with special focus on restricted antibiotics in tertiary care hospital of India. Asian J Pharm Clin Res 2016;9:256-9.

21. Malacarne P, Rossi C, Bertolini G, GiViTI Group. Antibiotic usage in intensive care units: A pharmaco-epidemiological multicentre study. J Antimicrob Chemother 54:221-4.

22. Lawrence KL, Kollef MH. Antimicrobial stewardship in the intensive care unit: Advances and obstacles. Am J Respir Crit Care Med 2009;179:434-8.

23. Banerjee T, Anupurba S, Singh DK. Poor compliance with the antibiotic policy in the intensive care unit (ICU) of a tertiary care hospital in India. J Infect Dev Countr 2013;7:994-8.

24. Usluer G, Ozgunes I, Leblebicioglu H. The Turkish antibiotic utilization study group. A multicenter point-prevalence study: Antimicrobial prescription frequencies in hospitalized patients in Turkey. Ann Clin Microbiol Antimicrob 2005;3:4-16.

25. Erbay A, Colpan A, Bodur H, Cevik MA, Samore MH, Ergonul O. Evaluation of antibiotic use in a Hospital with an antibiotic restriction policy. Int J Antimicrob Agents 2003;21:308-12.

26. Willemsen I, Anneke G, Diana B, Stuurman A, van Keulen P, Kluytmans J. Appropriateness of antimicrobial therapy measured by repeated prevalence surveys. Antimicrob Agents Chemother 2007;51:864-7.

27. Kshirsagar MJ, Langade D, Patil S, Patki PS. Prescribing patterns among medical practitioners in Pune, India. Bull World Health Organ 1998;76:271-5.

28. Das AK, Roy K, Kundu KK, Das N, Islam CN, Ram AK, *et al.* Study of rational utilization and cost analysis of antibiotic in a government teaching hospital. Ind J Pharmacology 2002;34:59-6.

29. Raveh D, Levy Y, Schlesinger Y, Greenberg A, Rudensky B, Yinnon AM. Longitudinal surveillance of antibiotic use in the hospital. QJM 2001;94:141-52.

30. di Giammarino L, Bihl F, Bissig M, Bernasconi B, Cerny A, Bernasconi E. Evaluation of prescription practices of antibiotics in a medium-sized Swiss hospital. Swiss Med Wkly 2005;135:710-4.

31. Thuong M, Shortgen F, Zazempa V, Girou E, Soussy CJ, Brun-Buisson C. Appropriate use of restricted antimicrobial agents in hospitals: The importance of empirical therapy and assisted reevaluation. J Antimicrob Chemother 2000;46:501-8.

32. White AC Jr, Atmar RL, Wilson J, Cate TR, Stager CE, Greenberg SB. Effects of requiring prior authorization for selected antimicrobials: Expenditures, susceptibilities, and clinical outcomes. Clin Infect Dis 1997;25:230-9.

33. Avorn J, Harvey K, Soumerai SB, Herxheimer A, Plumridge R, Bardelay G. Information and education as determinants of antibiotic use: Report of task force 5. Rev Infect Dis 1987;9(Suppl 3):S297-312.

34. Moleski RJ, Andriole VT. Role of the infectious disease specialist in containing costs of antibiotics in the hospital. Rev Infect Dis 1986;8:488-93.