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STUDY OF THE PREVALENCE OF MICRO ORGANISMS AND IMPACT OF USAGE OF RESTRICTED ANTIBIOTICS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

The study is to optimize the use of restricted antibiotics, to minimize the consequences of usage of Restricted Antibiotics (RA) & to determine the prevalence of resistant organisms. 316 patients receiving antibiotics in a tertiary care hospital in Kolkata, both restricted as well as non-restricted, were studied. The data was collected, analyzed for microbial & pharmacological impact analysis 316 patients under study, a total of 3218 antibiotics were dispensed, out of which 834 were restricted antibiotics (n=3218; 25.92%).The results showed that restricted antibiotic use consisted of 25.92%. According to the Society for Healthcare Epidemiology of America, the recommended use stands at 20%. In our study there is an increase of 5.92%. Recommended that health care institutions need robust infection control and antibiotic stewardship programs to prevent transmission of resistant bacteria and to decrease the selective pressure for resistance.

KEYWORDS: Antibiotic Stewardship Program, Drug Formulary, Restricted Antibiotic usage

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INTRODUCTION

Antibiotic resistance is a public health problem of increasing magnitude, and finding effective solutions to address this problem is a critical factor. Misuse of these agents can have an extremely negative effect on the society at large due to development of bacterial resistance. Antibiotic Stewardship Program (ASP) aims to optimize the use of restricted antibiotics by establishing a policy for its rational use & form strategies to prevent antibiotic resistance in patients. The usage of restricted antibiotics were monitored and documented on 316 patients in a tertiary care hospital in Kolkata. Documentation was done using the concept of Defined Daily Dose. Data were collected & assessments were made of the requirement for continuing antibiotic treatment, dose, duration & route of therapy. An evaluation audit tool was used to assess all patients on antibiotic treatment. The results showed that restricted antibiotic use consisted of 25.92%. According to the —Society for Healthcare Epidemiology of America, the recommended use stands at 20%. Thus there was an increase of 5.92%.

Antibiotic Steward

An antibiotic steward is a physician who is trained in infectious diseases and infection control or a microbiologist with training in infection control and antibiotic stewardship. They are responsible for giving a second opinion on higher-end antibioticusage.[1]

Antibiotic Stewardship Program

It is defined as a rational, systematic approach to the use of antimicrobial agents in order to achieve optimal outcomes. Optimal outcome include those of the patient (achievement of cure, avoidance of toxicity and other adverse effects) & of the larger population (avoidance of emergence or propagation of anti-microbial resistance).[1]

Drug Formulary

the official compilation of selected brand/generic drugs approved bythe committee to meet the clinical needs of the medicalteam.[1]

Restricted Antibiotic (RA)

those antibiotics that could contribute to development of multi- resistant organisms[1].

Antimicrobials are used to treat infections by different disease-causing microorganisms. In the vast majority of cases where antimicrobials are used, the microorganisms have found a way to evade or resist the antimicrobial agent[2]. Resistance occurs wherever antimicrobials are used -- in the community, in the farms for control of pests and in healthcare[3]. Antimicrobial resistance is emerging as challenge world-wide because of their irrational use & abuse a global problem, and poses one of the most significant global threats to us and our future generations, as resistant strains of microbes are emerging faster than ever thought[4]. Antibiotics are the most frequently prescribed group of drugs among hospitalized patients, especially in ICUs & surgical departments. While antimicrobial usage has undoubtedly reduced mortalities caused by infections, resistance to these drugs has also increased significantly. Antimicrobial resistance is a serious global challenge[5]. Each and every place on this globe is facing the ever increasing incidences of multi-drug resistant cases.Though, the extent and the severity of the problem vary. We may face the problems of pre antibiotic state, where many people could suffer or die from un-manageable cases infections[6].Infections with resistant bacteria were first reported over 60 years ago[7], but early on the problem was often overlooked, because if one antibiotic did not treat the infection another was usually available. Since then, infections with resistant bacteria have become more common in healthcare and community settings, and many bacteria have become resistant to more than one type or class of antibiotics[8]. Consequently, doctors and nurses today are faced with treating infections where antibiotic options are very limited, and in some cases, where no effective antibiotics exist. When treatment options are limited, healthcare providers might need to use antibiotics that are more expensive or more toxic to the patient[9]. When no antibiotic is effective, healthcare providers may be limited to providing supportive care rather than directly treating an infection -- similar to how medicine was practiced before antibiotics were discovered. As resistance increases, the patient‘s risk of dying from infection also increases[10]. Moreover, resistance is not just a problem for the patient who is infected. When an infection is not effectively treated because of resistance, the microorganisms will persist and potentially spread to others, further extending the resistance problem.The incidence of infections attributed to multidrug-resistant organisms (MDROs) among hospital patients continues to rise despite widespread efforts to control their spread. Infections caused by MDROs are associated with worsened clinical outcomes, including an increased risk of death & significantly increased costs, mostly attributable to increased length of stay. In response to this emerging concern, an Antibiotic Stewardship Program (ASP) has been created which aims at promoting rational antimicrobial prescribing with the goal of reducing the incidence of MDROs infections[11]. Antibiotic resistance is also an economic burden on the healthcare system. Resistant infections not only cost more to treat, but also can prolong healthcare use[12].Addressing antibiotic resistance requires a multifaceted approach to reduce inappropriate use, prevent disease transmission, and develop new antibiotic agents[13]. The incidence of antimicrobial resistance among health care–associated pathogens has been steadily increasing over the past 2–3 decades & still continues to grow as seen in the above graph. Preventing resistant infections provides the greatest opportunity to limit resistance. Strategies to prevent and control resistant bacteria vary by the pathogen and the setting in which the infection is acquired. For some diseases caused by bacteria like Streptococcus Pneumonia, there are vaccines to prevent infections[14]. Prevention of HAIs, such as MRSA, resistant gram-negative bacteria and C. difficile, can require different interventions than those infections that are community-associated, such as tuberculosis and pneumococcal pneumonia. In all cases, surveillance data are used to

monitor the effectiveness of prevention efforts. Currently, there is no functioning national antibiotic policy or a national policy to contain antimicrobial resistance in India. The policy published in 2011 has been put on hold due to non-implementation of major recommendations[15]. In India, there is unrestricted availability of even high end antibiotics, in every nook and corner pharmacy shops, without asking for valid prescription. Indian hospitals have reported very high Gram-negative resistance rates, with very high prevalence of Extended Spectrum of Beta Lactamase (ESBL) producers and also high Carbapenem resistance rates. Increasing Carbapenem resistance will invariably result in increased usage of Colistin, currently the last line of defense, with a potential for Colistin-resistant and Pan Drug Resistant bacterial infections[16]. As per data available from various studies, most accredited hospitals, though having a well written antibiotic stewardship and SOP, doctors do not comply in practice. India, with thousands of hospitals, with ever increasing population, wide cultural diversity, socio-economic disparity, and a large medical community of more than three-fourths of a million doctors with diverse back ground of practice of medicine, will find the resistance problem, an issue very difficult to tackle unless we take aggressive steps whole heartedly and join our hands in our efforts to tackle the menace on a national level[17].

Necessity of Antibiotic Stewardship Program

Major reasons for starting the ASP are

- Antimicrobial agents typically account for a large proportion of the pharmacy expenditures in a hospital.
- It has been estimated that 50% of antimicrobial use in hospitals isinappropriate.
- Inappropriate antibiotic use has been associated with propagation of antimicrobial resistance and other adverse effects.
- Appropriate use of antimicrobial agents may improve patient outcomes & reduce hospital costs.

Barriers to Implementation of ASP-

- ❖ Lack of awareness of the enormous adverse clinical and economic impacts of these infections
- ❖ Relative lack of engagement by prescribing clinicians with Microbiologists , who mostly confine themselves to the laboratory
- ❖ Absence of clinical pharmacists who support good quality prescribing
- ❖ The desire for clinicians to only be concerned with good clinical out-comes of individual patients, regardless of their commitment to the broader public good.

This study was carried out in a tertiary care hospital in Pune, with an aim of researching the prevalence of microorganisms and impact of usage of restricted antibiotics in a tertiary care hospital.We studied with the following objectives:

- To optimize the use of restricted antibiotics
- To minimize the consequences of usage of Restricted Antibiotics (RA)
- To determine the prevalence of resistant organisms

The study was restricted to patients in ICU, SICU, CCU, and Neuro-ICU.Since the study was conducted purely from the point of managerial issues, related to emergence of resistant organisms and impact of usage of restricted antibiotics on this microbial flora, there was no direct or indirect intervention in prescription by the doctors. Hence, keeping in view, that it was purely of an academic study, no ethical clearance was taken. Antimicrobial resistance is a known major public health issue and antimicrobial stewardship, the appropriate use of antimicrobial agents, is critical to stemming the continued emergence of antimicrobial-resistant organisms. Literature has shown that appropriate use of antimicrobials can reduce occurrences of antibiotic resistant organisms[16]. The increasing recognition of the health burden associated with hospital-acquired infections and the increasing evidence that the use of antimicrobials in hospitals is a critical determinant of infection rates due to the most important hospital-acquired pathogens, methicillin-resistant Staphylococcus aureus (MRSA) and Clostridium difficile, emphasize the urgency of developing and facilitating antimicrobial stewardship programs.

MATERIAL & METHODS

Area of study: ICU, CCU, SICU, Neuro-ICU
Place of study: Multi-super specialty Tertiary care Hospital in Kolkata
Sample size : 316
Sampling Technique: Convenient sampling Period of study: May 2015 to August 2015

Parameters of study

- ➢ Patient information
- ➢ Drug information
- ➢ Microbiological reports

316 patients receiving antibiotics, both restricted as well as non-restricted, were studied. The data was collected & tabulated under the following headings Table1): The clinical data was used to asses if the patient is showing any signs of infection &/or inflammation whereas the microbiological data was used to rationalize the usage of antibiotic. Based on the drug dosing information the total quantity of the drug dispensed to the patient was calculated and then the Daily Drug Dosage (DDD) of the drug was found out using the formulae:

Required DDD = Total Quantity dispensed*Conversion factor

In case of RA, the rationale was sought & checked for its appropriateness. The use of these antibiotics had to be justified & explained with a microbiological report. Sometimes the prescribers' clinical judgment could also suffice as a rationale. Based on this the RA was approved. If the rationale was not found to explain it sufficiently, then the necessary intervention was taken, i.e. either stopping the drug or changing them or deescalating them. Apart from this the Hospital's Pharmacy Department maintains daily records of the use of RA. The data for 3 months were studied for monitoring changes in resistance level in microorganisms and to analyze & co-relate antibiotic use with resistance development (Fig1).The percentage of resistance decreased over 3 months in cases of MDR & MRSA that is from 40 to 19 & 11 to 2 respectively. In case of ESBL, the percentage resistance decreased from February (20) to March (12) and then shot up in March (19).

Study of the Prevalence of Micro Organisms and Impact of usage of Restricted Antibiotics in a Tertiary care Hospital

Table 1
Data collection table

Patient Information	Drug Information	Microbiological Reports
Name	Antibiotic Name	Site of Infection
Age	Dose	Organism
Sex	Route	Sensitivity
Weight	Frequency	
UHID	Date of First Use	
Bed No.	Date of Last Use	

316 patients receiving antibiotics, both restricted as well as non-restricted, were studied. The data was collected & tabulated as per Table1)

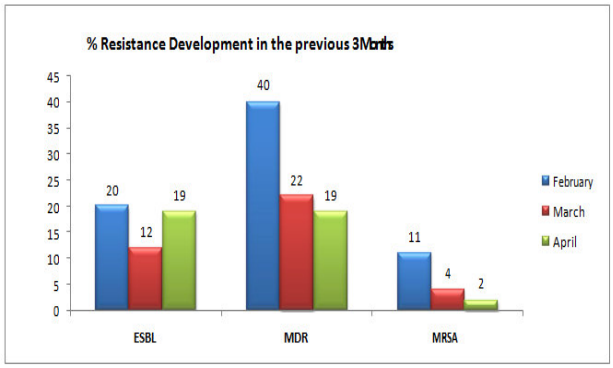

Figure 1
% Resistance Development in Patients in previous 3 months

The hospital's Pharmacy Department maintains daily records of the use of RA. The data for 3 months were studied for monitoring changes in resistance level in microorganisms and to analyze & co-relate antibiotic use with resistance development (Fig1).

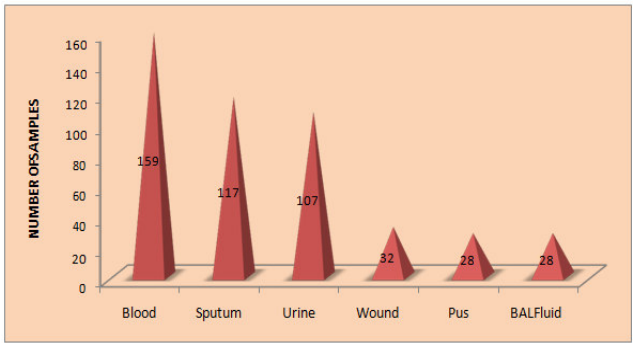

Figure 2
Number of samples collected from 316 patients

The highest number of samples collected from the 316 patients under study was blood (33.758%) followed by sputum (24.84%) urine (22.717%), wound (6.794%). The number of pus & BAL fluid samples stood at 5.945% each. In majority of the cases multiple samples were collected from each patient for microbiological testing.

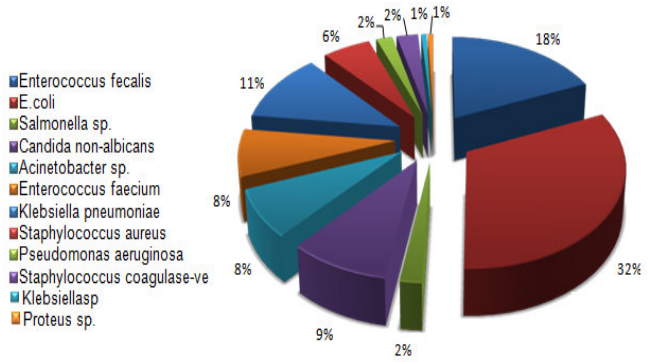

Figure 3
% of Organisms Isolated from Blood
Gram negative organisms were leading in the count from culture of Blood

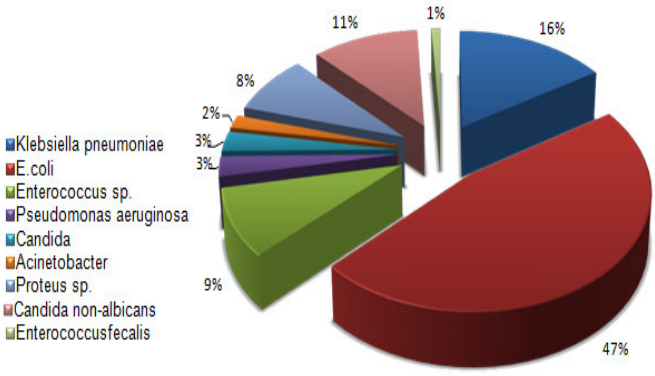

Figure 4
Organisms Isolated from Urine Culture

The rate of isolation of E. coli was the highest at 111 (n=471; 23.567%) (Fig8)& it is also the highest of all the organisms detected in blood 50 (n=159, 31%) & urine 50 (n=107, 47%) (Fig9) samples.

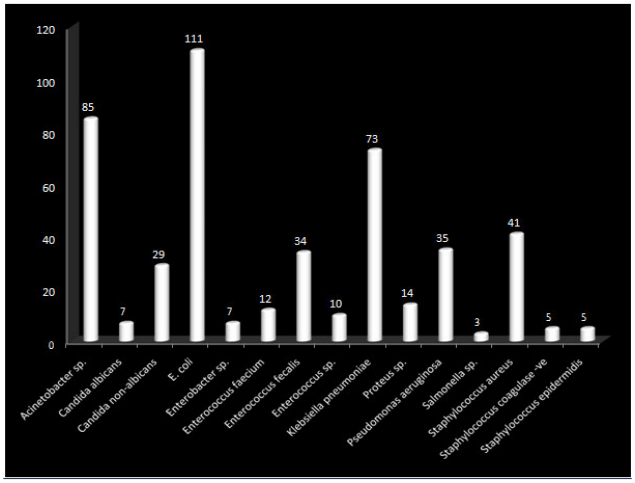

Figure 5
Number of resistant organisms isolated

E.Coli, Klebsiella pneumoniae & Acinetobacter species formed the other major chunk of organisms isolated mainly from sputum & BAL fluid. Staphylococcus aureus formed the majority of organisms isolated in pus 14 (n=28, 50%) & wound 12 (n=32, 38%). Salmonella species was the least isolated 3 (n=471; 0.637%) of all the organisms across all samples (Fig9).

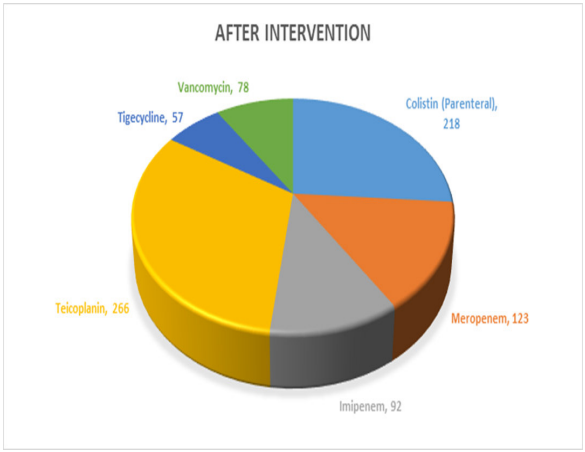

Figure 6
Antibiotic Usage after Educating Doctors

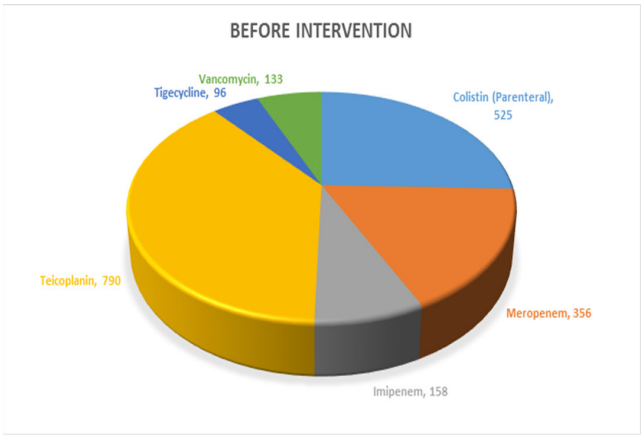

Figure 6
Antibiotic Usage before Educating Doctors

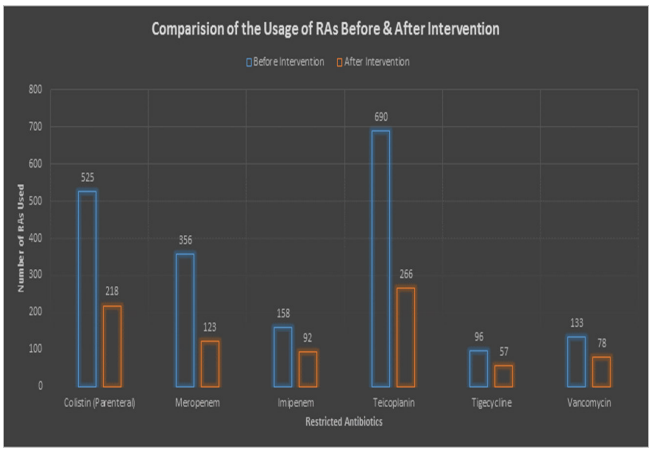

Figure 7
Comparison Before & After Training of Doctors, significant reduction in usage seen

Pharmacological Findings

Quantity of total antimicrobial dispensed (as per DDD) = 3218
Quantity of RA dispensed (as per DDD) = 834
Percentage of RA dispensed=
(834/3218)*100 = 25.92%

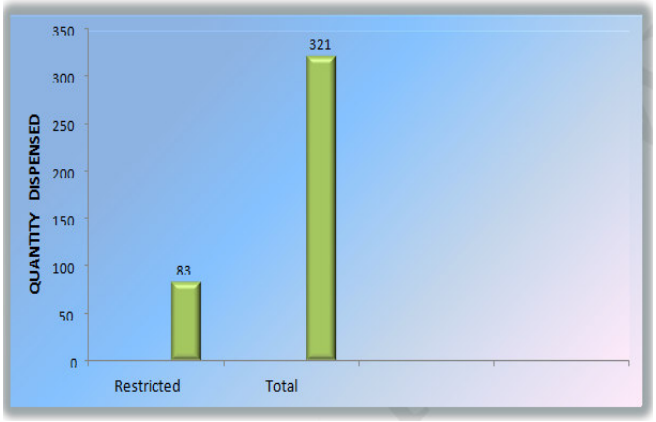

Figure 8
Quantity of Restricted Antibiotic used

OBSERVATIONS & DISCUSSION

Study of Microbial

The highest number of samples collected from the 316 patientsunder study was blood (33.76%) (Fig3) followed by sputum (24.84%) urine (22.72%), wound (6.79%). The number of pusBAL fluid samples stood at 5.95% each. In majority of the cases multiple samples were collected from each patient for microbiological testing. Gram negative organisms were the leading in the blood culture (Fig3).The rate of isolation of E. coli was the highest at 111 (n=471; 23.57%) (Fig 4)& it is also the highest of all the organisms detected in blood 50 (n=159, 31%) & urine 50 (n=107, 47%) samples. Klebsiella Pneumoniae & Acinetobacter species formed the other major chunk of organisms isolated mainly from sputum & BAL fluid. Staphylococcus aureus formed the majority of organisms isolated in pus 14 (n=28, 50%) (Fig 5) & wound 12 (n=32, 38%). Salmonella species was the least isolated 3 (n=471; 0.64%) of all the organisms across all samples. It thus shows that the Gram negative group of bacteria, are effectively escaping the effects 0f antibiotics that are being prescribed. A handful of these bacteria have also become pan-drug resistant in some patients, which means they show antimicrobial resistance to multiple antimicrobial drugs.

Antibiotic Usage

Based on the isolation of the said organisms & the diseases caused by them, Restricted Antibiotics along with other antibiotics were prescribed (Fig5,6&7). According to the —Society for Healthcare Epidemiology of America (SHEA) guidelines, the recommended RA use should be 20% of the total antibiotics dispensed. For the 316 patients under study, a total of 3218 antibiotics were dispensed, out of which 834 were restricted antibiotics (n=3218; 25.92%).This observed RA use was found to be 25.92% of the total. This value is 5.92% higher than the recommended value (20%) & it should be reduced by taking appropriate actions based on the rationales for the use of RA. An interesting thing that was noticed was that there has been a slight decline in cases of microbial infection & there has been a gradual decrease in resistance development. This shows that if the ASP is implemented extensively then there is no doubt that it will bring fruitful results (Fig8).

It was found that:

1. Quantity of total antimicrobial dispensed (as per DDD) =3218
2. Quantity of RA dispensed (as per DDD) =834
3. Percentage of RA dispensed= (834/3218)*100= 25.92%

Based on the study, the following recommendations are directed to the various stakeholders of the stewardship program in the hospital:

Appropriate use of Laboratory

- Utilize the hospital laboratory to undertake specialized microbiological testingas needed to support epidemiological investigations of hospital or community outbreaks of infection.
- Analyze laboratory data to produce surveillance reports for clinicians, for patterns of antimicrobial resistance among commonpathogens.
- It is to be ensured that the hospital laboratories can perform appropriate diagnostic testing and reproducible antimicrobial susceptibility testing of key organisms
- Utilize the hospital laboratory to undertake specialized microbiological testing as needed to support epidemiological investigations of hospital or community outbreaks ofinfection

Use of Antibiotics

- Limit the legal classification of antimicrobials to prescription only medicines (POM) wherever possible within the framework of individual nationalhealth provisionsystems
- Link the POM category to regulations controlling sales, supply and dispensingof medicines and to the scope of allowable promotional activities
- Encourage co-operative discovery efforts between industry and academia (public- private partnerships) with respect to new drugs and other modalities ofpreventing and managinginfection

Creating awareness in patients

- Educate patients regarding the inappropriate and appropriate uses of antibiotics
- Empower patients to participate in optimal medical decision-making
- Utilize behavior change theory to most effectively modify patient behavior with respect to antimicrobials
- Educate patients regarding the importance of adherence to prescribed antimicrobial regimens and the consequences of partial or intermittent therapy.

For those patients who have already developed resistance, following lines of treatment can be provided:

- Resort to a lower dosage
- Go for an oral alternative, if possible.
- Use no therapy when possible.
- Better clinical documentation on treatment plans and review processes for restricted antimicrobial use can be done during the transition from ICU to general wards.

Physicians

- Encourage use of problem-oriented decision making, clinical practice guidelines, and clinical algorithms that foster appropriate management and use of antimicrobials
- Develop educational programs for dispensers that enhance their understanding of appropriate and inappropriate use of antimicrobials and encourage them to educate patients regarding the importance of compliance with prescribed antibiotic regimens
- Control antimicrobial use by restrictive formularies that limit prescription to selected agents. Such formularies must provide appropriate antimicrobialchoices, however, and must be appropriate for the level/place ofcare
- Consider holding selected newer antimicrobials in reserve ‘at certain levels of care in order to slow the development of resistance to these newer agents

The study, however, found following limitations:

1. Lack of Resources-

- Staffing: Pharmacist &/or physicians availability

- Infectious Disease staff were not willing to participate, may be due to :

a. Fear of antagonizing colleagues.
b. Fear of decreasing referrals.
c. Lack of compensation of stewardship activities.

- IT Resources were not enabled in the hospital for monitoring drug usage.

2. Consistency between stewardship and Infectious Disease staff recommendations.
3. Hospital-Culture

- Antimicrobial stewardship was not a priority.
- Perceived loss of prescriber autonomy–gatekeeper mentality.
- Opposition for change, from administrator and/or prescribers.

CONCLUSION

With the growing development of antibiotic resistance, it is imperative that we no longer take the availability of effective antibiotics for granted. As a nation, we must respond to this growing problem, and our response needs to be multi-factorial and multi-disciplinary. Healthcare institutions need robust infection control programs and antibiotic stewardship programs to prevent transmission of resistant bacteria and to decrease the selective pressure for resistance.
Antibiotic Stewardship Programs show great promise and offer new opportunities for patient care and cost impact.

- They have the potential to reduce antimicrobialcosts.
- Limits overuse and inappropriate use of theseagents.
- Promotes active intravenous-to-per-oral (IV-to-PO) switchtherapy.

A well-designed ASP has the advantages of reducing:

- Risk of drug-related adverse events and their associatedcosts.
- Emergence ofresistance.
- Infections caused by resistantpathogens.

Therefore, by promoting the appropriate use of antimicrobials, ASPs can have a broad impact on improving clinical outcomes while reducing overall health care costs. Implementation of an antibiotic stewardship protocol as a component of an infection reduction campaign was associated with a decrease in resistant gram-negative healthcare-acquired infections in ICUs. These results further support widespread implementation of such initiatives.Authors are thankful to the tertiary care hospital of Pune, for their full-fledged support, for our study.

CONFLICT OF INTEREST

Conflict of interest declared none.

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