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RESEARCH ARTICLE

IMPACT OF ANTIBIOTIC STEWARDSHIP PROGRAM IN SURGICAL ICU'S AT TERTIARY CARE HOSPITAL IN SOUTH INDIA: AN AMBISPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: The surgical ICU's are the core areas in the hospital where antibiotics are frequently prescribed to treat number of infections. The consequence of irrational antibiotic use can result in drug resistance and associated rise in treatment expenditure. ***Aim:*** To study the impact of antibiotic stewardship program on antibiotic use in surgical ICU's and surgical wards at tertiary care hospital in south India. ***Methodology:*** All the patients in surgical ICU's and surgical wards who were prescribed with WHO watch and reserve antibiotics were included in the study regardless of sex. The data were collected retrospectively from October 2021 to January 2022 (pre-ASP) and prospectively, starting from February 2022 to May 2022 (Post-ASP). The consumption of watch and reserve antibiotics were compared in two time periods and drug use density is expressed as by anatomical therapeutic chemical (ATC)/defined daily doses (DDD) and normalized per 100 bed days. ***Results:*** From a total of 363 prescriptions, 274 appropriate prescriptions and 89 inappropriate prescriptions were observed. The result shows an increase in appropriate use and also gradual decrease in inappropriate use of targeted antibiotics. An overall -18.46% decrease in antibiotic consumption was observed between the pre-ASP and post-ASP phases measured in DDD/100 bed days for target antibiotics. The consumption of the targeted antibiotics reduced at the end of study. The consumption of vancomycin increased and the consumption of cefixime was reduced significantly (P-value = 0.015). ***Conclusion:*** As a conclusion, antibiotic stewardship program in hospital surgical ICU's are effective in reducing the antibiotic consumption.

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INTRODUCTION

Antibiotics are the one of the effective medications for the infectious diseases. One of the most significant breakthroughs in the history of medicine was the discovery and subsequent large-scale manufacture of antibiotics in the early twentieth century (1). Antibiotics are associated with a variety of toxicities, including specific-drug related adverse events, and the development of multidrug-resistant infections and CDI (2). One potential solution to mitigate the negative consequences associated with antibiotic use is the implementation of ASPs (Antibiotic Stewardship Program). The primary goal of ASPs is to optimize the appropriate usage of antibiotics to improve clinical outcomes while minimizing the overall use of antibiotics, by appropriate selection of drug and reducing the adverse events associated with the antibiotics (2).Along with the ASP, the AWaRe Classification of antibiotics was developed in 2017 by the WHO Expert Committee on Selection and Use of Essential Medicines as a tool to support antibiotic stewardship efforts at local, national and global levels.The primary objective of the study was to evaluate the impact of ASP in antibiotic consumption.

Antibiotic stewardship program in ICUs: The wide spread use of antibiotics in ICUS is due the development of infection which is the main cause of morbidity and mortality in intensive care units (ICUs) (3). It is reported that 41– 85% of ICU patients use at least one antibiotic which is 10 times higher in ICUs compared to other units (3). This inappropriate use of antibiotic causes the emergence of antibiotic resistance (3). Approximately 30–60% of patients in ICUs are prescribed unnecessary, inappropriate or suboptimal antibiotic treatment. (4).Implementation of ASP can lead to significant benefits in terms of clinical outcomes, reduced adverse events and lowered costs. As defined by the Society of Healthcare Epidemiology of America and Infectious Diseases Society of America (IDSA) Joint Committee on the Prevention of Antimicrobial Resistance in hospitals, 'stewardship of antimicrobials is an apt descriptor of related activities that help optimize antimicrobial therapy, ensuring the best clinical outcome for the patient while lowering the risk of subsequent development of antimicrobial resistance' (4). The main elements in successful implementation of ASP program in ICUs are leadership, prospective audit feedback, antibiotic timeout, rapid laboratory diagnostic assessment to reduce inappropriate use of antibiotics and computerised decision support (5).

Antibiotic stewardship program in surgical wards: For preventing post-operative procedures, antibiotics are given prior to the surgery, known as antibiotic prophylaxis (6). This practise of giving antibiotic prophylaxis has reduced the occurrence of surgical site infection. However, the widespread and prolonged use of broad-spectrum antibiotics has contributed to increased risks of antibiotic resistance (6). One of the role of ASP is the effective and rational use of antibiotics in surgical prophylaxis (6).

METHODOLOGY

Study design and subject selection: The single-centre, ambispective observational study was carried out in a tertiary care hospital in south India, Caritas hospital located in Thellakom, Kottayam. The subjects included were the patients who were prescribed with watch and reserve group antibiotics according to the WHO AWaRe criteria and patients who were admitted in the ICU's (Medical ICU -1, Medical ICU-2, Neuro ICU, Surgical ICU, Cardiac ICU) and surgical wards (surgical wars -1, surgical ward-2) of the hospital. The paediatric population, patients who were prescribed with dosage forms such as topical agents, liquid orals, powders and the patients who were prescribed with access group of WHO were excluded. The study was carried out for a period of 6 months, starting from December 2021 to May 2022.

Ethics, privacy and confidentiality: The ambispective observational study was approved by the ethics committee of Caritas hospital. The data of the study was strictly restricted to the investigators and all the data was used only for the research purpose with strict confidentiality.

Study period: Two time periods were considered for comparison, the pre-ASP (October 2021 to January 2022) and the post-ASP (February 2022 to May 2022).

Intervention: In the pre-ASP phase, the data regarding the consumption of antibiotics were obtained retrospectively from the hospital electronic medical records, pharmacy sales report and also from the medical records of the patients that had administered with the watch and reserve antibiotics according to WHO AWaRe criteria were analysed. In the post- ASP(February 2022), the ASP team consisting of clinical pharmacists, doctors, infectious disease specialists, microbiologists were started for the purpose of providing rational antibiotic use. The hospital guideline policy was revised in accordance with the national antibiotic prescribing guidelines by the clinical pharmacists and surgical ward rounds were carried out. The interventions observed were communicated to respective doctors via the prospective audit and feedback form and necessary changes were brought in the treatment. The micro-organism susceptibilities and resistance pattern were analysed by the hospital microbiologist before the implementation of ASP. All this activities helped in developing updated hospital antibiotic policy, which also includes the guidelines for optimizing antibiotic use in surgical treatments. The 72 hour antibiotic checklist was implemented with the aim of providing rational prescribing.

Study design and data collection: A pre-structured data collection form was prepared and validated by an expert panel under the Ethical clearance committee of Nirmala College of pharmacy. Data collection form includes, demographic details , watch and reserve antibiotics prescribed (include Brand name, Generic name, Indication, Dose, Route of administration), other antibiotics prescribed, duration of therapy, antibiotic therapy on 1st , 4th and 7th day, discharge medications, inpatient number, department name, 72- hour compliance, tests performed(chemical and microbial) etc. The drug use density were expressed in defined daily doses (DDD) and normalized per 100 bed days, the sales data was collected from the hospital pharmacy.

Statistical analysis: After transferring all the data to excel sheet, the statistical analysis (paired t-test) were carried out using the software IBM SPSS version 22. P-values < 0.05 are considered as significant.

RESULTS

A total of 363 patients were prescribed with target antibiotics during the post-ASP phase and the prescriptions were analysed prospectively with the hospital guidelines. Table 1 is the observed antibiotic prescribing during each month starting from January 2022 to May 2022. A total of 274 appropriate prescriptions and 89 inappropriate prescriptions were observed.

Table 1. Month-wise data of appropriate and inappropriate antibiotic therapy

Month	Appropriate		Inappropriate	
	n	%	n	%
Jan-22	42	54.5%	35	45.5%
Feb-22	118	82.5%	25	17.5%
Mar-22	62	72.9%	23	27.1%
Apr-22	19	86.4%	3	13.6%
May-22	33	91.7%	3	8.3%
Total	274	75.5%	89	24.5%

Table 2. Percent change in mean DDD/100 patient days during two phases of the study (pre and post - improvised ASP)

Antibiotics	DDD/100 Patient Days (mean value)		Percent of change (%)
	Pre-improvised ASP	Post-improvised ASP	
Watch group			
Cefuroxime	41.96	39.65	-5.83
Cefoperazone	8.43	5.85	-30.60
Levofloxacin	4.00	2.32	-41.86
Ceftriaxone	5.59	3.30	-40.96
Azithromycin	3.12	1.37	-55.97
Cefpodoxime	3.43	1.68	-51.13
Piperacillin	3.26	3.50	+7.36
Cefixime	1.37	0.59	-57.01
Cefotaxime	0.83	0.37	-55.42
Reserve group			
Meropenem	3.87	2.08	-46.25
Linezolid	1.29	0.91	-29.45
Faropenem	0.59	0.44	-25.42
Vancomycin	0.26	0.41	+57.69
Total	79.54	64.85	-18.46

Table 3. Defined daily dose per 100 patient-days in average value (mean ± SD) during two phases of the study

Antibiotics	Study phase		P-value
	Pre- improvised ASP	Post- improvised ASP	
Watch group			
Cefuroxime	41.96 ± 4.56	39.65 ± 2.65	0.164
Cefoperazone	8.43 ± 2.44	5.85 ± 1.40	0.133
Levofloxacin	4.00 ± 1.50	2.32 ± 0.66	0.097
Ceftriaxone	5.59 ± 2.41	3.20 ± 1.29	0.146
Azithromycin	3.12 ± 1.49	1.37 ± 0.35	0.083
Cefpodoxime	3.43 ± 0.98	1.68 ± 0.46	0.053
Piperacillin	3.26 ± 0.25	3.50 ± 1.31	0.732
Cefixime	1.37 ± 0.36	0.59 ± 0.17	< 0.015
Cefotaxime	0.83 ± 0.12	0.37 ± 0.26	0.065
Reserve group			
Meropenem	3.87 ± 1.42	2.08 ± 0.14	0.085
Linezolid	1.29 ± 0.47	0.91 ± 0.17	0.149
Faropenem	0.59 ± 0.40	0.44 ± 0.43	0.707
Vancomycin	0.26 ± 0.09	0.41 ± 0.54	0.655

The data shows increase in rationality in antibiotic prescribing from the month of February and this trend continue to increase at the end of the study (May 91.7%). Similarly gradual reduction in inappropriate prescribing is observed at the month of February and this trend continue to the end of the study (May 8.3%). An overall -18.46 % decrease in antibiotic consumption was observed between the pre-ASP and post-ASP phases measured in DDD/100 bed days for target antibiotics. The most significant reduction was observed in the consumption of cefexime (-57.01%), azithromycin (-55.97%) and cefotaxime (-55.42%) among the watch group. Also similar reduction in consumption was observed among reserve antibiotics after performing prospective audit and feedback at the level of prescription, whichincludes meropenem (-46.25%) and linezolid (-29.45%). Promising reduction was also observed in rest of the antibiotics, levofloxacin (-41.86%) and ceftriaxone (-40.96%). The consumption of antibiotics were increased in the use of piperacillin (+7.36%) among the watch group and vancomycin (+57.69%) among the reserve group (Table 2). Table 3 demonstrates the observed mean average value (mean±SD) of DDD per 100 patient days during the pre and post-ASP phase. After performing the statistical analysis, the reduction in the consumption of cefixime among the watch group was found to be significant (P-value = 0.015). The reduction in consumption of antibiotics azithromycin (P-value =0.083), cefpodoxime (P-value =0.053), cefotaxime(P- value =0.065) and meropenem(P- value =0.085) was close to the significant value. The short study period for both pre and post-ASP could be a reason for not reaching a significant value.

DISCUSSION

The surgical ICUS are the core areas of the hospital were the antibiotic are prescribed irrationally. This irrational use of watch and reserve antibiotics can lead to antibiotic resistance for such patients in future. Understanding the importance of antibiotic use, the WHO put forward the antibiotic stewardship program for preserving the effectiveness of antibiotics. However such an ASP program were not implemented in most of the hospitals and also effective execution of the strategies were also lacking. With the aim of optimizing antibiotic use, the ASP program was implemented in our hospital. The program was executed with the help of ASP team including clinical pharmacists, intensivists, microbiologists etc. Our results suggests reduction in the inappropriate prescriptions by the end of the study. The study by Michael et.al states that the medical practitioners experience pressure in prescribing antibiotics, since most often they fear of diagnostic error or missing information about the infection from both chemical and microbial test. In such cases, they follow a safety first approach in treating the patients and they prescribe antibiotics irrespective of what guidelines instructs (7).The influence on the medical practitioners by the suppliers for profit is also a reason for inappropriateness observed in our study and a similar kind of results was observed in a study conducted in Nepal which suggest that in the private sector, two factors were found to influence antibiotic use on the supply side: the profit motive and many of the private pharmacies being unlicensed. Both factors were seen to result in patients being prescribed or dispensed considerably more antibiotics than is clinically necessary (8). These all could be the reasons behind the inappropriate prescriptions. The daily ward round monitoring and PAAF were effective in reducing inappropriate prescriptions. Similar to other study results, the total reduction in the antibiotic consumption presented in DDD/100 days showed a considerable value.

The antibiotic consumption for the targeted antibiotics were reduced following PAAF except in the case of vancomycin. The increase in vancomycin consumption could be due to expansion of methicillin-resistant staphylococcus aureus at our hospital. Studies suggest the use of vancomycin as the initial choice for the MRSA bacteremia. However relevant reports shows that the excessive use of vancomycin in critically ill patients is associated with nephrotoxicity and vancomycin resistant enterococci (VRE), dosing adjustments should be carried out in such patients (9).Only reduction in the consumption for the cefixime is found to be significant. Rest of the antibiotic DDD values failed to attain a significant value. This could be due to the short pre and post-ASP time period. Limitations of the study include as stated short time period and also during the observation period, some of the patients who were affected with COVID-19 were shifted to isolation wards. The further data collection procedures from these patients were difficult. The collection of data from patients who left against medical advice (LAMA) was also difficult to follow-up. Future study regarding the increase in consumption of vancomycin and its probable cause at our hospital is also recommended.

Disclosure: Authors have no conflict of interest to declare.

CONCLUSION

In this study we could demonstrate the reduction in the consumption of targeted antibiotics in surgical ICUS. The implementation of ASP is feasible and effective in every south Indian hospitals, especially in surgical ICU'S. The results will be not only the optimal use of antibiotics, but also the economic benefits. The role of the clinical pharmacists are crucial for the success of the ASP and were empowered at our hospital. According to our single centre study, the implementation of ASP is helpful in providing effective clinical practice, reduction of antibiotic resistance and associated cost savings that can be beneficial for low income and developing countries.

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