Journal of Pharmaceutical Care
jpc.tums.ac.ir

Impact of Intervention by an Antimicrobial Stewardship Team on Rational Use of Antibiotics

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Received: 2021-06-10, Revised: 2021-08-14, Accepted: 2021-08-15, Published: 2021-09-30

ARTICLE INFO

Article type:
Original article

Keywords:
Antimicrobial Stewardship;
Clinical Audit;
Antibiotics

ABSTRACT

Background: : An antimicrobial stewardship program can be defined as the set of actions performed in hospitals for the rational use of antibiotics. Early conversion from intravenous to oral antibiotics plays an important role in reducing the cost of treatment, shortening the length of hospital stay, and decreasing the workload of nurses. The purpose of this study was to evaluate the impact of the implementation of antimicrobial stewardship program on duration of hospitalization and medication costs.

Methods: We performed an interventional study in Razi teaching hospital. All hospitalized patients aged 18 and older who met the inclusion criteria were included. This study comprised two groups. The interventional prospective group to assess the impact of intravenous to oral antibiotic conversion, and a retrospective group in which the intervention had not been applied, used as the comparator.

Results: A total of 260 cases were enrolled; 47 in the interventional group and 213 in the retrospective one. The length of hospitalization was significantly shorter in the intervention group compared to the retrospective one (5.2 vs7.9 days, $p<0.001$). The cost of intravenous antibiotics and total medication costs significantly decreased in the intervention group.

Conclusion: Our findings suggest that conversion from intravenous to oral antibiotics is effective for reducing the length of hospital stay, antibiotic cost, and excess use of intravenous antibiotics.

J Pharm Care 2021; 9(3): 137-140.

► **Please cite this paper as:**
Alikhani A, Babamahmoudi F, Khabbaz A, Abbaspour Kasgari H, Mohabbati S. Impact of Intervention by an Antimicrobial Stewardship Team on Rational Use of Antibiotics. J Pharm Care 2021; 9(3): 137-140.

Introduction

Antibiotics are frequently prescribed in clinical practice. The emergence of antibiotic-resistant microorganisms due to excessive and indiscriminate use of these drugs is a serious issue that is plaguing healthcare delivery throughout the world (1-2).

Antibiotic resistance can result in negative outcomes such as increased length of hospitalization, prolonged treatment duration, healthcare costs, and development of multidrug-resistant infections (3-5). Thus, it is important to develop an antimicrobial stewardship program (ASP). ASP is a rational systematic approach to the use of antimicrobial

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agents to achieve optimal outcomes (3).The primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms, and the emergence of resistance (4).

This strategy has numerous benefits for patients and results in lowering health care costs (6). In 2007 the infectious disease society of America (IDSA) and the society of healthcare epidemiology of America published guidelines that laid foundations to aid institutions in developing ASPs (7). Conversion from intravenous to oral administration of antibiotics in appropriate time is one of the major recommendations in these guidelines (8).

These guidelines must be customized for the specific health service and consider the local environment and available resources. Although the advantages of converting from intravenous to oral antibiotics administration have been reported in various studies, studies that investigate the clinical and financial effects of such intervention in Iran requires more attention. Hence, the antimicrobial stewardship team at Razi teaching hospital started an intervention to promote the conversion from intravenous to oral administration of antibiotics in December 2020, including daily antimicrobial prescription review and the intervention for IV to oral antibiotic conversion by organizing a team of infectious diseases physicians and pharmacists. In this study the economic impact of the intervention was evaluated.

Methods

This is a pre-post interventional study conducted in Razi teaching hospital. Patients over 18 who were hospitalized in infectious diseases wards were evaluated. The study comprised a retrospective phase (September 2019 to September 2020) in which the switch therapy was not applied and a post intervention group to assess the impact of intravenous (IV(to oral conversion over a six month (December 2020 to May 2021). In the pre intervention group, the data were extracted from medical records. In the prospective study, all patients receiving injectable antibiotics for more than 3 days and could take oral antibiotics were included for the intervention. The inclusion criteria for changing IV to oral antibiotics were improvement in the infection, absence of fever for at least 48 hours, hemodynamic stability(systolic blood pressure >100 mm hg and no unexplained tachycardia defined as heart rate greater than 100 beats per minute in last 12 hour), progressive reduction in white blood cell count and the following conditions were considered as non-including factors: patients who were in the intensive care units or protected isolation rooms at the time of screening, who were not able to take oral medications either due to dysphagia or tube feeding, who had malabsorption due to gastrointestinal surgery, whose medications had been converted to oral antibiotics or had been discharged from the hospital before the intervention. And those who received IV antibiotic due to treatment failure after the intervention were excluded from the analysis.

Patients who met all these conditions and signed the informed consent were included in the prospective interventional study. The study protocol was approved by the Institutional ethical committee through letter numbered IR. MAZUMS..REC.1400.4655

The intervention was regularly performed two times a week. A clinical pharmacist of the antimicrobial stewardship team identified study subjects and left a note of recommendation for the intervention. The note included the primary site of infection, type of antibiotic being administered, dosage, and treatment period. The drafted recommendation was validated by infectious diseases physicians who provided additional opinions and made the IV to oral conversions for those who meet the inclusion criteria such as absence of fever, normal blood pressure (BP), consciousness and ability to take drugs orally. Subsequently, a pharmacist of AMS team entered all information by the aid of developed data collection form.

Data were collected from medical records. Age, gender, type of antibiotics, duration of antibiotic consumption, length of hospitalization and period from intervention to discharge were extracted from medical records and the cost of medication was estimated. We compared these data between pre and post intervention phases to evaluate the effect of the intervention.

The duration of antibiotic administration was defined as the number of days in which antibiotics were administrated during hospitalization. Length of hospitalization was defined as the period between the day of admission and the day of discharge. For the patients admitted to the emergency room first, the commence day of hospitalization was considered as the day of admission. Medication cost was defined as the price of antibiotics administered based on the maximum drug cost according to the national insurance, and the number of administrations during hospitalization. Oral and intravenous medication costs were assessed separately.

Statistical analysis was performed using SPSS software version 22. Numerical variables were presented as the median and compared using the levene test. P-value of less than 0.05 was considered as statistically significant.

Results

A total of 260 evaluable patients were included (Table 1). There were 213 patients 121 men and 92 women with a median age of 53 ± 2 SD (standard deviation) Years (18-95) in the retrospective group, who did not switch to oral antibiotics and 47 patients, 29 men and 18 women with a median age of 52 ± 2 SD Years (22-86) were in prospective group.

Table 1. Demographic and clinical characteristics of the study cases.

	Intervention group (n = 47)	Retrospective group (n = 213)
Age, median	52.2(22-86)	53.3 (18-95)
Sex, n (%) Male Female	 29(61.7) 18(38.3)	 121(56.8) 92(43.2)
Medication, n (%)		
Ceftriaxone	38(80.8)	85(39.9)
Clindamycin	6(12.8)	27(12.7)
Clindamycin+Ceftriaxone	1(2.1)	3(1.4)
Piperacillin/Tazobactam	1(2.1)	17(8)
Metronidazole+Ceftriaxone	1(2.1)	2(0.9)

The duration of intravenous antibiotic administration was 7.6 days (SD:4.46) for the retrospective group and 3.8 days (SD:1.59) for the intervention group, showing a statistically significant decrease in the intervention group (P value<0.000). Besides, the length of hospitalization was significantly longer for the retrospective group (7.9 days, SD:4.7 vs 5.2 days, SD:1.8; P value< 0.001)

The cost of oral antibiotics was significantly lower in the interventional group (62 791.4 Iranian Rial, SD:50475.3) than the retrospective group (116 151.6 Iranian Rial, SD:108815.07, P value<0.000). There was a reduction in the cost of intravenous antibiotics in prospective patients compared to the retrospective group (440 638 Iranian Rial, SD:439428.5) vs (2 400 668 Iranian Rial, SD:3100629.9, P value<0.000). Total medication costs including IV therapy and oral medication were 15 880 306.3 Rial and 8 828 305.3 Rial, respectively, which was lower in the interventional group and the difference was statistically significant (p<0.000).

Table 2. Differences in duration of intravenous antibiotics administration, length of hospitalization, and cost of antibiotics therapy between intervention and retrospective group.

	Intervention group (n = 47)	Retrospective group (n = 213)	*P*-value	*SD for intervention group*	*SD for retrospective group*
Duration of IV administration (days)	3.8	7.6	< 0.001	1.59	4.46
Length of hospitalization (days) Median	5.2	7.9	< 0.001	1.8	4.7
Medication costs (Iranian Rial) IV, median	440 638.2	2400 668.5	< 0.001	439428.5	3100629.9
PO, median	62 791.4	11 6151.6	< 0.001	50475.3	108815.07
Total, median	8 828 305.3	15 880 306.3	< 0.001	4418407.2	11036065.1

Discussion

Early conversion from IV to oral antibiotics decrease the risk of antimicrobial resistance, medication cost, and eliminates a barrier to discharge. However, such intervention has not become pervasive in Iran due to the lack of proper and organized ASP implementation in public and private hospitals, besides, the consumption of antibiotics in Iran based on the available data is three times more than the mean global rate (9). Through this study, the intervention for IV to oral conversion was performed by the antimicrobial stewardship team and the effect of the intervention was evaluated.

This study found that AMS may have a significant impact on economic outcomes. Our intervention could decrease medical costs associated with intravenous injections, length of antibiotics administration, and hospitalization.

Previous studies analyzing the impact of ASPs have reported similar results. Vettese et al., found that a thrice-weekly ASP decreased total antibiotic expenditures by 6.4% in a 253-bed hospital. They could find a 3.7% cost reduction per

quarter with decreased antibiotic use (10). Another study conducted by Davis et al., conversion to oral administration in patients with community-acquired pneumonia resulted in a reduction in antibiotic cost and a significant increase in the success rate of clinical treatment in those who received the intervention (11). A study conducted in Taiwan also showed that pharmacist-managed IV to oral antibiotic conversion decreased the length of hospital stay as well as significant cost savings on both medications cost and total inpatient expenditures (12).

Our ASP could significantly reduce the average duration of IV therapy from 7.6 days to 3.8 days. Every day, our antimicrobial stewardship team monitored all IV antibiotics prescriptions and intervention performed by infectious diseases specialists. Many studies have shown that intervention by a healthcare provider can effectively reduce unnecessary use of intravenous antibiotics. The study by Fischer et al., showed that the intervention for oral conversion of five medications, including levofloxacin, reduced the use of intravenous medication by 34.5% (13). Another study by Avdic et al., showed similar results. They studied 127 patients with community-acquired pneumonia (CAP) and found that ASP helped to reduce the duration of therapy from 10 to 7 days; however, they found no difference in length of hospital stay between their pre-ASP and intervention groups (14).

A 12-month interventional study by Dominik et al revealed that the number of hours required for administering IV antibiotics was estimated to be reduced by 350 hours annually on the two wards (15). The impact of IV to oral conversion on the nursing workload and antimicrobial resistance were not assessed in this study, future studies are necessary for investigating these aspects.

The strengths of our study were that all classes of antibiotics and different types of infections were assessed and two infectious diseases specialists participated in the study, one was in the AMS and the other was not.

This study had several limitations. First, we compared a prospective group with a retrospective one in which certain data were difficult to extract. Second, the study conducted at a single center with limited population diversity, hence these findings need to be evaluated in a larger group.

In conclusion, the development of AMS is a vital component in improving treatment outcomes in healthcare facilities. Our data indicate the benefits of the implementation of active intervention for intravenous to oral antibiotics via the antimicrobial stewardship team.

Acknowledgments

We thank all the nurses on the infectious diseases wards for their excellent cooperation.

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