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Original Article

The Impact of Preprinted Antibiotic Order Forms on Vancomycin and Carbapenems Consumption

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Abstract

According to the increasing trend of antibiotic consumption all over the world, a rising concern is the emergence of resistant pathogens due to the inappropriate use of antibiotics, which increases the risk of treatment failure and mortality. Antibiotic Order Form (AOF) is an antimicrobial stewardship program protocol recommended to improve rational antibiotic use. We aimed to compare the antibiotic consumption rate, i.e., vancomycin and carbapenems, before and after preprinted AOFs were implemented. This study also evaluated physicians' compliance with AOFs as a secondary outcome. This prospective descriptive study was conducted from July to December 2015 in a 570-bed teaching hospital in Tehran, Iran. AOF includes demographics, microbiological, and clinical data on infection designed for vancomycin and carbapenems, including imipenem and meropenem. Prescribers were asked to fill out predesigned forms after prescribing the selected antibiotics and deliver them to the pharmacy on July 1, 2015. Collected data during this 6-month study period were compared with the same period times years 2011 to 2016 (4 years before and one year after implementation of AOF) to determine the effect of AOFs on the selected antibiotics consumption that had been calculated based on Daily Doses per 100-patients day (DDD/100-bed days). This study showed that although vancomycin had an increasing trend from 2011 to 2014, implementing the AOF program could stop this trend in 2015. Vancomycin consumption significantly decreased compared to the previous year ($P = 0.039$). This effect of the program was not the same on the use rate of carbapenems, and their use was increased nonsignificantly in 2015 ($P = 0.606$). The acceptance of prescribers in filling out the forms for vancomycin increased from 5.12% in the first month to 57.75% in December. This increase was from 4.20% to 37.26% for carbapenems. According to the increasing trend of antibiotic consumption in hospitals, we recommend improving utilization surveillance of antibiotics by choosing an appropriate antibiotic, optimal dosing, and desired duration of treatment that are important in decreasing the risk of developing resistant microorganisms due to misuse. The forms are much more effective when accompanied by the acceptance of prescribers.

Keywords: Antimicrobial stewardship program, Antibiotic order form, Carbapenem, Vancomycin, Meropenem, Imipenem, Defined daily dose.

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1. Introduction

Antibiotics, among the most prescribed drugs for hospitalized patients, play a crucial role in medical treatment. The US Centers for Disease

Control (CDC) has highlighted their extensive usage, revealing that 55.7% of patients from 323 hospital settings were given antibiotics during hospitalization [1]. This trend is not limited to a specific region, as a prior study covering 71 countries reported that antibiotic consumption increased by 36% between 2000 and 2010 [2]. In the United States alone, the prevalence of antibiotic prescriptions is 5 out of 6 people prescribed an antibiotic each year, and at least 30% of this is unnecessary. The implications of this widespread antibiotic administration are underscored by the Center for Disease Dynamics, Economics & Policy's (CDDEP) 2021 global analysis of antibiotic resistance, which shows that human antibiotic consumption increased by 65% between 2000 and 2015. If nothing changes, antibiotic consumption will increase worldwide by 200% between 2015 and 2030 [3]. These reports emphasize that we must rethink how we use antibiotics to minimize their potential adverse effects.

The World Health Organization (WHO) emphasizes that the misuse and overuse of antimicrobials in humans, animals, and plants are the leading cause of drug resistance, making it harder to treat common infections effectively and increasing the risk of treatment failure and mortality [4].

In the U.S., according to the CDC's 2019 Antibiotic Resistance (AR) Threats Report, more than 2.8 million antimicrobial-resistant infections occur each year, which leads to more than 35,000 deaths [5].

A Lancet report further reveals that antimicrobial resistance caused the death of at least 1.27 million patients worldwide in 2019 and is associated with nearly 5 million deaths [4].

Iran reports high resistance rates in bacteria of international concern, including Escherichia coli and Klebsiella pneumonia, exhibiting resistance to third-generation cephalosporins, fluoroquinolones, and carbapenems [6].

These findings underscore the urgent need for global efforts to address and control antimicrobial resistance.

To combat this global health challenge, The World Health Organization (WHO), the Infectious Diseases Society of America (IDSA), and other international public health organizations have begun their effort to implement and promote strategies to prevent antimicrobial resistance. For this purpose, IDSA has announced extensive strategies focusing on infection prevention and control and concurrently promoting antimicrobial stewardship programs (ASPs) implementation. These programs were defined by IDSA in 2012, "antimicrobial stewardship refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy and route of administration. These actions make ASPs essential in the global effort against antimicrobial resistance.

Antibiotic Order Form (AOF) is a significant protocol recommended within the ASP guidelines [7]. This prospective study compared the rate of antibiotics consumption, i.e., vancomycin and carbapenems, before and after implementation of preprinted AOFs intending to improve the utilization surveillance of antibiotics using these

forms to help to reduce the problem of increased multidrug-resistant pathogens in our country.

2. Materials and Methods

2.1. Setting and Study Population

This prospective observational study was conducted at the 570-bed Imam Hossein Medical Center in Tehran, Iran.

According to the ABC analysis results, the hospital's antimicrobial stewardship committee, which consisted of infectious disease and clinical pharmacy specialists, decided to prepare AOF to prescribe vancomycin, meropenem, and imipenem in April 2015. The hospital's pharmaceutical care unit developed the form based on a literature review and international guidelines, revised and finalized by the stewardship committee. It was approved by the Drug and Therapeutics Committee (D&T committee). The aof encompassed demographic data of patients and data related to diagnosis and treatment of infections, including suspicious/definite site of infection, hemodynamic and clinical conditions, culture results, and reason for choosing these broad-spectrum antibiotics.

A copy of the AOF and a cover letter explaining the purpose of the form and how to use it were sent to all prescribers at the hospital in May 2015. They were asked to fill out predesigned forms after prescribing the selected antibiotics and deliver them to the pharmacy on July 1, 2015. Collected data during this 6-month study period were compared with the same period from 2011 to 2016 (4 years before and one year after implementation of AOF) to determine the effect of AOFs on their consumption.

2.2. Outcome

The impact of preprinted aof on antibiotic consumption, i.e., vancomycin and carbapenems, was considered the study's primary outcome. We also evaluated physicians' compliance with filling out the AOFs as a secondary outcome.

2.3. Calculation of the rate of Antimicrobial Consumption

Consumption of selected antibiotics has been calculated based on the WHO-defined method of daily doses per 100 patients per day (DDD/100-bed days) [8].

2.4. Statistical Analysis

All statistical analyses were performed using SPSS for Windows (version 16.0). We used the Mann-Whitney and Kruskal–Wallis tests to compare changes in antibiotic usage before and after the AOF implementation. P-value < 0.05 was considered significant. Antimicrobial consumption was presented as a chart using Microsoft Excel.

3. Results and Discussion

Of 1722 patients who received vancomycin during the 6-month study period, AOF was filled out for 681 patients (39.54%), and just 347 (20.15%) were completed. We detected a significant decrease in vancomycin consumption compared to 2014 (P = 0.039). This study showed an increasing trend in using vancomycin from 2011 to 2014, with a nonsignificant difference between the mean of differences (P = 0.087). In 2015, this trend was stopped, and vancomycin consumption was significantly decreased compared to the previous year. However, it increased again in 2016 (**Figure 1A**).

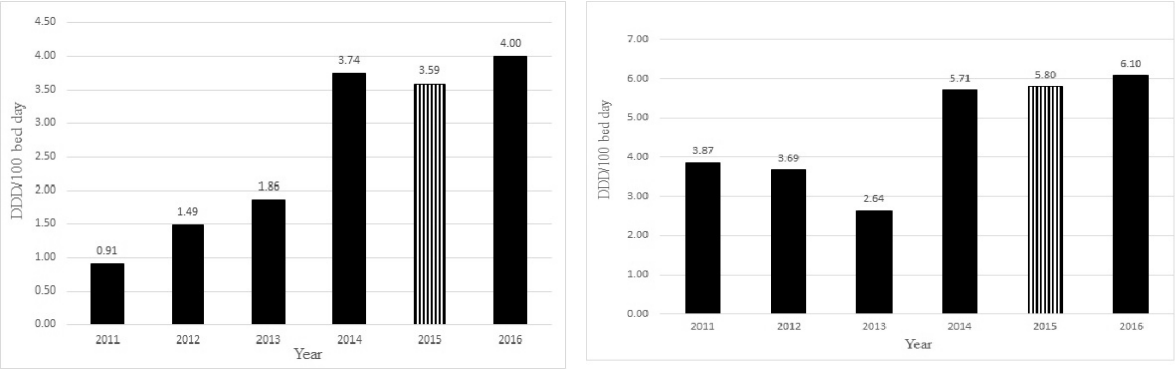

Figure 1. The consumption of antibiotics based on Daily Doses per 100-patients day (DDD/100-bed days) from July 1st till the end of December of 2011-2016, A) vancomycin, B) carbapenems.

Of 1649 patients who received carbapenems during the study period, 480 AOFs were received at the pharmacy (29.10%), and just 239 forms were filled out completely (14.49%). Data showed a significant increase in the use of carbapenems from 2013 to 2014. In 2015, carbapenem consumption increased but not significantly (P = 0.606). This increasing trend continued also in 2016 (**Figure 1B**).

Implementing the aofs has proven to be a successful strategy, positively impacting the quality and accuracy of antibiotic prescriptions for hospitalized patients.

The initial design of the aof by Durbin et al. encouraged physicians to thoroughly review basic, clinical, and laboratory information, categorizing antimicrobial drug use as prophylactic, empirical, or therapeutic [9].

In diverse healthcare settings, AOF implementation demonstrated notable success. An 800-bed hospital reported a substantial reduction in antibiotic treatment courses, highlighting the positive impact of AOFs on antibiotic utilization [10]. Duc Chien Vo and colleagues observed a significant influence of AOFs on prescribing patterns in a tertiary hospital, with a commendable 92% compliance rate and a notable impact on prescribing behavior [11].

Economic evaluations emphasized the potential for AOFs to contain costs and promote rational antimicrobial use. A study in a 900-bed tertiary-care medical school hospital aimed to guide physicians in providing explicit information on diagnoses and suspected resistance patterns, underlining the potential benefits of AOFs cost containment and rational antimicrobial use through order form [12]. Surveillance data from AOFs contributed to improved antibiotic use, facilitating the prospective evaluation of the quantity and quality of antibiotic use [13, 14].

In addressing surgical prophylaxis and antibiotic use, AOFs played a crucial role. Pilot studies showcased their effectiveness in reducing the duration of surgical prophylaxis and the irrational use of specific antibiotics [15]. Multiple investigations reported broader positive impacts of AOFs, including reductions in mortality, costs, and the risk of developing resistant pathogens [10-13, 15-17].

However, the utility of AOFs exhibited context-dependent effectiveness. While

successful in reducing inappropriate surgical prophylaxis [15], their impact on reducing vancomycin use in pediatric inpatients remains inconclusive [16].

The improvement in physician compliance, illustrated in **Figure 2**, demonstrated increased acceptance and utilization of AOFs for specific antibiotics, highlighting their role in shaping prescribing behavior.

The findings in Figure 2 highlight a significant improvement in physicians' compliance with filling out and completing Antibiotic Order Forms (AOFs) throughout the study period. Notably, the acceptance of filling out forms for vancomycin saw a substantial rise, increasing from 5.12% in the initial month to 57.75% by December (**Figure 2A**). Similarly, for carbapenems, the acceptance increased from 4.20% to 37.26% over the same timeframe (**Figure 2B**). This upward trend in acceptance aligns with the observations made by Gilbert et al. in their study, where acceptance increased from 58% in the first two weeks following introduction to 76% in the 5-11th week [17].

The limitations of this intervention, which affected the outcome, could be a small number of pharmacists per bed, lack of consistent human resources, and many defects in the hospital's internal system (such as lack of an auto-stop system) [18].

4. Conclusion

According to the increasing trend of antibiotic consumption in hospitals, we recommend implementing AOFs to enhance surveillance and ensure appropriate antibiotic treatment selection, dosing, and duration. The effectiveness of aofs is significantly augmented when accompanied by the acceptance of prescribers.

Acknowledgments

MH, MAM, SS, MF, FH, and MS created the concept. Literature review and drafting of the proposal were done by MF, MS, and EP. MF and EP recruited the patients and gathered clinical data and MF and MS analyzed the data. All authors reviewed and helped to finalize the article for publication.

Conflict of interest

The authors declare to have no conflict of interest.

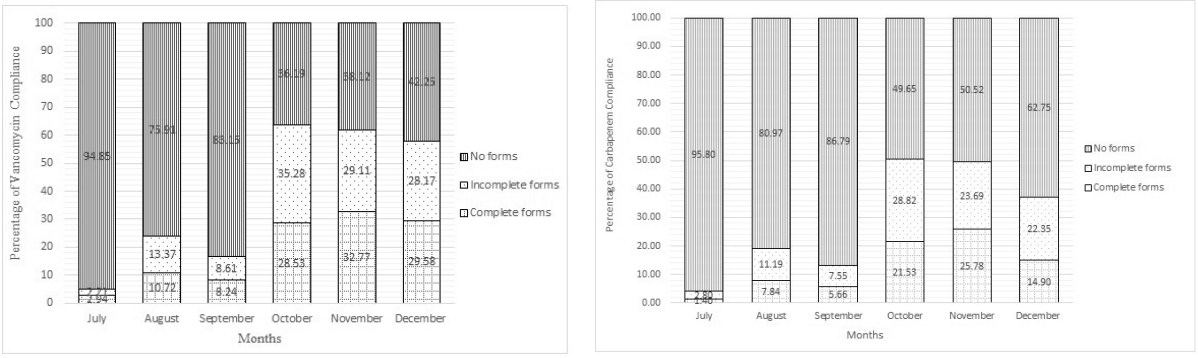

Figure 2. The compliance of physicians to fill out and complete the preprinted antibiotic order forms during the 6-month study, A) vancomycin, B) carbapenems.

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