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Original Article

Evaluation of the physician's acceptance to clinical pharmacy interventions after antibiotic stewardship implementation in the ICU in a general hospital in Egypt

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ABSTRACT

Background: Physicians' perception of the role of the clinical pharmacist role plays a cornerstone in accepting interventions suggested by pharmacists to correct DRPs and in complying with guidelines of a pharmacist-led Antibiotic stewardship program (ASP). This study aimed at evaluating the acceptance of physicians' to pharmacists interventions to antibiotic prescribing and the change in antibiotic consumption in Al-Haram general hospital Intensive care unit (ICU).

Methods: This study was performed in Al-Haram general hospital ICU from July 2014 till December 2015. Medication review of antibiotics started in Al-Haram hospital ICU in July 2014 by responsible clinical pharmacists. An on-job physician education program about antibiotics started in June 2015. Implementation of ASP started in July 2015. The antibiotic related interventions and response of physicians to interventions were recorded all along the study period. The pattern of physicians' acceptance along with antibiotic consumption (in Daily define dose per 1000 patient-days) were reported.

Results: The number of accepted interventions had increased along the study. The overall antibiotic consumption increased after implementation of ASP, however the individual pattern of antibiotic prescribing changed.

Conclusion: The physicians in Al-Haram hospital appeared to accept the role of clinical pharmacist in correcting antibiotic-related DRPs as well as in implementing ASP.

1. Introduction

Antimicrobial resistance is growing due to emergence of new strains and the pipeline for new antibiotics production is running dry. This is more prominent with multidrug-resistant Gram-negative bacteria [1]. Suggested approaches to address this problem are either discovering new antibiotic or improvement of antimicrobial use by developing of antimicrobial stewardship program (ASP) [2]. The Infectious Diseases Society of America (IDSA) introduced the concept of establishing a multidisciplinary team to improve the antimicrobial prescribing within hospitals [3]. This team is responsible for ensuring optimal use of antimicrobials within the institution. The team consists of infectious diseases (ID) physician who is the leader of the program, infection control practitioner, a clinical microbiologist and a clinical pharmacist [4]. The clinical pharmacist has been considered as a core member of the team together with the ID physician since 2007, with recommendations that the pharmacist should receive training in infectious diseases [4,5]. This recommendation has been reinforced by the Joint Commission International in its 6th edition by developing new standards associated by the antimicrobial resistance. This new standard, Medication Management and Use (MMU.1.1), requires organizations to develop and implement a program for antibiotic stewardship to enhance the patient safety [6]. In the US, approximately 2 million people develop an infection that is resistant to antibiotics, and about 23,000 of these people die as a result of the infection [6].

According to the Infectious Diseases Society of America (IDSA), ASP is defined as a program consisting of coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting optimal selection of antimicrobial drug regimen, dose, duration of therapy, and route of administration. Antimicrobial stewards seek to achieve optimal clinical outcomes related to antimicrobial use, minimize toxicity and other adverse events [7–9].

For implementation of an antibiotic policy, physician education is an integral part for change. The pharmacist can control antimicrobial

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cycling, de-escalation of the therapy, dose optimization and parental to oral conversion [10]. This necessitates the physician accepting the role of the pharmacist in correcting antibiotic related problems in patients and being an integral member in the team responsible for ASP.

This study aimed to evaluate the acceptance of the role of the pharmacist in implementing the antibiotic stewardship by physicians by following the pattern of physician acceptance to pharmacist interventions to antibiotic related problems and following the antibiotic consumption pattern in Al-Haram general hospital ICU.

2. Materials and methods

2.1. Study design

This study was approved by the Ethics Committee of the Faculty of Pharmacy, Cairo University. This was a prospective observational study that was conducted in the ICU of Al-Haram Hospital, Giza, Egypt, from July 2014 till December 2015. Al-Haram hospital is one of the governmental major hospitals in Egypt of multispecialty with 270 beds including 13 beds in the ICU. The ICU of the hospital handles about 1000 patients per year. It is divided into 3 sections: trauma and surgery, cardiology and internal medicine. In July 2014 clinical pharmacy services were established in the ICU of Al-Haram hospital by three pharmacists. Previously, the role of the pharmacist was restricted to receiving the physicians' orders and dispensing the available medication.

The study was divided into three six-month phases. The first phase was the preparation phase during which clinical pharmacy services were introduced in the ICU and recommendations on the rational prescribing of antibiotics were made by the pharmacists. The second phase involved on-job education of physicians and setting up the ASP in the hospital. Physician education focused on bacterial resistance, rational prescribing of antibiotics, mechanism of action, stability and compatibility of different antibiotics, and how to use the hospital antibiotic policy for prescribing. The third phase involved the implementation of the ASP in the hospital. Throughout the three phases antibiotic drug related problems (DRPs) in the ICU were recorded by the pharmacists as well as antibiotic consumption.

2.2. Data collection

2.2.1. Medication related problems and interventions

The clinical pharmacist in charge reviewed the patient files, identified drug related problems (DRPs), and discussed them with the physicians and documented the data The medication review was a service implemented during the eighteen month period, all the pharmacists involved were requested to review as many patients' files as possible and to record any identified DRPs together with any suggested interventions. The interventions were discussed with the physicians. All DRP's, interventions and the acceptance or rejection of the physicians were documented. The definition of DRPs followed the American Society of Health-System pharmacists (ASHP) classification [11]. For the purpose of this study the antibiotics DRPs as well as interventions were only considered. The acceptance rate of the physicians to the clinical pharmacist's interventions was recorded as well.

2.2.2. Antibacterial usage retrieval

ICU antibacterial drug use was obtained from infection control department in the hospital records for the ICU department during the period of the study (July 2014–December 2015). Aggregated annualized monthly reports of antibiotics were included. The antibiotic consumption was calculated using the daily defined dose (DDD) based on the World Health Organization (WHO) recommendation. All DDDs were based on the 2015 version of the Anatomical Therapeutic Chemical Classification System and the DDD index [12]. To express the aggregate use of antibiotics, total DDDs were normalized per 1000 patient-days to control for differences of ICU census [13].

2.3. Data analysis

The physicians' perception of the clinical pharmacist service was assessed in terms of the accepted percentage of the interventions and the analysis was done using the statistical Package, SPSS version 22. The physician's acceptance rate to the clinical pharmacist interventions was calculated by dividing the number of accepted interventions on antibiotic related problems to the total number of recorded antibiotic related problems measured through each individual phase in the ICU. Chi-Square test was used to compare the interventions during the three periods. A P value of < 0.05 was considered significant. DDD per 1000 patient-days trends were followed across the three study phases.

3. Results

3.1. Medication related problems and clinical pharmacist's interventions

3.1.1. Frequencies and types of medication problem

Overall, a total of 680 pharmacist's interventions were recommended for 805 patients during the eighteen months period of study. More than half of the total interventions (412) involved antibiotics, 51 of the interventions (12.3%) were not applicable due to death, discharge or transfer to another hospital or other reasons) The rest of the interventions (361) were categorized into 145 accepted by the physicians (35.2%) and 216 (52%) were not accepted (Table 1). DRPs detected for antibiotics were indication with no medication prescribed, medication without indication, inappropriate selection of antibiotic, therapeutic duplication, improper dosage regimen and interaction or contraindication. The interventions concerning antibiotics were categorized by the study phase and their frequencies were compared.

3.1.2. Preparation period

The total number of antibiotic interventions made by the pharmacists during the preparation phase were 180 interventions, 61 (33.38%) were accepted while 109 (60.56%) were rejected. There were 10 interventions that were not applicable (5.56%) as the patient was either discharged or died. The most prevalent DRP for which interventions were made was inappropriate selection of antibiotic followed by medication without indication.

3.1.3. Education period

During the education phase, there were 128 antibiotic interventions by the pharmacists, 80 (62.5%) accepted interventions, 25 (19.5%) unaccepted and 23 (17.9%) not applicable. The most prevalent DRP for which interventions were made was still inappropriate selection of antibiotic followed by inappropriate dosage regimen.

3.1.4. Implementation period

During the implementation phase of the ASP, the total number of interventions made by the pharmacists was 104 interventions. The accepted interventions were 70 interventions (68%), the unaccepted were 18 interventions (17.5%) and there were 16 interventions that were not applicable (14.7%). The most prevalent DRP was inappropriate selection of the antibiotic followed by inappropriate dosing schedule. Using Chi-square test, there was a significant increase in accepted interventions across the study periods which means increase the physician's compliance to the clinical pharmacist's intervention ($P < 0.001$).

3.2. Antibiotic consumption

The overall antibiotic consumption expressed as DDD per 1000 patient-days increased after implementation of the ASP (Table 2). The preparation and education phases had similar DDDs per 1000 patient-days. The consumption of some categories decreased like third generation cephalosporins, penicillin's and carpabenem. These changes

Table 1
Incidence of accepted and unaccepted interventions during the three study phases expressed as numbers (percentage of 412 interventions along the whole study period).

	Preparation		Education		Implementation	
	Accepted	Unaccepted	Accepted	Unaccepted	Accepted	Unaccepted
Medication with no indication	1 (0.24%)	61 (14.8%)	5 (1.21%)	4 (0.97%)	4 (0.97%)	1 (0.24%)
Indication and no medication prescribed	6 (1.45%)	5 (1.2%)	2 (0.48%)	2 (0.48%)	10 (2.42%)	0.0
Inappropriate selection of the antibiotic	30 (7.28%)	35 (8.49%)	35 (8.49%)	9 (2.18%)	23 (5.58%)	6 (1.45%)
Therapeutic duplication	4 (0.97%)	1 (0.24%)	13 (3.15%)	2 (0.48%)	7 (1.7%)	4 (0.97%)
Inappropriate dosage regimen	19 (4.61%)	7 (1.69%)	17 (4.12%)	4 (0.97%)	24 (5.82%)	2 (0.48%)
Actual or potential clinically significant drug-drug, drug-disease interaction	1 (0.24%)	0.0	8 (1.94%)	2 (0.48%)	2 (0.48%)	5 (1.21%)
Total accepted and unaccepted	61 (14.8%)	109 (26.45%)	80 (19.41%)	23 (5.58%)	70 (16.99%)	18 (4.36%)
Inapplicable	10 (2.42%)		25 (6.06%)		16 (3.88%)	
Total number of interventions in each period/total number of interventions (412)	180 (43.68%)		128 (31.06%)		104 (25.24%)	

Table 2
Defined daily dose (DDD) per 1000 patient-days during the three phases of the study (preparation, education and implementation).

	Preparation (DDD)	Education (DDD)	Implementation (DDD)
Carbapenem	150.185	124.68	172.71
Aminoglycosides	110.42	141.03	337.595
Third generation cephalosporins	72.205	34.9975	96.77
Quinolones	32.86	33.775	38.84
Penicillin	122.29	88.865	128.155
Lincosamide	173.6	174.6	229.05
Vancomycin 500 mg	16.94	62.28	9.26
Cefazolin 1 g			58.14
Azithromycin			1.96
Clarithromycin			3.73
Tecoplanin			1.05
Total	678.5	660.22	1077.64

were accompanied by marked increase in the use of vancomycin. The DDDs of quinolones, aminoglycosides and lincosamide increased. During the implementation phase, there was an increase in the total consumption of antibiotics probably due to the difference in the average age of patients and number of ventilated patients as well as introduction of antibiotics that were not previously used in the ICU. However, vancomycin consumption decreased. A trend of antibiotic consumption could not be constructed due to the relatively short duration of the study.

4. Discussion

Our study describes the physicians' acceptance to pharmacist-led interventions in antibiotic prescription through physician education and ASP implementation. To our knowledge, this is the first study that describes the role of clinical pharmacists as specialists in the ICU in detecting, avoiding, and correcting DRPs focusing on antibiotic prescribing in an Egyptian public general hospital and whether physician's education would affect antibiotic prescribing or not. It was shown that pharmacists were effectively able to intervene and correct many of the audited errors while physicians were more resistant to interventions within the preparation phase. This resistance decreased after ending of the stewardship preparation and the acceptance was increased during the implementation of ASP. In the preparation phase, approximately 34% only of the total interventions were accepted, most of them were medications prescribed inappropriately for a particular condition like prescribing meropenem for a patient for more than 21 days with no fever and normal total leukocyte count (TLC) or prescribing ceftriaxone for a patient for which the microbiological culture was resistant to ceftriaxone (documented DRPS by pharmacists). Sixty percent of the total interventions were unaccepted like prescribing prophylactic antibiotic for a patient only to protect him/her from getting an infection or prescribing two antibiotics covering the same spectrum of activity. However, the number of interventions decreased during the education and implementation phases and acceptance of these interventions increased due to physician education and the presence of hospital guidelines. The need for pharmacist interventions and the need of proper physician education to minimize DRPs were previously documented in Egyptian and Middle Eastern Studies. Poor knowledge of medicines by physicians partially accounted for medication problems in the Middle East as pointed out in the systematic review by Alsulami et al. [14]. The physicians' education program in antibiotic use was developed specifically for ASP implementation, but it was one of the most difficult obstacles in our process as there was a time contradiction between work and training. The workload of the physicians did not permit them to attend lectures, and the training program was modified to be on job training that consumed a long time. This was also a challenge found in the Chinese medical practice in urban communities [15].

Medication reviews previously performed in Egypt and the Middle East reflected similar problems and outcomes. In a cross-sectional evaluation of medication reviews carried out in a private Egyptian general hospital of multiple specialties, the most common errors were prescribing errors, administration errors and overdoses. Factors associated with an increased risk of such problems were physicians' resistance, shortage of nursing staff, and renal impairment [16]. In another study that was carried on in Kasr El-Ainy hospital, Cairo, Egypt, emphasizing the role of clinical pharmacist in inpatient services as a medication reviewer and establishing a method for reporting any identified medication related problems was recommended [17]. A study performed in AlKhor Hospital (HMC) in Doha, Qatar concluded that the participation of clinical pharmacists reduced drug costs for the patient as well as for the hospital. The acceptance rate of interventions by the physicians was increasing by time. The difference of this study from our study that this study was carried on medical ward not the ICU, it also included all interventions on all types of medications but our

study focused only on antibiotics [18]. A similar study in Pakistan evaluating the prescribers approach towards a rational drug practice showed that the drug practice among the hospitalized patients was irrational, with high levels of medication errors. An accurate prescribing and a rational use of drugs are the major needs to ensure a safe medication practice [19]. This further emphasizes the findings in our study which used some of the strategies recommended in previous studies to decrease DRPs, namely physician education and hospital prescribing guidelines.

During the education and implementation phases, the total number of interventions decreased along with an increase in acceptance of interventions by physicians. It was observed in the preparation phase, that the regimens of antibiotics were similar in ICU patients despite different diagnosis; all patients of the ICU were prescribed mainly third generation cephalosporins (ceftriaxone or cefoperazone/sulbactam) whether for prophylaxis or treatment irrespective of diagnosis. This has significantly changed after the implementation of the antibiotic policy, the prophylaxis regimen was changed to first generation cephalosporins (cefazolin) except for special cases (e.g. ventilated patients) as reflected by antibiotic consumption pattern. Physicians started to request antibiotics other than third generation cephalosporins that were previously prevalent in the ICU. They also started to add new categories of antibiotics to the hospital formulary.

An additional factor proposed in influencing decision for prescribing antibiotics was sales promotion by pharmaceutical companies [20]; however physician education and implementation of ASP might limit this role by having clear guidelines for prescription.

In the education phase although the total consumption of antibiotics did not change from the preparation phase, the consumption of different categories changed especially the third generation of cephalosporins as the physicians were focusing only on the pattern of resistance irrespective to the guidelines. But when comparing the preparation with the implementation period, we will find that the antibiotic consumption has increased with the appearance of new antibiotics due to physicians' adherence to the hospital guidelines. On the other hand, there was a decrease in the use of vancomycin as the physicians used to prescribe vancomycin previously for any treatment failure. However, after ASP education they used to refer to the hospital guidelines for second line options according to diagnosis. A limited resource of purchasing different categories of antibiotics was one of the main obstacles to achieve much better remodeling of antibiotic consumption. All governmental hospitals have the same problem as they are restricted to certain types of antibiotics and certain cost determined by the Ministry of Health.

A review article performed on English papers published from 1999 to 2015 determined the impact of ASP on: antibiotics use and cost, the changing of the resistance pattern and Clostridium difficile prevalence and the length of stay and patient outcomes. It was found that 21 papers stated that the ASP affected the antibiotics use and cost and changing the pattern of prescribing. The majority of the studies that reported significant cost savings did not provide the cost of implementing the program [21].

Although numerous methods were developed by healthcare professionals for an improvement in the antibiotic use, the major problem which is prevalent throughout our study and the world is the excessive and inappropriate antibiotic prescribing. In the United States, approximately 60% of the hospitalized patients were prescribed an antimicrobial agent and about 50% of those antibiotics were unnecessary [22]. The main consideration for the rational prescribing of antibiotics is to select the optimal agent with a proper dosage and duration, to minimize the risk of emergence of resistance and provide affordable health care. This consideration greatly affects the consumption of antibiotics especially third generation cephalosporin which consequently will affect the pattern of resistance [23,24].

5. Limitations and recommendations

Even though our study showed change in the antibiotic prescription pattern along with the decrease in the need of intervention by pharmacists, further analysis is needed to investigate whether this change is truly correlated with reduced cost and improve in resistance pattern in the hospital over a longer time period. Due to the short period of the study a rigorous explanation for the overall increase in antibiotic consumption as expressed by DDD per 1000 patient-days could not be provided and comparison to studies in other countries [25–27] was not possible. The short duration also led to the inability to rigorously evaluate the ASP in this hospital. Application in the ICU ward only in one hospital is a major limitation as well. Multicenter studies covering all wards are needed to give an accurate perspective on the unmet needs in Egyptian hospitals regarding rational antibiotic prescribing and minimizing antibiotic resistance.

6. Conclusion

This study suggests that physicians in an Egyptian general hospital are accepting the role of clinical pharmacists in advising physicians about proper selection of antibiotics according to effectiveness and safety. The interventions needed as a result of DRPs decreased accompanied by an increase in acceptance of these interventions by physicians. Greater effort needs to be directed towards increasing physician's awareness about the importance of rationale prescribing of antibiotics with the accurate doses. A thorough evaluation of ASP implementation in Egyptian hospitals over longer periods of time is greatly needed.

Conflict of interest

None.

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