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SHORT RESEARCH REPORT

Impact of the pharmacist on a multidisciplinary team in an antimicrobial stewardship program: a quasi-experimental study

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Abstract *Background* Antimicrobial stewardship programs (ASP) have been implemented to promote rational use of antimicrobial drugs. Multidisciplinary teams are needed to form effective committees. *Objective* Assess the impact of ASP, with and without the presence of a pharmacist, in a cardiology hospital in Brazil. *Methods* The program started with an infectious disease (ID) physician, and after 22 months, a pharmacist started to work in the ASP team. We present data related to: stage 1—before the program implementation; stage 2—with the ID physician; and stage 3 with the inclusion of a pharmacist. Analysis was made by segmented regression of time series. *Results* After the start of ASP there was a significant reduction of consumption of all antimicrobials. The pharmacist contributed to the significant reduction in consumption of fluoroquinolones, clindamycin and ampicillin/sulbactam and in increase in total cephalosporins use in stage 3. Adherence rate to the ASP team recommendations was 64.1%. There was a significant reduction of 69% in hospital antibiotics costs. *Conclusion* A non-expensive ASP in a limited resource country resulted in reductions in antimicrobial consumption and costs. The multidisciplinary team contributed to maximize the impact of interventions.

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Keywords Antibiotics · Antimicrobial stewardship program · Brazil · Infection control pharmacist · Pharmacopidemiology

Impact of findings on practice

- Clinical hospital pharmacist can complement physicians in the management of antimicrobial therapies.
- Pharmacist interventions are effective to guide the antimicrobial prescription according the local antibiotic policies.
- Clinical Pharmacists can effectively participate in health education to promote the rational use of antimicrobial agents.

Introduction

The prescription of antimicrobial drugs is an exercise in balance between the benefits of an aggressive empirical therapy and the risks of emergence of antimicrobial-resistant pathogens [1].

Antimicrobial stewardship programs (ASP) have been implemented to promote rational use of antimicrobial drugs. The Infectious Diseases Society of America (IDSA) guideline emphasize the importance of an infectious disease (ID) physician and a pharmacist being part of ASP team [2].

Aim of the study

We assessed the impact of an intervention-prospective audit with feedback to prescriber, with and without the

presence of a pharmacist in ASP team, in a cardiology hospital in Brazil.

Method

A quasi-experimental study was conducted at Instituto de Cardiologia, a 250-bed hospital for cardiology patients in southern Brazil. Instituto de Cardiologia atends adult and pediatric, surgical and clinical cardiology patients. Also, the hospital has a cardiac transplant service. The hospital has three intensive care units, which account for 16% of institution's beds. The infection control team was composed by an infectious disease physician, a nurse and a nurse assistant.

Antibiotic consumption was measured for 30 months (January 2003 to July 2005) before program implementation (Stage 1). The ID specialist was responsible for the ASP from July 2005 to April 2007 (Stage 2). From May 2007 to December 2008 the ID physician and the pharmacist worked together for the ASP program (Stage 3).

The ID physician was assigned to 2 h a day for the program, but was available for consultation at all times, usually by phone. In this program, all antimicrobial written order forms were reviewed daily, and a written reply, with the recommendations of the infection control team (ICT) was put on patient's records within 24 h. However, the decision to follow the recommendation was at the discretion of the attending physician.

In stage 3, a trained pharmacist joined the team, assigned 4 h a day for antibiotic control. The pharmacist was trained on the antimicrobial stewardship program during oral discussions and seminars with ICT. The pharmacist role was to follow all patient-cases prospectively, recording the clinical data associated with the antimicrobial agent and the patient illness. After culture results, an order to deescalate therapy was done. Furthermore, on the third day of therapy, if feasible, an order to switch the intravenous to oral route, was released. At the end of the therapy, a stop order was put on the patient's records.

Antibiotic policy was based on restriction of fluoroquinolones and third-generation cephalosporins because of the associated risk of resistance. The use of vancomycin and carbapenems were also restricted. The use of penicilins were stimulated by the ICT.

Definitions and outcomes

Antibiotic use was computed for the entire hospital. Data from carbapenems, fluoroquinolones, cephalosporins, piperacilin/tazobactam, vancomycin and total antibiotic use was analyzed. On a monthly basis, consumption were counted as number of defined daily doses (DDD), expressed as DDD per 100 patient-days [3, 4]. Adherence rate to the ASP team's suggestions was also reviewed from November 2005 to December 2006 and from May 2007 to December 2008.

Statistical analysis

Time series segmented regression analysis was applied to determine significant changes in antibiotic consumption. The 2-rate X^2 test was used to compare resistant bacteria rates between pre- and post-intervention periods. All P values less than 0.05 were considered statistically significant. All collected data was stored in Excel® 2000 version and analyzed using SPSS® 14.0 program.

Results

Trends in antibiotic use throughout the three stages are shown in Fig. 1 and Table 1. Before the implementation of the ASP (Stage 1), there was an increasing consumption of carbapenems, fluoroquinolones, cephalosporins, vancomycin and of the total amount of antibiotics. Whereas, the consumption of second-generation cephalosporins, showed a significant decreasing trend.

During stage 2, there was an immediate decrease in the consumption level of carbapenems, cephalosporins and vancomycin. For carbapenems and cephalosporins there was, also, a significant decreasing trend in consumption, along the months after the first intervention. There was an increase in level and trend of piperacillin/tazobactam use. For fluoroquinolones there was an immediate increase in level of use and after that, a decreasing trend in the subsequent months. Finally, there was a decreasing trend in consumption in the total amount of antibiotic use (Table 1).

In stage 3, segmented regression model showed an immediate increase in the level of cephalosporins consumption and a decrease in the piperacillin/tazobactam level. For carbapenems and cephalosporins, there was an increasing trend of use during this period. For fluoroquinolones, the decreasing trend was maintained. Finally, there was an increasing trend of total antibiotic consumption (Table 1).

There was a significant increase in ceftazidime-resistant *Klebsiella* spp., 12% and 16% in stages 1 and 2, to 42% in stage 3 ($P < 0.001$); and an increase in ceftazidime-resistant *Pseudomonas* spp., 4 and 3% in stages 1 and 2, and 14% during the last period of observation ($P = 0.005$). The rate of carbapenem-resistant *Pseudomonas* spp. decreased from 6 to 7% in stages 2 and 3, to 1% in stage 3 ($P = 0.01$). The rate of ceftazidime-resistant *Klebsiella* spp., but not of

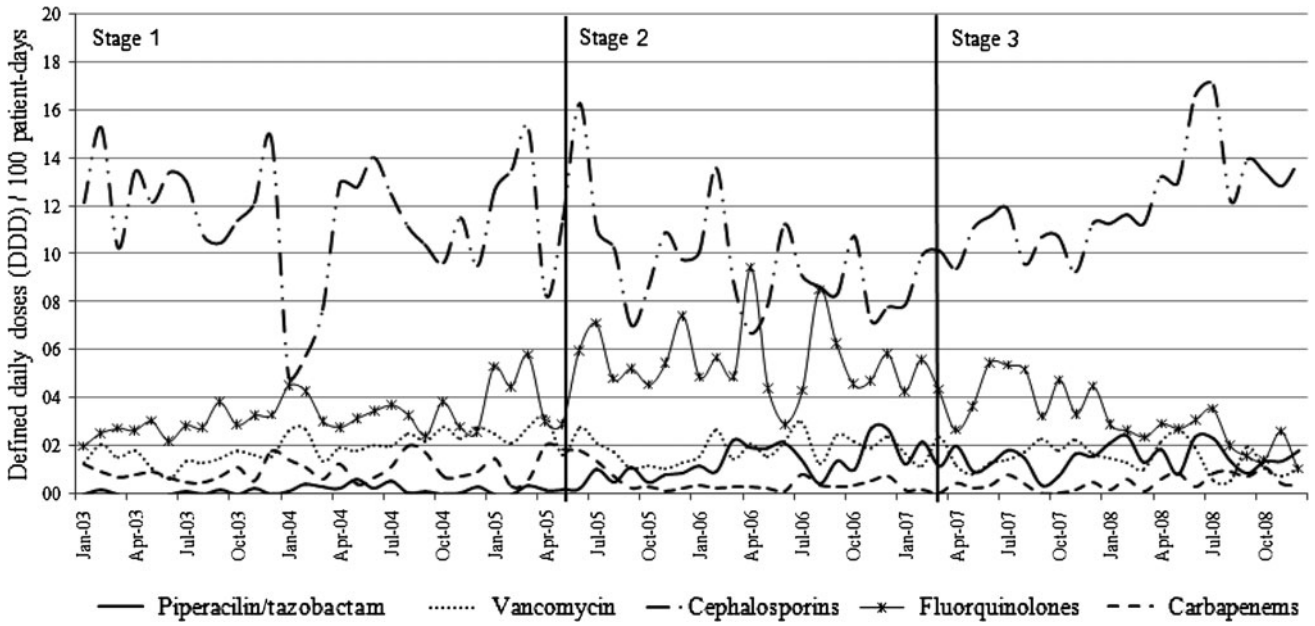

Fig. 1 Montlhy antibiotics consumption in DDD/100 patient-days—stages 1, 2 and 3. Cephalosporins—cefazolin, cefalexin, cefuroxime, cefoxitin, ceftazidime, cefotaxime, ceftriaxone, and cefepime; fluroquinolones—norfloxacin, ciprofloxacin and levofloxacin; carbapenems—meropenem and imipenem

Table 1 Trends in antibiotic consumption in DDD/100 patient-days, from stages 1, 2 and 3

Antimicrobial use	Stage 1		Stage 2				Stage 3			
	Trend coefficient	*P*	Level coefficient	*P*	Trend coefficient	*P*	Level coefficient	*P*	Trend coefficient	*P*
Carbapenems	0.21	0.01	−0.81	<0.001	−0.34	0.03	−0.028	0.91	0.036	0.05
Fluoroquinolones	0.06	0.01	1.87	0.004	−0.13	0.004	0.45	0.51	−0.104	0.05
Cephalosporins	0.11	0.006	−2.42	0.02	−0.16	0.03	4.05	0.001	0.26	0.005
2nd-generation cephalosporins	−0.03	0.03	0.45	0.16.	0.03	0.14	0.39	0.26	0.03	0.28
3rd-generation cephalosporins	−0.01	0.34	−0.32	0.16	−0.01	0.55	0.18	0.46	0.01	0.52
4th-generation cephalosporins	0.14	<0.001	−2.55	0.007	−0.18	0.005	1.21	0.23	0.1	0.20
Piperacilin/tazobactam	0.005	0.60	0.56	0.03	0.05	0.007	−0.76	0.01	−0.03	0.16
Vancomycin	0.05	<0.001	−1.09	0.001	−0.031	0.15	−0.24	0.48	−0.04	0.13
Total antibiotic consumption	1.22	<0.001	−1.31	0.78	−2.65	<0.001	4.69	0.37	1.20	0.004

ceftazidime-resistant *Pseudomonas* spp, correlated with the increase in total cephalosporin use ($r = 0.239$; $P = 0.04$).

The mean adherence rate to the ASP suggestion was 62.4% in stage 2, and 64.1% in stage 3 ($P = 0.55$).

Finally, comparing stage 1 and 3, there was a significant reduction of 25% in antimicrobial consumption and 69% in hospital antibiotic costs after implementation of ASP. The global consumption fell from 48.9 (mean monthly consumption in DDD/100 patient-days) during the first period, to 36.9 in the third period ($P = 0.001$). The mean monthly antibiotic cost, during the first stage, was US$ 30,727.56 (American dollars), US$ 18,034.89 in the second period, and US$ 9,623.73 in the last period of the study ($P < 0.001$).

Discussion

A non-confrontational back-end prospective audit, giving feedback to the prescribers, contributed to the dissemination of the antimicrobial policy in the hospital. During the study period, most changes in antimicrobial prescription were not related to any other external factor, such as new physicians on service, new antibiotic availability, or new guideline. Thereby, most changes in antimicrobial consumption was associated with the ASP. After the decrease in consumption of cephalosporins and increase in piperacillin + tazobactam in the second stage, an attempt to counter-balance this tendency by changing the recommendations in favor of

cephalosporins use to the third period. Also, the increase in quinolone in stage 2 was related to the introduction of levofloxacin in the antimicrobial panel.

Several relevant studies, examining the impact of an ASP, have been published. In a study, with a hospital-wide multidisciplinary antibiotic management program, to minimize the inappropriate use of third-generation cephalosporins, there was a 22% reduction in the use of broad-spectrum antibiotics, and a significant decrease in nosocomial infections caused by Enterobacteriaceae [5]. An educational intervention, in relation to levofloxacin and ceftazidime prescriptions, resulted in a 41% reduction of unnecessary antibiotic use [6]. Furthermore, hospitals that practice a carbapenems restriction strategy reduced carbapenem-resistant *P. aeruginosa* [7]. In accordance to these studies, the intervention to reduce fluoroquinolone, carbapenems, and vancomycin was successfully achieved.

The reduction in DDD of carbapenems resulted in a reduction of carbapenems-resistant *Pseudomonas* spp. On the other hand, there was an increase in ceftazidime-resistant *Pseudomonas* spp. and ceftazidime-resistant *Klebsiella* spp. The latter correlated with an increase in cephalosporins prescriptions in stage 3. This might be related to the phenomenon known as "squeezing the balloon" or "collateral damage", which is the ability of antimicrobials to cause unintended ecological resistance, despite an intervention aimed to reduce bacterial resistance [8, 9]. The increase in bacterial resistant trends, resulted in the increase in total antimicrobial use in stage 3. Besides, there was an increasing pressure for carbapenem use in this period. Nevertheless, there was a reduction in the total antimicrobial costs, which reinforce the ASP team (and pharmacist) recommendations towards more cost-effective therapies, reducing inappropriate use of drugs.

Thus, the introduction of a pharmacist in a multidisciplinary team was sufficient to incorporate important contributions in prescribing practices. In Europe, hospitals with the prescribing advice from pharmacist had lower median levels of antibiotic consumption [10]. In one particular study, the decisions made by the team had more favorable outcomes when compared to the ID specialist alone [11]. In Brazil, the pharmacist's advice is underrecognized. Brazilian hospitals, in general, do not offer full-time residency programs or post-graduate training in antimicrobial stewardship for pharmacists.

This is not a controlled study which enables us to make only inferences about the contribution of the pharmacist. The pharmacist contributed mostly in the prospective follow-up of the patient, allowing consultant physicians to make more accurate recommendations, since they do not actually see all the patients. This informal mode of consultation (without seeing the patient) probably resulted in the 35% of non-adherence by the prescriber, considering that the attending physician had more information about the patient than the ICT at distance.

Conclusions

In developing nations, traditional barriers to the implementation of ASPs are difficult to overcome. A non-expensive program, with co-working from the ID physician and pharmacist, may contribute to a more rational prescription of antimicrobial drugs, saving costs and changing bacterial resistant patterns.

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