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Impact of an interdisciplinary strategy on antibiotic use: a prospective controlled study in three hospitals

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Objectives: Evaluation of the impact of the implementation of practice guidelines, with or without their reinforcement by a pharmacist, on the intra-hospital use of antibiotics.

Materials and methods: The duration of antibiotic treatment, their cost, and the length of patient stay were compared in three secondary-care hospitals, before and after interventions that were designed to promote rational antibiotic use. After randomization, hospital A received no intervention (control), local practice guidelines were implemented in hospital B (low grade intervention), and these guidelines were reinforced by a clinical pharmacist in hospital C (high grade intervention). Adherence to the guidelines was measured in hospitals B and C. Multivariable statistical analyses were carried out to adjust for confounding factors.

Results: None of the outcomes measured in the 1200 included patients decreased between the two study periods in any hospital. Hospital A was significantly and independently associated with an increase in the duration of antibiotic treatments, the cost of antibiotics (acquisition and global costs), and the length of stay. Although these differences were not statistically significant, increases in hospital B were higher than in hospital C. Adherence to guidelines was significantly higher in hospital C.

Conclusions: Even though interdisciplinary interventions aiming at rationalizing antibiotic use could not diminish the duration of treatments, their costs or the length of stay, they proved useful to control the progression of these parameters.

Keywords: practice guidelines, antibiotic use, costs, interdisciplinary team, pharmaceutical services

Introduction

Antibiotics represent approximately 30% of acute care hospitals' drug expenditures; they are prescribed for 20–50% of inpatients, and contribute to the emergence of resistant microorganisms. Surveys have shown that 22–65% of antibiotic prescriptions are either inappropriate or incorrect.[1] Indeed, several organizations have written action plans to control the costs of antibiotics and limit their selective pressure on resistant microorganisms through surveillance and interventions promoting their rational use. Every health care professional, including pharmacists, may play an important role in these efforts.[2]

Different interventions have been described to guide a more appropriate and cost-effective use of antibiotics in hospitals: some are restrictive (automatic stop orders, restricted antibiotic list, mandatory approval by infectious diseases specialists). Others focus on education (face-to-face discussion, conferences, distribution of printed material, audit with feed-back), or are based on tools to help physicians in their decision making (practice guidelines, computer programs). The importance of combining strategies to enhance the success of any intervention has been emphasized.[3] Clinical practice guidelines are used to promote the rational use of antibiotics. They need to be adequately prepared, implemented and supported to have a positive impact.[4] Several studies support the role of the clinical pharmacist as a

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drug therapy advisor in institutional settings,[5] fewer demonstrate his/her impact on quality or cost in the implementation of antibiotic guidelines.[6]

The aim of this controlled 'before–after' study was to evaluate the impact of the implementation of local practice guidelines, with and without their reinforcement by a clinical pharmacist, on the intra-hospital use of antibiotics.

Materials and methods

Setting and study design

The general medical wards and intensive care units of three comparable secondary-care non-university affiliated public hospitals in western Switzerland (100–120 acute-care beds each, 5000–6000 admissions per year each, and similar case-mix indexes) were studied during two 6 month periods (November 2001 to April 2002 and November 2002 to April 2003). Over each period of time, the first 200 patients admitted to these wards of each hospital were enrolled into the study provided they received antibiotic therapy. Hospitals were randomly assigned to no intervention (hospital A, control), implementation of guidelines only (hospital B, low grade intervention), or implementation of guidelines with their reinforcement by a clinical pharmacist (hospital C, high grade intervention). Local practice guidelines, based on published recommendations, a common drug formulary, and regional antibiotic susceptibility patterns, were developed and implemented in hospitals B and C between the two study periods by infectious diseases physicians,

pharmacists, and the heads of internal medicine of these two hospitals. In hospital C, a clinical pharmacist reviewed the medical charts and participated in clinical rounds twice weekly during the intervention period. She informed the physicians on any deviation from the guidelines, necessity to adjust dosages, and possibilities to narrow the spectrum of activity of antibiotics or to switch to oral therapy.

Data collection

Data were collected from the medical charts. The outcome variables were the length of hospital stay, the duration of the antibiotic treatment (distinguishing oral and intravenous administrations), and costs expressed as the cost of the substances and the global cost of treatment including substances, devices, and nursing time for the administration of the treatment. The adherence to guidelines in the second study period was evaluated, in hospitals B and C, by a blinded investigator.

Other collected variables included the age, the gender, the Charlson comorbidity index, microbiological results, the antibiotics used, their indication, dosage and route of administration.

Statistical analysis

Proportions and medians were compared between hospitals and study periods in univariate analysis by using χ^2, Fisher's exact, Kruskal–Wallis or Mann–Whitney tests, as appropriate.

After exclusion of outliers based on the inspection of histograms and clinical appraisal, multivariable models were developed to obtain adjusted outcome comparisons between hospitals and study

Table 1. Patients' characteristics in the intervention and control hospitals during the pre- and post-intervention periods

Characteristic	Hospital A, control	Hospital B, low grade intervention	Hospital C, high grade intervention	P value[a]
Pre-intervention period	$n = 200$	$n = 200$	$n = 200$	
patients admitted,[b] n	850	685	746	
median age, years (extremes)	72.1 (14–94)	76.6 (15–97)	69.4 (19–97)	0.078
males, n (%)	94 (47)	89 (44.5)	98 (49)	0.665
Charlson comorbidity index, n (%)				0.027
0	83 (41.5)	56 (28)	60 (30)	
1–3	92 (46)	106 (53)	101 (50.5)	
>3	25 (12.5)	38 (19)	39 (19.5)	
nosocomial infections,[c] n (%)	10 (5)	9 (4.5)	12 (6)	0.788
difficult-to-treat infections,[d] n (%)	20 (10)	22 (11)	20 (10)	0.931
difficult-to-treat pathogens,[e] n (%)	2 (1)	8 (4)	7 (3.5)	0.153
Post-intervention period	$n = 200$	$n = 200$	$n = 200$	
patients admitted,[b] n	746	616	850	
median age, years (extremes)	73.7 (14–95)	71.7 (16–103)	74.0 (18–98)	0.428
males, n (%)	90 (45)	93 (46.5)	98 (49)	0.720
Charlson comorbidity index, n (%)				0.245
0	77 (38.5)	61 (30.5)	58 (29)	
1–3	95 (47.5)	101 (50.5)	106 (53)	
>3	28 (14)	38 (19)	36 (18)	
nosocomial infections,[c] n (%)	6 (3)	1 (0.5)	10 (5)	0.025
difficult-to-treat infections,[d] n (%)	14 (7)	16 (8)	24 (12)	0.181
difficult-to-treat pathogens,[e] n (%)	2 (1)	8 (4)	4 (2)	0.161

[a]χ^2, Fisher's exact or Kruskal–Wallis test.
[b]Number of admissions necessary to reach the 200 pre-planned patients with criteria for inclusion.
[c]Defined as infections occurring more than 48 h after admission and not in incubation at the time of admission.
[d]Infections involving the bone or joints, the central nervous system, the vascular system (e.g. endocarditis), associated with a bacteraemia, or occurring in a neutropenic patient.
[e]*Acinetobacter* sp., *Enterobacter* sp., *Pseudomonas* sp., *Serratia marcescens*, methicillin-resistant *Staphylococcus aureus* (MRSA), and *Stenotrophomonas maltophilia*.

Table 2. Durations of treatment, costs, and length of stay in the intervention and control hospitals during the pre-intervention (PRE) and post-intervention (POST) periods

Outcomes	Hospital A, control				Hospital B, low grade intervention				Hospital C, high grade intervention			
	PRE	POST	TR or CR[a] [95% CI]	P value	PRE	POST	TR or CR[a] [95% CI]	P value	PRE	POST	TR or CR[a] [95% CI]	P value
Median duration of iv antibiotics, days (IQ range)[b]	2.0 (2.0)	2.5 (2.0)	1.11 [0.94–1.30]	0.230	5.0 (4.0)	5.0 (4.5)	1.10 [0.95–1.27]	0.203	4.0 (2.0)	4.0 (2.0)	1.05 [0.90–1.22]	0.533
Median duration of all antibiotics, days (IQ range)	6.0 (5.0)	8.0 (5.0)	1.18 [1.06–1.31]	0.002	8.0 (7.0)	8.0 (7.0)	1.08 [0.97–1.20]	0.183	7.0 (5.0)	7.0 (5.0)	1.02 [0.91–1.13]	0.753
Median cost of antibiotics,[c] Euros (IQ range)	27.5 (53.5)	37.4 (63.1)	1.35 [1.07–1.70]	0.011	68.4 (103.5)	82.3 (118.3)	1.22 [0.96–1.54]	0.099	45.9 (67.6)	46.0 (101.4)	1.11 [0.88–1.40]	0.391
Median global cost,[c,d] Euros (IQ range)	51.9 (84.5)	65.4 (85.3)	1.30 [1.05–1.60]	0.014	128.2 (184.1)	149.9 (196.5)	1.20 [0.98–1.48]	0.085	80.8 (110.4)	83.3 (158.6)	1.07 [0.87–1.32]	0.520
Median length of stay, days (IQ range)	9.0 (6.0)	10.0 (7.0)	1.14 [1.03–1.26]	0.013	10.0 (9.0)	10.0 (9.0)	1.11 [1.00–1.23]	0.058	10.0 (9.0)	11.0 (8.0)	1.05 [0.95–1.17]	0.322

[a]TR (time ratios) and CR (cost ratios) correspond to ratios of the changes of outcomes between the two study periods in each hospital compared with the others, controlling for potential confounding factors (see text).
[b]The numbers of patients treated with intravenous antibiotics during the pre- and post-intervention periods among the 200 patients included in the study for every hospital and every period were 102 and 114 in hospital A, 137 and 149 in hospital B, and 128 and 118 in hospital C, respectively.
[c]The mean hospital acquisition costs per dose in year 2002 were used for every antibiotic prescribed during the two study periods.
[d]Including the cost of antibiotics, plus devices and nursing time (see text).

periods. Independent variables in the final models included the dummy-coded hospitals and study periods, and confounding factors remaining after a backward selection from the following variables: age, gender, Charlson comorbidity index, nosocomial infection, difficult-to-treat infection and difficult-to-treat pathogen, as defined in Table 1. P values were two-tailed; $P \leq 0.05$ was considered to be significant.

Results

The characteristics of the 1200 included patients are shown in Table 1. Significant differences were found only for the proportion of patients with no comorbidities which was higher in hospital A in the pre-intervention period, and for the proportion of patients suffering from nosocomial infections which was higher in hospital C in the post-intervention period.

Inter-hospital differences were however present in the baseline values of the measured outcomes. Hospital A (control) had lower median values for the total duration of antibiotic treatments ($P < 0.001$), costs of antibiotics ($P = 0.003$), global costs of antimicrobial treatments ($P < 0.001$), and length of stay ($P = 0.003$).

No decrease in the outcomes as defined in Table 2 was observed in any of the participating hospitals. However, significant increases were found only in hospital A (control) when comparing it with the two other participating institutions while adjusting for any potential changes in the patients' characteristics between the two study periods. Moreover, although the differences were not statistically significant, the observed increases in the parameters investigated were higher in hospital B (low grade intervention) than in hospital C (high grade intervention).

During the post-intervention period, 95/170 patients (56%) in hospital B and 122/170 (72%) in hospital C were treated in accordance to the guidelines ($P = 0.002$). Thirty patients in each hospital were excluded because their indication to receive antibiotics was unclear or not included in the guidelines.

Discussion

In a previous study, Gums et al.[7] attributed a decrease in the length of patients' stay to antibiotic control programmes including consultations by multidisciplinary teams. In this study, the implementation of practice guidelines by infectious disease consultants, pharmacists, and in-house physicians, with or without their reinforcement by a clinical pharmacist, was not associated with any decrease in the duration of hospital antibiotic treatments, their costs, or the length of patients' stays. However, a significant increase in the parameters investigated was observed only in the control hospital, compared with the hospitals which benefited from an intervention. Moreover, although these differences were not statistically significant in the intervention groups, the observed increases were higher in the hospital with a low grade intervention than in the hospital with a high grade intervention. The impact of the high grade intervention, which included the reinforcement of the guidelines by a clinical pharmacist, is demonstrated by a higher adherence to the guidelines (72%), compared with 56% in the hospital without reinforcement or to published rates of 40–60%.[8] These results suggest a positive effect of the implementation of practice

guidelines for antibiotic use, particularly when they are reinforced by a clinical pharmacist, thus arguing in favour of multifaceted interventions and confirming the results of previous studies that demonstrated the lack of efficacy of the distribution guidelines, in the absence of additional measures.[9]

This study used a prospective, controlled, 'before–after' design. The same months were chosen for each observation period to avoid seasonal biases. The different interventions were randomly allocated to different hospitals to avoid contamination biases. These institutions were similar in terms of size, activities, and case-mix indexes, thus minimizing the risk of inappropriate comparisons. In addition, the multivariable analyses took potential confounding factors into account, allowing us to estimate the independent association of each of the interventions with the measured outcomes.

Nevertheless, the control hospital had significantly lower baseline durations of antibiotic treatments, costs and length of stays than the others. In addition, although these parameters increased significantly in this hospital between the two study periods, they remained lower than in the others. As discussed by Avorn & Solomon,[10] many factors, other than the patients' characteristics or their type of infection, may influence antibiotic use. Such factors that may be cultural or economical, are difficult to capture in a study on antibiotic use and could have played an unseen role in our results. Other limitations of this study suggest caution while interpreting its results. First, outcomes such as mortality, resistance rates to antibiotics or quality of care were not assessed and may vary independently from the costs, the duration of treatments or the length of stay. Second, this study addressed only in-hospital antibiotic use and did not include the treatments of patients transferred or discharged on antibiotics. Third, it was not designed to determine the cost-effectiveness of the implemented interventions.

In conclusion, this study illustrates the difficulties encountered when measuring the impact of interventions to promote the rational use of antibiotics. Nevertheless, it suggests a positive impact of the development and implementation of local guidelines, particularly when they are reinforced by a clinical pharmacist.

Acknowledgements

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