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ABSTRACT

Objectives: Antimicrobial stewardship (AMS) teams around the world include pharmacists; however, their impact is relatively unknown. This study aimed to explore the relationship between pharmacists' actions and antibiotic consumption.
Methods: Hospital pharmacists involved in the French antibiotic consumption surveillance network (ATB-Raisin) were invited to participate in a retrospective observational multicentre study. Collected data were: the previous year's (2016) antibiotic consumption expressed in daily defined dose per 1000 patient-days; AMS measures, including pharmacist-specific actions; and use of a computerised prescription order entry (CPOE) system. Associations between antibiotic consumption and AMS measures were assessed by linear regression, after adjustment for hospital activities.
Results: Annual data for 2016 from 77 hospitals (7 260 000 bed-days in 24 000 beds) were analysed. Pharmacists were involved in AMS programs in 73% of hospitals, and were the antibiotic advisor in 25%. Pharmaceutical review of prescriptions was organised in almost all hospitals (97%). The univariable analysis identified five measures associated with lower overall antibiotic consumption: CPOE use (if >80% of prescriptions or 100%), pharmaceutical review (if >80% of beds or 100%) and the antibiotic advisor being a pharmacist ($P = 0.04$, $P = 0.004$ and $P = 0.003$, respectively). In the multivariable analysis, two explanatory variables were significantly and independently associated with a lower overall antibiotic consumption: the antibiotic advisor being a pharmacist and a pharmaceutical review covering all beds (−19.9% [−31.6%; −8.1%], $P = 0.002$ and −18.3% [−34.0%; −2.6%], $P = 0.03$, respectively).
Conclusions: Antibiotic consumption was lower when the antibiotic advisor was a pharmacist and when the pharmaceutical team reviewed all prescriptions. These results highlight that actions initiated by pharmacists have a positive impact and should be supported.

1. Introduction

Infections due to multi-drug resistant bacteria cause 23 000 and 25 000 deaths each year in USA and Europe, respectively [1,2], making the worldwide burden of antibiotic resistance a major threat to public health [3]. In this context, antimicrobial stewardship (AMS) programs were developed [4] and their implementation has been associated with improvements in antibiotic consumption [5–7], reduction in associated costs [5,6] and bacterial resistance [8]. AMS programs are based on multidisciplinary actions involving all health professionals. The impact of pharmacists actions in these programs is well documented in the USA [9] and the UK [10], where pharmacists are invariably involved in AMS programs [11]. Worldwide, pharmacists actions in AMS teams have been shown to be associated with a reduction in antibiotic consumption [12–14], associated costs [13] and

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mortality [15]. In these countries, most of the pharmacists involved in AMS programs are clinical pharmacists with specific infectious disease (ID) training, and this training has been associated with lower antibiotic consumption [11]. In France, AMS programs are led by ID physicians; however, French pharmacists are widely involved in AMS programs and consider themselves as having the role of overseeing good prescribing practices [16,17] and managing antimicrobial agents, including pharmaceutical review, restriction policy, prospective audit and feedback, and monitoring antibiotic use and consumption.

If the global impact of pharmacists in AMS teams is now well known, the specific impact of every single pharmacist's action in these programs has not yet been precisely documented. Therefore, the aim of the current study was to determine which specific pharmacists' actions were associated with decreased antibiotic consumption.

2. Materials and methods

2.1. Study design

A retrospective, observational, multicentre study (performed between January–April 2017) collected 2016 data (AMS measures and antibiotic hospital consumption). A pilot study of five hospitals was carried out, then hospitals involved in the French antibiotic consumption surveillance network (ATB-Raisin) were invited to participate. Hospitals that did not send complete data after one email reminder were excluded.

2.2. Antimicrobial stewardship data collection

An auto questionnaire exploring AMS programs was developed by a multidisciplinary team comprising an epidemiologist and clinical pharmacists with ID training. The survey was based on the literature about the pharmacist's role in AMS [16] on Regional Health Authority requirements on prudent and efficient use of medicines (care quality and efficiency improvement contract, CAQES) and on a Governmental guidelines (instruction no 2015-212 of 19 June 2015). This survey was filled in by hospital pharmacists. The survey explored pharmaceutical and multidisciplinary actions, computerised prescription order entry (CPOE) and overall organisation. Emphasis was put on specific training and pharmaceutical review, defined as a structured evaluation of patients' medicines in order to optimise the use of medicines and improve health outcomes [18]. For CPOE systems and pharmaceutical reviews, results were analysed with two thresholds: 80% of beds (target set in CAQES); and 100% of beds, which is the ideal objective. Furthermore, data on AMS teams were collected, especially regarding the role of pharmacists (antibiotic advisor or not). In France, an antibiotic advisor is a healthcare professional with specific training in antibiotherapy, whose mission is to help prescribers choose the best antibiotic treatment, and to lead educational and assessment actions regarding antibiotic use.

2.3. Antimicrobial consumption and administrative data collection

Hospitals were asked to provide a copy of the Excel® form that had been filled out for the ATB-Raisin network annual survey. This file contained annual antibiotic consumption and administrative data on hospitals: hospital status (public teaching hospital, public hospital, private hospital, rehabilitation centre or psychiatric hospital); and number of beds and patient-days (PD) for the whole hospital and for each type of ward (medical, surgical, intensive care unit, rehabilitation, long-term care). Antibiotic consumption was expressed in defined daily doses (DDD [19]) for 1000 PD, according to the ATB-Raisin methodology.

2.4. Judgement criteria and statistical analysis

Data were analysed using R version 3.4.2 software (R Development Core Tam, Vienna, Austria). The primary endpoint was the overall antibiotic consumption, expressed in DDD per 1000 PD, in relation to AMS actions. Linear regression was used to identify relationships between overall antibiotic consumption and AMS actions. All models were added a random intercept accounting for hospital type and were adjusted on hospital activity (considering the number of PD for the different types of clinical activity). A multivariable model was built, from the variables identified during the univariate analysis, using stepwise regression to identify covariates independently associated with global antibiotic consumption. Regression coefficients were reported as relative variations from the intercept with their 95% confidence intervals (95% CI). *P*-value was set at 0.05 for all tests.

3. Results

3.1. Participating hospitals

Among the 1470 hospitals of ATB-Raisin network, 88 (6.0%) hospitals responded to the survey. Eleven were excluded due to missing data on antibiotic consumption or PD. The 77 included hospitals were mainly public hospitals with >33% of acute care beds (n = 25; 32%) and acute care private hospitals (n = 20; 26%). These hospitals accounted for 7 260 000 PD and > 24 000 beds, with a median of 213 beds (IQR [99–384]).

3.2. AMS measures

The AMS measures in hospitals are described in Table 1. Of note, a pharmacist dedicated time for AMS in 56 hospitals (73%), and was the antibiotic advisor in 19 (25%) cases. The mean of this dedicated time was 3.4 h each week (IQR [1.1–4.0]). Thirty-five of these pharmacists had specific ID training (45%). CPOE systems were present in 76 hospitals (99%) and covered all beds in 61% of hospitals. Antibiotic-specific modules such as computerised protocols, automatic stop-order or requirement to document indication were less common (19%, 44% and 40%, respectively). Pharmaceutical review was organised in 75 hospitals (97%) and implemented for 100% of the beds in 48 hospitals (62%).

3.3. Relationship between overall hospital antibiotic consumption and AMS measures

The univariable analysis identified five measures associated with lower total antibiotic consumption: CPOE use (if >80% of prescriptions or 100%), pharmaceutical review (if >80% of beds or 100%), and the antibiotic advisor being a pharmacist (Table 2, *P* = 0.04, 0.004 and 0.003, respectively). Among these measures, CPOE use and pharmaceutical review were identified as significant explanatory variables for the two thresholds (>80% and 100%). Moreover, hospitals with CPOE available for 100% of the beds used less antibiotics than hospitals with 80–99% computerised prescriptions (−33.3%; *P* < 0.001). Consumption did not differ whether the pharmaceutical review was implemented in 100% beds or in 80–99% beds (−17.2%, *P* = 0.17). Conversely, reassessment of prescription after 48–72 h was associated with higher antibiotic consumption (+24.3%, *P* = 0.04).

In the multivariable analysis, the selected model identified two explanatory variables independently associated with lower total antibiotic consumption: pharmacists as antibiotic advisors and

Table 1
Antimicrobial stewardship actions carried out by participating hospitals (n = 77 hospitals, 2016).

	Hospitals	
	Number	%
Multidisciplinary measures		
Institutional committee for anti-infective agents	66	86%
Annual meetings: ≤2	12	16%
Annual meetings: ≥3	54	70%
AMS mobile team	22	29%
With a pharmacist	11	14%
Facility-specific clinical practice guidelines on infectious diseases	73	95%
Dematerialised diffusion by local network	64	83%
Physical diffusion by a paper guide	34	44%
Annual monitoring of antibiotic consumption	76	99%
With feedback to clinical wards	21	27%
Annual audits about antibiotic use	71	92%
Re-assessment of prescriptions after 48–72 h	50	65%
With automatised extraction of concerned patients	38	49%
Re-assessment of prescriptions after 7 days	22	29%
With automatised extraction of concerned patients	14	18%
Pharmacist-specific actions		
Pharmacist with time dedicated to AMS	56	73%
This pharmacist is the local antibiotic advisor	19	25%
This pharmacist has a specific training in antibiotic therapy	35	45%
Preauthorisation by a pharmacist	68	88%
For fluoroquinolones	49	64%
For third-generation cephalosporins	44	57%
For carbapenems	66	86%
Pharmaceutical review of prescriptions	75	97%
>80% of hospital beds	57	74%
100% of hospital beds	48	62%
Time dedicated for delocalised clinical pharmacy activities	36	47%
Computerised order entry system		
Computerised prescribing system	76	99%
Covering >80% of hospital beds	58	75%
Covering 100% of hospital beds	47	61%
Inclusion of antibiotic treatment protocols in CPOE system	15	19%
Inclusion of stop-order in CPOE system	34	44%
Documentation of antibiotic indication mandatory in CPOE system	31	40%

Abbreviations: AMS, antimicrobial stewardship; CPOE, computerised prescription order entry.

Table 2
Relationship between overall antibiotic consumption in hospitals and antimicrobial stewardship measures.

AMS actions, type	Actions, number (%)	Univariate analysis		Multivariate analysis	
		DDD/1000 PD[a]	*P*-value	DDD/1000 PD[a]	*P*-value
Reassessment of prescriptions after 48–72 h	50 (65)	24.3% [1.8%; 46.8%]	0.04	–	–
Antibiotic advisor is a pharmacist	19 (25)	−22.5% [−36.6%; −8.5%]	0.003	−19.9% [−31.6%; −8.1%]	< 0.002
Computerised prescription ≥80% of hospital beds	58 (75)	−21.3% [−40.7%; −1.9%]	0.04	–	–
Computerised prescription = 100% of hospital beds	47 (61)	−22.3% [−40.4%; −4.2%]	0.02	–	–
Pharmaceutical review ≥ 80% of hospital beds	57 (74)	−27.5% [−45.3% ; −9.8%]	0.004	–	–
Pharmaceutical review = 100% of hospital beds	48 (62)	−35.4% [−49.5%; −21.3%]	< 0.001	−18.3% [−34.0%; −2.6%]	<0.03

Abbreviation: AMS, antimicrobial stewardship; PD, patient-days.
[a] Regression coefficients reported as relative variations from the intercept with their 95% confidence intervals.

100% of beds with pharmaceutical analysis (−19.9% and −18.3%, $P < 0.002$ and $P < 0.03$, respectively). For example, mean consumption in local public hospitals was 419.7 DDD/1000 PD versus 367.0 DDD/1000 PD if the antibiotic advisor was not a pharmacist (−52.7).

4. Discussion

It is believed that this study is the first to analyse the association between AMS single action of pharmacists and antibiotic consumption. It showed that pharmacists were the antibiotic advisor in a substantial proportion of hospitals (25%) and that this was associated with a lower antibiotic consumption (−20%); this could be related to greater versality of pharmacists than ID specialists, who usually focus on more complex situations. Greater efforts can be quantitively made on antibiotic consumption for the most simple and classic situations (non-severe infection and non-resistant bacteria). This study also showed that pharmaceutical review is a useful tool to limit antibiotic use (−18%), especially if it covers all hospital beds. However, if pharmaceutical review is widely present in French hospitals (97%), it does not always apply to all beds (62%). Facility-specific guidelines may also support the antibiotic advisor's decision in relatively simple situations.

As previously described [16,17], pharmacists are widely integrated into AMS programs in French hospitals, despite a lack of official guidelines describing their role. Specific training of

French pharmacists in ID and antibiotic use has not yet been developed, with no such university certificate [16,17], although multidisciplinary training courses in infectious diseases or hospital hygiene are frequently offered by universities. In order to limit consumption and in fine resistance to antibiotics, in view of the current results, harmonisation and enhancement of the training of pharmacists seems to be an interesting concept.

Even if a small number of hospitals was included (77), their distribution is comparable with the national antimicrobial consumption surveillance network (ATB-Raisin) repartition [20], with a small over-representation of University Hospitals (data not shown). The overall antibiotic consumption of the current sample was not different to ATB-Raisin national data.

This study had some limitations. First, as it was based on voluntary participation, the included hospitals were certainly those most involved in AMS. Moreover, a risk of bias was introduced as the respondents were pharmacists, in that pharmacists who were confident that their actions impacted antibiotic use might have been more likely to respond to the survey. However, even among these hospitals, there was room for improvement in feedback, pharmaceutical review and information technology systems. Second, due to the observational design, causality could not be inferred from the associations between pharmacists' AMS action on antimicrobial consumption. Third, the profession of antibiotic advisor was unknown when it was not a pharmacist. Therefore, the benefits of a pharmacist being an antibiotic advisor could not be compared with other professions (physician, ID specialists).

In conclusion, this study showed that antibiotic consumption was lower in France when the antibiotic advisor was a pharmacist and when the pharmaceutical team reviewed prescriptions for all hospital beds. This highlights the need for dedicated time and acknowledgement of pharmaceutical activities to improve antibiotic use and, ultimately, to control antimicrobial resistance.

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Competing interests

No conflicts of interest to declare.

Ethical approval

Not required.

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