



The use of an antibiotic order form in a tertiary hospital: Influence on physicians' prescribing patterns

[El uso de un formulario de pedido de antibióticos en un hospital de tercer nivel: influencia en los patrones de prescripción de los médicos]

Duc Chien Vo¹, Tuan Anh Mai², Thu Thao Nguyen³, Dang Thoai Nguyen⁴, Thi Ha Vo^{3,4*}

¹Department of Respiratory Medicine, Nguyen Tri Phuong Hospital, Ho Chi Minh, V-70000, Vietnam.

²Department of Pharmacy, Hanoi Pharmacy University, Ha Noi, 100000, Vietnam.

³Department of Pharmacy, Nguyen Tri Phuong Hospital, Ho Chi Minh, V-70000, Vietnam.

⁴Faculty of Pharmacy, Pham Ngoc Thach University of Medicine, Ho Chi Minh, V-70000, Vietnam.

*E-mail: havt@pnt.edu.vn

Abstract

Context: Vietnam is one of the countries at the high alert of antibiotic resistance.

Aims: To evaluate the compliance rate and changes in physicians' prescribing patterns in patients with community-acquired pneumonia (CAP) before and after using the antibiotic order form (AOF) in a tertiary hospital.

Methods: 120 inpatient medical records having antibiotic use and 115 patient medical records diagnosed with CAP at a Department of Respiratory Medicine during 3 months before and 3 months after using the AOF were retrospectively collected for assessment.

Results: The compliance rate was 92%, and the average rate of filling in information fields was 58%. Comparison of prescribing behavior of CAP in control and intervention group showed that the rate of bacterial culture increased from 70% to 77% ($p = 0.690$), in which the rate of culture prior prescribing administration increased from 14% to 45% ($p < 0.001$), the initial antibiotic regimen with narrow-spectrum increased from 26% to 36% ($p = 0.353$), the proportion of patients improved clinically after 72 hours increased from 64% to 89% ($p = 0.138$), and the de-escalation decreased from 23% to 20% ($p = 0.713$). The treatment failure at hospital discharge decreased from 12% to 6% ($p = 0.447$). However, the length of treatment and the days of antibiotic treatment were not significantly different.

Conclusions: The compliance rate was high, but the AOF filling rate was incomplete. Improving prescribing patterns and treatment efficacy in CAP patients is a suggestion to combine the AOF into multifaceted interventional efforts for specific patients.

Keywords: antibiotic order form; antibiotic stewardship program; community acquired pneumonia; prescribing; Vietnam.

Resumen

Contexto: Vietnam es uno de los países en alerta máxima de resistencia a los antibióticos.

Objetivos: Evaluar la tasa de cumplimiento y el cambio en los patrones de prescripción de los médicos en pacientes con neumonía adquirida en la comunidad (NAC) antes y después de usar el formulario de pedido de antibióticos (AOF) en un hospital terciario.

Métodos: Se recolectaron retrospectivamente 120 historias clínicas de pacientes hospitalizados con uso de antibióticos y 115 historias clínicas de pacientes diagnosticados con NAC en un Departamento de Medicina Respiratoria durante los 3 meses antes y 3 meses después de usar la AOF para su evaluación.

Resultados: La tasa de cumplimiento fue del 92% y la tasa promedio de llenado de los campos de información fue del 58%. La comparación del comportamiento de prescripción de CAP en el grupo de control y de intervención mostró que la tasa de cultivo bacteriano aumentó del 70% al 77% ($p = 0,690$), en el que la tasa de cultivo antes de la administración de prescripción aumentó del 14% al 45% ($p < 0,001$), el régimen antibiótico inicial con espectro estrecho aumentó del 26% al 36% ($p = 0,353$), la proporción de pacientes que mejoraron clínicamente después de 72 horas aumentó del 64% al 89% ($p = 0,138$) y la disminución del 23% al 20% ($p = 0,713$). El fracaso del tratamiento al alta hospitalaria disminuyó del 12% al 6% ($p = 0,447$). Sin embargo, la duración del tratamiento y los días de tratamiento con antibióticos no fueron significativamente diferentes.

Conclusiones: La tasa de cumplimiento fue alta, pero la tasa de llenado de la AOF fue incompleta. Mejorar los patrones de prescripción y la eficacia del tratamiento en pacientes con NAC es una sugerencia para combinar la AOF en esfuerzos intervencionistas multifacéticos para pacientes específicos.

Palabras Clave: formulario pedido antibióticos; neumonía adquirida en la comunidad; prescribir; programa administración antibióticos; Vietnam.

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INTRODUCTION

Antibiotic resistance (ABR) has been recognized as a global health issue. Inappropriate antibiotic use is one of the major causes leading to ABR. A systematic review in 2015 indicated that inappropriate empirical antibiotic utilization rates ranged from 14.1% to 78.9% (Marquet et al., 2015).

Vietnam is one of the countries at the high alert of ABR (Bordier et al., 2018). In 2016, the Vietnam Ministry of Health (VNMOH) approved a national program in effort to prevent spread of ABR and a guideline on the implementation of “Antibiotic stewardship programs (ASP) in hospitals” (Vietnam Minister of Health, 2016). ASP is a multifaceted, multidisciplinary team approach to combat antibiotic misuse (Barlam et al., 2016).

An exclusive antibiotic order form (AOF) has been used in many hospitals worldwide since the 1980s to reduce antibiotic use and increase appropriate antibiotic use (Durbin et al., 1981; Echols et al., 1984; Boyles et al., 2013). An AOF is designed to “focus antibiotic prescribing on distinct infection episodes” (Boyles et al., 2013), in which the physicians are required to fill in patient-related, disease-related, and antibiotic-related information. A national survey of ASP in France found that 69.9% hospitals used nominative prescription and 57.8% applied nominative delivery form (Miliiani et al., 2008).

The use of AOF has been issued in a tertiary hospital since May 2019. This study aimed to evaluate compliance with AOF use and its’ impact on antibiotic use and prescribing patterns for treating community-acquired pneumonia.

MATERIAL AND METHODS

Study setting

Nguyen Tri Phuong Hospital (NTPH), the 800-bedded tertiary teaching hospital, offers medical and surgical care. In order to improve clinical pharmacy practice in NTPH, four lecturers on clinical pharmacy from Pham Ngoc Thach University of Medicine have worked as part-time clinical

pharmacists with four hospital clinical pharmacists in the Clinical Pharmacy Unit (CPU) in NTPH since January 2019. Beginning in May 2019, the study piloted the introduction of a dedicated AOF.

Antibiotic order form (AOF)

The AOF was designed after review of similar antibiotic prescription chart used in other studies (Durbin et al., 1981; Echols et al., 1984; Boyles et al., 2013) and the restricted antibiotic order form of the Ministry of Health (Vietnam Ministry of Health, 2016) and was modified by one author and underwent content validation by a peer group comprising two clinical pharmacists, one surgical physician, and one medical physician. It was pre-tested on a group of 9 patients to ensure that AOF was unambiguous and appropriate. Afterward, AOF was used in NTPH for a pilot during one month (April 2019). All feedbacks and suggestions of physicians were carefully considered to complete the final form. The final AOF was presented on a 2-side A4 page: the front side includes 4 sections (patient-related section; disease-related section; antibiotic-related section, and administrative section); while the backside presents a list of restricted antibiotics and details of risk stratification of an infectious patient (risk factors, bacterial agents, and recommended antibiotic treatment) (Fig. 1).

Physicians were asked to fill in a new AOF whenever they wanted to start/initiate antibiotic prescribing or change their antibiotics regime. The AOF was used solely for antibiotics and antifungals, but not for antiviral drugs, for both prophylactic and treatment antibiotics.

NTPH still uses a global drug dispensation for each ward daily, does not yet implement a nominative drug dispensation, and does not have electronic medical records. It means that nurses summarized daily antibiotic amounts for all patients in their ward and send it to pharmacy for validation and dispensation. Therefore, pharmacists cannot access to specific patient information and AOF before dispensing antibiotics. Pharmacy only conducts a retrospective audit for AOF use.

		<h2 style="text-align: center;">ANTIBIOTIC ORDER FORM</h2> <p style="text-align: center;">(Apply for each time starting antibiotic or changing antibiotic)</p>			Department:	
<i>Note: fields marked * are obligatory</i>						
PATIENT	Full name*:		Age:	Gender:	Medical record ID:	
	Weight:		Height:		eGFR/CrCl:	
	Allergy*: <input type="checkbox"/> No <input type="checkbox"/> Yes (specify):					
Infection	Diagnosis	<input type="checkbox"/> Pneumonia <input type="checkbox"/> Meningitis <input type="checkbox"/> Skin-soft tissue infection <input type="checkbox"/> Diuretic infection <input type="checkbox"/> Abdominal infection <input type="checkbox"/> Other (specify):				
	Indication*	<input type="checkbox"/> Prophylaxis <input type="checkbox"/> Empiric <input type="checkbox"/> Specific treatment				
	Risk stratification	<input type="checkbox"/> Community-acquired pneumonia <input type="checkbox"/> Medical-care infection <input type="checkbox"/> Hospital-acquired pneumonia				
	Clinical signs	<input type="checkbox"/> Fever..... <input type="checkbox"/> Other (specify):				
	Laboratory signs	<input type="checkbox"/> WBC..... <input type="checkbox"/> NEU..... <input type="checkbox"/> CRP..... <input type="checkbox"/> Procalcitonin..... <input type="checkbox"/> Other (specify).....				
	Culture sample	<input type="checkbox"/> Send before antibiotic prescribing <input type="checkbox"/> Send after antibiotic prescribing <input type="checkbox"/> Do not send				
	Sample	<input type="checkbox"/> Blood <input type="checkbox"/> Tissue <input type="checkbox"/> Pus <input type="checkbox"/> Sputum <input type="checkbox"/> Urine <input type="checkbox"/> Blood <input type="checkbox"/> Other(specify).....				
Culture result (attach antibiogram)	<input type="checkbox"/> Negative <input type="checkbox"/> Positive (<input type="checkbox"/> Negative Gr <input type="checkbox"/> Positive Gr)					
	Bacteria 1:		Sensitive:			
	Resistant:					
ANTIBIOTIC	Record	<input type="checkbox"/> New course <input type="checkbox"/> Change antibiotic (<input type="checkbox"/> De-escalation <input type="checkbox"/> Escalation <input type="checkbox"/> Other)				
	Antibiotic name*	Route of administration*	Dose*	Duration	Start day*	End day
Date: .../.../.....						
Physician* (sign & full name)		Head of clinical department (sign & full name)		Pharmacy Department (sign & full name)		

Figure 1. Antibiotic order form (front side).

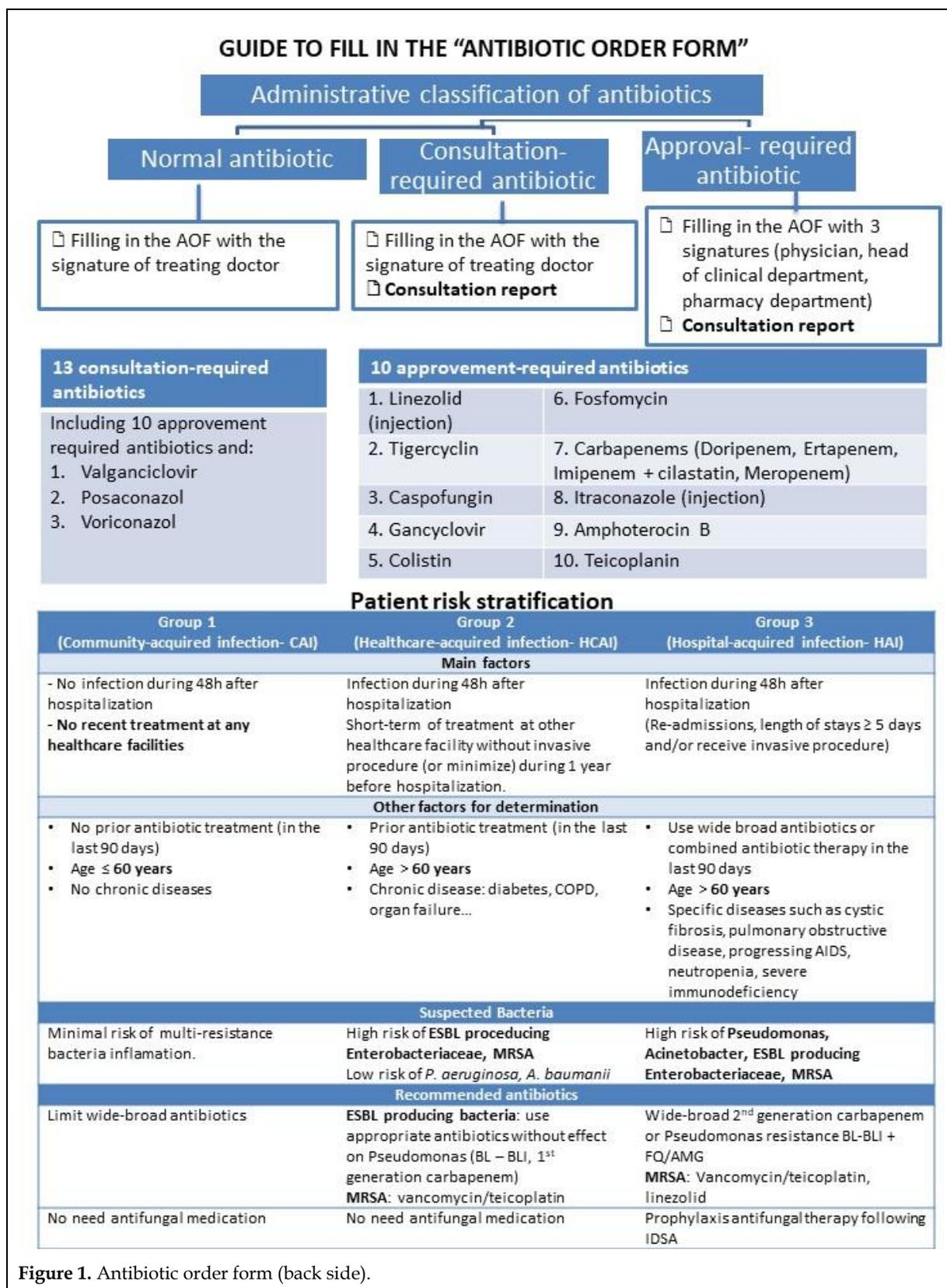


Figure 1. Antibiotic order form (back side).

Training of AOF use

A local hospital guideline of AOF use was issued and sent to each clinical ward in paper and uploaded into the hospital's intranet. Print AOFs were placed in the emergency unit and all clinical wards who prescribed antibiotics. One-hour direct training on AOF use was conducted for physicians by a senior clinical pharmacist.

Audit of AOF use

To determine compliance with AOF use, 120 medical records in which physicians prescribed antibiotics in June 2019 were collected randomly. The use of AOF when prescribing antibiotics was recorded. In addition, the rate of completion of 30 separate indicators on AOF was also assessed.

Prescribing patterns for patient with community-acquired pneumonia

To evaluate whether AOF changes physicians' prescribing patterns, a retrospective study of 54 medical records of patients with community-acquired pneumonia treated during June, July, and August 2019 (intervention period), compared to 60 medical records of the patient treated during January, February, and March 2019 (control period) was conducted.

The socio-demographic data, which was collected, comprised of age, gender. The clinical profile of patients consisted of infection-related data (CURB 65, timing of culture, culture site, Gram stain, antibiotic susceptibility testing), antibiotic treatment, and outcomes.

Ethics statement

The study was approved by the local hospital ethical review board (N87-2018/NTP-CĐT). The study was conducted in the spirit of respecting the private information related to patients and health care providers. Information, which was collected

from routine data of drug charts was anonymized.

Statistical analysis

All data were analyzed by using SPSS software version 20.0. Two means were compared by the t-test, and two percentages were compared by the Chi-squared test. The results are presented as mean \pm SD or %. $P < 0.05$ was considered statistically significant.

RESULTS

Audit of AOF implementation

In the audit of 120 patients who had been prescribed antibiotics, the rate of medical records using at least one AOF was 92%. Since one AOF was required for either starting or changing antibiotics, the required number of AOF for 120 patients was 182. However, only 162 AOFs were obtained, corresponding to 89%. The more times antibiotics were changed, the lower compliance rate of filling in AOF was obtained.

Of 30 information fields required to fill in the AOF, the fill rate of each field varied from 0% to 100%. The average fill rate was 58% for all fields. The fields most likely to be omitted from charts were "Bacterial name" (73%) and antibiogram of "Sensitivity" (79%) and "Resistance" (80%).

Prescribing patterns for the patient with community-acquired pneumonia before and after using the AOF

The characteristics of two patient groups with CAP before and after using AOF were considered similar in age, gender, and CURB 65 (Table 1).

Control of ABR depends greatly on the rational prescribing behavior of physicians. Changes in prescribing patterns between control and intervention periods were summarized in (Table 2).

Table 1. Characteristics of community-acquired pneumonia patients before and after using the antibiotic order form.

	Patient before using AOF (%)	Patient after using AOF (%)	p-value
No. of patient	60	55	
Age			
< 65	13 (22%)	21 (38%)	
≥ 65	47 (78%)	34 (62%)	
Mean ± SD	71.76 ± 15.34	67.96 ± 18.97	0.685
Gender			
Male	24 (40%)	21/55 (38%)	0.876
Female	36 (60%)	34/53 (62%)	0.900
CURB 65			
Mean ± SD	2.3 ± 0.8	2.1 ± 0.9	0.655

AOF: antibiotic order form; SD: standard deviation; CURB 65: score for severity of community-acquired pneumonia.

Table 2. Prescribing patterns and outcomes of community-acquired pneumonia patients before and after using the antibiotic order form.

Parameter/Outcome	Patient before using AOF (%)	Patient after using AOF (%)	p-value
Number of patients	60	55	
Bacteria culture	42 (70%)	42 (77%)	0.690
Obtaining culture before antibiotic administration	8 (14%)	25 (45%)	0.001*
Initial empirical antibiotic therapy			
Narrow spectrum	16 (26%)	20 (36%)	0.353
Broad spectrum	47 (74%)	35 (64%)	
Clinical improvement after 72 h	38 (64%)	48 (89%)	0.138
Changing in antibiotic	23 (38%)	16 (28%)	0.395
De-escalation	11/47 (23%)	7/35 (20%)	0.713
DOT# (mean ± SD)	12.5 ± 7.13	12.17 ± 7.27	0.351
LOT* (mean ± SD)	8.18 ± 4.32	8.08 ± 4.50	0.478
Length of stay (mean ± SD)	7.52 ± 3.22	8.57 ± 3.25	0.173
Treatment failure at discharge	7 (12%)	4 (6%)	0.447

*p < 0.05; AOF: antibiotic order form; DOT: duration of treatment; LOT: length of treatment; SD: standard deviation.

DISCUSSION

Most hospitals still have a lot of difficulties in implementing the ASP. The ASP in another Vietnamese hospital has initially shown promising results

(Nguyen et al., 2017) but impact of specific intervention of ASP is not reported. This is the first study to introduce the AOF and evaluate its impact in Vietnam.

Antibiotic order form

Since 2016, VNMOH has provided a nominative prescribing order for restricted antibiotics, and physicians have to fill in this order in order that patient's antibiotics will be reimbursed by health insurance (Vietnam Ministry of Health, 2016). However, this form still lacks some important information fields, and the information is not presented in logical clinical reasoning.

The final AOF used in NTPH was designed to print on paper, be filled by physicians whenever starting or changing any antibiotics and be inserted into patient medical records. Therefore, the antibiotic prescription form is short-formatted with many fields in check-list forms so that it does not take much time to complete. The AOF covers the main information fields for physicians' antibiotic prescribing reasoning. Each AOF was used only once, although more than one antibiotic could be prescribed simultaneously.

There were some differences between the implementation of AOFs in this study and in other studies. Firstly, solely physicians were empowered to write AOFs without other prospective audits and feedback. Secondly, there was not an automatic discontinuation after a fixed duration of antibiotics (like "after two days (prophylactic), three days (empirical), or seven days (therapeutic)" in the study of Durbin et al. (1981) or "after 2 days (prophylaxis) or five days (other indications)" in the study of Echols et al. (1984)) because the hospital ASP team did not have enough clinical pharmacists to follow up in order to prevent inadvertent or premature discontinuation. Thirdly, the limited resources of NTPH did not allow clinicians to use a nominative drug delivery for each patient. Pharmacists then cannot contribute to validate individual antibiotic therapies to prevent medication errors (Labrosse et al., 2010). Fourthly, there were no antibiotic stewardship multi-professional ward rounds like in the study of Boyles et al. (2013) though it is likely that a major factor affecting prescribing behavior change was ward round.

Audit of AOF implementation

In the similar research of Boyles et al. (2013), there was a similar high compliance rate of AOF use (92% vs. 96%). The average fill rate was 58% for all fields. Boyles et al. (2013) reported the median of unfilled fields was two per 12 fields chart (range 0-6). The fields most likely to be omitted from charts were "Bacterial name" and antibiotic of "Sensitivity" and "Resistance". These results are reasonable because most AOFs were filled in starting empiric antibiotics when lacking bacterial identification and antibiotic susceptibility testing results.

Prescribing patterns for the patient with community-acquired pneumonia before and after using the AOF

There are many metrics to study the impact of an intervention of ASPs with its own advantages and disadvantages (Morris, 2014). This study aimed to evaluate disease-specific consumption measures in order to focus more on physicians' prescribing behaviors.

Microbiological testing is an important tool in the rational prescribing of antibiotics (Giuliano et al., 2019). It is essential to carry out antibiotic-susceptibility testing because the local annual antibiogram data can guide clinicians in selecting an appropriate empirical treatment regimen for an infection (Barlam et al., 2016). There was an increase in obtaining culture (from 70% to 77%, $p = 0.690$), of which ordering culture before antibiotic administration significantly increased from 14% to 45% ($p = 0.001$). This was a positive impact since obtaining cultures prior to antibiotic administration can help physicians in identifying a causative organism, allowing potential de-escalation. If cultures are drawn after antibiotic administration, the likelihood of culture positivity is greatly reduced, which can increase the cost and length of stay for the patient (Murphy et al., 2015). Bacterial detections declined with increasing time between inpatient antibiotic administration and specimen collection (Harris et al., 2017). With using AOF, physicians were likely to order specimen collections

more promptly, preferably before antibiotics, providing data for improved antibiotic selection.

Concerning antibiotic prescribing behavior between group using AOFs compared to control groups, physicians were likely to prescribe more often a narrow spectrum on day 1 (from 26% to 36%, $p = 0.353$), and patients' clinical improvement after 72 hours was better (from 64% to 89%, $p = 0.138$). Then physicians were less likely to have to change antibiotics (from 38% to 28%, $p = 0.395$), or de-escalation (23% to 20%, $p = 0.713$). However, these changes were not statistically significantly different ($p < 0.05$).

The guidelines state that antibiotic therapy should be reassessed between 48 and 72 hours after treatment initiation in order to narrow the spectrum of antibiotics if possible (Pérut et al., 2019). Using AOFs was not likely to improve de-escalation. In a French study by Pérut et al. (2019), 44% of antibiotic therapies with a broad spectrum on day 1 benefited from a de-escalation at 72 hours, which was higher in this study. Pérut et al. concluded that clearly recorded reassessment at 72 hours was associated with de-escalation ($p = 0.025$).

Many studies confirmed that antibiotic prescribing was infrequently influenced by microbiological culture results (Maraha et al., 2000). However, in this study, using AOFs was statistically significantly associated with increasing microbiological analysis but not statistically significantly associated with antibiotic prescribing change. This finding was similar to a study by Roger et al. (2013) in which they found microbiological findings were not contributive to a modification of the initial antibiotic treatment.

There was no statistically significant difference in days of therapy (DOT), length of therapy (LOT), length of hospital stays (LOS) between the two groups. In the study of Echols et al. (1984), the introduction of the AOF showed a significant decline in the number of antibiotic treatment courses and the percentage of patients receiving any antibiotics. Durbin et al. (1981) described the use of a prescription form used exclusively for antibiotic orders in surgical and medical wards and found this

antibiotic prescribing system has a substantial impact on antibiotic use, including a decrease in prophylactic antibiotics from 68% to 60%, decrease in duration of prophylaxis from 4.9 ± 2.4 days to 2.9 ± 1.6 days. Similarly, another study in South Africa (Boyles et al., 2013), which applied an AOF, and weekly antibiotic stewardship ward rounds, represents a 19.6% decrease in volume with a cost reduction of 35% of the pharmacy's antibiotic budget.

Response to treatment of an infection can be assessed using both clinical, biochemical, and microbiological parameters. Many factors contribute to an antibiotic treatment failure at discharge (Basseti et al., 2018). The rate of antibiotic treatment failure at hospital discharge in the group using the AOF was lower compared to the control group (6% and 12%, respectively, $p = 0.447$). In another Vietnamese study, the overall treatment response rate was 87.7% (Nguyen et al., 2017).

In order to change antibiotic prescribing patterns, multifaceted interventional efforts are the need for an effective antimicrobial stewardship program (Miliani et al., 2008; Barlam et al., 2016). The sole AOF introduction as physicians' self-reflection had only a modest impact on changing prescribing behavior. The effect of organizational changes such as continuous audit and feedback, educational sessions, ward rounds, nominative drug delivery cannot be ignored.

This study remains some limitations, which need to be considered when interpreting the results. Firstly, the sample size was small but suitable for the purpose of audit and evaluation in detail of prescribing behavior related to CAP. Secondly, audit-related to filling in AOF did not evaluate whether the filled information was accurate.

CONCLUSIONS

The key finding of this study is that the introduction of a AOF itself as physicians' antibiotic prescribing reasoning had a very high compliance rate and impacted antibiotic prescribing patterns related to CAP treatment. However, change in physicians' prescribing behavior was still limited, which needs integration of the AOFs into other

interventions like multi-discipline ward rounds or retrospective audit and feedback.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTION:

Contribution	Vo DC	Mai TA	Nguyen TT	Nguyen DT	Vo TH
Concepts or ideas	x	x	x	x	x
Design	x	x	x	x	x
Definition of intellectual content	x	x	x		x
Literature search	x			x	x
Experimental studies	x			x	x
Data acquisition	x			x	x
Data analysis	x			x	x
Statistical analysis	x			x	x
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Manuscript editing	x	x	x	x	x
Manuscript review	x	x	x	x	x

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