

# Evaluation of prescription practices of antibiotics in a medium-sized Swiss hospital

Loriana Di Giammarino<sup>a</sup>, Florian Bibl<sup>a</sup>, Marco Bissig<sup>b</sup>, Beatrice Bernasconi<sup>a</sup>, Andreas Cerny<sup>a</sup>, Enos Bernasconi<sup>a</sup>

<sup>a</sup> Division of Infectious Disease and Department of Internal Medicine and

<sup>b</sup> Hospital pharmacy, Ospedale Regionale di Lugano, Switzerland

## Summary

**Background:** The use of guidelines standardises prescription practices for antibiotics against the most common infectious diseases (ID) and favours an early switch from intravenous (IV), to oral (PO) therapy. The goals of this observational study were to evaluate adherence to guidelines and streamlining of antibiotics.

**Methods:** Hospitalised patients, diagnosed with a possible ID and receiving antibiotics (ABs) for at least five days were included. Data for all patients receiving ABs in the Intensive Care Unit, medical and surgical ward were collected. The collected information was reviewed for indication of AB prescription. Patient's data were assigned into one of eight groups based on the ID diagnosis.

**Results:** Over a period of six months, 129 patients from three hospital wards were included; 124 patients with a confirmed ID diagnosis were considered for further analysis. The four most frequent diagnoses were: community acquired pneumonia, urinary tract infection, skin and soft tissue infection, and infection of surgical sites and of in-

travenous catheters; the remaining diagnoses were grouped together. Two-thirds of all antibiotics prescribed were for the four most frequent diagnoses. Overall adherence to the guidelines was 71% and was highest in the most frequent diagnostic groups (76%). Eighty-one patients (65%) received IV antibiotic treatment. Forty-seven patients (58%) had a delayed switch from IV to PO (mean delay of 5.1 days) with 240 days of cumulative delay. This delay resulted in additional pharmacy costs and supplementary hospitalisation costs.

**Conclusion:** In general there was a good adherence to the local AB guidelines but we observed an unjustified delay in the switch from IV to PO in more than half of the patients, which started an IV antibiotic treatment.

**Key words:** antibiotics; antibiotic guidelines; antibiotic switch; cost analysis; oral antibiotic administration; intravenous and oral antibiotic therapy; pharmacy costs

## Introduction

For many years, proper application of antibiotics (ABs) has been difficult to regulate and to control. Several studies have shown that administration of antibiotics was inappropriate in 22% to 65% of patients that received treatment [1, 2]. AB costs have increased dramatically over the years with an overall trend to prescribe expensive broad-spectrum rather than narrow-spectrum antibiotics [3, 4]. Clinicians were warned of the dire consequences overuse of ABs would bring; now these predictions are reality, with a multitude of antibiotic-resistant organisms and inflated hospital pharmacy costs [5]. Today, ABs are one of the most expensive drug expenditures in hospitals, accounting for 20% to 50% of total pharmacy spending [4, 6], with intravenous (IV) antibiotics accounting for the most expensive category of ABs in hospitalised patients. Furthermore, patients on IV therapy

often have prolonged hospital stays to complete antibiotic treatment; a switch from IV to oral (PO) therapy could favour an earlier discharge and directly save health care costs [7].

Various interventions including restricted AB formularies, AB control programs and improved accessibility to guidelines have been proposed to improve the use of ABs. Antibiotic guidelines have proven to be a simple, yet effective, intervention while encouraging appropriate choices of antibiotic therapies and recommending a timely switch from IV to PO therapy [8–16].

Guidelines were released in 2001, by a group of infectious disease (ID) specialists in Southern Switzerland, in order to facilitate AB choice. The intention was to standardise antibiotic prescription for the most common ID and to favour a suitable switch from IV to PO therapy. These guidelines

were printed as a small easy-to-carry booklet and handed out to physicians in all public and various private hospitals from the Italian-speaking area of Switzerland. The guidelines were introduced in our hospital with a presentation seminar and at the end of the study a feedback session was given to all involved physicians.

## Patients and methods

This prospective study was performed in a 300-bed hospital, a secondary care centre in Southern Switzerland, over a six-month period from May to October 2002. Data for all patients receiving antibiotics in the medical ward (63 beds), surgical ward (58 beds) and Intensive Care Unit (12 beds) were collected.

Patients diagnosed with a possible ID and receiving AB treatment for at least five days were included in this study. Antibiotic prescription was considered correct if there was clinical and/or radiological evidence (eg infiltrate on chest X-ray) with or without microbiological proof of bacterial infection.

Data were collected twice per week in the selected departments. Data collection included: date of hospital entrance, admission diagnosis, information concerning the ID diagnosis; microbiological results; choice, dosage and route of administration of ABs, and the time point of the switch from IV to PO treatment. Nursing charts and medical records were used to gather these data. Direct (chart statements) or indirect data (clinical, radiological, microbiological findings) were reviewed for indication of antibiotic prescription. The study team included ID specialists, ID fellows, one research nurse and the hospital pharmacist. Duration of IV therapy until the switch to PO formulation was measured and compared to the recommendations of the guidelines (table 2). The criteria for switching from IV to PO therapy were based on a consensus among ID specialists and on the literature. However, a patient was a candidate for a switch from IV to PO when a clinical improvement was observed (improvement of general conditions, decrease of body temperature and white blood count) and if the patient was able to take oral medication, assuming that oral antibiotics were available. A transition

The aims of this study were to evaluate overall adherence to the local guidelines on antibiotic therapy, and the timely switch from IV to PO therapy in a medium-sized hospital. Furthermore the potential economical impact of delayed transitional therapy from IV to PO was estimated.

to PO ABs was not expected when a patient's condition was unstable, in case of malabsorption, or impossibility of oral intake (eg patients after abdominal surgery).

Patients meeting the following criteria were excluded: under 16 years old, pregnant, concomitant antiviral, anti-fungal or anti-parasitic treatment, or incapable of oral therapy.

Patients' data were assigned to one of eight groups based on ID diagnosis: 1) community acquired pneumonia, 2) urinary tract infection, 3) skin and soft tissue infection, 4) infection of surgical sites and of intravenous catheters, 5) lower respiratory tract infection, 6) diverticulitis, 7) cholangitis, and 8) less frequent diagnosis (which were grouped together and included: hospital acquired pneumonia, bacterial peritonitis, upper respiratory tract infection, osteomyelitis, meningitis, fever of unknown origin, endocarditis and septic shock).

## Statistics

Fisher's exact test was used to calculate the difference between proportions of two categories. With one-way ANOVA, or Kruskal Wallis when appropriate, we analysed mean values of multiple groups using GraphPad Prism Software for Macintosh, version 3, S. Diego, USA. A p-value higher than 0.05 was considered statistically not significant (NS). The calculated pharmacy costs were based on the prices of acquisition of the pharmacy and expressed in Swiss Francs (1 CHF = 0.70 Euro). Drug prices and hospitalisation costs remained constant during the entire study period.

## Results

A total of 129 patients were enrolled in this study: 85 male (66%) and 44 female (34%), median age 66.4 years (16-100 y) (table 1). Five patients receiving antibiotics without any clinical or radiological sign of an ID (closed leg fracture, deep venous thrombosis, pancreas carcinoma, tongue carcinoma, asthma) were excluded from further analysis. One hundred and twenty-four patients had a diagnosis of ID and were included in the analysis. All patients were assigned to one of eight ID groups: community acquired pneumonia (29.8%), urinary tract infection (14.5%), skin and soft tissue infection (13.7%), infection of surgical sites and of intravenous catheters (8.9%), lower respiratory tract infection (6.5%), diverticulitis (5.6%), cholangitis (5.6%) and others (15.3%) (table 1). The four most frequent diagnostic

groups comprised two-thirds (67%) of patients prescribed antibiotics in this study. Considering that many patients received two or more ABs concurrently, the most frequently prescribed ABs for empirical therapy were amoxicillin/clavulanic acid (51% patients) and cefepime (43%), followed by ciprofloxacin (30%), cefazolin (17%), clarithromycin (17%), ceftriaxone (10%) and vancomycin (9%).

## Consistency with guidelines

In 71% of patients empirical AB treatment was congruent with the local guidelines (table 2); the best adherence was in the community-acquired pneumonia group with 86%, followed by 71% for skin and soft tissue infection, 67% for urinary tract infection, 64% for infections of surgical site and of

intravenous catheters and 61% for the other diagnostic groups. The difference of the consistency to the guidelines between the 4 most frequent diagnostic groups (76%) and the less common diagnostic groups (61%) was not statistically significant (table 3). Diverticulitis was the only group with a

significant difference between the prescription practice and the local guidelines, because all patients (7/7) were treated with cefazolin IV while ciprofloxacin and metronidazole PO were recommended ( $p < 0.001$ ). All patients in this group had uncomplicated diverticulitis and oral AB intake would have been possible.

**Table 1**  
Baseline characteristics and principal diagnosis of 129 patients included in the study.

Age	66.4 (16–100)
Sex	
Male	85 (66%)
Female	44 (34%)
Wards of patients recruitment n = 124	
Internal Medicine	76
Surgery	36
Intensive Care Unit	12
Principal ID diagnosis	
Community acquired pneumonia (CAP)	37 (29.8%)
Urinary tract infection (UTI)	18 (14.5%)
Skin and soft tissue infection (SSTI)	17 (13.7%)
Surgical sites and intravenous catheters infection	11 (8.9%)
Lower respiratory tract infection	8 (6.5%)
Cholangitis	7 (5.6%)
Diverticulitis	7 (5.6%)
Others	19 (15.3%)

**Switch from IV to PO therapy**

Eighty-one patients received IV therapy as initial AB treatment. This was determined as congruent with the guidelines in 54 cases (67%) and non-congruent in 27 (33%). Out of 81 patients with intravenous treatment, 34 (42%) switched to oral treatment in accordance to the local guidelines, and 47 (58%) were delayed in the transition from IV to PO. A mean delay of 5.1 days (SD 4.1) was observed for these 47 patients, while a statistical significance in the delay was observed only for urinary tract infection (table 3). Cumulatively 240 days of delayed switch from intravenous to oral treatment were calculated for these 47 patients.

**Cost analysis**

Only extra costs attributable to excessive duration of IV therapy were considered for the cost analysis. These extra costs were estimated as followed: if recommendations of guidelines have

**Table 2**  
Antibiotic recommendation for the four most frequent therapeutic groups derived from the local guidelines.

Diagnosis	Duration IV/PO/tot	Suggested empiric IV therapy		Switch to PO therapy	
		PRIMARY	ALTERNATIVE	PRIMARY	ALTERNATIVE
Community Acquired Pneumonia	2–3/8–11/10–14	Amoxicillin/clavulanic acid 2.2 g/8 h ± Clarithromycin 500 mg/12 h	Ceftriaxone 2 g/24 h ± Clarithromycin 500 mg/12 h	Amoxicillin/clavulanic acid 625 mg/8 h ± Clarithromycin 500 mg/12 h	Cefuroxime 500 mg/12 h ± Clarithromycin 500 mg/12 h
Uncomplicated Urinary Tract Infection	0/14/14			Ciprofloxacin 500 mg/12 h	
Skin and Soft Tissue Infection	5/5/10	Amoxicillin/clavulanic acid 1.2 g/8 h	Cefuroxime 1.5 g/8 h	Amoxicillin/clavulanic acid 625 mg/8 h	Cefuroxime 500 mg/12 h
Infection of Surgical Sites	5–7/5–7/10–14	Cefepime 2 g/12 h ± Metronidazole 500 mg/8 h	Piperacillin/Tazobactam 4.5 g/8 h or Imipenem 500 mg/6 h	Ciprofloxacin 500 mg/12 h + Clindamycin 300 mg/6 h	

**Table 3**  
Guidelines adherence and switch of route of administration.

Disease	No. of cases	Guideline adherence	Delayed switch IV → PO*	Mean switch delay (days)
Community acquired pneumonia (CAP)	37	86% (32/37)	38% (14/37)	3.3 (SD 3.3)
Urinary tract infection (UTI)	18	67% (12/18)	100% (6/6)	7.2 (SD 5.0)
Skin and soft tissue infection (SSTI)	17	71% (12/17)	35% (6/17)	5.8 (SD 3.1)
Infection of surgical sites and of intravenous catheters (ISSIV)	11	64% (7/11)	27% (3/11)	9 (SD 11.3)
Other diagnostic groups	41	61% (25/41)	44% (18/41)	5.4 (SD 2.3)
Total	124	71% (88/124)	58% (47/81)	5.1 (SD 4.1)

\* Between UTI and the 4 groups is a significant difference in switch delay (CAP  $p = 0.006$ , SSTI  $p = 0.009$ , ISSIV  $p = 0.006$ , others  $p = 0.012$ )

been followed in all patients, the hospital pharmacy would have had a pure AB cost saving of 7984 CHF for 240 days of delayed AB switch for 47 patients.

In this estimation we did not take into account several hidden, but important factors contributing to the total cost of antibiotic therapy: cost of each intravenous infusion equipment, nurses' workload, direct and indirect charges for therapeutic monitoring of antibiotics, and costs related to adverse effects of IV administration.

As a maximum theoretical estimate of cost analysis one could assume that every day of unjustified IV therapy causes an additional day of hospitalisation. Since the cost of one day of hospitalisation was 630 CHF (for a common bed in the medical or surgical department), the 240 cumulated days of delayed IV to PO adjustment, resulted in an excess hospitalisation cost of 153'720 CHF.

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## Discussion

This study, performed one year after the introduction of local guidelines, demonstrates a generally good adherence to local AB guidelines (71%), as previously reported from similar hospital settings. Berild et al. [8] indicated in a point-prevalence investigation, conducted 18 months after the introduction of guidelines, that compliance was more than 95%. Similarly, Lutters et al. [17] showed in an interventional cohort study that, after an intensive intervention period consisting of a physicians' educational program, the guidelines were correctly implemented in 75% of surveyed patients.

However, unlike Moss et al. and Bugnon-Reber et al. [18, 19] who found 47% AB misuse overall after the distribution of guidelines, this study found that only a small minority of patients (3.9%) received ABs despite a lack of indication. This surprisingly low number of AB misuse could be explained through our inclusion criteria, ie patients >5 days on an AB treatment. In fact, ID physicians are frequently involved in the discussion of unclear cases and only few patients will remain more than 2-3 days on an AB treatment that is not indicated. However, the results suggest that guidelines had an impact on the choice of the antibiotic drug, but showed only a limited effectiveness in prompting a switch from IV to PO therapy. Indeed, with the exception of community-acquired pneumonia, where the switch was made faster in comparison to the other ID diagnoses (3.3 versus up to 9 days), 47 out of 81 patients (58%) with various ID diagnoses had a delay in switching from IV to PO formulations. Although the relationship between duration of IV AB therapy and length of hospital stay is well recognized, in this study the delayed switch produced additional costs of more than 150000 CHF, which corresponds to nearly 3300 CHF for each of the 47 patients, per hospitalisation [9, 20]. These results concur with findings in comparable studies, where savings from 450 CHF to 6500 CHF per patient were achieved with a timely transition from IV to PO therapy [20-23]. Savings were achieved through reduced costs for oral antibiotics and due to a shortened pe-

riod of hospitalisation. Since there is a compelling reason to change the current prescribing practice, an important question to ask is: how can these practices be altered? Physician education alone is generally not effective [24]. Control of antibiotic use seems to require a multidisciplinary approach involving ID physicians, microbiologists, pharmacists and administrators. However, no consensus has been reached regarding which intervention is the most feasible and most effective to change AB use [25-28]. A recent review of 25 years experience in improving physicians knowledge of how to use ABs, showed some encouraging trends, but more detailed economic assessments are needed to determine the most cost-effective approaches for settings with constrained resources [29]. Interestingly, more than two-thirds of all antibiotic prescriptions in this study were found in four diagnostic groups. In all probability, a strict surveillance of these patient groups could help to avoid possible switch delays resulting in a reduction of pharmacy costs and length of hospital stay.

Some of the limitations of this study were its short-term design (6 months) and absence of control data on prescribing habits of physicians prior to the introduction of the guidelines. However, the most important wards of the hospital, in terms of capacity and patient turnover, were considered; and the observation time was long enough to evaluate a considerable number of patients.

In conclusion, this study showed a good adherence to the local AB guidelines in terms of a correct empirical antibiotic therapy choice, but showed an unjustified delay in the switch from IV to PO therapy. However, the best method for assisting clinicians to optimise the timing of the switch from IV to PO AB therapy is not yet determined but the presence of local AB guidelines together with ID consultants or clinical pharmacists are a potential aid for significant reduction of hospital AB cost. Adequate antibiotic prescription practice and a timely switch to PO formulations can be obtained with these interventions in conjunction with a narrow surveillance of the most common IDs.



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### Correspondence:

Enos Bernasconi MD  
Division of Infectious Diseases  
Ospedale Regionale di Lugano  
Via Tesserete 46  
CH-6903 Lugano, Switzerland  
E-Mail: enos.bernasconi@eoc.ch

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