International Journal of Antimicrobial Agents 46 (2015) 428–433

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

# Earlier switching from intravenous to oral antibiotics owing to electronic reminders☆,☆☆

Patrick E. Beeler[a], Stefan P. Kuster[b], Emmanuel Eschmann[a], Rainer Weber[b], Jürg Blaser[a,*]

[a] Research Center for Medical Informatics, University Hospital Zurich and University of Zurich, Zurich, Switzerland
[b] Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich and University of Zurich, Zurich, Switzerland

ARTICLE INFO

*Article history:*
Received 27 April 2015
Accepted 17 June 2015

*Keywords:*
Anti-infective agents/administration & dosage
Decision support systems, clinical
Medical informatics, reminder systems
Antibacterial agents

ABSTRACT

Paper-based interventions have been shown to stimulate switching from intravenous (i.v.) to oral (p.o.) antibiotic therapies. Shorter i.v. durations are associated with a lower risk of iatrogenic infections as well as reduced workload and costs. The purpose of this study was to determine whether automated electronic reminders are able to promote earlier switching. In this controlled before-and-after study, an algorithm identified patients who were eligible for i.v.-to-p.o. switch 60 h after starting i.v. antimicrobials. Reminders offering guidance on the re-assessment of initial i.v. therapy were displayed within the electronic health records in 12 units during the intervention period (year 2012). In contrast, no reminders were visible during the baseline period (2011) and in the control group (17 units). A total of 22 863 i.v. antibiotic therapies were analysed; 6082 (26.6%) were switched to p.o. therapy. In the intervention group, 757 courses of i.v. antibiotics were administered for a mean ± standard deviation duration of 5.4 ± 8.1 days before switching to p.o. antibiotics in the baseline period, and 794 courses for 4.5 ± 5.5 days in the intervention period ($P = 0.004$), corresponding to a 17.5% reduction of i.v. administration time. In contrast, in the control group the duration increased; 2240 i.v. antibiotics were administered for a mean duration of 4.0 ± 5.9 days in the baseline period, and 2291 for 4.3 ± 5.8 days in the intervention period ($P = 0.03$). Electronic reminders fostered earlier i.v.-to-p.o. switches, thereby reducing the duration of initial i.v. therapies by nearly a day.



## 1. Introduction

Studies have shown that antimicrobial therapies among hospitalised patients are inappropriate 30–50% of the time [1–4]. Antimicrobial stewardship programmes intend to optimise the use of antimicrobial agents, curb resistance, minimise the risk of adverse effects and reduce costs [2,4].

One strategy to improve antimicrobial regimens is earlier switching from an intravenous (i.v.) to an oral (p.o.) route of administration [4,5]. Such i.v.-to-p.o. switches are often considered ca. 3 days after starting empirical therapy if the patient is clinically stable and is able to swallow [6,7]. Changing the administration route may be performed while ordering the same or a different antimicrobial agent, depending on the microbiological susceptibility results. Important advantages associated with an early i.v.-to-p.o. switch include a lower risk of catheter-associated infections, reduced nursing workload, and decreased direct and indirect costs [5,7–9]. A number of studies have demonstrated reduced durations of initial i.v. therapies owing to paper-based checklists fostering the i.v.-to-p.o. switch [9–11].

Dellit et al. [4] and Pestotnik [12] summarised the literature on computer-based decision support for antimicrobial stewardship purposes. One study investigated a commercial decision support system that generated various alerts to reduce inappropriate antimicrobial use, e.g. suggested switches to equivalent p.o. agents [13]. Other investigators presented a sophisticated algorithm that recommended the p.o. administration route for quinolones in some patients, and successfully increased the use of p.o. administration of levofloxacin and ciprofloxacin [14]. Shojania et al. displayed

☆ Parts of the data were presented during an oral presentation at the Swiss eHealth Summit 2014, 8–9 September 2014, Bern, Switzerland; and an abstract was presented at the American Medical Informatics Association (AMIA) 2014 Annual Symposium, 15–19 November 2014, Washington, DC.

☆☆ ClinicalTrials.gov identifier: NCT01499927.

* Corresponding author. Present address: Research Center for Medical Informatics, Directorate of Research & Education, University Hospital Zurich, University of Zurich, Moussonstrasse 2, CH-8091 Zurich, Switzerland. Tel.: +41 44 255 3618; fax: +41 44 634 5503.
*E-mail address:* juerg.blaser@usz.ch (J. Blaser).

http://dx.doi.org/10.1016/j.ijantimicag.2015.06.013
0924-8579/

guidelines at the time of computerised physician order entry and thereby reduced the duration of i.v. vancomycin [15].

The aim of the present clinical trial was to encourage early i.v.-to-p.o. switch using computerised clinical decision support (CDS) in order to reduce the duration of initial i.v. antimicrobials. Since 'alert fatigue' is a well known issue in electronic approaches [16], the algorithm featured enhanced specificity by checking in real time whether patient parameters allowed for switching from i.v. to p.o. therapy.

## 2. Materials and methods

### 2.1. Design and site

The study was designed as a prospective, controlled, before-and-after trial. The baseline period lasted from 1 January 2011 to 31 December 2011 and the intervention period from 1 January 2012 to 31 December 2012. These study periods were defined in order to mitigate seasonal influences on infectious diseases [17]. No reminders were displayed during the baseline period and in the control group. In the intervention group, reminders were activated at the beginning of the intervention period.

The University Hospital Zurich (Zurich, Switzerland) has ca. 850 beds and covers all specialties except for orthopaedic surgery and paediatrics. All inpatients receiving i.v. antimicrobials ordered via computerised physician order entry were included. A total of 29 units of the hospital cared for inpatients during the study periods.

Allocation of the 29 inpatient units to either the intervention or the control group was based on feasibility and safety considerations by infectious diseases specialists. Twelve units served as the intervention group (angiology, cardiology, endocrinology & diabetology, gastroenterology, immunology, infectious diseases, internal medicine, nephrology, neurology, pulmonology, rheumatology and urology) and seventeen as the control group (abdominal surgery, cardiac & vascular surgery, dermatology, gynaecology, haematology, neonatology, neuroradiology, neurosurgery, obstetrics, oncology, ophthalmology, oral & maxillofacial surgery, otolaryngology, radiation oncology, reconstructive surgery, thoracic surgery and traumatology). It was clear from the beginning that the two study groups would not be comparable due to differences between the patient populations. We controlled for this issue by comparing the baseline period with the intervention period in both study groups separately.

The Ethics Committee of the University Hospital Zurich approved the study, and patient consent was waived. Under consideration of anticipated improvements due to the intervention (increased patient safety and reduced workload and costs) [2,4,5,7–9] and of available studies with similar interventions that reported no higher incidence of adverse events [9,11,13,18], a waiver for informed consent was requested because (i) limiting the study to patients who could give informed consent would decrease the generalisability of the results and (ii) even attempting to obtain informed consent from such a large number of patients would result in financial costs that are prohibitive and a potentially poor use of limited resources. The study was registered at ClinicalTrials.gov (NCT01499927).

### 2.2. Clinical information system

Inpatient care is comprehensively documented and managed by the clinical information system (KISIM; Cistec AG, Zurich, Switzerland), including all pharmacological therapies, other treatments and diagnostic procedures on all wards except for intensive care units.

### 2.3. Computerised reminders

At 60 h after the start of an i.v. antimicrobial therapy, an algorithm automatically checked whether: (i) the therapy was scheduled for an additional 24 h or longer; (ii) the neutrophil count of the patient exceeded $0.5 \times 10^9$ cells/L; (iii) the body temperature was <38 °C; and (iv) the patient had the ability to swallow as indicated by orders of p.o. medication. If the conditions were met, a non-interruptive reminder was displayed as a red bar within the top section of the electronic health record.

By clicking on the reminder bar, a window appeared offering guidance on whether or not an i.v.-to-p.o. switch was appropriate: At first, the window contained a short explanation of why the reminder was displayed. Further, it recommended re-assessing the initial i.v. treatment under consideration of five suggestions: (i) switching from i.v. to p.o. therapy; (ii) narrowing the antimicrobial spectrum; (iii) stopping the antimicrobial treatment if no longer indicated; (iv) no change; or (v) consulting an infectious diseases specialist. Finally, a table listed the need-to-knows about the advantages of i.v.-to-p.o. switches, when a switch was possible, and also contraindications to switch.

The reminder was displayed in the electronic health record from 60 h onwards until a physician acknowledged the notification or the i.v. therapy triggering the reminder was stopped. However, the reminder was automatically terminated 10 days after it appeared. Therefore, the immediate influence of the reminders is considered to be reflected by i.v.-to-p.o. switches during the time frame of 60–300 h.

### 2.4. Definition of 'switch'

Antimicrobials were defined using the Anatomical Therapeutic Chemical (ATC) classification system of the World Health Organization (WHO). Drug orders according to ATC codes of the categories J01 (antibiotics), J02 (antifungals), J04 (antimycobacterials) and J05 (antivirals) were included.

The only 'antimycobacterial' ordered was rifampicin. However, i.v. rifampicin—switched to p.o. in the process—was always used, and therefore considered, as an antibiotic and was never prescribed for the treatment of tuberculosis or leprosy during the study.

At the end of an i.v. antimicrobial therapy, the time frame 'i.v. stop time ±12 h' was used to check for an 'p.o. start time': if the stopped i.v. therapy and the starting p.o. therapy were among the same ATC category, then an i.v.-to-p.o. switch had been performed by definition. Durations of i.v. and p.o. administrations were only considered throughout the hospital stay.

### 2.5. Statistics

Continuous variables are presented as the mean ± standard deviation. Comparisons of the duration of therapy and tests of Kaplan–Meier curve differences were performed using the log-rank test. *P*-values of ≤0.05 were considered statistically significant. Kaplan–Meier curves were plotted for i.v.-to-p.o. switches that reflected the reminders' impact, i.e. within the time frame 60–300 h.

The primary endpoint was the duration of i.v. administration of antimicrobial therapies until switching to p.o. administration. Secondary analyses included changes in numbers and durations of switched antibiotics. Furthermore, secondary endpoints were i.v.-to-p.o. switches within 60–300 h in the years 2011 and 2012.

Calculations were performed using R v.3.0.2 (R Foundation for Statistical Computing, Vienna, Austria).