Evaluation of intravenous to oral antimicrobial switch at a hospital with a tightly regulated antimicrobial stewardship program

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Abstract

Timely intravenous (IV) to oral antimicrobial switch (IV-oral-switch) is a key antimicrobial stewardship (AMS) strategy. A retrospective audit was undertaken to determine concordance with IV-oral-switch guidelines in the context of a long-standing, tightly regulated AMS program. Data from 107 general medical and surgical patients in an Australian hospital were analysed. Median duration of IV antimicrobial courses before switching to oral therapy was 3 days (interquartile range, 2.25-5.00). Timely IV-oral-switch occurred in 57% (n=61) of patients. The median delay to switching was 0 days (IQR 0 to 1.25). In most courses (92/106, 86.8%), the choice of oral alternative after switching was appropriate. In 45% (47/105) of courses, total duration of therapy (IV plus oral) exceeded the recommended duration by >1.0 day. Excessive IV antimicrobial duration was uncommon at a hospital with a tightly regulated AMS program. Total duration of therapy was identified as an AMS target for improvement.

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What is already known about this subject:

Timely intravenous (IV) to oral antimicrobial switch (IV-oral-switch) has proven benefits for patients and hospitals. However, timely IV-oral-switch only occurs in approximately half of eligible patients.

Previous studies examining strategies to improve IV-oral-switch were typically undertaken shortly after IV-oral-switch interventions were implemented. It is not known whether the reported benefits reflect longer-term outcomes, especially in the context of a long-standing, tightly regulated antimicrobial stewardship (AMS) program.

What this study adds:

- Our results suggest a multifaceted AMS approach that includes guidelines and a preauthorisation system with short duration of approvals for target antimicrobials is associated with sustained good IV-oral-switch practice.
- The total duration of therapy (IV plus oral) was identified as an area for improvement.

Abstract

Timely intravenous (IV) to oral antimicrobial switch (IV-oral-switch) is a key antimicrobial stewardship (AMS) strategy. A retrospective audit was undertaken to determine concordance with IV-oral-switch guidelines in the context of a long-standing, tightly regulated AMS program. Data from 107 general medical and surgical patients in an Australian hospital were analysed. Median duration of IV antimicrobial courses before switching to oral therapy was 3 days (interquartile range, 2.25-5.00). Timely IV-oral-switch occurred in 57% (n =61) of patients. The median delay to switching was 0 days (IQR 0 to 1.25). In most courses (92/106, 86.8%), the choice of oral alternative after switching was appropriate. In 45% (47/105) of courses, total duration of therapy (IV plus oral) exceeded the recommended duration by >1.0 day. Excessive IV antimicrobial duration was uncommon at a hospital with a tightly regulated AMS program. Total duration of therapy was identified as an AMS target for improvement.

Main text

Introduction

Timely intravenous (IV) to oral antimicrobial switch (IV-oral-switch) is a well-studied antimicrobial stewardship (AMS) activity to optimise prescribing, recommended in best-practice guidelines because of its proven benefits to the patient and hospital (reduced IV line-related complications, antimicrobial costs and length of hospital stay) [1],[2]. Despite its effectiveness and safety, international studies have demonstrated that timely switch only occurs in approximately half of eligible hospitalised patients [3, 4, 5, 6].

Previous studies examining strategies to improve IV-oral-switch were typically undertaken immediately or shortly after IV-oral-switch interventions were implemented or without providing details of existing over-

arching AMS programs [3, 4, 5]. It is not known whether the reported benefits reflect longer-term outcomes or whether they are applicable to settings with an existing AMS program.

Austin Health, a tertiary public hospital in Melbourne, Australia, has a long-established interdisciplinary AMS program that includes strategies to support IV-oral-switch. Included in this program are formulary restrictions requiring preauthorization for target antimicrobials (e.g. broad-spectrum agents) that limits empiric therapy to two or three days after which a new authorisation is required. Such a system encourages early re-assessment and consideration of key AMS interventions (IV-oral-switch, de-escalation or discontinuation of therapy). The preauthorization system is a combination of phone approval via an Infectious Diseases (ID) physician and computerised approval [7], with daily oversight from ID pharmacists. Since November 2017, the AMS program also included a local IV-oral-switch guideline and pocket-sized summary cards for clinicians outlining criteria for IV-oral-switch and recommendations for oral alternatives (Supplement).

The aim of this study was to explore concordance with IV-oral-switch guidelines in the context of a long-standing, tightly regulated AMS program.

Methods

A retrospective review of general medical and surgical patients on four wards prescribed one or more IV antimicrobials for [?]48 hours was undertaken over two months (29 October to 21 December 2018). Patients were identified via electronic prescribing records and excluded if: antimicrobial(s) were prescribed for a non-infective condition; infection required a prolonged course of IV treatment (e.g. endocarditis); patient unable to take oral therapy or no oral option available; patient transferred to another ward, hospital or outpatient parenteral antimicrobial therapy; or patient died during IV antimicrobial therapy.

An IV antimicrobial course was defined as receiving one or more IV antimicrobials. If the timing of IV-oral-switch was deemed inappropriate for one agent in a combination, the entire course was considered inappropriate.

Data was collected from patients' electronic medical records and included: variables listed in the IV-oral-switch guideline (Supplement), infection type, antimicrobial(s) prescribed, antimicrobial allergy history, microbiology test results and total duration of therapy (IV plus oral). The timing of IV-oral-switch, choice of oral antimicrobial(s), and total duration of therapy were assessed by an ID pharmacist and ID physician against local and national antimicrobial prescribing guidelines [8].

The primary outcome was the proportion of patients switched to oral antimicrobial(s) within 24 hours of meeting switch criteria. Secondary outcomes were: median number of days of IV antimicrobial(s) before IV-oral-switch, time delay to switch (difference in days between the actual switch date and 24 hours after meeting switch criteria), appropriateness of choice of oral alternative(s), and total duration of antimicrobial therapy (IV plus oral). All outcomes were compared across medical and surgical patients to identify differences in IV-oral-switch and total duration of therapy. Statistical analyses were performed using Microsoft Excel (2016) and Stata version 15. Ethical approval was obtained from the Austin Health Human Research Ethics Committee (LNR/18/Austin/369) and Monash University Human Research Ethics Committee (18733).

Results

One hundred and sixty-one IV antimicrobial courses of [?]48-hour duration were screened, with 107 courses in 107 patients eligible for the study (Figure 1). Characteristics of patients and antimicrobial use are shown in Table 1.

IV-oral-switch occurred within 24 hours of meeting switch criteria in 61/107 (57%) patients. The median duration of IV antimicrobial courses before IV-oral-switch was 3 days (IQR, 2.25 to 5.0). The median delay to switching was 0 days (IQR 0 to 1.25). In the patients who did not receive timely IV-oral-switch (n =46), the median delay to switching was 1.75 days (IQR 1.0 to 2.25). Data on primary and secondary outcomes measures, and comparisons between medical and surgical patients, are shown in the Table 2.

Discussion

Our study demonstrates that in a setting with a long-standing AMS program the median duration of IV antimicrobial use was short (3 days) and a majority of patients (57%) received timely IV-oral-switch. Although a substantial proportion (43%) did not receive timely IV-oral-switch, the excess IV treatment duration in these patients was typically short (median 1.75 days). Results for general medical and surgical patients were similar.

Numerous IV-oral-switch studies have been conducted in similar patient groups, however many were undertaken over two decades ago when AMS programs were in their infancy. Two recent studies examined IV-oral-switch in patient populations similar to ours. Mouwen *et al.* reviewed 138 (84 pre- and 54 post-intervention) surgical patients to evaluate a combination of interventions to improve IV-oral-switch. Interventions included educating physicians via a single presentation, provision of pocket-sized cards containing a flowchart of switch criteria plus additional information (e.g. indications for prolonged IV therapy), and switch advice in the electronic prescribing record [9]. The percentage of courses with timely IV-oral-switch and the median duration of IV therapy improved significantly following intervention (from 35.4% to 67.7%, and 5 to 3 days, respectively). Sze and Kong reviewed 148 medical patients (72 pre-and 76-post intervention) to evaluate printed IV-oral-switch guidelines and recommendations attached to the medical notes of patients on the day they became eligible for switch [10]. The proportion of IV-to-oral switches that occurred in a timely manner significantly increased from 24.1% to 88.3% post-intervention, and delays to switching (mean days between switch and when switch criteria were met) fell from 1.8 days to 0.2 days. The median duration of IV therapy was also significantly shorter, falling from 4.1 to 2.8 days. In our study, the median duration of IV therapy was shorter than the baseline (pre-intervention) findings of these two recent studies (3.0 days versus 4.1-5.0 days), and comparable to their post-intervention findings (3.0 days versus 2.8-3.0 days). The percentage of courses switched in a timely manner approximated the post-intervention results of Mouwen *et al.* [9] but was lower than that of Sze and Kong [10]. A limitation of Sze and Kong's study, however, is that the post-intervention data collection occurred immediately after implementation of IV-oral-switch interventions, so the longer-term effects are unknown.

To the best of our knowledge ours is the first study to examine usual practice within a long-standing environment of tightly regulated AMS and IV-oral-switch guidelines. Our findings are important given post-intervention audits in previous studies were undertaken soon after IV-oral-switch interventions were implemented and thus may not reflect longer-term outcomes. This is illustrated by findings from van Niekerk*et al.* who reported that a significant improvement in timely IV-to-oral switch after implementation of an IV-oral-switch guideline (from 16%, 19/119 to 43%, 47/107) was not sustained three months later, when IV-oral-switch rates had returned close to the pre-intervention level (20.8%, 25/120) [11].

A limitation of our study was the lack of a comparison group not exposed to our AMS program. We are unable to ascertain which element(s) of our multi-faceted AMS approach contributed to the findings of generally short IV treatment duration and timely IV-oral-switch. Studies have shown improved IV-oral-switch practice with a combination of interventions including prescriber education, printed guidelines inserted in patients' case notes, reminder stickers on medication charts, prospective audit and feedback and electronic alerts [3], [5], [9, 10, 11, 12, 13]. Unfortunately, few IV-oral-switch studies have described what AMS programs were already in place prior to the IV-oral-switch intervention, making comparisons difficult. Given that the two most commonly prescribed IV antimicrobials in our study (ceftriaxone and amoxicillin-clavulanate) were agents requiring prior approval before prescribing, it's likely our preauthorization system (with time-limited approvals) helped ensure IV-oral-switch was considered by day 2–3 of therapy. Preauthorization has been shown to optimise empiric choices, reduce antibiotic use and costs, increase rates of susceptible pathogens and decrease rates of*Clostridioides difficile* infection [14], [15]. However, to the best of our knowledge no studies have specifically examined preauthorization as a strategy to improve other AMS targets such as timing of IV-oral-switch.

An interesting finding of our study concerns the total duration (IV plus oral) of antimicrobial therapy. There is growing evidence that shorter therapy durations are as effective as longer durations for common infections [16]. We found that 45% of patients received an excessive total duration of therapy, and this may underesti-

mate the magnitude of this issue. For example, at the time of our study national antimicrobial prescribing guidelines recommend seven days of treatment for community-acquired pneumonia (CAP) [8]. However, these guidelines recently changed to incorporate a shorter duration of five days for mild to moderately severe CAP based on recent evidence [17, 18]. There were fifteen (14.0%) patients with CAP in our cohort that received antibiotic treatment for a median of seven days. Longer durations of therapy are associated with increased risk of antimicrobial resistance, secondary infections and greater costs [19, 20, 21]. Therefore, future AMS activities should incorporate the most recent evidence for treatment duration to further optimise therapy and reduce associated hazards.

In summary, the practice of IV-oral-switch at our hospital was generally concordant with guidelines, suggesting that a tightly regulated AMS program with preauthorisation for target IV antimicrobials may lead to sustained good IV-oral-switch practice. Total duration of therapy was identified as an AMS target to improve antimicrobial prescribing and patient safety.

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4. **Data availability statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.
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Table caption: Table 1: Characteristics of patients and antimicrobial use

Characteristic (n=107)
Age (years), median (IQR)
Gender, n (%) female
Clinical unit, n (%) Medical Surgical
Infection type (n=112) (%) intra-abdominal lower respiratory tract urinary tract skin and soft tissue prophylaxis gastro-inte
Intravenous antimicrobials (n=164) (%) ceftriaxone amoxicillin-clavulanate metronidazole benzylpenicillin cefazolin azithron

Table caption:

Table 2: Timeliness and appropriateness of IV-oral-switch, and total duration of therapy

Variable	All patients N=107 courses	Medical N=63 courses	Surgical N=44 courses	P-value (medical vs. surgical)
Patients switched from IV to oral antimicrobial within 24 hours of meeting IV-oral-switch criteria, n (%)	61 (57.0)	35 (55.5)	26 (59.0)	0.71[a]

Variable	All patients N=107 courses	Medical N=63 courses	Surgical N=44 courses	P-value (medical vs. surgical)
Duration (days) of IV antimicrobial, median (IQR)	3.0 (2.25 to 5.00)	3.0 (2.25 to 5.00)	3.0 (2.75 to 4.50)	0.44[b]
Time delay to switch (days), median (IQR)	0 (0 to 1.25)	0 (0 to 1.75)	0 (0 to 1.00)	0.55[b]
Time delay (days) to switch in subgroup that did not switch within 24 hours of meeting switch criteria, median (IQR)	1.75 (1.00 to 2.25) (*n*=46)	2.0 (1.00 to 2.75) (*n*=28)	1.25 (1.00 to 2.00) (*n*=18)	0.30[b]
Patients prescribed an inappropriate choice oral alternative after switching, n (%)	14 (13.2) (*n*=106) *	9 (14.3%) (*n*=63)	5 (11.6%) (*n*=43)	0.69[a]
Total duration (days) of antimicrobial therapy (IV plus oral), median (IQR)	9.0 (7.00 to 12.75) (*n*=105) ^	9.5 (7.00 to 12.25) (*n*=61)	9.5 (7.25 to 12.75) (*n*=44)	0.69[b]
Proportion of courses where the total duration of therapy (IV plus oral) exceeded the recommended duration by >1.0 day, n (%)	47/105 (44.8%) (*n*=105) ^	22 (36.1%) (*n*=61)	25 (56.8%) (*n*=44)	0.03[a]
[a] Chi-square test; [b]Mann-Whitney U-test. Statistical significance was set at $p < 0.05$. * Denominator is 106 because one eligible patient was not switched to oral therapy. ^ Denominator is 105 because two patients were switched to prolonged oral therapy.	[a] Chi-square test; [b]Mann-Whitney U-test. Statistical significance was set at $p < 0.05$. * Denominator is 106 because one eligible patient was not switched to oral therapy. ^ Denominator is 105 because two patients were switched to prolonged oral therapy.	[a] Chi-square test; [b]Mann-Whitney U-test. Statistical significance was set at $p < 0.05$. * Denominator is 106 because one eligible patient was not switched to oral therapy. ^ Denominator is 105 because two patients were switched to prolonged oral therapy.	[a] Chi-square test; [b]Mann-Whitney U-test. Statistical significance was set at $p < 0.05$. * Denominator is 106 because one eligible patient was not switched to oral therapy. ^ Denominator is 105 because two patients were switched to prolonged oral therapy.	[a] Chi-square test; [b]Mann-Whitney U-test. Statistical significance was set at $p < 0.05$. * Denominator is 106 because one eligible patient was not switched to oral therapy. ^ Denominator is 105 because two patients were switched to prolonged oral therapy.

Figure legends:

Figure 1: Identification of patients eligible for review

Supplementary information: Austin Health's 'Early switch from intravenous to oral antimicrobials: IV-STOP' flowchart