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Early switch from intravenous to oral antibiotics: guidelines and implementation in a large teaching hospital

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In recent years 'switch therapy' has been advocated: short intravenous antibiotic therapy, for 2–3 days, followed by oral treatment for the remainder of the course. Little is known about the number of patients that could benefit from early switch therapy and the consequences of introducing this strategy in everyday practice. We prospectively registered all antibiotic courses on wards for Internal Medicine, Surgery, and Pulmonology during a 2 month period, before (*n* = 362, inventorial phase) and after (*n* = 281, implementation phase) the introduction of guidelines for switching therapy. Approximately 40% of all patients who started on iv antibiotics were candidates for an early iv–oral switch. During the inventorial phase, 54% (52/97) of eligible patients were switched to oral treatment, after a median of 6 days (range 2–28 days). After implementation of the guidelines, this percentage rose to 83% (66/80) (difference 29%, 95% CI 16–42%; *P* < 0.001). Therapy was also switched earlier, after a median of 4 days (range 2 to 16 days). In the 6 weeks after completion of the oral course, recurrence of infections, or readmissions due to reinfections did not occur. Compared with the inventorial phase, 43% of iv administrations could be avoided, that is >6000 per year. This means a potential annual reduction of dfl.60,000 (*c.* US$30,000) of administration costs. The potential savings in purchase costs of the antibiotics were dfl.54,000 (US$27,000) annually. In conclusion, a substantial number of patients starting on iv antibiotics were candidates for an early iv–oral switch. The guidelines were well accepted by the physicians and substantial savings in costs and nursing time were achieved.

Introduction

For serious infections most clinicians consider intravenous administration as the preferred route for administering antibiotics. However, in recent years several authors have advocated a regimen of relatively short intravenous therapy—2–3 days—followed by oral treatment for the remainder of the course: 'switch therapy' or 'sequential antibiotic therapy'.[1–3] Switch therapy has become feasible through the development of antibiotics with reliable absorption, providing adequate blood levels. Examples are a number of third-generation cephalosporins (cefixime, cefpodoxime), claritromycin, quinolones, and fluconazole. There are also a number of older antibiotics with good bioavailability. Advantages of an early iv–oral switch are a decreased risk of infection of the iv catheter, increased comfort and mobility for the patient, and the possibility of earlier discharge from the hospital. Oral therapy is less labour intensive for the nursing staff, and economic benefits are clear, since preparation and administration costs are smaller. In addition, the acquisition costs for iv formulations are usually substantially greater than those of the oral form.[1]

A large number of comparative clinical trials have been performed, randomizing patients between iv therapy for the entire treatment course, and iv therapy for a few days

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followed by oral therapy.[4–15] All studies reported equal efficacy for the two treatment strategies. A number of recent reviews have therefore concluded that the evidence available clearly supports the use of 'early switch therapy'.[1–3,16]

Little is known, however, about the number of patients that could benefit from early switch therapy, and the consequences of introducing this strategy in daily practice. After documenting the baseline situation, guidelines for switching from iv to oral therapy were introduced in our hospital. We report the results of the implementation of these guidelines with regard to the number and characteristics of patients that were candidates for an early iv–oral switch, acceptance rate of the guidelines, long-term results, and potential savings obtained.

Materials and methods

Development of guidelines for iv–oral switch

In accordance with the literature[1,3,16–20] the members of the study group proposed the following guidelines for iv–oral switch after at least 48–72 h of iv therapy:

(1) The patient should be haemodynamically stable. The condition of the patient should be improving, with a trend towards normalization of the body temperature and the peripheral leucocyte count.

(2) With the oral regime adequate drug levels can be attained at the site of infection. This means that oral therapy is usually not possible in the case of meningitis, intracranial abscesses, endocarditis, mediastinitis, legionella pneumonia and exacerbations of cystic fibrosis, inadequately drained abscesses and empyema, severe soft tissue infections such as group A streptococcal infections, infections of foreign bodies, e.g. iv catheters, and *Staphylococcus aureus* or *Pseudomonas aeruginosa* bacteraemia. Treatment for liver abscesses, adequately drained abscesses and empyemas, osteomyelitis, and arthritis can be changed to oral therapy after $\geqslant$2 weeks of iv therapy. Oral therapy is not advisable for severe infections during chemotherapy-related severe neutropenia.

(3) The patient must be able to take oral medication and must have a functioning gastrointestinal tract, without signs of malabsorption. In the use of calcium- or magnesium-containing antacids, or sucralfate, the uptake of quinolones or clindamycin will be disturbed if there is not an adequate interval between intake.

(4) When a microorganism is isolated, the resistance pattern of the microorganism determines the choice of the oral regimen. When no microorganism is isolated, the antibiotic must be changed to its oral formulation, and if the iv antibiotic has no oral formulation the oral regimen will be established after consultation with the infectious diseases physician or the medical microbiologist.

Inventorial (baseline) phase

To document the baseline situation, during a 2 month period (18 November 1996 to 18 January 1997) all antibiotics prescribed on wards for Internal Medicine (66 beds), Surgery (64 beds), and Pulmonology (23 beds) were registered. These wards were selected because of their high antibiotic use. Recognized surgical prophylactic schemes lasting $<$24 h were excluded. An antibiotic course was defined as a course of antibiotics given for an episode of clinical or suspected infection. A prescription was defined as a written order to start or change antibiotics.[21] A distinction was made between prescriptions for prophylaxis (other than established perioperative prophylaxis, e.g. endocarditis prophylaxis and PCP prophylaxis in HIV patients), prescriptions for documented therapy (when a microorganism was cultured or the clinical picture was typical for one specific pathogen), and prescriptions for empirical therapy (when no microorganism has yet been cultured).[21]

For every patient, age, sex, and length of stay in the hospital were recorded. For each course, data were collected on duration, indications for therapy, final diagnosis, and culture results. The day on which fever resolved ($<$37.5°C) and the peripheral leucocyte count normalized ($<10 \times 10^9$/L) was recorded. For each prescription, data were collected on route of administration, dosage, and duration of treatment. For iv prescriptions, we registered whether an oral alternative was present which would result in adequate levels at the site of infection, and whether the patient had a functioning gastrointestinal tract. All decisions on the duration and route of administration of the antibiotics prescribed were made by the attending physicians.

Implementation phase

The guidelines for iv–oral switch were introduced during a joint meeting of the study group and the staff members and attending physicians of the departments involved. During the first 2 months after the guidelines' introduction (June–August 1997, implementation phase) all antibiotics prescribed were registered, using the same methods as during the inventorial phase. The study physician (FS) identified on a daily basis all patients fulfilling the criteria for iv–oral switch, and recorded when the antibiotics were in fact switched to an oral formulation. When a patient fulfilling the criteria for switch continued iv therapy, she contacted the attending physician to remind them of the guidelines, and to ask whether there were compelling reasons not to change the route of administration.

For all patients who were switched to oral treatment, reasons for readmittance to our hospital within 6 weeks after discharge were recorded. In addition all bacteriological culture results obtained during this period were retrieved.

Results

Characteristics of antibiotic use

The total number of patients present in the wards during the two study periods, the number of patients treated with antibiotics, and their duration of stay in the hospital are shown in Table I. A high percentage of patients received one or more antibiotic courses during their stay, especially in the Internal Medicine and the Pulmonology wards.

During the inventarization phase, a total of 271 patients received 362 antibiotic courses. The mean number of courses per patient was comparable between the different wards (Table II). During the implementation phase, 234 patients received 281 antibiotic courses. The percentage of patients treated with antibiotics and the mean number of courses per patient were slightly lower than in the first study period. This was because, unlike in the baseline phase, courses that had already been started before the introduction of the guidelines could not be included. The median length of the antibiotic courses was 7 days during both phases of the study. The final indications for therapy are shown in Table II.

During the baseline phase we recorded 775 prescriptions. Sixty-two prescriptions were given as prophylaxis, 287 for documented therapy, and 426 as empirical therapy. Prescriptions for empirical therapy were given predominantly intravenously (75%), whereas prescriptions for documented therapy were given predominantly orally (53%). During the implementation phase we recorded 581 prescriptions.

Iv–oral switch

Using the guidelines, we established for all courses started intravenously whether an iv–oral switch would have been justified. During the baseline phase, in 36% of cases

Table I. Characteristics of antibiotic use during the baseline (I) and implementation (II) phases

	Medicine		Surgery		Pulmonology		All	
Department	I	II	I	II	I	II	I	II
Patients admitted (*n*)	234	270	276	293	142	111	652	674
% of patients treated with antibiotics	49	39	31	29	49	40	42	35
Duration of stay of antibiotic-treated patients (days)[a]	13	9	11	12	9	12	11	10

[a]Median.

Table II. Antibiotic courses during the inventorial (I) and implementation (II) phases

	Medicine		Surgery		Pulmonology		All	
Department	I	II	I	II	I	II	I	II
Number of courses (*n*)[a]	1.33	1.19	1.30	1.23	1.39	1.18	1.34	1.20
Duration of course (days)[b]	8	7	6	6	8	8	7	7
Final indication *n* (%)								
respiratory tract	33 (22)	25 (20)	15 (13)	12 (12)	54 (56)	31 (60)	102 (28)	68 (24)
urinary tract	26 (17)	13 (10)	8 (7)	16 (16)	3 (3)	2 (4)	37 (10)	31 (11)
cholangitis	11 (7)	14 (11)	7 (6)	8 (8)	–	–	18 (5)	22 (8)
abdominal abscess	5 (3)	4 (3)	17 (15)	12 (12)	–	–	22 (6)	16 (6)
erysipelas	–	7 (6)	2 (2)	4 (4)	–	–	2 (1)	11 (4)
intravascular catheter	3 (2)	4 (3)	–	2 (2)	–	–	3 (1)	6 (2)
oral candidiasis	3 (2)	7 (6)	2 (2)	4 (4)	11 (11)	4 (8)	16 (4)	15 (5)
other	29 (19)	33 (26)	40 (36)	31 (30)	17 (18)	8 (15)	86 (24)	72 (26)
prophylaxis	28 (18)	13 (10)	16 (14)	10 (10)	4 (4)	4 (8)	48 (13)	27 (10)
no definite infection	15 (10)	6 (5)	5 (5)	4 (4)	8 (8)	3 (6)	28 (8)	13 (5)
Total	153 (100)	126 (100)	112 (100)	103 (100)	97 (100)	52 (100)	362 (100)	281 (100)

[a]Mean number per patient.
[b]Median.

antibiotics were given orally during the entire course. An iv–oral switch would have been justified in 97/230 (42%) of courses where antibiotics were started intravenously (Table III). The criteria were met on day 3 (median). The main reasons for a patient not meeting the criteria for switch are given in Table IV. Fifty-two (54%) of the 97 patients who met the criteria switched to oral therapy. This was done on day 6 (median; range 2–28).

During the implementation phase, in 35% of courses antibiotics were given orally during the entire course. For the patients starting on iv antibiotics, 80/182 (44%) met the criteria for iv–oral switch. In 66/80 (83%) of courses meeting the criteria, antibiotics were switched from iv to oral (difference from baseline phase 29%, 95% CI 16–42%; $P < 0.001$). Whereas the criteria for switch were met on day 3 (median), the switch was actually done on day 4 (median; range 2–16). Fourteen patients meeting the criteria for switch received their entire course intravenously. In two of these patients, the criteria were met during a weekend, and antibiotic therapy was stopped on the Monday. One patient was suffering from a terminal illness. One patient complained of nausea, and already had an iv catheter for another indication. In the other ten patients there were no compelling reasons for not switching, according to the opinion of the study group. During the implementation phase, the mean duration of iv therapy was clearly shorter, and the duration of oral treatment was longer than during the first study phase (Table III).

Seven of the 66 patients who were switched to oral treatment during the implementation phase were readmitted to the hospital within 6 weeks after termination of the antibiotic course. In all cases, readmittance was for non-infectious disorders. During that period, two positive bacteriological cultures were retrieved from these patients. In one patient, who had been treated for asymptomatic *Escherichia coli* bacteriuria, *E. coli* was cultured from the urine. However, based on the resistance pattern this was a different strain. In the other patient, treated for aspiration pneumonia, after 1 month oral flora was again cultured from the sputum. However, this was a terminally ill patient, in whom repeated aspiration was likely. Therefore, we believe these two positive cultures could not be attributed to the early iv–oral switch.

Table III. Courses suitable for iv–oral switch during the inventorial (I) and implementation (II) phases

	I	II
Total number of courses	362	281
Courses starting on iv antibiotics	230	182
Courses meeting criteria for switch	97	80
Courses switched to oral therapy	52 (54%)	66 (83%)
Day of switch[a]	6 (2–28)	4 (2–16)
Duration of therapy[b]		
iv (days)	9.6	6.0
oral (days)	3.4	5.4

[a]Median (range).
[b]In patients meeting the criteria for switch; mean.

Table IV. Main reason precluding early iv–oral switch during the inventorial (I) and implementation (II) phases

	I	II
Persisting fever	15 (11%)	6 (6%)
No oral alternative	4 (3%)	10 (10%)
No adequate drug level at infection site with oral antibiotic	43 (32%)	31 (30%)
Leucopenia	6 (5%)	1 (1%)
Nil by mouth	36 (27%)	44 (43%)
Malabsorption	–	2 (2%)
Course <72 h	20 (15%)	8 (8%)
More than one reason	9 (7%)	–
Total	133	102

Economic analysis

The preparation and administration costs (including materials and labour) per iv dose were conservatively estimated to be dfl.10.00 (1990 currency values), that is *c.* US$5.00.[22,23] The costs of administering one oral dose are negligible.[23] In patients meeting the criteria for iv–oral switch, the total number of iv administrations during the inventorial phase (97 courses) was 2620, compared with 1240 during the implementation phase (80 courses). So, when we take an average of 90 courses amenable for early switch in 2 months, the potential number of iv administrations that can be avoided is $(90/97 \times 2620) - (90/80 \times 1240) = 1036$, in 2 months, or over 6000 per year, for the selected wards. This means a reduction of 6000 × dfl.10.00 = dfl.60,000 (US$30,000) in administration costs. The purchase costs of all antibiotics used (antiviral, antifungal, and antituberculous medication excluded) were dfl.18,442 during the inventorial phase, compared with dfl.7156 during the implementation phase. Again taking an average of 90 courses amenable for early switch in 2 months, the potential savings in purchase costs were dfl.9059 in 2 months, or dfl.54,000 (US$27,000) per year for our hospital.

Discussion

Approximately 40% of all patients started on iv antibiotics in the wards studied were candidates for an early switch. During the first phase of the study, before implementation of switch guidelines, only 54% of patients who could have been switched were actually switched to oral treatment,

after a median of 6 days of iv therapy. After implementation of the guidelines, this percentage rose to 83%, and therapy was also switched earlier, after a median of 4 days of therapy. In the analysis of reasons for not switching when the criteria were met, no consistent or compelling reasons for not switching were apparent. During the 6 weeks following completion of the oral course, recurrence of infections, or readmissions due to reinfection did not occur.

The percentage of patients treated with antibiotics, the length of hospitalization of these patients, the number of courses per patient, the length of the courses, and the indications for therapy were comparable for the two periods, as was the percentage of patients treated orally during the entire course, and the percentage of patients starting on iv treatment who met the criteria for iv–oral switch. Hence, the patient groups and a number of indicators of the physicians' antibiotic policy were comparable for the two periods.

With an early switch considerable savings can be achieved: when we extrapolate the results of the study periods, over dfl.100,000 per year, that is *c.* US$50,000, can be saved for the wards studied. These figures are only an estimate. The exact figures are dependent on local purchase prices, and dfl.10.00 (US$5.00) is probably a low estimate for the administration costs. Additional savings might have been achieved by earlier discharge of patients, which we could not include in our analysis. On the other hand, the costs of the study doctor, or the costs of other means to ensure implementation of the guidelines, were not taken into account. These results are in accordance with the literature. In a number of comparative, randomized studies, savings reached per patient with an early iv–oral switch ranged from £220 to US$5600.[5,9,14,15] These savings were achieved by lower purchase costs for oral antibiotics, but also by a shortened period of hospitalization. The estimated annual reduction for an average hospital in purchase and administration costs of antibiotics ranged from US$30,000 to US$80,000.[1,18,20]

The present study was not designed to prove in a double-blind fashion that an early switch to oral therapy has the same efficacy as a full iv course. In accordance with a number of recent reviews[1–3,16] and a consensus statement of the American Thoracic Society concerning the management of community-acquired pneumonia,[24] we believe that the available studies provide sufficient evidence to switch to oral treatment if the condition of the patient has improved after a few days. Since there is a compelling reason to change the current prescribing practices, an important question is how to alter these practices. Education alone is usually not effective.[25] Intervention programmes that are successful usually provide immediate feedback, directed to the physician-in-charge, about a specific patient, and consisting of clear, unambiguous advice.[17–20,26] During the implementation phase of our study, this was done by the study doctor. In other studies of early switch therapy it was done by the hospital pharmacist[18–20] or a specially trained audit nurse.[17] High acceptance rates (80–85%) of such direct feedback programmes have been reported,[18,19,26] which is comparable to the 83% in our study. The savings reached in this way usually outweigh the salaries of these pharmacy workers. Electronic drug-ordering systems, which can provide computer-assisted decision support, might be an additional aid in streamlining the use of antibiotics.[27]

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