Early switch and early discharge strategies in patients with community-acquired pneumonia: a meta-analysis

Authors' objectives
To evaluate the various criteria used in studies of community-acquired pneumonia (CAP) for early switch from parenteral to oral antibiotics, to determine which is a safer strategy. In addition, to assess the impact of early switch and early discharge strategies on clinical outcomes and length of stay (LOS).

Searching
MEDLINE, HealthSTAR, EMBASE, the Cochrane Library and Best Evidence were searched using the following subject headings: 'pneumonia', 'respiratory tract infections', 'community-acquired infections', 'infection', 'guidelines', 'economics', 'meta-analysis', 'prospective studies', 'randomised controlled trials', 'controlled clinical trials', 'treatment outcome', 'treatment failure', 'hospitalisation', 'antibiotics', 'patient discharge', 'length of stay', 'quality of health care', 'outcome and process assessment (health care)', 'quality assurance (health care)', and 'total quality management'.

A literature search was also conducted using the following title words: 'switch', 'conversions', 'intravenous to oral', 'parenteral to oral', 'community-acquired', 'pathway', 'guideline', 'quality', 'outcome', and 'discharge'.

The search was limited to clinical trials of humans, published in English between January 1, 1980 and March 31, 2000. Additional studies were located by reviewing the bibliographies of all selected articles, and by contacting local experts in infectious disease, pulmonary and critical care, and health services research. Letters and editorials were excluded.

Study selection
Study designs of evaluations included in the review
Prospective trials, retrospective trials, meta-analyses and systematic reviews were eligible for inclusion. Studies had to include criteria for switch, recommended day for switch, or recommended minimum number of days of parenteral treatment. Non-clinical evaluations, studies with less rigorous design (retrospective or non-interventional study, review article, case study, or decision analysis), consensus statements, highlights from conferences, and abstracts were excluded.

Specific interventions included in the review
Strategies of early switch and early discharge, when defined as interventions designed to shorten LOS by recommending early switch from parenteral to oral antibiotics, early discharge from hospital, or both.

The strategies described for switch needed to consider the criteria for switch, recommended day for switch, or the recommended minimum number of days of parenteral treatment.

The switch criteria were applied to those studies describing specific clinical requirements for switching from parenteral to oral antibiotics. The discharge criteria were applied when those studies meeting the switch criteria also described requirements for discharging the patient from hospital.

Studies that compared parallel groups with different recommended days of parenteral and oral antibiotic treatments were considered if the intervention recommending the shortest time to starting an oral antibiotic also involved a switch from parenteral to oral antibiotics.

Participants included in the review
Adults aged at least 18 years with bacterial CAP were eligible. The mean age was 61 years, based on 8 (2,463 patients) of the 10 studies. Studies were excluded if they examined patients with non-bacterial pneumonia or specific patient populations, or were non-specific for CAP. The specific patient populations included out-patients, patients aged less than 18 years, those with acquired immunodeficiency virus syndrome or infected with human immunodeficiency virus,
those that had undergone transplantation, and those with cystic fibrosis.

Outcomes assessed in the review
The primary outcome evaluated was LOS. The criteria for switch and for early discharge were also evaluated. Other outcomes included complications of therapeutic failures, mortality, readmission, health-related quality of life, therapeutic success, patient satisfaction with care, intensive care unit admission, any adverse outcome, and relapse.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected titles. The abstracts and articles were independently reviewed, and the inter-rater agreement was assessed using a Kappa value. The Kappa values for the abstract and article reviews were 0.80 and 0.65, respectively.

Assessment of study quality
No formal assessment of validity was undertaken.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. The data were extracted and presented in tables. Data were extracted for the categories of author and year of publication; the number of patients per treatment group; time to switch; length of stay; early switch criteria and recommendations; and early discharge criteria and recommendations.

Methods of synthesis

How were the studies combined?
Studies of outcomes were classified according to two groups: prospectively controlled studies, and prospectively uncontrolled or historically-controlled studies. The random-effects model described by Fleiss (see Other Publications of Related Interest) was used to combine the LOS across the five prospective controlled studies reporting that outcome. Uncontrolled and historically-controlled studies were combined in a narrative review.

How were differences between studies investigated?
A chi-squared analysis was used to evaluate the variation in LOS between studies.

Results of the review
A total of 10 prospective studies were included (total number of patients unclear); of these, one trial randomised sites rather than patients.

Criteria for switch (9 studies).

The most common criteria used were afebrile (100%), improvement or resolution of respiratory signs and symptoms (89%), and ability to take oral antibiotics (67%). Afebrile was the only criterion reported in all 9 studies, although several different definitions were employed.

Four of the 9 studies recommended a specific post-switch antibiotic, 5 studies recommended a specific day for switching, and 4 studies recommended a specific day for discharge.

Criteria for discharge (5 studies).

The most common criterion was care of co-morbid conditions. The 5 studies applied four different combinations of discharge criteria.

Switch on specific day (3 studies) or minimum parenteral treatment (5 studies).

The median recommended day of switching to oral antibiotic was day 3 (range: 2 to 10). The median recommended
duration of parenteral antibiotics was 3 days (range: 2 to 10).

Outcomes (10 studies).

1. LOS (5 studies)

LOS ranged from 3.5 to 11 days. The drop-out rates ranged from 0 to 37%.

Six studies (458 patients) applied an early switch and early discharge strategy to an intervention and control group, and 5 studies provided standard deviations for LOS. The mean change in LOS was -1.64 days (95% confidence interval, CI: -3.30, 0.02, P=0.05); this did not differ significantly between intervention groups. Following the exclusion of 2 studies, which recommended an intervention LOS longer than or equal to the control LOS, the mean LOS was -3.04 days (95% CI: -4.90, -1.19).

2. Clinical outcomes. No significant differences were found between intervention groups for the following outcomes: complications of therapeutic failures (4 studies), mortality (3 studies), readmission (3 studies), health-related quality of life (3 studies), therapeutic success (2 studies), patient satisfaction with care (2 studies), intensive care unit admission (1 study), any adverse outcome (1 study), and relapse (1 study). No supporting data were presented.

3. Uncontrolled or historically-controlled studies (4 studies, 985 patients). Early switch strategies were applied to 710 (72%) of the patients in these studies. Where data were available, the mean time to switch and the mean LOS appeared less for patients receiving the intervention than for the control patients.

**Authors' conclusions**

There was considerable variation in the criteria used in studies of CAP for early switch from parenteral to oral antibiotics. Early switch and early discharge strategies may significantly and safely reduce the mean LOS when the recommended LOS is shorter than the actual LOS.

**CRD commentary**

The aims were stated and the inclusion criteria were defined in terms of the study design, participants, outcome and intervention; however, the emphasis appeared to have been on exclusion criteria. The criteria used to define patients with CAP were not specified, and the inclusion criteria for study design were broad. Several relevant databases were searched and attempts were made to locate unpublished material. By limiting the included studies to those published in English, it is possible that other relevant studies might have been omitted.

The methods used to select the primary studies were described and inter-rater agreement was assessed. Validity was not formally assessed or discussed. There was insufficient information on the primary studies, in particular: whether the prospective studies were randomised or non-randomised; the criteria used to diagnose CAP; characteristics of patients other than age; intervention, in terms of the specific drug and dose; definitions of criteria used for early switch or discharge; whether analysis was on an intention to treat basis; and side-effects.

Studies were pooled on the grounds that 'all patients were diagnosed as having CAP and the mean age is similar'. This was inappropriate since significant statistical heterogeneity was found. As the authors state, confounding factors such as death, complications, readmissions, intolerance of oral antibiotics and losses to follow-up, may have influenced the results. The discussion mentions the possibility that secular trends and geography may have contributed to the variation in LOS between studies.

The evidence supported the variation in LOS between studies, but there was insufficient evidence to support any other conclusions.

**Implications of the review for practice and research**

Practice: The authors state that early switch and early discharge strategies may significantly and safely reduce the mean LOS when the recommended LOS is shorter than the actual LOS. They further recommend that clinicians should...
ensure that early switch and discharge strategies should contain at least the following criteria: resolution of fever, improvement in respiratory signs and/or symptoms, and the ability to take oral medication.

Research: The authors state that further prospectively-controlled intervention studies with baseline LOS assessments are needed to verify the review's findings.

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