Community-acquired pneumonia: a clinical approach to hospital admission, diagnosis and treatment
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Chapter 6

Evaluation of an algorithm for switching from IV to PO therapy in clinical practice in patients with community-acquired pneumonia

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Abstract

**Background:** In patients with community-acquired pneumonia (CAP), switching from parenteral to oral antimicrobial agents offers advantages over IV therapy alone, including improved cost-effectiveness through reductions in the length of hospital stay and treatment costs.

**Objective:** The aim of this study was to determine whether a method for applying switch therapy in daily practice could be used in patients with CAP and whether differences were found between the five risk classes of the Pneumonia Severity Index concerning duration of parenteral treatment and length of stay after applying switch therapy.

**Methods:** In a prospective observational study, switch to oral antibiotic therapy was performed when the patient’s temperature had been normalized for 72 hours and respiratory symptoms (dyspnea, coughing and thoracal pain) had improved.

**Results:** One hundred and eighty patients with CAP were included. Clinical cure was seen in 174 patients (97%). Overall, patients with CAP switched on day 5 of treatment. After conversion to oral antibiotics CRP decreased in all risk classes and was normalized by follow-up. Patients from risk class V remained hospitalized for a significantly longer period than patients from risk classes I-IV (p<0.001).

**Conclusions:** The results of this study show that criteria for switch to oral therapy, consisting of an absence of fever for 72 hours and a reduction in respiratory symptoms, showed a high success rate in patients with CAP. Furthermore, patients with a lower risk of mortality had a shorter length of hospital stay than high risk patients.
Introduction

Traditionally, hospitalized patients with uncomplicated community-acquired pneumonia (CAP) have generally been treated with a course of intravenous (IV) antibiotic therapy. Patients were normally discharged after completing this course. During the past decade there has been a tendency to switch to oral antibiotics in an earlier phase of treatment. Theoretically, switch therapy from IV to oral agents benefits the patient, because of a decline in complications such as thrombophlebitis, and there is the possibility of mobilizing patients sooner. Furthermore, it could be cost-effective because the hospital stay can be shortened, and less expensive treatment can be used.¹

Switch therapy needs to be as safe and as effective as a complete course of IV antibiotic therapy. Regardless of the presence of effective antibiotics CAP can still be a severe illness, as evidenced by the high percentages of Intensive Care Unit (ICU) admissions and the high mortality figures.² ³ Therefore, it is necessary to determine at what stage it is safe to switch to oral therapy, and which patients can be considered candidates for switch therapy. Several studies have been performed in order to determine the right moment for conversion from parenteral to oral antibiotics. In some studies the criteria for switch therapy were based on a fixed duration of IV antibiotic therapy, ranging from one to three days.⁴⁻¹² In other studies conversion to oral antibiotics was performed after reaching a state of clinical stability.¹³⁻¹⁶ However, important limitations, such as the absence of reporting the severity of CAP, the presence of patients with lower respiratory tract infections other than CAP, the use of a single antibiotic agent and the exclusion of patients with atypical bacterial pathogens were present in most studies.

Therefore, we have attempted to develop a method for performing switch to oral therapy in daily practice. A prospective observational study was therefore performed, investigating whether switch to oral therapy could be applied in patients with CAP who had been afebrile for 72 hours and whose respiratory symptoms had improved. Furthermore, the relation between the pneumonia severity index (PSI) and the duration of IV antibiotic treatment as well as length of hospital stay (LOS) were investigated after applying switch therapy.
Patients and Methods

Setting and patient selection
A prospective observational study was performed between December 1998 and November 2000 in the Departments of Pulmonary Diseases and Internal Medicine of the Medical Center Alkmaar, which is a teaching hospital with 900 beds. The study protocol was approved by the medical ethical committee of our hospital. Patients who fulfilled the following criteria were enrolled in the study after giving written informed consent: 1) age of 18 years or older 2) clinical presentation with an acute illness including one or more of the following symptoms suggesting CAP: presence of fever (temperature $\geq 38^\circ$C), dyspnea, cough (with or without expectoration of sputum), chest pain; 3) presence of a new consolidation on the chest radiograph. Patients were excluded from the study if they met one of the following criteria: severe immunosuppression (HIV infection; high dose of immunosuppressive agents, like prednisone $> 35$ mg/day; chemotherapy); presence of malignancy; pregnancy; documented severe allergy for antibiotics; presence of obstruction pneumonia; signs of pneumonia within 8 days after previous hospital discharge. Furthermore, from a pharmacokinetic and pharmacodynamic point of view, patients were excluded from switch therapy if they had been referred to the ICU before switch therapy could be performed, or if empyema, lung abscess or a state of abnormal gastro-intestinal absorption was present. Patients who could not ingest oral antibiotics were also excluded from switch therapy. If patients were referred to the ICU after switch had been performed, they were included in the study. Comorbidities were defined as diseases that were actively treated at the moment of admission.

Antibiotic treatment and time of conversion to oral antibiotic therapy
IV antibiotic treatment ranged from a pathogen-specific therapy to broad-spectrum empirical treatment. The IV antibiotics most frequently used were: the combination of erythromycin and amoxicillin-clavulanate (46%); penicillin (20%); amoxicillin-clavulanate (18%); erythromycin (6%) and amoxicillin (3%). Patients received the same oral drug after switch as was used in parenteral form. An important consideration was that the oral drug possessed good pharmacodynamic and pharmacokinetic properties.
Conversion to oral therapy was performed when the patient's temperature had been normalized (temperature < 38°C) for 72 hours and when respiratory symptoms had improved. Respiratory symptoms were defined as coughing with or without production of sputum, thoracic pain and dyspnea. Improvement of respiratory symptoms was determined by clinical judgement of the treating physician. If these conditions were not fulfilled before performing switch therapy, this was defined as a protocol violation.

**Assessment of clinical outcome after switch therapy**
Patients were considered cured when a good clinical response was observed on oral therapy and when signs and symptoms of pneumonia were improved at follow-up, one month after discharge. If signs and symptoms of pneumonia returned after switch to oral therapy or if patients were admitted to the ICU after switch had been performed or if patients died before follow-up this was considered to be a failure. C-reactive protein (CRP) and white blood cell count (WBC) were determined on days 1, 2, 7 and 14 of treatment and at follow-up.

**Severity classification**
Patients were stratified into the 5 risk classes of the PSI. All data necessary for calculating the PSI were prospectively collected at admission. A comparison was made between the different risk classes concerning day of switch therapy, total duration of antibiotic use, LOS, CRP and WBC count and clinical failure. No criteria for discharge were given to the treating physician, nor were they informed about the contribution of LOS as an outcome parameter for this observational study.

**Microbiological investigations**
On admission a sputum specimen for Gram's stain (presence of > 25 polymorphonuclear leukocytes and < 10 squamous cells per low-magnification field [x10]), semi-quantitative culture and *Streptococcus pneumoniae* antigen detection (latex agglutination, Murex, Dartford, Kent, UK) was obtained; 3 sets of blood cultures were drawn and on clinical suspicion a urine sample for *Legionella pneumophila* type I antigen detection (immunoenzymatic method, Binax-NOW, Binax, Portland, Maine, USA) was obtained, preferably before the start of antibiotic treatment. If indicated,
bronchoalveolar lavage (BAL) and protected specimen brush (PSB) were performed; specimens were investigated by Gram's stain, quantitative culture and *S. pneumoniae* antigen detection. All patients were analysed for the presence of *S. pneumoniae* antigen (Binax-NOW, BINAX, Portland, Maine, USA) in the urine samples obtained at admission. Thoracentesis with Gram's stain, *S. pneumoniae* antigen detection and culture for aerobic and anaerobic bacteria was performed when pleural fluid was present. Blood samples for serology (Serion ELISA classic, Virion GmbH, Würzburg, Germany) were obtained at day 1 and 14 of treatment to detect antibodies to *Mycoplasma pneumoniae, Chlamydia pneumoniae, L. pneumophila*, influenza A virus and influenza B virus, parainfluenza virus 1-3, respiratory syncytial virus (RS) and adenovirus.

The microbial diagnosis was established by: 1. Identification of a pathogen from blood, representative sputum, BAL, PSB, and/or pleural fluid. 2. Presence of detectable pneumococcal antigen in sputum, BAL, PSB, pleural fluid and/or urine. 3. Threefold rise in antibody titers of *L. pneumophila, M. pneumoniae, C. pneumoniae, influenza A virus and influenza B virus, parainfluenza virus*1-3, RS virus, or adenovirus or a single elevated IgM titer of $> = 17$ U/ml for *M. pneumoniae*.

**Statistical analysis**

Data were compared and analyzed with one-way analysis of variance (ANOVA) with post hoc Bonferroni correction for continuous variables and chi-square test for nominal data using SPSS Version 11.5 for Windows (SPSS Inc, Chicago, Illinois, USA). Data were expressed as means with standard deviation. Variables were considered to be clinically meaningful when $p < 0.05$. 

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Results

Patient characteristics
Three hundred and two patients were initially included; 42 patients did not have pneumonia according to the inclusion criteria and were consequently misdiagnosed at admission and excluded. Another 80 patients were not eligible for switch therapy, from this group 50 patients did not fulfill the criteria for starting oral therapy. The results of the remaining 180 patients were evaluated (figure 1).

Figure 1: Flow diagram of inclusion and primary outcome.

302 patients enrolled

42 patients misdiagnosed:
- lungcancer (n = 7)
- bronchitis (n = 6)
- congestive heartfailure (n = 4)
- pulmonary embolism (n = 3)
- other (n = 22)

260 patients with CAP

80 patients excluded for switch therapy:
- ICU admission before performing switch therapy (n = 22)
- Lungabscusses (n = 2)
- Empyema (n = 6)
- Protocol violation (n = 50):
  - Switch to oral therapy > 72 hours without fever (n = 22)
  - Switch to oral therapy < 72 hours without fever (n = 28)

180 patients with CAP included

Clinical failure: n = 6 (3%)
Risk class I: n = 0 (0%)
Risk class II: n = 1 (2%)
Risk class III: n = 1 (2%)
Risk class IV: n = 4 (6%)
Risk class V: n = 0 (0%)

Clinical cure: n = 174

\(^{a}\)CAP = community-acquired pneumonia.
The main demographic characteristics of the study population are described in Table 1. The median age of the patients was 69 years (range 19-97 years). Male and female populations were almost equally distributed (52% versus 48%). The most common comorbidity was chronic obstructive pulmonary disease (COPD), present in 77 patients (43%), followed by diabetes mellitus in 19 patients (11%) and asthma in 19 patients (11%).

**Table 1**: Demographic characteristics of the study population.

<table>
<thead>
<tr>
<th>Variables</th>
<th>no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>180</td>
</tr>
<tr>
<td>Age, range (years)</td>
<td>69(^a), 19-97</td>
</tr>
<tr>
<td>Male</td>
<td>93 (52)</td>
</tr>
<tr>
<td>Female</td>
<td>87 (48)</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Respiratory symptoms</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>109 (61)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>112 (62)</td>
</tr>
<tr>
<td>Coughing</td>
<td>167 (93)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>77 (43)</td>
</tr>
<tr>
<td>Asthma</td>
<td>19 (11)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>13 (7)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>12 (7)</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Other neurologic disorder</td>
<td>12 (7)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19 (11)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>≥ 10 cigarettes/day</td>
<td>40 (22)</td>
</tr>
<tr>
<td>&lt; 10 cigarettes/day</td>
<td>7 (4)</td>
</tr>
<tr>
<td>ex-smoker</td>
<td>68 (38)</td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
</tr>
<tr>
<td>&gt; 3 units/day</td>
<td>8 (4)</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)(^b)</td>
<td>159 ± 127</td>
</tr>
<tr>
<td>White blood cell count (10(^9)/L)(^b)</td>
<td>13.8 ± 6.9</td>
</tr>
</tbody>
</table>

\(^a\)median value. \(^b\)mean value ± SD.
**Etiology**
In 93 patients (52%) a microbial diagnosis could be established. The most common pathogen in all risk classes was *S. pneumoniae*, present in 64 patients (36%), followed by *Haemophilus influenzae* identified in 14 patients (8%) and *M. pneumoniae* in 11 patients (6%) (table 2).

**Table 2**: Etiology determination by routine microbiological research and serological investigation.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Class I, n = 14</th>
<th>Class II, n = 44</th>
<th>Class III, n = 46</th>
<th>Class IV, n = 65</th>
<th>Class V, n = 11</th>
<th>Total, n = 180</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pneumoniae</em> no. (%)</td>
<td>3 (21)</td>
<td>16 (36)</td>
<td>17 (37)</td>
<td>23 (35)</td>
<td>5 (45)</td>
<td>64 (36)</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em>, no. (%)</td>
<td>1 (7)</td>
<td>6 (14)</td>
<td>2 (4)</td>
<td>4 (6)</td>
<td>1 (9)</td>
<td>14 (8)</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em>, no. (%)</td>
<td>3 (21)</td>
<td>1 (2)</td>
<td>2 (4)</td>
<td>5 (8)</td>
<td>0 (0)</td>
<td>11 (6)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em>, no. (%)</td>
<td>1 (7)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>2 (3)</td>
<td>0 (0)</td>
<td>4 (2)</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em>, no. (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (3)</td>
<td>1 (9)</td>
<td>3 (2)</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em>, no. (%)</td>
<td>2 (14)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>5 (3)</td>
</tr>
<tr>
<td><em>E-coli</em>, no. (%)</td>
<td>1 (7)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (3)</td>
<td>0 (0)</td>
<td>3 (2)</td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em>, no. (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td><em>Haemophilus parainfluenzae</em>, no. (%)</td>
<td>0 (0)</td>
<td>2 (5)</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>3 (2)</td>
</tr>
<tr>
<td><em>Adenovirus</em>, no. (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td><em>Parainfluenza virus</em>, no. (%)</td>
<td>1 (7)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Etiology unknown, no. (%)</td>
<td>4 (29)</td>
<td>23 (52)</td>
<td>24 (52)</td>
<td>32 (49)</td>
<td>4 (36)</td>
<td>87 (48)</td>
</tr>
</tbody>
</table>

**Clinical outcome**
Switch to oral therapy was successfully performed in 174 patients (97%). Switch therapy failed in six patients (3%) (figure 1). In two patients respiratory symptoms increased after switch to oral therapy, caused by progressive symptoms of COPD. In three other patients, a relapse of fever
occurred after conversion to oral antibiotics. In one of these patients, the oral antibiotic initially started was replaced by another oral antibiotic; the other two patients continued on the same oral antibiotic. All five patients were clinically cured at follow-up, one month after discharge. The sixth patient died after 16 days of hospitalization due to non-CAP related cardiac disease. No significant difference in the number of clinical failures was found between the five different risk classes (p=0.6). No failures occurred in risk classes I and V.

When applying the criteria for switch therapy in the study population, conversion to oral antibiotic therapy was performed after a mean of 4.6 days of IV therapy (table 3). After classification into the five PSI risk classes, oral antibiotic therapy was initiated on day 5 of treatment in patients stratified into class I-III and class V. Patients stratified into risk class IV switched to oral antibiotics on day 6 of treatment. Overall, the duration of antibiotic therapy was 10 days, with no significant difference between the five risk classes.

Besides clinical response, the efficacy of applying the criteria for switch therapy were supported by a decrease in CRP (figure 2) and WBC count. After conversion to oral antibiotics CRP declined in all risk classes. Normalization of CRP was observed on day 14 in risk class I, II and III. The WBC returned to normal in all risk classes 14 days after starting IV antibiotic treatment.

The mean LOS for all patients with CAP was 12.3 days (table 3). High risk patients stratified in risk class V remained in the hospital for a significantly longer period (23.5 days) than patients from risk classes I-IV (8.3, 9.7, 11.6 and 14 days respectively; p<0.001). A significant difference in LOS was also seen between patients stratified into risk class IV compared to risk class II (p=0.004). Reasons for the prolonged LOS in patients from the higher risk classes were treatment of comorbid conditions and social circumstances, as waiting for referral to a nursing home. The presence of comorbid illness showed an increasing trend across the risk classes (p=0.004) (table 3). Furthermore patients with comorbidities had to remain in the hospital for a longer period than those without comorbidities (mean of 14.1 days and 10.2 days, respectively; p=0.001) (figure 3).
**Table 3:** Duration of total and intravenous antibiotic therapy, length of hospital stay and presence of comorbid illness in patients with community-acquired pneumonia, stratified into five risk classes of the pneumonia severity index.

<table>
<thead>
<tr>
<th></th>
<th>Class I, n = 14</th>
<th>Class II, n = 44</th>
<th>Class III, n = 46</th>
<th>Class IV, n = 65</th>
<th>Class V, n = 11</th>
<th>Total, N = 180</th>
<th>p-value f</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abiv</strong>, days (±SD)</td>
<td>4.0 (±1.0)</td>
<td>4.5 (±1.3)</td>
<td>4.4 (±1.1)</td>
<td>5.0 (±2.3)</td>
<td>4.5 (±1.1)</td>
<td>4.6 (±1.7)</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>AB</strong>, days (±SD)</td>
<td>9.5 (±2.9)</td>
<td>9.8 (±3.0)</td>
<td>9.3 (±2.1)</td>
<td>10.3 (±4.4)</td>
<td>8.6 (±1.4)</td>
<td>9.8 (±3.2)</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>LOS</strong>, days (±SD)</td>
<td>8.3 (±3.8)</td>
<td>9.7 (±3.7)</td>
<td>11.6 (±3.6)</td>
<td>14 (±8.3)</td>
<td>23.5 (±16.7)</td>
<td>12.3 (±7.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidity, no. of patients (%)</td>
<td>3 (21)</td>
<td>19 (43)</td>
<td>29 (63)</td>
<td>42 (65)</td>
<td>8 (73)</td>
<td>101 (56)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Data are expressed as mean values ± standard deviation, with exception of comorbidity which is expressed as absolute number.

- Abiv = length of intravenous antibiotic therapy.
- AB = total duration of antibiotic therapy.
- LOS = length of stay; d = p = 0.004 compared to risk class II; e = p < 0.001 compared to risk class I-IV, after post-hoc Bonferroni correction.
- Calculated with one-way analysis of variance, with exception of comorbidity which was calculated with chi-square test.
**Figure 2:** Results of CRP during treatment in the five risk classes of the pneumonia severity index (mean; 95% confidence intervals).

![Graph showing CRP levels over time for different risk classes.]

**Figure 3:** Kaplan-meier curve showing length of hospital stay for patients with and without comorbidity.

![Graph showing Kaplan-meier curve for hospital stay.]

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*Chapter 6*

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Discussion

A method for performing an early switch to oral antibiotic therapy was prospectively studied in 180 patients with CAP. Clinical failure on switch to oral therapy occurred in only six patients (3%); five patients were clinically cured by follow-up, one month after discharge. The sixth patient died after 16 days of hospitalization due to non-CAP related cardiac disease. Following the criteria set down, it was decided to count this patient as a failure, although whether this patient was a clinical failure of switch therapy could be a point for discussion. No significant difference was observed between the five risk classes concerning day of starting oral therapy. The clinical success of switch to oral therapy can be supported by the course of the WBC counts and CRP. CRP is a sensitive marker of pneumonia. A persistently high CRP level suggests antibiotic treatment failure. After conversion to oral antibiotics CRP decreased in all risk classes and was normalized by follow-up. The WBC counts were reduced in all risk classes after starting IV antibiotic treatment and normalized on follow-up, one month after discharge. The results of this study are comparable to the results reported in other studies (clinical cure 84%-100%).

When we designed the protocol, reports in the existing literature showed that patients switched after being treated for 2-5 days with IV antibiotic therapy. Traditionally, patients were treated with IV antibiotics solely. Therefore, it was decided to convert to oral antibiotics when the patient’s temperature had been normalized for 72 hours and when an improvement of respiratory symptoms was seen. The reason for choosing these criteria was because of the limitations we encountered in literature concerning the application of a safe way for performing switch therapy in daily practice. We realized that 72 hours after normalization of fever is a long period before performing switch to oral therapy. In a study performed by Castro et al. patients with non-severe CAP had a favorable outcome after treatment with oral therapy alone (failure of 10%) compared to switch to oral therapy after 72 hours without fever (failure of 32%). Furthermore, Castro et al. showed that patients with severe CAP could switch to oral therapy after 48 hours without fever (failure of 25%) instead of being treated with IV therapy alone (failure of 24%). The percentages of therapy failure are higher than the results of our study. This could partly be explained by the more elaborate criteria for therapy failure used in the study of Castro et al.
The high cure rate of the present study could partly be explained by the inclusion of low risk patients (32%), stratified in risk class I and II. According to the PSI these patients could safely be treated at home.\textsuperscript{3} The patients in our study were hospitalized because of various reasons, like treatment of comorbid illness (56%) or lack of improving on outpatient antibiotic therapy (18%). The percentage of these low risk patients in our study population is similar to a study performed by Roson et al.\textsuperscript{22} Moreover, in other studies reasons for admitting low risk patients are described.\textsuperscript{23,24} This leads to the question as to whether these low risk patients, once hospitalized, could exclusively be treated with oral antibiotics. Some studies, comparing oral with IV therapy, showed encouraging results for certain groups being treated with oral antibiotics alone.\textsuperscript{1,7,25} Unfortunately, these studies were not performed on large numbers of patients and the severity of CAP was not reported in these patient populations. Castro et al.\textsuperscript{16} showed in the study described above, that in patients with non-severe CAP no difference was seen between initial therapy with oral antibiotics or starting with IV antibiotics.

A significant difference in LOS was seen between the risk classes I, II and III and the risk classes IV and V. One of the reasons for a prolonged LOS in the higher risk classes was treatment of comorbid illness. Furthermore, social indications, as lack of immediate outpatient supportive care facilities prolonged hospital stay in several cases. It should be emphasized that this study had an observational character and that no criteria for discharge were given to the treating physician. The decision for hospital discharge was based on clinical judgement. Patients from class I and II usually remained in the hospital for three to four days after switch to oral therapy. Some authors suggest that a patient could be discharged directly after changing from IV to oral therapy.\textsuperscript{26-28} Often, the only reason for prolonged hospitalization is to be sure that a patient does not suffer a clinical failure after starting oral antibiotic therapy. At this moment, insufficient evidence is available to justify observing patients for some days in the hospital after switching them to oral antibiotic therapy. On some occasions patients cannot be discharged immediately after switch to oral therapy. In the present study some patients, especially from risk class IV and V, had to remain hospitalized for a longer period because of treatment of comorbid illness and social circumstances, an observation that is also described in two other studies.\textsuperscript{23,29} However,
if patients are discharged immediately after antibiotic switch is initiated, than it is advisable to implement an early follow-up visit. Although the study was not designed to evaluate criteria for hospital discharge, attention has to be made for the difference in LOS between studies about CAP in Europe and USA.\textsuperscript{14,22,23,30} Regional differences, like more economic pressure in the USA, may explain the variability in LOS. A closer evaluation of the hospital discharge criteria, as mentioned earlier, could lead to a reduction in LOS, which will reduce medical care costs and will eventually improve patients' comfort.\textsuperscript{14,30,31}

In several studies about switch therapy a single antibiotic agent, often consisting of a broad-spectrum second or third generation cephalosporin, was chosen.\textsuperscript{4-6,8-12} In contrast, in the present study antibiotic therapy ranged from a pathogen-directed to empirical broad-spectrum therapy, reflecting daily practice. Of the six patient failures, four had received empiric antibiotic broad-spectrum therapy and two had received a pathogen-directed therapy. These results are encouraging for the application of switch therapy with different antibiotics.

In summary, the results of this study show that criteria to perform switch to oral therapy in daily practice, consisting of an absence of fever for 72 hours and a reduction in respiratory symptoms, can be applied in patients with CAP. The encouraging results from this study could partly be explained by the inclusion of patients from PSI risk class I and II, who in most instances could be treated at home. In the future, possible alternatives may be evaluated. We speculate that in patients where CRP is frequently monitored, switch to oral therapy may be initiated when CRP starts declining to normal. Furthermore, discharge may be possible once parenteral therapy is discontinued. Further research is needed to determine whether patients from risk class I and II could solely be treated with oral antibiotic therapy.
Reference List


Evaluation of an algorithm for switching from IV to PO therapy


