Conversion of intravenous to oral/nasogastric antibiotics in critically ill patients with pneumonia

Léna Lauzon, Marc M. Perreault and Michael Tierney

ABSTRACT

BACKGROUND: Considering the fiscal restrainst on health care, an intravenous (IV) to oral/nasogastric (PO/NG) conversion program for critically ill patients with community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) was developed.
OBJECTIVE: Our purpose was to evaluate the feasibility of implementing an IV to PO/NG conversion program in this population and to assess patient outcomes.
METHODS: Intensive care unit (ICU) patients diagnosed with CAP and HAP were eligible for enrollment. Patients that met predefined criteria were converted to an enteral regimen. Temperature, white blood cell counts and oxygen requirements were evaluated at baseline, time of conversion and end of oral therapy. Treatment courses were evaluated for clinical and microbiological outcomes.
RESULTS: During a 5-month period, 26 ICU patients were entered into this trial (13 CAP and 13 HAP). Mean age (± SD) was 61 (17.3) and 55.8 (20) years old, and mean Acute Physiology and Chronic Health Evaluation II (APACHE II) scores 24 (6.7) and 19 (6.7) in the CAP and HAP groups respectively. Mechanical ventilation was required in 69.2% of patients. Conversion occurred in 77% and 92% of CAP and HAP patients after a mean of 6.6 and 5 days. Twenty patients were clinically evaluable and cure or improvement occurred in all cases. Seventeen patients had positive microbiological cultures and eradication was observed in 13 of these patients (76%).
CONCLUSION: An IV to PO/NG conversion program for critically ill patients with CAP or HAP is feasible and effective.

Key words: Pneumonia, antibiotics, intensive care unit, switch therapy.

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BACKGROUND

With the current fiscal restraints in health care, it is crucial to develop effective treatment at the lowest possible cost. Sequential, transitional, stepdown or switch therapy refers to the practice of limiting the use of intravenous antibiotics to the early stages of infection, and then converting to an effective oral agent(s) for the duration of treatment. Three main benefits are associated with the use of this approach: economic benefits, patient benefits and benefits to the health care provider.[1,2]

The economic benefits consist of significant cost reductions that result from the conversion of intravenous (IV) to oral/nasogastric (PO/NG) therapy because of lower drug acquisition costs, a reduction in pharmacy time in the preparation and mixing of drugs, and a reduction in the length of hospital stay.[3,4] Although less quantifiable, patient-related benefits are nevertheless important. The use of oral instead of intravenous drugs increases patient comfort and mobility. In critically ill patients this benefit is minimal, but by avoiding the use of intravenous lines there is possibly less risk of phlebitis and line-related infections.[1,2] An earlier discharge from hospital decreases the risk of development of nosocomial infections and increases the patient's quality of life.[5] Finally, there is less personnel time associated with drug delivery, which may free the individual for other patient care activities.[1,2]

Reports of successful IV to PO conversion of antibiotics for treatment of serious infections have been published. However, to our knowledge this has never been studied specifically in an intensive care unit (ICU)

population. An IV to PO conversion program is currently in place in other wards at our hospital, whereby clinical pharmacists initiate the conversion if the patient meets predefined criteria. However, due to the severity of the condition of ICU patients, there was reluctance from the ICU staff to participate.

OBJECTIVES

The objectives of this study were to evaluate the feasibility of implementing an IV to PO/NG conversion program in critically ill patients with community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP), and to assess patient outcomes.

METHOD

This was a descriptive study carried out in the ICU of The Ottawa Hospital General Site, a 16-bed Medical–Surgical Unit. All patients with a clinical diagnosis of CAP or HAP were identified during the 5-month study period. Pneumonia was diagnosed by the ICU physician on the basis of the following criteria: presence of pulmonary infiltrate on chest x-ray, fever, leukocytosis, new onset of cough or sputum production, and proper sputum sample for Gram's staining and culture.[6] Patients receiving steroids could be included in the study. Exclusion criteria were neutropenia (defined as an absolute neutrophil count less than 500 cells/mm^3), concomitant endocarditis, meningitis, severe sepsis or septic shock, and cystic fibrosis.[7] We excluded patients who were taking immunosuppressive medications such as cyclosporine and azathioprine, as well as patients who were enrolled in any clinical trial involving antimicrobials.

Before implementation of this conversion program, a computerized literature search (Medline) was completed using the following key words: pneumonia, antibiotics, intensive care unit, switch therapy. Guidelines for intravenous antibiotics were developed based on the Canadian Consensus Conference on Community and Hospital-Acquired Pneumonia and other references.[8–12] Oral antibiotic alternatives were identified for the treatment of the isolated pathogen(s), considering the antibiotic spectrum of activity, bioavailability, pharmacokinetic profile and gastrointestinal tolerance. The patient's allergy status, the presence of concomitant diseases and the potential for drug interactions also influenced the choice of the oral antibiotic(s). Criteria for conversion to an oral alternative were developed from the existing literature and consisted of continued need for an antibiotic; functional gastrointestinal tract as evidenced by tolerance to enteral feeds; afebrile (T < 38°C) for 24 hours; and, reduced white-blood-cell (WBC) count. Patients were also required to present at least 2 of the following signs of clinical improvement: reduction in the quantity of sputum production; change in the colour of sputum; improvement in oxygenation as evidenced by a reduction in the fraction of inspired oxygen (FiO_2); or signs of radiographic improvement.[6,12–13]

Data were collected by family interview and chart review, and from the ICU Clinical Database, a computer program that allows the collection and analysis of selected clinical parameters on all patients admitted to the ICU. The patient characteristics collected included gender, age, smoking history, alcohol use or history, prior exposure to antibiotics (within 7 days), number of chronic conditions (such as diabetes mellitus, renal insufficiency and chronic obstructive pulmonary disease), baseline creatinine, Acute Physiology and Chronic Health Evaluation II (APACHE II) score on admission to ICU, duration of ICU stay, requirement for mechanical ventilation, ventilation hours and survival during the ICU admission. The clinical pharmacist followed the eligible patients and promoted the conversion from an IV to PO/NG regimen once the conversion criteria were met.

When criteria for IV to PO/NG conversion were met, an oral agent was chosen according to available sputum culture and sensitivity information (i.e. tracheal aspirates and bronchoscopic samples). If cultures were negative and the patient was responding, an oral alternative covering a similar spectrum as the IV regimen was chosen.

Temperature, WBC and FiO_2 required were noted at time of diagnosis of pneumonia in ICU. These measurements were also recorded daily prior to conversion to an oral antibiotic, at the time of conversion and daily thereafter, until the end of enteral therapy.

Treatment courses were evaluated for clinical and microbiological outcomes, which were assessed by the investigators. Clinical response to antibiotic therapy was classified as cure, improvement, failure or relapse. Cure was defined as the resolution of clinical signs and symptoms (including elevated temperature and WBC count) with no evidence of pulmonary infection at time of discontinuation of therapy and no evidence of relapse during the 5-day immediate follow-up period. Cure was

assumed when the patient was discharged from hospital while on oral therapy, or when discharged before the end of the 5-day follow-up period. Improvement was defined as a significant reduction in clinical signs and symptoms with incomplete resolution of clinical evidence of infection at the time of treatment course discontinuation. Failure was defined as no apparent clinical and microbiological response to therapy. Finally, relapse was defined as recurrence of similar signs and symptoms with the same pathogen isolated within 5 days of discontinuation of the oral treatment.

Microbiological outcome was evaluated when positive blood or sputum cultures were available prior to initiation of antibiotic therapy. Microbiological response was categorized as eradication, persistence, eradication with recurrence, superinfection and colonization. Eradication was defined as negative follow-up cultures. When the follow-up specimens were not obtained within 48 hours of study drug discontinuation, eradication of initial pathogen(s) was assumed if a clinical cure or an improvement was determined. Persistence was defined as the failure to eradicate the same pathogen from the same site. Eradication with recurrence was defined as negative repeat cultures with subsequent positive cultures within 5 days. Superinfection was defined as the appearance of a new infecting pathogen in cultures obtained after 48 hours of therapy associated with the development of fever or other clinical evidence of infection. Colonization was defined as the appearance of any potentially pathogenic organism at least 48 hours after initiation of therapy, but without signs and symptoms of infection.[14]

Clinical and microbiological outcomes were unevaluable when active acute care of a patient was withdrawn while the patient was receiving antibiotics, when switch therapy was not performed, when randomization to a clinical trial involving antimicrobials occurred, or when the patient developed an illness that interfered with the clinical evaluation of pneumonia (e.g. acute respiratory distress syndrome) or died from a cause other than pneumonia.

RESULTS

From March 11–August 28, 1996, 26 critically ill patients with pneumonia qualified for entry into the study. The population demographics are outlined in Table I. Of the 26 cases, 13 had CAP and 13 had HAP. The majority of patients were above 50 years of age and had several underlying conditions including heart disease (46%) and diabetes mellitus (31%). The APACHE II scores on admission to ICU were less than 10 in 11% of patients, 11–20 in 35% of patients, 21–30 in 46% of patients and above 30 in 8% of patients. Patients with CAP tended to have higher APACHE II scores than patients with HAP. Fifteen (57.7%) patients required mechanical ventilation at study entry and 18 (69.2%) patients required it during their ICU stay. Intravenous antibiotics were initiated in the emergency room for four patients with CAP whereas all treatments courses for HAP were started in the ICU. Among the 13 cases of HAP, 9 were acquired in the ICU.

Switch therapy was achieved in 10 (77%) patients with CAP and 12 (92%) patients with HAP. Conversion occurred after an average of 6.6 days and 5 days of IV therapy for patients with CAP and HAP respectively. Four patients (15%) were not converted to oral therapy, 2 because they failed to meet our criteria for conversion, and 2 for other reasons (IV therapy discontinued, misunderstanding from the prescriber).

Parenteral antibiotics were combined in 62% of CAP treatment courses. The most frequent combination, cefuroxime and clindamycin, was used in 62.5% of patients that had polytherapy. Antibiotics used in monotherapy included cefuroxime (25%), cloxacillin (25%), clindamycin (25%) and penicillin G (25%).

Table I — Demographics of critically ill ICU patients with pneumonia, undergoing conversion from iv to oral/nasograstric antibiotics during a 5-month study period. CAP=Community-acquired pneumonia. HAP=Hospital-acquired penumonia. APACHE II= Acute Physiology and Chronic Health Evaluation II.

Factor	Type of pneumonia	
	CAP	HAP
No. of treatment courses	13	13
Female/male	6/7	7/6
Mean age in years (±SD)	61.0 ± 17.3	55.8 ± 20.0
With history of smoking	7	5
Signficant alcohol use or history	6	2
Average number of chronic conditions (± SD)	2.2 ± 1.6	2.5 ± 2.0
Baseline creatinine (± SD) (mmol/l)	115.4 ± 32.6	92.7 ± 38.8
APACHE II score (± SD)	24.0 ± 6.7	19.0 ± 6.7
Duration of ICU stay in hours (± SD)	228.6 ± 207.8	169.56 ± 91.45
Hours of ventilation (± SD)	193.0 ± 22.6	99.0 ± 74.0
Number of patients mechanically ventilated	11	7

Combination therapy was also used initially in 62% of HAP treatment courses, and consisted of cefotaxime and clindamycin in half of the patients that received combination therapy. When monotherapy was used, antibiotics included cefuroxime (60%) and cefotaxime (40%). Antibiotics selected for switch therapy in the CAP group included cotrimoxazole (40%), amoxicillin/clavulanic acid (30%), clindamycin (30%) and cloxacillin (10%). Oral antibiotics were combined in one patient only (cotrimoxazole and clindamycin). In the HAP group, the antibiotics selected for switch therapy were ciprofloxacin (33%), cotrimoxazole (25%), amoxicillin/clavulanic acid (25%), clindamycin (17%), cloxacillin (8%), erythromycin (8%) and cephalexin (8%). Combination with oral antibiotics occurred in 3 patients (ciprofloxacin and clindamycin, ciprofloxacin and erythromycin, cephalexin and clindamycin). Switch therapy occurred while in the ICU for 20 (91%) patients.

Values for temperature, WBC and FiO_2 requirements at baseline, at time of conversion and at the end of oral therapy are presented in Table II. Clinical outcome was evaluated in 9 (69%) treatment courses for CAP and 11 (85%) treatment courses for HAP. The reasons for the lack of assessment of clinical response were failure to convert to an oral antibiotic (n=4) and care withdrawal (n=2). Of the evaluable patients, clinical cure was observed in 8 (89%) patients with CAP and 9 (82%) patients with HAP. Improvement occurred in 1 (11%) patient with CAP and 2 (18%) patients with HAP.

Only one study patient had a positive blood culutre. Sputum cultures were positive in 10 (77%) patients with CAP and 7 (54%) patients with HAP. Culture results are presented in Table III.

Table II—Mean temperature (and SD), white-blood-cell count (WBC) and FiO_2 requirements during study period. CAP=Community-acquired pneumonia. HAP=Hospital-acquired pneumonia.

	Time of value (and SD of values)		
Type of measure	Baseline	IV to PO conversion	End of oral therapy
CAP (n=13)			
Mean temperature (°C)	38.2 (1.1)	37.1 (0.6)	37.0 (0.4)
Mean WBC (x 10^9/L)	12.1 (8.2)	7.3 (2.8)	8.5 (4.8)
Mean FiO_2 (%)	53 (19.0)	29 (10.0)	22 (3.0)
HAP (n=13)			
Mean temperature (°C)	37.6 (1.2)	37.1 (0.9)	36.8 (0.7)
Mean WBC (x 10^9/L)	15.1 (5.9)	12.5 (3.8)	12.3 (3.5)
Mean FiO_2 (%)	39 (11.0)	26 (12.0)	22 (0.0)

Microbiological outcome was assessed in 10 patients with CAP and 7 patients with HAP. In the CAP group, 7 of the 10 patients had eradication as microbiological outcome while the remaining 3 patients, despite positive cultures, were unevaluable because conversion to an oral antibiotic had not occurred. In the HAP group, 6 of the 7 patients with positive cultures had eradication while one patient was unevaluable again because of failure to convert to an oral antibiotic.

DISCUSSION

Numerous reports regarding the successful use of intravenous followed by oral antibiotics for treatment of serious infections, especially pneumonia, have been published.[15–21] Our study results are in agreement with those reports. To our knowledge, this is the first evaluation of switch therapy done strictly in an ICU population. Our results suggest that a switch to the enteral route provides safe and effective therapy.

Patients with CAP were switched to oral antibiotics after an average of 6.6 days of intravenous therapy. The time before conversion to oral therapy was greater in patients with CAP than in patients with HAP, where switch therapy occurred after a mean of 5.0 days. This is likely due to the severity of illness of the patients with CAP, as demonstrated by a higher mean APACHE II score and longer duration of ventilation (24 ± 6.7 and 193 ± 226 hours, respectively). However, the patients in the HAP group may not accurately reflect our typical ICU population with nosocomial pneumonia. The reason for this bias is that during our study, a company-sponsored clinical trial comparing 2 IV antibiotics for nosocomial pneumonia was taking place in the ICU. Priority for enrollment was given to the company-sponsored trial, and we excluded all patients in any clinical trial involving antimicrobials. Mean APACHE II scores and duration of ventilation for HAP patients in our study versus those enrolled in the sponsored trial were 19 ± 6.7 and 99 ± 74 hours versus 23 ± 6.4 and 285 ± 253 hours respectively. None of the patients in the HAP group died compared to a mortality rate of 22% in the clinical trial.

Clinical assessments of the 20 patients with evaluable data indicated that all were clinically cured or improved. Among the 17 patients that had positive microbiological cultures, 13 patients (76%) had eradication of the causative pathogen(s). No adverse effects from the PO/NG

Table III—Culture results among study patients

Type of pneumonia	Type of culture: Sputum — Patients with positive cultures (N), organisms and frequency	Type of culture: Blood — Patients with positive cultures (N), organisms and frequency
Community-acquired (N=13)	N=10 S. pneumoniae 6 S. aureus 5 H. influenzae* 2 E. coli 1 H. alvei 1 C. freundii 1 P. aeruginosa 1 L. pneumonphila 1	N=1 S. aureus 5
Hospital-acquired (N=13)	N=7 S. aureus 4 E. coli 2 H. influenzae† 2 P. aeruginosa 1 S. marcescens 1	N=0

* Both beta-lactamase negative.
† One beta-lactamase positive and one beta-lactamase negative.

antibiotics were noted. These results clearly suggest a favorable outcome for patients that underwent switch therapy.

Pathogens most frequently isolated in the CAP group were consistent with those reported in ICU patients with CAP by the Canadian Community-Acquired Pneumonia Consensus Conference.[8] All organisms, except *H. influenzae*, isolated in the HAP group, were frequently identified in severe HAP by the Canadian Hospital-Acquired Pneumonia Consensus Conference.[9]

Limitations of this study include the small sample size of the 2 groups of patients, and the exclusion of sicker patients who were entered into the company-sponsored clinical trial. In addition, a control group to assess the characteristics of drug usage in the absence of our program was not used. Since no other studies on conversion to PO/NG antibiotics for pneumonia in the ICU setting have been published, comparative information is lacking and data can only be retrieved from a nonICU setting. Ramirez reported the results of a conversion program for CAP as well as for HAP in the absence of a control group. Conversion occurred after a mean time of 2.8–3.2 days for CAP and 4.5 days for HAP. Our results for CAP differ because our patients were more severely ill and required ICU admission. Data for HAP, however, are similar. Ramirez also compared the length of hospital stay with a historical matched control group and observed that an IV to PO conversion program led to a significant reduction in length of hospital stay.[15] However, we feel that such a program in the ICU setting is unlikely to be associated with a reduction in the ICU length of stay or duration of ventilation.

Efforts to promote early conversion to PO/NG antibiotic are still ongoing and are part of the daily workload of the ICU pharmacist.

CONCLUSION

An IV to PO/NG conversion program for critically ill patients with community or hospital-acquired pneumonia provides effective therapy. Clinical and microbiological assessments revealed that the majority of patients were clinically cured and had eradication of the causative pathogen(s).

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N.B. Guidelines for the empiric treatment of CAP and HAP at our hospital are available upon request.

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