Comparison Of Clinical Outcome3 Quality Of Life And Cost In Patients With Community Acquired Pneumonia Treated With Home Iv Antibiotics Vs. Inpatient Iv Antibiotics

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A. Introduction and Background

Community-acquired pneumonia (CAP) is an illness which affects over 4 million people each year in the U.S., and for which an estimated 1,000,000 patients are hospitalized yearly [Fine, pred. rule; Siegel -rand study]. The etiology and pathophysiology of pneumonia is well elucidated in the scientific literature, and the pharmacologic therapy is well established [ATS] with some degree of variation. Recent literature has suggested that there is a significant percentage of patients hospitalized with CAP who are not severely ill, and may be candidates for shortened courses of intravenous (IV) antibiotics [Siegel] as well as IV antibiotic treatment provided at home without compromising clinical outcome (ref PORT]. With the availability of home-delivered IV antibiotic therapy (Williams], we propose a study to identify those patients that are traditionally hospitalized who could be successfully treated at home.

Although the diagnosis and treatment of this illness are considered to be straightforward, criteria that determine need for hospitalization have traditionally been based on subjective physician assessment and are, therefore, inconsistent among physicians and institutions. One survey [Fine et.al. - hosp. adm decision] revealed that physicians relied heavily on clinical factors such as respiratory status, comorbid illness, clinical appearance, lung involvement of more than I lobe on radiography, and oral intake in the decision to hospitalize. Two psychosocial. factors were identified by practitioners as important in this decision: patient reliability and level of home care support. This survey also revealed that physicians often overestimate the risk of mortality in these patients, suggesting that a reliable rule to predict prognosis might increase appropriate use of outpatient treatment of CAP.

At this time, reliable prediction rules designed to stratify patients with CAP into low, moderate and high risk categories with regard to severity of illness have been developed. Fine et.al. have published such a prediction rule [Fine, pred. rule] which they show to be valid and reliable in analysis of two large databases of patients with CAP. These data suggest that there is a significant percentage of patients hospitalized for CAP (class II and III as described below) that have a low mortality of 0.6 percent in class II in both cohorts and 0.9 percent to 2.8 percent in class III in the two cohorts. In addition, these risk classes were found to have a high likelihood of clinical cure and could potentially be treated safely and effectively at home via VNA services that currently exist and with appropriate physician follow-up.

The aim of our study is to compare the treatment of patients with CAP who have an illness of moderate severity (as defined below) in their homes versus the traditional inpatient setting via a randomized, prospective study in order to demonstrate home treatment of CAP as a safe and practical option for a significant percentage of patients with this illness. This has important implications for improving patients' quality of life while maintaining effective treatment as reflected by clinical improvement, low rates of subsequent admission to the hospital, low 30 day mortality and complication rate, and significant reductions in the cost of treating CAP.

B. Study design and statistical analysis:

Patients presenting to the CPMC or Allen Pavilion (and NY Hospital and other consortium sites) Emergency Departments with suspected CAP will be evaluated by a physician in order to conduct initial assessment and data gathering required for risk stratification via the prediction rule developed by Fine et.al.[ ] - see Figure I. Those patients found to be in risk classes II and III will be considered for inclusion. Patients identified to be eligible (see exclusion criteria in section G.) will be randomized from the

emergency room to receive inpatient IV antibiotics or to receive IV antibiotics at home to be delivered by VNA (Visiting Nurses Association) services. Patients in the home treatment group will be followed daily by a nurse who will perform basic clinical evaluation (vitals, physical exam) and ensure that IV antibiotics are delivered through a properly functioning intravenous catheter. A physician contact from each site will be available at all times to answer questions and provide guidance to the patient and nurse.

All patients will receive 5 days of IV antibiotics prior to switch to oral antibiotics. Although a few randomized controlled trials have found early switch (2 to 3 days) to be a safe option, no standardized length of IV antibiotic treatment exists currently. The ATS guidelines suggest that resolution of fever and improvement of clinical symptoms indicate a reasonable timepoint to begin oral therapy [ATS].

Data will be collected regarding demographics and home environment, comorbid illnesses, physical exam findings and laboratory findings as per figure I at initial evaluation. Additional data regarding pertinent symptomatology, physical exam and laboratory findings will be collected at day 7 and at day 30 at the time of followup physician evaluations (see Figure 2), and at time of readmission if this event should occur. A health-related quality-of-life survey to be completed by the participating patients will be collected at day 30. Data will be analyzed on an intent-to-treat basis. Analysis of covariance will be performed on all data to control for undetected confounders in comparing primary and secondary outcomes between groups.

a. **Outcomes measured will include the following:**
  i. **Primary outcomes:**
     - Treatment failure as defined by readmission to the hospital. This will be defined as any admission in the home treatment group within 30 days of the initial emergency room evaluation for illness due to relapsed or continued and progressive pneumonia. Treatment failure in the inpatient group will be defined as re-admission to the hospital within - days of discharge or-transfer to an ICU, indicators of failure of initial therapy-
  ii. **Secondary outcomes:**
     - Health-related quality of life, as measured by the SF-36 health survey instrument;
     - Cost of treatment (will refer to data re. avg. cost for treatment of inpatient CAP at CPMC from 1996 data as well as average cost of VNA and infusion services/day);
     - Mortality at 30 days.

Data from the Pneumonia PORT Cohort Study allow us to estimate that approximately 10 percent of patients in classes II and III who were treated as outpatients required subsequent hospitalization for reasons due to their pneumonia, with a subsequent mortality of 0.4 percent (one death in class II) and zero percent respectively. We have made the assumption that an admission rate from the home treatment group that is greater than 10 percent higher than readmission rate in the inpatient group would be a true marker of poor clinical outcome in the home treatment group, and a difference that we must be able to detect. A difference of less than 10 percent will be acceptable due to the low mortality rate in this group and due to the anticipated benefits of improved quality of life and significant cost reduction. In order to detect a difference in primary outcome of greater than 10 percent between groups in this study we will require 220 subjects in each group, with an 80 percent probability of detecting a true difference of this size.

It is estimated that approximately 22 eligible patients will be available for recruitment to the study per month based on review of total admissions for 1996 to CPMC and the Allen Pavilion. If we anticipate a 50% rejection rate at all sites, and match this recruitment rate via all other participating sites (NY Hospital and all consortium hospitals), the patient enrollment period can be expected to last approximately 20 months.

C. **Description of study procedures**

Home IV antibiotic therapy will be provided by VNA services, who will provide a visiting RN daily to ensure proper functioning of peripheral IV's and to administer antibiotic dosages in a timely fashion. Inpatient IV antibiotic therapy will be provided by hospital RN staff. A physician contact to discuss concerns and questions will be made available daily for visiting nurses.

D. Study Drugs

Patients in each group will receive a second- or third- generation cephalosporin OR a beta-lactam/ beta-lactam aB inhibitor +/- a macrolide as described in the American Thoracic Society's official recommendation for hospitalized patients with CAP. ***[length of treatment up to discretion of MD, in each case?]

E. Medical Devices

Peripheral intravenous catheters will be required in all patients in each group, to be changed according to standard hospital procedure to prevent infection, or if there is evidence of infection at the placement site or if the catheter is not functioning properly.

F. Study questionnaires

A health-related quality-of-life survey will be administered to the patient at the 30 day follow-up meeting.
** [choose an instrument]

G. Description of study subjects and method of recruitment

Enrollment will be open to any male or female age 18 or older who meet the eligibility criteria as described above. Subjects will be recruited from patients evaluated in the Emergency Dept. at either CPMC or at the Allen Pavilion. Approximately 220 patients will be required in each group in order to detect a significant difference in the primary outcome if such a difference exists.

As treatment of nosocomial pneumonia will not be considered in this study, patients will be ineligible for enrollment if they have been transferred from another hospital, or discharged from an acute-care hospital within ten days prior to presentation to the emergency department. Patients known to be HIV-positive will be excluded from this study. Patients with a witnessed aspiration event, prior organ transplantation, recent use of myelosuppressive drugs, neutropenia due to chemotherapy, or severe neuromuscular disorders [Stone et.al.] will be excluded from this study. In addition, patients who fall into risk categories II or III will be ineligible if they have an oxygen saturation of less than 90 percent or a partial pressure of oxygen of less than 60 percent while breathing room air on initial evaluation. An attempt will be made to obtain reason for exclusion for all patients found to be ineligible at the time of initial evaluation.

H. Confidentiality of study data

Each patient enrolled in the study will be identified by a unique number. All data will be stored in Dr. Richard Greene's office in the Milstein Building, 8th floor. Any information presented as a result of this study will refer to individual patients by number only.

I. Location of study

Patients will be initially evaluated in the E.D. at either CPMC or the Allen Pavilion. Follow-up visits for all patients at day 7 and day 30 will be conducted in the Irving Center Outpatient Clinic on the tenth floor of the Harkness Building, or at the bedside if the patient is in the hospital.

J.   Risks and benefits

The primary risks of participation in the study include the following: intolerance of antibiotics due to side effects such as GI disturbance (nausea, vomiting, diarrhea), allergy (rash, bronchospasm); complications due to placement of intravenous catheter (phlebitis and irritation). In addition, the risk of complications of CAP includes worsening respiratory status due to pleural effusion or increased lobar involvement and suppurative complications (e.g. empyema, meningitis, bacterial seeding of heart valves and joints). The rate of such complications in this subgroup of patients is expected to be very low, as the expected mortality is less than 2.8 percent for all patients, and less 1.0 percent for outpatients subsequently admitted to the hospital.

A mechanism will be in place for daily contact with patients in the home treatment group should their clinical condition require re-evaluation.

The benefits of participation in the study include improvement in patient quality of life while maintaining the high clinical cure rate and low mortality rate already shown to exist with standard therapy in this subgroup of patients. The home treatment group will avoid risk of hospital-related complications such as nosocomial infections. Additional benefits will be the increased participation of outpatients in their own care. Benefits to the health care system will be realized mainly in improved patient satisfaction and in lowering costs associated with treating patients with CAP within the subgroup we are studying.

K.   Alternative therapies

There is currently no proven alternative therapy for patients with CAP requiring IV antibiotics who are not severely ill. There are antibiotics (e.g. fluoroquinolones) that are effective against the spectrum of bacteria that cause CAP, but questions remain as to problems with creation of resistance among bacteria exposed to certain classes of these drugs. ATS recommended therapy continues to be the standard at this time.

L.   Compensation and costs to subjects

Subjects will not incur any costs for their involvement. In addition, $20 dollars per visit will be provided to patients to cover travel, meal or other costs.

M.   Minors and research subjects

N/A

N.   Radiation and radioactive substances

N/A