



Original Contribution

Failure of outpatient antibiotics among patients hospitalized for acute bacterial skin infections: What is the clinical relevance? ☆☆☆☆



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ABSTRACT

Background: Infectious Diseases Society of America guidelines recommend that patients hospitalized for acute bacterial skin infections after failure of outpatient antibiotic therapy be managed as “severe” infections; however, the clinical relevance of apparent failure of outpatient therapy is not clear.

Methods: This was a secondary analysis of a multicenter, retrospective cohort of adults and children hospitalized for cellulitis, abscess, or wound infection. We compared clinical features, laboratory and microbiology findings, antibiotic treatment, and outcomes among patients who received outpatient antibiotics prior to admission and those who did not.

Results: Of 533 patients, 179 (34%) received outpatient antibiotics prior to admission. Compared with those who did not, patients who received antibiotics prior to admission less frequently had fever (18% vs 26%, $P = .04$) and leukocytosis (33% vs 51%, $P < .001$). In the 202 cases where a microorganism was identified, *Staphylococcus aureus* was more common among those who received antibiotics prior to admission (75% vs 58%, $P = .02$), particularly methicillin-resistant *S aureus* (41% vs 27%, $P = .049$), whereas aerobic gram-negative bacilli were less common (3% vs 13%, $P = .03$). After hospitalization, clinical failure occurred with similar frequency between the 2 groups (12% vs 11%, $P = .73$).

Conclusions: Patients hospitalized with skin infections after apparently failing outpatient therapy had clinical features suggestive of less severe infection and similar outcomes compared with patients who did not receive antibiotics prior to admission. Our results suggest that inpatient treatment for patients not responding to outpatient therapy should focus on methicillin-resistant *S aureus*, not gram-negative pathogens.

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1. Introduction

Acute bacterial skin infections result in approximately 14 million ambulatory care visits [1] and 900 000 hospitalizations [2] per year and are among the leading indications for antibiotic use in hospitals [3]. In prior cohorts of patients requiring hospitalization for acute bacterial skin infections, 28% to 51% had failed an initial attempt at outpatient antibiotic therapy [4,5]. However, the determination of whether a patient is responding to outpatient therapy can be challenging for emergency department (ED) providers, particularly in cases of cellulitis, given that the skin may remain inflamed despite eradication of the causative pathogen. Whether failure of outpatient therapy as judged

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by clinicians is associated with an increased breadth of microbial pathogens or affects clinical outcomes has not been previously studied.

Current Infectious Diseases Society of America (IDSA) guidelines for the management of skin infections stratify treatment recommendations based on a clinical classification of mild, moderate, or severe infection [6]. Patients who have failed outpatient antibiotic therapy, have systemic signs of infection, are immunosuppressed, or have clinical signs suggestive of necrotizing infection are classified as having “severe” infection. In the case of severe nonpurulent cellulitis, an antibiotic regimen with a broad spectrum of gram-positive and gram-negative activity is recommended (eg, vancomycin plus piperacillin-tazobactam). Given the frequency of failure of outpatient therapy, adherence to this suggested treatment approach would lead ED providers to start broad-spectrum antibiotics in a sizeable proportion of cases. It is thus important to gain a better understanding of the clinical relevance of failure of outpatient therapy as judged by clinicians. We used a large cohort of patients requiring hospitalization for treatment of an acute bacterial skin infection to determine whether an initial attempt at outpatient therapy prior to admission impacted the microbiology, treatment, and clinical outcomes.

2. Methods

2.1. Study design

We previously described a multicenter, retrospective cohort of patients requiring hospitalization for acute bacterial skin infection between June 1, 2010, and May 31, 2012 [7]. Using this cohort, we performed a secondary analysis comparing patients who were initially attempted to be treated with outpatient antibiotic therapy prior to admission with those who were not.

2.2. Study setting and population

The study was performed in 7 Colorado hospitals including a Veteran's Affairs hospital, tertiary referral center, public safety-net hospital, children's specialty hospital, and 3 private community hospitals.

Detailed study entry criteria have been described previously [7]. Briefly, adults and children with a principal discharge diagnosis of cellulitis, cutaneous abscess, or wound infection were identified through *International Classification of Diseases, Ninth Revision, Clinical Modification* codes (680.* , 681.* , 682.* , 686, 035). Cases were manually reviewed to confirm eligibility. The main exclusion criteria were infections with deep tissue involvement (eg, necrotizing fasciitis, osteomyelitis, and myositis) and clinical scenarios that require specialized management, including the following: infected ulcers, surgical site infection, periorbital or perineal infection, infected human or animal bites, health care-associated infections, and hidradenitis suppurativa. At each hospital, for cases meeting the study entry criteria, a clinician with experience in the management of skin infections abstracted clinical and pharmacy data from the medical record using a standardized data collection form. Each clinician underwent training to standardize data collection across sites. The study was approved by each hospital's institutional review board.

2.3. Definitions and study outcomes

Outpatient antibiotic therapy prior to admission was defined as the receipt of one or more systemic antibiotic for the current episode of skin infection leading up to hospitalization, as documented in the medical record (Figure A). Both parenteral and oral antibiotics prescribed at ambulatory care visits prior to admission were included in this definition; this information was obtained from provider documentation and pharmacy fill data. When it was specifically noted in the medical record that a patient was prescribed an antibiotic but either did not fill the prescription or did not take any doses of the antibiotic, this was not classified as antibiotic therapy prior to admission. Antibiotic courses for a previous, distinct episode of skin infection were also not classified as antibiotic therapy prior to admission. The specific antibiotics received leading up to hospital admission were recorded; however, the number of days of therapy and the timing in relation to admission were not collected as this information was frequently not available in the medical record.

Fever and leukocytosis were defined as a core body temperature of at least 38.0°C and a serum white blood cell count greater than

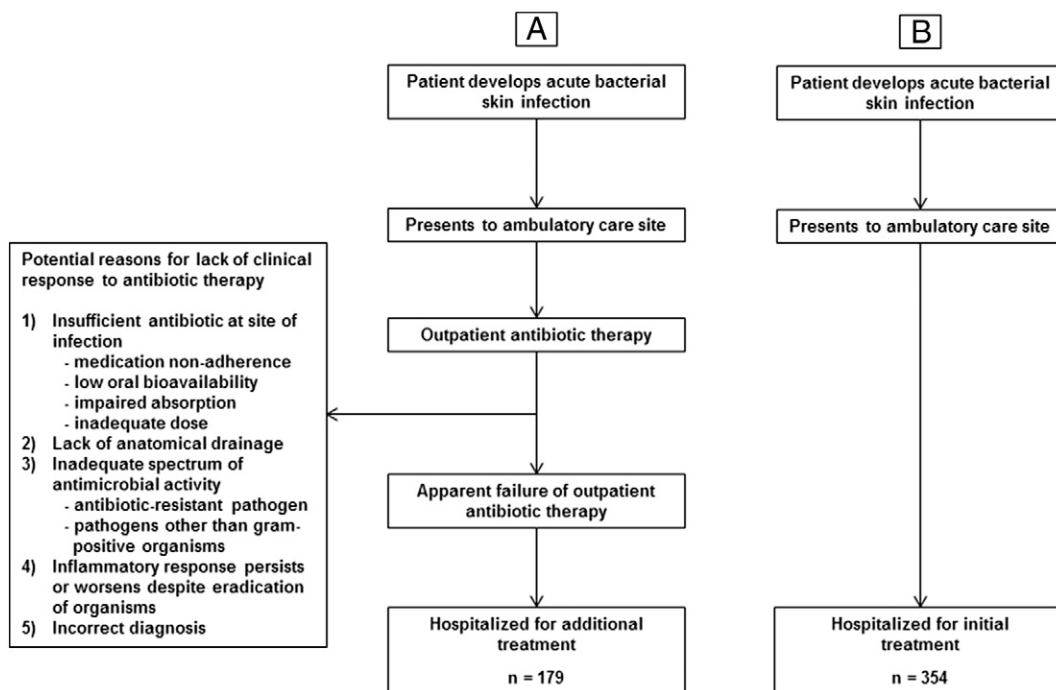


Figure. Conceptual framework of the process of care for patients requiring hospitalization for treatment of acute bacterial skin infections. A, Patients who appear to fail an initial attempt at outpatient antibiotic therapy and a list of potential reasons for the lack of response to therapy. B, Patients hospitalized for initial treatment with no attempt at outpatient antibiotic therapy. Ambulatory care refers to EDs, urgent care, and outpatient clinics.

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