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Infectious diseases specialist management improves outcomes for outpatients diagnosed with cellulitis in the emergency department: a double cohort study☆

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ABSTRACT

Three hospital emergency rooms (ERs) routinely referred all cases of cellulitis requiring outpatient intravenous antibiotics, to a central ER-staffed cellulitis clinic. We performed a retrospective cohort study of all patients seen by the ER clinic in the last 4 months preceding a policy change (ER management cohort [ERMC]) (n = 149) and all those seen in the first 3 months of a new policy of automatic referral to an infectious disease (ID) specialist–supervised cellulitis clinic (ID management cohort [IDMC]) (n = 136). Fifty-four (40%) of 136 patients in the IDMC were given an alternative diagnosis (noncellulitis), compared to 16 (11%) of 149 in the ERMC ($P < 0.0001$). Logistic regression–demonstrated rates of disease recurrence were lower in the IDMC than the ERMC (hazard ratio [HR], 0.06; $P = 0.003$), as were rates of hospitalization (HR, 0.11; $P = 0.01$). There was no significant difference in mortality. Automatic ID consultation for cellulitis was beneficial in differentiating mimickers from true cellulitis, reducing recurrence, and preventing hospital admissions.

1. Introduction

Cellulitis is an acute or subacute inflammation of the dermis and/or subcutaneous tissue, characterized by erythema, warmth, edema, pain, and in some cases systemic signs, such as fever. In patients presenting with cellulitis, there are many factors that determine the type and duration of treatment, as outlined in the Infectious Diseases Society of America guidelines on skin and soft tissue infections (Stevens et al., 2014). Despite these guidelines, variation among emergency physicians has been well documented in the treatment of presumed cellulitis, and treatment failure rates remain high (Dong et al., 2001; Hoogewerf et al., 1999; Murray et al., 2005; Peterson et al., 2014; Quirke et al., 2016; Zed et al., 2001).

Several modifiable risk factors for the development and recurrence of cellulitis have been identified (e.g., tinea pedis, chronic ulcers, etc.) (Björnsdóttir et al., 2005; Dupuy et al., 1999; Halpern et al., 2008; Peterson et al., 2014; Roujeau et al., 2004). This suggests that in some cases, recurrent cellulitis results from an underlying condition that requires management beyond simple antibacterial antibiotics. Additionally, several mimickers of cellulitis have been identified that can lead to overdiagnosis of cellulitis (and therefore inappropriate antibiotic use), and undertreatment of the true presenting condition (Arakaki et al., 2014; Levell et al., 2011). Studies have suggested that dermatologist consultation for cellulitis diagnosed in the primary care setting reduces the use of unnecessary antibiotics (Arakaki et al., 2014; Levell et al., 2011). A recent study suggested that across a number of cellulitis trials, reported treatment failure rates vary between 6 and 37%, likely due in part to the wrongful inclusion of cellulitis mimickers, as well as to the mistreatment of complicated or atypical cases of cellulitis (Obaitan et al., 2016). We hypothesized that infectious diseases (ID) specialist consultation may be beneficial in differentiating true cellulitis from its mimickers, and also in identifying and treating underlying conditions that lead to recurrence and treatment failure.

To our knowledge, there is no published literature on the effects of ID consultation on the management of cellulitis diagnosed in the primary care setting. Our study aims to determine whether or not automatic

☆ Article summary: automatic infectious diseases consultation for cellulitis treated with intravenous antibiotics in the outpatient setting significantly decreased rates of hospitalization and disease recurrence when compared to ongoing management by the emergency room physicians.

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ID consultation for presumed cellulitis diagnosed in the emergency room (ER) reduces rates of disease recurrence, hospitalization, or mortality.

2. Methods

2.1. Study design and population

This study was conducted in London, Ontario. Prior to October 2014, 2 tertiary and 1 primary care hospital ERs routinely referred all cases of cellulitis requiring outpatient intravenous (IV) antibiotics, to a central ER physician–staffed cellulitis clinic. These 3 hospitals provided all emergency care services in the city of London (population 380,000). In October 2014, the policy was changed to refer all these patients from the ER to a board-certified ID specialist–supervised cellulitis clinic located in the same facility as the prior ER-run cellulitis clinic, after receiving at least 1 dose of IV antibiotics in the ER. Six ID physicians rotated call to the clinic. We completed a retrospective cohort study of all adult patients seen in the ER cellulitis clinic in the last 4 months prior to the change in policy (n = 149) (ER management cohort [ERMC]) and all those seen by ID in the first 3 months of the automatic ID consult policy (n = 136) (ID management cohort [IDMC]). This sample size was selected, as this was a quality of care initiative pilot program assessed as part of a student project, with the sample sizes taken to be feasible within the allotted time. All patients referred electively to other specialist services by either the ER or ID physicians remained part of their respective cohorts for the purposes or our analysis. More specifically, 4 patients who were managed by the ER cellulitis clinic were electively referred to ID for consultation. These patients were considered part of the ERMC for all analyses. Patients below the age of 18, and those who were admitted to hospital directly on their first visit to the ER were excluded. Research ethics approval was obtained from the Health Sciences Research ethics board at Western University, as well as the Lawson Health Research Institute.

2.2. Data collection and definitions

A combination of paper charts and electronic medical records was used to collect data from the 3 hospital ERs, inpatient wards, and clinics. Furthermore, a regional database of all laboratory and radiological studies done in the community during the study period was reviewed to identify any testing done outside the study institutions. Patient variables that were collected and analyzed included age, sex, site of presumed cellulitis, presence of diabetes, coronary artery disease, chronic obstructive pulmonary disease, pulmonary hypertension, obstructive sleep apnea, congestive heart failure, chronic kidney disease, liver disease, hypertension, dyslipidemia, previous surgery to the affected body site, history of lymphedema, history of lymph node resection, venous insufficiency, chronic ulcers, immunosuppression (including active cancer, HIV infection, and immunosuppressive medications), documented methicillin-resistant *Staphylococcus aureus* (MRSA) carriage or infection within the last year, history of IV drug use, history of previous cellulitis, history of recent antibiotic use at the time of initial presentation, and trauma to the affected site. These variables were chosen based on published literature outlining the predisposing factors for development and recurrence of cellulitis, as well as risk factors identified to contribute to treatment failures in the ER (Björnsdóttir et al., 2005; Dupuy et al., 1999; Halpern et al., 2008; Murray et al., 2005; Peterson et al., 2014; Roujeau et al., 2004).

We determined whether or not a predisposing condition was identified and treated by either ER or ID physicians (e.g., compression stockings prescribed for recurrent venous stasis). We recorded the final diagnosis established for each patient, and determined whether it changed to an alternate diagnosis (noncellulitis diagnosis), either upon ID specialist consultation or following ongoing care in the ER cellulitis clinic.

2.3. Outcomes

Primary outcomes included disease recurrence, hospitalization, and mortality. *Recurrence* was defined as a patient presenting to the ER or ID cellulitis clinic with disease involving the same anatomical location, requiring the re-institution of IV therapy within 90 days of initial presentation. If a patient's antibiotics were extended or changed for worsening or persistence of disease while on antimicrobial therapy, this was not counted as a recurrence. *Hospitalization* was defined as any hospitalization related to the presenting condition within a 90-day period. *Mortality* was defined as any cause of mortality within a 90-day period, as determined by hospital electronic records.

Secondary outcomes included *Clostridium difficile* infection within a 90-day period, as well as allergic reaction following antibiotic administration. Antibiotic discontinuation practices, total duration of antibiotics prescribed, duration of IV antibiotics, and duration of broad-spectrum therapy before step-down to narrow-spectrum therapy were also included. Broad-spectrum therapy included piperacillin-tazobactam, carbapenems, fluoroquinolones, second and third generation cephalosporins, amoxicillin-clavulinic acid, clindamycin, and any combination of antibiotics. *Narrow-spectrum therapy* was defined as single therapy with penicillin, cloxacillin, a first-generation cephalosporin, vancomycin, cotrimoxazole, or doxycycline.

2.4. Statistical analysis

Descriptive statistics were used to determine baseline and clinical characteristics of study subjects in each management cohort. Bivariate analysis of patient variables was performed using the chi-square test for equal proportion, Student *t* test for normally distributed continuous variables, and Mann–Whitney U test for nonnormally distributed variables. The efficacies of the 2 treatment approaches were assessed using bivariate analysis. Multivariate logistic models were constructed using stepwise selection and backwards elimination procedures with all variables from the bivariate analysis ($P < 0.2$) being considered for inclusion. All analysis was performed using SPSS version 21 (IBM Institute, Armonk, NY, USA). A 2-sided *P* value of 0.05 was considered to be statistically significant.

3. Results

One hundred forty-nine patients received treatment by ER physicians, and 136 by ID specialists. Patient demographics and underlying variables across cohorts are demonstrated in Table 1. Although many of the variables did not reach statistical significance across the 2 cohorts, there is a general trend toward patients in the IDMC having more comorbid conditions (Table 1). This is likely a result of more complete documentation on the patients seen in consultation by ID as compared to those seen in the ER, rather than a reflection of a true difference between cohorts.

Although all patients in our study were initially referred by the ER for management of cellulitis, 54 (40%) of 136 patients who were managed by ID were given an alternative diagnosis (noncellulitis), compared to 16 (11%) of 149 patients followed by the ER staff ($P < 0.0001$) (Table 2). When the final diagnosis was deemed to be cellulitis, the frequency of identification and treatment of an underlying etiology or predisposing factor was higher in the IDMC than in the ERMC (21/82 [26%] versus 3/133 [2%], $P < 0.0001$) (Table 3).

Table 4 demonstrates the results of the bivariate analysis of our study outcomes. Frequency of 90-day recurrence was lower in the IDMC than the ERMC (10/136 [8%] versus 48/148 [34%], $P = 0.001$) (Table 4). Using multiple backward logistic regression for adjustment of the roles of other covariates (age, diabetes, dyslipidemia, previous surgery of the affected site, lymphedema, chronic ulcer, MRSA colonization and noncellulitis diagnosis), receiving treatment by the IDMC (rather than ERMC) was the only variable which remained significantly