

Introduction: Current guideline recommendations for optimal management of non-purulent skin and soft tissue infections (SSTIs) are based on expert consensus. There is currently a lack of evidence to guide emergency physicians on when to select oral versus intravenous antibiotic therapy. The primary objective was to identify risk factors associated with oral antibiotic treatment failure. A secondary objective was to describe the epidemiology of adult emergency department (ED) patients with non-purulent SSTIs. **Methods:** We performed a health records review of adults (age 18 years) with non-purulent SSTIs treated at two tertiary care EDs. Patients were excluded if they had a purulent infection or infected ulcers without surrounding cellulitis. Treatment failure was defined any of the following after a minimum of 48 hours of oral therapy: (i) hospitalization for SSTI; (ii) change in class of oral antibiotic owing to infection progression; or (iii) change to intravenous therapy owing to infection progression. Multivariable logistic regression was used to identify predictors independently associated with the primary outcome of oral antibiotic treatment failure after a minimum of 48 hours of oral therapy. **Results:** We enrolled 500 patients (mean age 64 years, 279 male (55.8%) and 126 (25.2%) with diabetes) and the hospital admission rate was 29.6%. The majority of patients (70.8%) received at least one intravenous antibiotic dose in the ED. Of 288 patients who had received a minimum of 48 hours of oral antibiotics, there were 85 oral antibiotic treatment failures (29.5%). Tachypnea at triage (odds ratio [OR]=6.31, 95% CI=1.80 to 22.08), chronic ulcers (OR=4.90, 95% CI=1.68 to 14.27), history of MRSA colonization or infection (OR=4.83, 95% CI=1.51 to 15.44), and cellulitis in the past 12 months (OR=2.23, 95% CI=1.01 to 4.96) were independently associated with oral antibiotic treatment failure. **Conclusion:** This is the first study to evaluate potential predictors of oral antibiotic treatment failure for non-purulent SSTIs in the ED. We observed a high rate of treatment failure and hospitalization. Tachypnea at triage, chronic ulcers, history of MRSA colonization or infection and cellulitis within the past year were independently associated with oral antibiotic treatment failure. Emergency physicians should consider these risk factors when deciding on oral versus intravenous antimicrobial therapy for non-purulent SSTIs being managed as outpatients.

Keywords: cellulitis, antibiotics, treatment failure

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Intravenous cefazolin plus oral probenecid vs. oral cephalexin for the treatment of skin and soft tissue infections: a randomized controlled trial

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Introduction: Skin and soft tissue infections (SSTIs) are a common reason for presentation to an emergency department (ED). Although many patients with mild SSTI are managed with oral antibiotics, those with mild-moderate infections are often treated with parenteral antibiotics, managed in EDs as outpatients using once daily intravenous cefazolin combined with oral probenecid. The purpose of our study was to determine if cephalexin 500 mg orally four times daily was non-inferior to cefazolin 2 g intravenously daily plus probenecid 1 g orally daily in the management of uncomplicated mild-moderate SSTIs patients presenting to the ED. **Methods:** This was a prospective, multicenter, double dummy-blind, randomized controlled non-inferiority trial conducted at two tertiary care teaching hospitals in Canada. Patients were enrolled if they presented to the ED with an uncomplicated SSTI, in a 1:1 fashion to oral cephalexin or intravenous cefazolin plus oral probenecid for up to 7 days. The primary outcome was failure of therapy

at 72 hours. Clinical cure at 7 days, intravenous to oral step-down, admission to hospital and adverse events were also evaluated. **Results:** 206 patients were randomized with 104 patients in the cephalexin group and 102 in the cefazolin and probenecid group. The proportion of patients failing therapy at 72 hours was similar between the treatment groups (4.2% and 6.1%, risk difference 1.9%, 95% CI (-3.3% to 7.1%), p-value for non-inferiority = 0.001). Clinical cure at seven days was not significantly different (100% and 97.7%, risk difference -2.3%, 95% CI (-4.9% to 0.3%), p-value for non-inferiority = 0.008). **Conclusion:** Cephalexin at appropriate doses appears to be a safe and effective alternative to outpatient parenteral cefazolin and probenecid in the treatment of uncomplicated mild to moderate SSTIs who present to the ED.

Keywords: skin and soft tissue infection, antimicrobial therapy, emergency department

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Prospective multicenter validation of the Canadian syncope risk score

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Introduction: The Canadian Syncope Risk Score (CSRS) was developed to identify patients at risk for serious adverse events (SAE) within 30 days of an Emergency Department (ED) visit for syncope. We sought to validate the score in a new cohort of ED patients. **Methods:** We conducted a multicenter prospective cohort study at 8 large academic tertiary-care EDs across Canada from March 2014 to Dec 2016. We enrolled adults (age 16 years) who presented within 24 hours of syncope, after excluding those with persistent altered mentation, witnessed seizure, intoxication, and major trauma requiring hospitalization. Treating ED physicians collected the nine CSRS predictors at the index visit. Adjudicated SAE included death, arrhythmias and non-arrhythmic SAE (myocardial infarction, serious structural heart disease, pulmonary embolism, severe hemorrhage and procedural interventions within 30-days). We assessed area under the Receiver Operating Characteristic (ROC) curve, score calibration, and the classification performance for the various risk categories. **Results:** Of the 2547 patients enrolled, 146 (5.7%) were lost to follow-up and 111 (4.3%) had serious condition during the index ED visit and were excluded. Among the 2290 analyzed, 79 patients (3.4%; 0.4% death, 1.4% arrhythmia) suffered 30-day serious outcomes after ED disposition. The accuracy of the CSRS remained high with area under the ROC curve at 0.87 (95% CI 0.82-0.92), similar to the derivation phase (0.87; 95% CI 0.84-0.89). The score showed excellent calibration at the prespecified risk strata. For the very-low risk category (0.3% SAE of which 0.2% were arrhythmia and no deaths) the sensitivity was 97.5% and negative predictive value was 99.7% (95% CI 98.7-99.9). For the very high-risk category (61.5% SAE of which 26.9% were arrhythmia and 11.5% death) the specificity was 99.4% and positive predictive value was 61.5% (95% CI 43.0-77.2). **Conclusion:** In this multicenter validation study, the CSRS accurately risk stratified ED patients with syncope for short-term serious outcomes after ED disposition. The score should aid in minimizing investigation and observation of very-low risk patients, and prioritization of inpatient vs outpatient investigations or following of the rest. The CSRS is ready for implementation studies examining ED management decisions, patient safety and health care resource utilization.

Keywords: syncope, risk stratification, validation