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Trimethoprim-Sulfamethoxazole Therapy Reduces Failure and Recurrence in Methicillin-Resistant *Staphylococcus aureus* Skin Abscesses after Surgical Drainage

Lucy Holmes, MD[1,2], Changxing Ma, PhD[1], Haiping Qiao, MBBS, MS[2], Cheryl Drabik, MSN[2], Colleen Hurley, MSN[2], Donna Jones, MS[2], Sarah Judkiewicz, MSN[2], and Howard Faden, MD[1,2]

Objective To determine whether a 3-day vs 10-day course of antibiotics after surgical drainage of skin abscesses is associated with different failure and recurrence rates.

Study design Patients age 3 months to 17 years seeking care at a pediatric emergency department with an uncomplicated skin abscess that required surgical drainage were randomized to receive 3 or 10 days of oral trimethoprim-sulfamethoxazole therapy. Patients were evaluated 10-14 days later to assess clinical outcome. Patients were followed for 6 months to determine the cumulative rate of recurrent skin infections.

Results Among the 249 patients who were enrolled, 87% of wound cultures grew *Staphylococcus aureus* (*S aureus*) (55% methicillin-resistant *S aureus* [MRSA], 32% methicillin-sensitive *S aureus*), 11% other organisms, and 2% no growth. Thirteen patients experienced treatment failure. Among all patients, no significant difference in failure rates between the 3- and 10-day treatment groups was found. After we stratified patients by the infecting organism, only patients with MRSA infection were more likely to experience treatment failure in the 3-day group than the 10-day group (P = .03, rate difference 10.1%, 95% CI 2.1%-18.2%) Recurrent infection within 1 month of surgical drainage was more likely in patients infected with MRSA who received 3 days of antibiotics. (P = .046, rate difference 10.3%, 95% CI 0.8%-19.9%).

Conclusion Patients with MRSA skin abscesses are more likely to experience treatment failure and recurrent skin infection if given 3 rather than 10 days of trimethoprim-sulfamethoxazole after surgical drainage. *(J Pediatr 2016;169:128-34)*.

Trial registration ClinicalTrials.gov: NCT02024867.

In the last 15 years, there has been a sharp increase in the incidence of skin and soft-tissue infections (SSTIs).[1-7] Currently, most infections are abscesses caused by community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) and CA methicillin-sensitive *Staphylococcus aureus* (MSSA).[2,8-12]

Open incision and drainage alone, in otherwise-healthy patients, has been shown to be sufficient treatment in patients with skin abscesses[13,14] and traditionally was considered the standard of care.[15] Currently, it is less clear whether abscesses caused by CA-MRSA require adjunctive antibiotic treatment. The Infectious Diseases Society of America guidelines for the treatment of MRSA SSTI state that incision and drainage alone likely is sufficient treatment for simple abscesses or boils, although further studies are needed to determine the role for antibiotics.[16] Despite these guidelines, most practitioners prescribe adjunctive antibiotics.[17-19]

Some studies did not find any difference in outcome between patients given an active compared with an inactive antibiotic after incision and drainage of a MRSA skin abscess.[20,21] In contrast, 2 retrospective studies in adults showed that patients with CA-MRSA SSTI had improved outcome when given an active antibiotic, although not all patients in these studies had surgical drainage of their abscess.[11,22]

Two randomized controlled trials showed no difference in failure rates between 7 or 10 days of trimethoprim-sulfamethoxazole (TMP-SMX) and placebo among patients who had surgical drainage of their skin abscesses, although all the abscesses were not caused by MRSA.[23,24] In contrast, both studies showed that patients receiving placebo were more likely to experience a new infection within 1 month, suggesting that antibiotics may be beneficial in the prevention of recurrent infection.

CA	Community-associated
ED	Emergency department
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin-sensitive *Staphylococcus aureus*
SSTI	Skin and soft-tissue infection
TMP-SMX	Trimethoprim-sulfamethoxazole

From the [1]University at Buffalo; and [2]Women & Children's Hospital of Buffalo, Buffalo, NY

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A universally accepted empiric treatment regimen has remained elusive because of the lack of sufficiently large studies with adequate follow-up to determine failure and recurrence rates. The present study was designed to assess the effect of the duration of TMP-SMX treatment on the failure of cure and recurrence rates of surgically drained skin abscesses.

Methods

Patients were eligible to participate in the study if they were 3 months to 17 years of age and sought care at a pediatric emergency department (ED) for an uncomplicated skin abscess that required surgical drainage (induration ≥1 cm in diameter). An abscess was defined as a localized collection of pus causing soft-tissue swelling and tenderness. The measured size was based on the area of induration.

Exclusion criteria included patients who, in the judgment of the ED provider, required immediate hospitalization for parenteral antibiotic therapy, as well as patients who had received 2 or more doses of antibiotics in the previous 36 hours. Also excluded were patients who had a concurrent additional infection other than the abscess, an underlying medical condition predisposing them to more severe infections (ie, diabetes mellitus, sickle cell disease, an immune deficiency, or renal disease), or an allergy to TMP-SMX.

This study was a randomized, noninferiority trial approved by the Children and Youth Institutional Review Board at the Women and Children's Hospital of Buffalo. Clinical trial registration was obtained late for administrative reasons. The study design and primary outcome measure did not differ from the initial Institutional Review Board application and this article. Informed written consent was obtained from the parent or legal guardian. Assent was obtained from children ages 7-17 years. Patients were randomized to receive 3 or 10 days of oral TMP-SMX dosed at 10 mg TMP per kg per day divided twice a day, to a maximum of 320 mg TMP per day. No placebo pills or liquid were used for the subsequent 7 days in those randomized to the 3-day group. The randomization procedure was carried out by following a randomization table and implemented after informed consent was obtained. Study personnel and patients were not blinded to the treatment groups.

All patients had their abscess drained surgically with a minimally invasive surgical technique that is associated with a greater cure rate than open incision and drainage.[25-27] After a procedural sedation, a stab incision was made at each end of the abscess cavity, leaving a skin bridge over the abscess intact. The abscess was then probed with a hemostat to break up loculations. Purulent material was drained by manual compression, and the abscess cavity irrigated through the incisions. Finally, a subcutaneous drain, also known as a vessel loop, was inserted through the abscess cavity via the 2 incisions and tied together to keep the incision sites open and allow the abscess to drain further. Patients with multiple or larger abscesses had additional incisions and subcutaneous drains inserted.

If patients also had physical evidence of cellulitis, some ED providers routinely administered one parenteral dose of clindamycin before discharge from the ED. Providers were allowed to continue this practice at their discretion, with the assumption that this would occur in an equal distribution in the 2 treatment arms. No patient received decolonization therapy with additional antibiotics at the time of enrollment.

Patients were asked to return to surgery clinic 10-14 days after the surgical procedure to remove the drain and assess clinical outcome. Some patients chose to return to the ED to have their drain removed. In this situation, clinical resolution was based on the ED medical records if study personnel were not present. Otherwise, study personnel in the ED assessed for clinical resolution. Other patients chose to have their primary health care provider, and a few patients had a family member, remove the drain. In these situations, clinical outcome was based on a telephone interview with the patient's legal guardian. Parents were contacted by telephone monthly for 6 months, starting 1 month after recruitment, to assess for new skin infections since the previous phone contact.

Outcome Measures

The primary outcome measure was treatment failure or cure. Treatment failure was defined as persistent or increased size of the original abscess requiring additional antibiotic therapy or surgical incision and drainage. Treatment cure was defined as no or minimal tenderness, erythema, fever, wound drainage, warmth, fluctuance, or induration at the 10- to 14-day follow-up.

A secondary outcome measure was the cumulative rate of recurrent skin infection among follow-up responders from 1 to 6 months after surgical drainage. Patients who were treatment failures were excluded from this analysis because they all received additional medical interventions that could affect the secondary outcome measure. Infections involving the same site more than 2 weeks after clinical resolution of the original infection were considered a recurrent infection. Both outcome measures were stratified for analysis based on the infecting organism.

Statistical Analyses

The sample size of 120 per group was calculated according to an assumed treatment cure rate of 95% with 10 days of antibiotics, and a noninferiority margin of 7% (allowing up to 88% cure rate with 3 days of antibiotics), to achieve a power of 0.80 (alpha = 0.05). An additional 25 patients were recruited to account for an estimated 10% lost to follow-up. Continuous variables were summarized using the following descriptive summary statistics: the number of subjects (n), median, and range. Categorical variables were summarized using counts and percentages. The primary comparisons between 3 days and 10 days of therapy were carried out by 2-sample t tests for continuous measures and the χ^2 or Fisher exact test for categorical variables. The rate differences and corresponding CIs also were calculated. Because the use of clindamycin was significantly different between the 2 groups,