Randomized, Controlled Trial of Antibiotics in the Management of Community-Acquired Skin Abscesses in the Pediatric Patient

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**Study objective:** Emergency department visits for skin and soft tissue infections are increasing with the discovery of community-acquired methicillin-resistant *Staphylococcus aureus*. Whether abscesses treated surgically also require antibiotics is controversial. There are no published pediatric randomized controlled trials evaluating the need for antibiotics in skin abscess management. We determine the benefits of antibiotics in surgically managed pediatric skin abscesses.

**Methods:** This was a double-blind, randomized, controlled trial. Pediatric patients were randomized to receive 10 days of placebo or trimethoprim-sulfamethoxazole after incision and draining. Follow-up consisted of a visit/call at 10 to 14 days and a call at 90 days. Primary outcome was treatment failure at the 10-day follow-up. Secondary outcome was new lesion development at the 10- and 90-day follow-ups. Noninferiority of placebo relative to trimethoprim-sulfamethoxazole for primary and secondary outcomes was assessed.

**Results:** One hundred sixty-one patients were enrolled, with 12 lost to follow-up. The failure rates were 5.3% (n=4/76) and 4.1% (n=3/73) in the placebo and antibiotic groups, respectively, yielding a difference of 1.2%, with a 1-sided 95% confidence interval (CI) (−∞ to 6.8%). Noninferiority was established with an equivalence threshold of 7%. New lesions occurred at the 10-day follow-up: 19 on placebo (26.4%) and 9 on antibiotics (12.9%), yielding a difference of 13.5%, with 95% 1-sided CI (−∞ to 24.3%). At the 3-month follow-up, 15 of 52 (28.8%) in the placebo group and 13 of 46 (28.3%) in the antibiotic group developed new lesions. The difference was 0.5%, with 95% 1-sided CI (−∞ to 15.6%).

**Conclusion:** Antibiotics are not required for pediatric skin abscess resolution. Antibiotics may help prevent new lesions in the short term, but further studies are required. [Ann Emerg Med. 2010;55:401-407.]

**INTRODUCTION**

The incidence of skin and soft tissue infections has increased markedly during the last decade. From 1993 to 2005, there was nearly a 3-fold increase in skin infections diagnosed by emergency physicians in the United States, from 1.2 to 3.4 million cases.1 There are numerous reports indicating that this overall increase is primarily due to a dramatic increase in the number of infections caused by community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), an organism that often presents with skin and soft tissue infections in the pediatric population.2,3 In the past, surgical drainage of skin abscesses has been the accepted standard of care. With the emergence of CA-MRSA causing serious and even fatal infections in immunocompetent pediatric patients, many have recommended the addition of antibiotic therapy.3-5 Several published studies have suggested that skin abscesses can be cured with adequate drainage alone, according to the finding that many patients improve despite receiving antibiotics to which their infecting organisms are not susceptible.6-8 Rajendran et al9 reported no benefit with the addition of cephalaxin to the management of surgically drained CA-MRSA skin abscesses in adult patients, but a retrospective study by Ruhe et al5 reported an association between delayed initiation of active antibiotic and treatment failure of CA-MRSA skin abscesses in adults.
To our knowledge, there are no published randomized controlled studies evaluating the benefits of antibiotic treatment of adequately drained skin abscesses in the era of CA-MRSA, either in adults or in the pediatric population.

The purpose of this study is to demonstrate noninferiority of placebo relative to antibiotic use in pediatric patients who undergo incision and drainage of acute skin abscesses.

**MATERIALS AND METHODS**

**Setting**

This study was conducted in the emergency department (ED) at the Cardinal Glennon Children’s Medical Center, Saint Louis University in St. Louis, MO, from July 2006 to February 2008. It is a Level I pediatric trauma center, with annual visits of 41,000 patients.

**Selection of Participants**

The study population consisted of pediatric patients aged 3 months to 18 years, who had skin abscesses and were nontoxic, with temperature less than 38.4 °C (101.1 °F). Skin abscesses were diagnosed clinically and by bedside ultrasonography, performed by emergency physicians, when available. Diagnostic criteria for skin abscess included the presence of all of the following features: (1) acute onset within 1 week, (2) fluctuance, (3) erythema, (4) induration, and (5) tenderness, with or without purulent drainage. Subjects who had skin abscesses and met the inclusion criteria were recruited by qualified pediatric emergency medicine attending physicians or fellows. Subjects or their parent or guardian had to be able to read and comprehend English sufficiently to provide informed written consent (and assent when applicable).

Children were excluded from the study if they had known chronic health problems, such as diabetes; were receiving immunosuppressive medications, such as oral steroids for asthma; had recent (within the last week) or current antibiotic usage; or had any contraindication to trimethoprim-sulfamethoxazole, such as a history of hypersensitivity to sulfonamides or trimethoprim. Minor or superficial skin infections such as folliculitis were excluded because these infections tend to resolve spontaneously or with warm compresses or topical antibiotics, and surgical drainage is not required.

**Study Design, Interventions, and Data Collection and Processing**

This study was a double-blinded, prospective, randomized, controlled trial approved by the Institutional Review Board of Saint Louis University. Once written consent (or assent when applicable) was obtained, patient information (age, sex, race, history of skin abscesses, and family history of skin abscesses) and the largest diameter (in centimeters) of erythema and induration of the abscess were recorded. When ultrasonography was available, measurements were made in 2 dimensions, diameter and depth. Local anesthetic or procedural sedation was used at the discretion of the attending physician. The skin overlying all skin abscesses was cleansed with 10% povidone-iodine solution and then incised with a no. 11 blade, probed for loculations, and irrigated with normal saline solution. Abscess cultures obtained on Dacron swabs (Starplex Scientific Inc., Etobicoke, Ontario, Canada) were obtained immediately after surgical incision and sent for culture and antibiotic sensitivity testing. Antibiotic susceptibilities to *S aureus* isolates were performed at the microbiology laboratory at our institution. Isolates were tested with the Microscan systems by methods established by the Clinical and Laboratory Standards Institute for antibiotics, including amikacin, cefazolin, cefotaxime, ceftriaxone, chloramphenicol, gentamicin, penicillin, clindamycin, erythromycin, oxacillin, trimethoprim-sulfamethoxazole, and vancomycin. Pathogens that were erythromycin resistant but clindamycin sensitive had a disk diffusion test (D-test) performed to evaluate the organism for inducible clindamycin resistance.10

Decisions concerning the need for procedural sedation, the incision size, and 24-hour wound packing were physician dependent. With a computer randomization program, subjects were then randomized in permuted blocks of 50 to receive a 10-day course of placebo or trimethoprim-sulfamethoxazole. The placebo consisted of a Maalox and tonic water combination that resembled the antibiotic in color, texture, and taste. The antibiotic dose was a standard trimethoprim-sulfamethoxazole dose for mild bacterial infections (10-12 mg trimethoprim/kg/day divided into 2 doses, with a maximum dose of 160 mg trimethoprim/dose). Only the liquid formulation of the antibiotic was used because teenagers could be persuaded to take
liquids more readily than smaller children could be to take large tablets. The concentration of the antibiotic solution was 200 mg sulfamethoxazole/40 mg trimethoprim per 5 mL. The medications were prepared, stored, and dispensed by the inpatient pharmacist who also generated the randomization sequence and assigned the participants to their groups. The patient, parents, and clinician who assessed the clinical outcome were blinded to group assignment.

Patients and their parents were asked to monitor study subjects for any adverse effects of the medication and to call if they had any questions or concerns. At home, they were instructed to remove and discard the gauze packing, if used, 24 hours after it was placed in the ED and to perform warm water soaks at least twice a day per standard of care. They were instructed to keep the wound clean and covered by a layer of gauze with taping around the edges and to avoid using topical antibiotic ointment/cream, hydrogen peroxide, alcohol, or Betadine to decrease the chance of confounding factors.

Updated telephone numbers were verified before the patient’s discharge on the initial and day 10 visits to increase the likelihood of a telephone follow-up at 2 to 3 days, 10 to 14 days, and 90 days later. With the 2- to 3-day follow-up call, patients were reminded to remove packing if present, to do warm soaks, and to take their medications. Any patient concerns were addressed at that time, and a 10- to 14-day follow-up appointment was set up.

Compliance was evaluated by quantifying study medication that remained on the follow-up clinic visit or by parental report over the telephone. The participants were asked to bring their medicine and its container back at the 10-day follow-up visit. The remaining volume was recorded and categorized as 0%, 1% to 24%, 25% to 49%, 50% to 74%, and greater than 75% of medication remaining. Compliance was defined as greater than 50% of the medication taken by the patient. Patients and parents were also asked the number of days it took for them to notice healing of the wound at the 10-day follow-up visit or call. The 90-day telephone interview of the parent or guardian consisted of 2 questions: (1) whether there was there any recurrence of skin abscesses or spread to other body parts and (2) whether anyone else in the family developed skin abscesses.

Methods of Measurements and Outcome Measures

The primary outcome measure was clinical resolution or failure. Clinical resolution was defined as absence of erythema, warmth, induration, fluctuance, tenderness, and drainage at the 10-day follow-up. The secondary outcomes of interest included the development of new lesions at a different site (>5 cm away from original skin abscess) on day 10 clinical follow-up or self-report and 3-month telephone follow-up. Management of these new lesions was recorded. The spread to other family members (household contacts) by report at the 10-day and 3-month follow-up, as well as the presence of any adverse effects from the medications at the 10-day follow-up, was noted.

Treatment failure was defined as the presence of any of the above signs or symptoms at the 10-day follow-up or worsening signs or symptoms before the 10-day follow-up requiring further surgical drainage, change in medication, or hospital admission for intravenous antibiotics. New lesions within 5 cm of the original abscess site were also considered treatment failures. New lesions may consist of folliculitis, furuncles, carbuncles, or abscesses. Physicians involved in the enrollment and assessment of clinical outcome received training or education about the study design and protocol by the primary investigator.

The study was approved by our institutional review board. A data and safety committee was formed to meet quarterly to monitor patient safety. More specifically, they reviewed the adverse effects of the medications, frequency of treatment failures, frequency of new lesion development, and subsequent managements and outcomes of these patients.

Primary Data Analysis

This was a noninferiority study. The sample size of 81 per group was calculated according to assumed treatment failure rate of 3.3% with antibiotics, an equivalence threshold of 7% (allowing up to 10.3% failure rate with placebo), to achieve a power of 0.80 (α=0.05), using nQuery 7.0 Module PTE0. To assess noninferiority, a 95% 1-sided confidence interval (CI) was computed on the difference of the proportions between the 2 groups. If the upper limit of the CI was less than the equivalence threshold of 7%, then noninferiority could be inferred.

Our definition for CA-MRSA is a methicillin-resistant S. aureus isolate obtained from skin abscesses of patients from the community that is “relatively susceptible” to other antibiotics, including vancomycin, trimethoprim-sulfamethoxazole, tetracyclines, and clindamycin. Our definition is not based on molecular characterization of the isolates.

RESULTS

Characteristics of Study Subjects

A total of 1,305 patients who presented to our ED were identified with the International Classification of Disease coding for cellulitis and skin abscesses during the study period. This was not a convenience sampling. Among this group of potential study subjects were 161 individuals who agreed to participate in the trial after the protocol was reviewed with them. These subjects were then randomly assigned treatment with either placebo or trimethoprim-sulfamethoxazole. Twelve subjects were lost to follow-up (8 from the placebo group and 4 from the trimethoprim-sulfamethoxazole group), resulting in a final cohort of 149 evaluable participants (Figure). The other potential study subjects were not enrolled because they did not meet inclusion criteria, refused to consent, or were not enrolled by the examining physician. No formal record was kept of the reasons for not enrolling the potential subjects who did not participate.

Subjects in the 2 study groups were similar in baseline characteristics (Table 1). The patients in our study were primarily female (58%) black children (86%) younger than 5
years (53%), with a median age of 4 years and an interquartile range of 1 to 12 years. Forty-one percent of the patients had a history of skin abscesses and 47% had a family history of skin abscesses.

The skin lesions were most often located in the diaper region: gluteus (43%), perineum/labia (5.4%), and inguinal (7.4%). Other locations for the skin abscesses included the upper leg (8.1%), lower leg (8.7%), axilla (13.4%), forearm (2.7%), abdomen (8.1%), and head (3.3%). The mean diameter of erythema and induration was 3.8±2.3 cm and 3.6±1.9 cm, respectively. There were 52 abscesses with erythema greater than or equal to 5 cm, 26 in the placebo group and 26 in the antibiotic group. For lesions measured by ultrasonography, the mean diameters were 2.2±1.5 cm, and mean depth was 1.6±1.1 cm. Procedural sedation was performed in 69% of the patients and wound packing in 72%. There was no statistically significant difference between the 2 groups in terms of patient or abscess characteristics.

Fifty-two percent of the patients received placebo (83) and 48% received trimethoprim-sulfamethoxazole (78). The overall compliance rate was 66%, 55% among subjects assigned to the placebo group and 46% among subjects assigned to the treatment group. Approximately 90% of the patients did not have any adverse effects. There were no reports of serious or potentially life-threatening adverse effects from the medications (Table 2).

The bacterial pathogens isolated from the skin abscesses were primarily CA-MRSA (80%), with 18% clindamycin resistance but 100% trimethoprim-sulfamethoxazole and vancomycin sensitivity (Table 3).

One hundred sixty-one subjects were enrolled, with 12 lost to follow-up. The patients who were lost to follow-up did not differ from the rest of study participants in terms of demographics or clinical presentation. For the patients who were lost to follow-up, 92% were black, with a mean age of 7 years. These patients had mean ultrasonographic diameter,
Table 3. Skin abscess culture results.

<table>
<thead>
<tr>
<th>Culture Results</th>
<th>Placebo (%)</th>
<th>Trimethoprim-Sulfamethoxazole (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA-MRSA</td>
<td>61 (81)</td>
<td>58 (79)</td>
<td>129 (80)</td>
</tr>
<tr>
<td>MSSA</td>
<td>6 (8)</td>
<td>7 (10)</td>
<td>14 (9)</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>4 (5)</td>
<td>2 (3)</td>
<td>6 (4)</td>
</tr>
<tr>
<td>GAS</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1)</td>
<td>3 (4)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>No culture/growth</td>
<td>3 (4)</td>
<td>2 (3)</td>
<td>6 (3)</td>
</tr>
</tbody>
</table>

MSSA, Methicillin sensitive S. aureus; GAS, group A streptococcus.

depth, erythema, and induration of 1.0±0.8 cm, 0.8±0.8 cm, 2.5±1.5 cm, and 2.2±1.0 cm, respectively. Twenty-five percent (3/12) of these patients lost to follow-up had a history of skin abscesses, and 50% of them had a family history of skin abscesses. Eight of these patients had been randomized to receive placebo, and 4 were randomized to receive trimethoprim-sulfamethoxazole.

Of the 149 participants, the 10-day clinical follow-up occurred in 60% of the patients (90/149), with 40% requiring telephone follow-up. Sixty percent of the placebo group (46/76) and 60% (44/73) in the antibiotic group received clinical follow-ups. The 3-month telephone follow-up was 65% (98/149).

The frequency of adverse effects was similar for the 2 treatment groups (Table 2).

For clinical resolution, noninferiority was demonstrated for placebo relative to antibiotic. The failure rate was 5.3% (4 of 76) in the placebo group versus 4.1% (3 of 73) in the antibiotic group, yielding a difference of 1.2%, with a 1-sided 95% CI of −∞ to 6.8%. The upper limit (6.8%) of this CI for the difference in failure rate did not exceed the previously specified equivalence threshold of 7%.

The treatment failures in the antibiotic groups had antibiotic change before the 10-day follow-up, which was not by design, and all investigators were blinded until the study end date. Of the 7 treatment failures, all had persistent purulent drainage, 2 had surgical reexploration for loculations and drainage, and none were hospitalized. They were all discharged home, receiving oral trimethoprim-sulfamethoxazole or clindamycin. Of the treatment failure patients, the pathogens were CA-MRSA (4) and Proteus mirabilis (3), which were all sensitive to trimethoprim-sulfamethoxazole.

To address concerns that patients who are aged 14 years and older may respond better than patients younger than 14 years and thus bias our results, subanalysis of patients younger than 14 years was performed. Treatment failure was 2 of 58 (3.4%) in the placebo group and 1 of 62 (1.6%) in the antibiotic group, yielding a difference of 1.84%, with 95% CI (−∞ to 6.5%). With the 7% margin, noninferiority was established for this subgroup analysis of patients younger than 14 years.

There was no statistically significant difference between placebo and antibiotic groups in new lesion development at the 3-month follow-up, but there was one at the 10-day follow-up.

New lesions occurred in 28 patients (19%) at the 10-day follow-up: 19 in the placebo group (26.4%) and 9 in the antibiotics group (12.9%), yielding a difference of 13.5, with 95% 1-sided CI (−∞ to 24.3%).

Of the 28 patients with new lesion development at the 10-day follow-up, 8 required incision and draining (5 in the placebo and 3 in the antibiotic group), 1 in the placebo group was hospitalized for intravenous antibiotics, 4 began receiving oral antibiotics, 5 had spontaneous drainage, and 10 spontaneously resolved (Table 4).

At 3 months, only 98 patients could be followed up (52 in the placebo and 46 in the antibiotic group): 28.8% of the patients in the placebo group and 28.3% in the antibiotics group developed new lesions, yielding a difference of 0.5%, with 95% 1-sided CI (−∞ to 15.6%).

**LIMITATIONS**

Limitations to this study include possible selection bias, with a large proportion of potential patients not being enrolled from July 24, 2006, to February 2, 2008, by the examining physician. Another source of selection bias may come from the 12 participants (7%) who were lost to follow-up, but this is a relatively small number, and analysis of available data for them indicates similarity with the studied subjects. Forty percent of our follow-ups occurred by telephone calls, which is another source of bias with inaccurate data gathering and unreliable self-reporting.

Because of the patient population who most often present to our ED (ie, lower social economic group with less stable living conditions), it was not surprising to find a larger loss in follow-up at 3 months (40%), which could have affected our interpretation of long-term skin abscess recurrence rate.
No molecular studies were performed to verify that the methicillin-resistant \textit{S. aureus} were truly community acquired, as distinct from hospital-acquired methicillin-resistant \textit{S. aureus}. Our definition of CA-MRSA is based on clinical presentation of previously healthy pediatric patients to an outpatient setting (the ED) and the pathogen’s antibiotic susceptibility pattern, but this is in compliance with the Centers for Disease Control and Prevention’s (CDC’s) definition of CA-MRSA. The CDC defines CA-MRSA as “MRSA infections that are acquired by persons who have not been recently (within the past year) hospitalized or had a medical procedure (such as dialysis, surgery, catheters).”

The compliance rate of 66% is poor but comparable to that of other clinical studies. Llera and Levy\(^8\) reported a compliance rate of 68% in adults for a 7-day antibiotic course, but their definition of compliance was greater than 78% medication completion. The compliance rate in our study would be much lower if compliance were defined as greater than 75% medication completion as opposed to greater than 50%. The compliance rate might be higher if the duration of antibiotic therapy were reduced from 10 to 7 days. As mentioned above, further limitations include the unreliability of self-reporting of medication compliance in the patients who were followed up by telephone calls.

The sample size was calculated according to a clinical tolerance of treatment failure rate of 7%, which some may find unacceptable. However, the treatment failures were not severe and required minimal change in management (such as receiving a susceptible oral antibiotic). It is impractical to conduct a study with a set clinical tolerance of treatment failure of 1%, which would require more than 4,500 patients.

This study was conducted on previously healthy pediatric patients and may not be generalized to adults or pediatric patients who have comorbidities and present with skin abscesses.

**DISCUSSION**

Across the nation, there has been a dramatic increase in the diagnosis of skin and soft tissue infections.\(^1\) There is no doubt that CA-MRSA has emerged as a common pathogen causing skin abscesses in adult and pediatric patients throughout the United States. Young\(^7\) reported that 63% of skin abscess cultures in adults were CA-MRSA (median age 42 years; range 1 to 89 years). Moran et al\(^2\) reported 76% CA-MRSA skin and soft tissue infections in adults, which is comparable to that in the pediatric population presented here, with CA-MRSA isolates of 80% from the skin abscesses.

Geographic variation of antibiotic resistance is well established. California and Baltimore have reported 6% clindamycin resistance\(^12,13\) and Detroit has reported 46% clindamycin resistance\(^14\) among their CA-MRSA isolates. The proportion of CA-MRSA isolates that was clindamycin resistant in this study was 18%, which concurred with a retrospective review at our institution in 2005, demonstrating a clindamycin resistance of 17% (unpublished data).

The standard of care for the management of skin abscesses is incision and draining. Recommendations for the addition of antibiotics, which would be effective against CA-MRSA, in the management of skin abscesses stemmed from an increase in CA-MRSA skin and soft tissue infections and associated complications. In concordance with the articles written by Llera and Levy\(^8\) and Rajendran et al,\(^9\) our study demonstrated that antibiotics are not needed for skin abscess resolution after incision and draining. However, the treatment group in these other randomized control trials in the adult population used antibiotics (cephradine and cephalexin) that would not be active against CA-MRSA. No difference in treatment failure rates was found between the placebo and antibiotic groups in a subanalysis of data from skin abscesses caused by CA-MRSA. The current study suggests that systemic antibiotics are not required in the treatment of skin abscesses after incision and draining, even in the era of CA-MRSA. There were no correlations between treatment failure and other factors such as medical history or family history, use of wound packing, or use of procedural sedation for the incision and draining. In fact, the placebo group had more history of skin abscesses compared with the antibiotic group, which further supports our conclusion that antibiotic is not needed for skin abscess resolution.

Lee et al\(^6\) reported a treatment failure rate of 8%, with an increased risk of treatment failure in skin abscesses that were greater than 5 cm. On ultrasonography, our mean skin abscess diameter was only 2.2±1.5 cm, which suggests that our skin abscesses may have been smaller than the ones reported by Lee et al,\(^6\) with a selection bias for healing without antibiotics. Our treatment failure rate was slightly less, at 5%, but treatment failure did not correlate with clinical assessment of abscess size, erythema, or induration greater than or equal to 5 cm (Table 1). The presence of cellulitis with these skin abscesses did not correlate with treatment failure.

There is a paucity of data on the usefulness of antibiotics in skin abscess management in terms of healing time or prevention of recurrence. In our patients, antibiotics decreased new lesion developments at the 10-day follow-up. There was no significant difference between the 2 groups in new lesion development at the 3-month follow-up. In the short term, antibiotics may be useful in preventing recurrent skin abscesses but provided no long-term benefits in terms of new lesion development. Further studies are required to further elucidate this issue.

Despite the potential advantage of antibiotic use in the management of skin abscesses, with the continuing evolution of bacterial pathogens, poor patient compliance with medications, and increasing antibiotic resistance, it is prudent to minimize...
the use of antibiotics in this setting, given such low treatment failure rates.

After incision and draining of skin abscesses in children, 95% of the skin abscesses demonstrated clinical resolution; therefore, antibiotics are not required. The potential benefit of preventing distal lesion development with the use of antibiotics will require further study and evaluation.

By avoiding unnecessary antibiotic use, potential adverse effects, allergic reactions, and natural selection of more resistant organisms may be avoided. Furthermore, the cost saving of unnecessary antibiotic use is significant, considering the dramatic increase in skin abscess diagnoses.

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