FEATURE ARTICLE

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Primary Care Management of Pediatric Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Skin and Soft Tissue Infections

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ABSTRACT

Background: The prevalence of pediatric community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) skin and soft tissue infections (SSTIs) have been well documented, yet evidence supporting treatment standards for short- and long-term resolutions is equivocal.

Objective: To review the healthcare challenge of pediatric CA-MRSA SSTIs and describe current evidence concerning treatment of uncomplicated infections. Implications and recommendations for primary care practice are presented.

Review of Literature: Databases were searched using the keywords CA-MRSA, skin, soft tissue infections, antibiotics, incision and drainage, clindamycin, and trimethoprim-sulfamethoxazole to locate the highest level of evidence available. Further searches were conducted to investigate the epidemiology, history of antibiotic resistance, and past treatment of SSTIs including CA-MRSA.

Results: When treating a pediatric patient for an uncomplicated CA-MRSA SSTI, the primary care practitioner needs to consider patient history and comorbid conditions, location of the infection, size of lesion, community prevalence of CA-MRSA and its susceptibility, history of antibiotic use, family or close contact history of CA-MRSA, immunocompetence, and physical signs of the patient.

Conclusion: Treatment changes are paramount in the fight against CA-MRSA, and practitioners must follow the clinical practice guidelines and begin to utilize incision and drainage more frequently and antibiotics less frequently.

Key words: CA-MRSA, Pediatric, SSTIs, Uncomplicated

Treatment of pediatric patients with community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) skin and soft tissue infections (SSTIs) is a major challenge and concern in the global healthcare community. These infections are rapidly becoming more prevalent (McCaig, McDonald, Mandal, & Jernigan, 2006), and prevention of further antibiotic resistance is of paramount importance (World Health Organization, 2010). Primary healthcare providers need to know the most effective method of treatment and control of CA-MRSA SSTIs in the pediatric population to achieve resolution of infection, prevent adverse health outcomes, and limit spread of the infection.

Despite current recommendations for incision and drainage (I&D) to be the primary treatment for uncomplicated CA-MRSA SSTIs (Gorwitz, 2008; Liu et al., 2011), substantial practice variation in use of I&D and antibiotic prescription persists (Baumann et al., 2011; Hersh, Cabana, Gonzales, Shenkin, & Cho, 2009). Increasing consistency and use of evidence-based care is important to both prevent inadequate treatment and improve patient outcomes. Appropriate antibiotic prescribing practices are particularly important to help reduce the spread of antibiotic resistance (Gorwitz, 2008). Evidence-based practice can potentially both improve patient outcomes and reduce the risk of adverse outcomes.

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The authors declare no conflicts of interest.

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DOI: 10.1097/JDN.0b013e31824138f3

The purpose of this article is to review the healthcare challenge of pediatric CA-MRSA SSTIs and describe current evidence concerning treatment of uncomplicated infections. Implications and recommendations for primary care practice are presented.

BACKGROUND

CA-MRSA

Although antibiotic-resistant bacteria are not a new phenomenon, the World Health Organization (2010) has identified the development of antibiotic resistance as one of the most significant public health threats of the 21st century. MRSA is one of these antibiotic-resistant bacteria, prevalent in the community, contagious, difficult to treat and eradicate, and, at times, lethal (Newland & Kearns, 2008). In the 1960s, the first occurrence of MRSA was observed in the hospital setting (Barrett, McGehee, & Finland, 1968), hence the label hospital-acquired MRSA (HA-MRSA). Risk factors associated with HA-MRSA include prolonged hospitalization, surgical intervention, dialysis, close contact with other patients with MRSA, implanted medical devices, and admission into intensive care or burn units (Newland & Kearns, 2008).

Until the 1980s, MRSA remained a major problem in the hospital but had not yet become a major pathogen in the community (Fergie & Purcell, 2001). In the 1980s, the first individual case of MRSA in the community without the risk factors of HA-MRSA was observed. This type of MRSA became known as community-acquired MRSA (CA-MRSA). Herold et al. (1998) reported an increasing trend in the 1990s in SSTIs caused by CA-MRSA in patients with none of the known risk factors previously associated with HA-MRSA. CA-MRSA has become a major pathogen in the community, specifically affecting the pediatric population in SSTIs (Centers for Disease Control [CDC], 2010). CA-MRSA is a common and serious problem, usually involving skin, especially among children (Fridkin et al., 2005).

Most CA-MRSA infections occur in infants, children, and teenagers (CDC, 2010). In this population, 80% of the CA-MRSA infections present as SSTIs. Community onset SSTI accounts for most MRSA infections in children (Gorwitz, 2008). Children who are enrolled in child-care centers, athletes, tattoo recipients, and neonates are at increased risk for CA-MRSA SSTIs. Additional risk factors include age (<2 years), being of minority race or ethnicity, and low socioeconomic status (CDC, 2010).

Treatment

Worldwide, clinicians and researchers are addressing the healthcare challenge of CA-MRSA SSTIs. A key concern associated with treatment of CA-MRSA SSTIs is that *S. aureus* will continue to develop resistance to these remaining antibiotics and further limit treatment options. A focus of research has been to identify the most efficacious way of treating CA-MRSA SSTIs that will also be the least likely to create further antibiotic resistance. A parallel concern has been to avoid unnecessary treatment with antibiotics when clinical situations warrant. Although there are significant variations in regional susceptibility, options for outpatient empiric antimicrobial treatment include elindamycin, doxycycline, minocycline, trimethoprim-sulfamethoxazole, rifampin, and linezolid (Centers for Disease Control [CDC], 2007). It must be noted that only clindamycin, trimethoprim-sulfamethoxazole, doxycycline (for children 9 years or older), and minocycline (for children 9 years or older) are used for treating the outpatient pediatric CA-MRSA SSTI.

Antibiotic Resistance

In 1928, Professor Alexander Fleming recognized that a mold was inhibiting the growth of bacteria (National Institute of Health, 2009). He remarked that this mold was able to repel and destroy other bacteria. Fleming's discovery effectively ushered in the era of antibiotics. For over 70 years, antibiotics have been used to treat innumerable amounts of infections and prolong countless lives. However, after many decades of use and over use of antibiotics, bacteria have developed resistance to them (National Institute of Health, 2009). After being exposed to antibiotics, the bacteria have altered their genetic structure so that they are no longer susceptible to certain types of antibiotics.

Another important part of the etiology of antibiotic resistance is the process of selectively eliminating, intentionally or unintentionally, bacteria from the body. Bacteria normally colonize the skin of humans. When an individual's skin is intact, these bacteria are not harmful and are believed to be in some ways beneficial. However, when individuals take or receive antibiotics, these medications theoretically kill or inhibit the growth of all bacteria that are susceptible to the antibiotic. The bacteria that are left on the skin are the ones that are resistant to the antibiotic and are then freely able to multiply and become the dominant bacteria.

The problem arises the next time the integrity of the skin is broken or the individual has another infection, because these bacteria are no longer susceptible or are developing resistance to that type of antibiotic. A different type of antibiotic is needed to treat the bacterial infection. After continual cycles of taking antibiotics, it becomes increasingly difficult to find antibiotics that are effective against the bacteria that remain. It is interesting to note that several of the antibiotics used to treat CA-MRSA, such as trimethoprim-sulfamethoxazole, are older medications that had fallen out of favor of the medical community for treatment of infections. It is these medications that had not been extensively used for some time that are now at times the first line of defense against CA-MRSA SSTIs (Liu et al., 2011).

Epidemiology

Although there is evidence that SSTIs are rapidly increasing across the United States, the exact incidence and prevalence of noninvasive MRSA and CA-MRSA are not known (CDC, 2010). A major barrier to measuring the incidence and prevalence data is that MRSA is not a nationally reportable disease. In the literature, incidence and prevalence data are often taken from individual studies and standardized for the United States. One such study that is accepted by the CDC as representative of prevalence for the United States used the National Ambulatory Medical Care Surveys and National Hospital Ambulatory Medical Care Surveys to estimate the prevalence of CA-MRSA SSTIs (McCaig et al., 2006). These researchers estimated that, in 2005, there were 14 million outpatient visits that were suspected *S. aureus* and SSTIs.

Because neither CA-MRSA nor MRSA are notifiable diseases according to the CDC, neither are included in the morbidity and mortality weekly report published by the CDC (2010). Therefore, morbidity and mortality statistics are not officially known nationally or locally. According to the CDC (2010), the most accurate, currently available assessment of morbidity and mortality associated with CA-MRSA is a study conducted by Klevens et al. (2007). From July 2004 through December 2005, these researchers conducted a population-based surveillance for invasive MRSA in nine sites across the United States. The researchers standardized the results from their surveillance and derived a standardized mortality rate of 6.3 per 100,000 for all cases of MRSA and 0.5 per 100,000 for CA-MRSA.

REVIEW OF RESEARCH

Current clinical practice guidelines (Liu et al., 2011; Stevens et al., 2005) recommend I&D alone for treatment of uncomplicated CA-MRSA SSTIs in pediatric primary care patients. Despite consensus on recommended management, use of I&D alone is limited (Hersh et al., 2009; McCaig et al., 2006), and antibiotic prescribing practice patterns vary substantially (Baumann et al., 2011). Although both internal and external barriers to increased use of I&D in primary care pediatric practice have been identified (Hersh et al., 2009), clinical practice guidelines also include caveats to recommendations for treatment of pediatric patients based on limitations in existing research. Prospective controlled trials with pediatric patients are scarce; thus, clinical judgment and local prevalence and susceptibility patterns should inform treatment decisions (Deleo, Otto, Kreiswirth, & Chambers, 2010). Considerations related to use of antibiotics in addition to I&D include severity of local symptoms, presence of systemic symptoms, an infection that is refractory to management with I&D or which progresses rapidly or that is located in a site not easy to manage with I&D, very young patient age, or associated patient comorbidities or immune suppression (Gorwitz, Jernigan, Powers, & Jernigan, 2006).

When antibiotics are considered clinically necessary, it is important to use antibiotics active against CA-MRSA (Liu et al., 2011; Stevens et al., 2005). Furthermore, it has been noted that when prevalence of CA-MRSA within a community exceeds 10%–15%, empiric use of antibiotics should be initiated for SSTI treatment instead of basing the decision solely on clinical characteristics (Gorwitz et al., 2006; Lawrence, Golik, & Davidson, 2009).

Pediatric-specific research regarding the management of uncomplicated CA-MRSA SSTIs is quite limited as well as varied in approach and methodology. Only one randomized controlled trial (Duong, Markwell, Peter, & Barenkamp, 2010) and a single prospective observational study (Lee & Lieberman, 2006) has been conducted; otherwise research designs have been retrospective (Hyun, Mason, Forbes, & Kaplan, 2009; Teng et al., 2009). Although these studies intended to answer questions about the most effective treatment for pediatric CA-MRSA SSTIs, only two (Duong et al., 2010; Lee & Lieberman, 2006) were designed specifically to investigate whether antibiotics are necessary in addition to I&D. The remaining two studies (Hyun et al., 2009; Teng et al., 2009) compare effective versus ineffective antibiotics (effective means active against MRSA) without testing the effect of I&D.

The existing pediatric-specific research examines management of patients presenting to the emergency department for treatment of CA-MRSA SSTIs (Duong et al., 2010; Lee & Lieberman, 2006; Teng et al., 2009) or outpatient management after hospitalization for CA-MRSA SSTIs (Hyun et al., 2009). However, pediatric patients presenting to emergency departments for treatment of skin abscesses tend to have larger infected areas (Baumann et al., 2011; Magilner, Byerly, & Cline, 2008) compared with children presenting to primary care or pediatricians for management. A single study (Elliott et al., 2009) investigated treatment of pediatric SSTI in a primary care setting; however, this study did not seek to identify MRSA as the causative organism of its included infections, focused on nondrained, noncultured SSTI without distinguishing type of infection (e.g., presence of abscess) and, thus, does not include information or findings relevant for the present discussion.

Hyun and colleagues focused on outpatient management of pediatric patients after hospitalization for CA-MRSA SSTIs, comparing effectiveness of trimethoprim-sulfamethoxazole versus clindamycin and not examining the effect of I&D. Findings indicated no difference between the two groups with respect to treatment failure, suggesting that the antibiotics may be equally effective as postdischarge management for pediatric patients hospitalized for CA-MRSA SSTIs.

Teng and colleagues compared outcomes for pediatric patients with CA-MRSA SSTIs who received effective versus ineffective antibiotics. Treatment was successful for

most of the sample, despite ineffective antibiotic use, suggesting that treatment of uncomplicated SSTIs without antibiotics is possible. Whether treatment success was associated with the use of I&D was not examined, although most patients underwent this procedure. Of the two studies designed to determine if I&D alone is effective for treatment of CA-MRSA SSTIs in otherwise healthy children (Duong et al., 2010; Lee & Lieberman, 2006), findings were similar, suggesting that antibiotics, in addition to I&D, are not needed for effective treatment. However, Lee and Lieberman (2006) identified an association related to abscess size (abscess of >5 cm in diameter at initial evaluation predicts hospitalization at follow-up), but this finding was not confirmed by the Duong et al. (2010) investigation.

A further consideration is whether antibiotics may offer some benefit with respect to subsequent SSTI development. In adults, trimethoprim-sulfamethoxazole provided after I&D for CA-MRSA SSTI, although not associated with reduced incidence of treatment failure compared with placebo, may protect against development of subsequent infections (Schmitz et al., 2010). Research investigating the long-term outcomes of management with I&D alone for uncomplicated CA-MRSA SSTIs in adults or pediatric patients has not been conducted. Therefore, a risk for subsequent development of recurrent, more severe, and even life-threatening infections is a possibility.

RECOMMENDATIONS FOR PRACTICE

When treating a pediatric patient for an uncomplicated CA-MRSA SSTI, the primary care practitioner needs to consider patient history and comorbid conditions, location of the infection, size of lesion, community prevalence of CA-MRSA and its susceptibility, history of antibiotic use, family or close contact history of CA-MRSA, immunocompetence, and physical signs of the patient. In an immunocompetent pediatric patient older than 3 months of age who has no signs of systemic infection or comorbid conditions, an uncomplicated SSTI can be defined as an acute single infectious erythematic lesion of the skin or soft tissue without progressing cellulitis that is anatomically located in an area in which I&D can adequately be performed and does not involve adjacent deep tissue structures. CA-MRSA is defined clinically as a specimen positive for MRSA, obtained on an outpatient visit or within 48 hours of hospital admission, and also lacking all of the risk factors for HA-MRSA. Given these definitions, treatment with I&D alone is recommended for uncomplicated CA-MRSA SSTI in pediatric patients.

How CA-MRSA is defined and identified is important. In one study (Teng et al., 2009), CA-MRSA is defined as a specimen positive for MRSA, obtained on an outpatient visit or within 48 hours of hospital admission, and also lacking all of the risk factors for HA-MRSA. Duong et al. defined CA-MRSA as MRSA obtained from a patient from the community with an SSTI susceptible to other antibiotics, including vancomycin, trimethoprim-sulfamethoxazole, clindamycin, and tetracyclines. Newland and Kearns (2008) recommend molecular determination, clinical presentation, and presence of risk factors to identify CA-MRSA. Inconsistent identification of the infection being treated means that some interventions may be considered to have an effect on CA-MRSA that does not exist, because the SSTI was not actually caused by CA-MRSA. Practitioners must reflect on their organization's definition of CA-MRSA when deciding a treatment method.

Although I&D is the recommended treatment, practitioners should be aware that the procedure used for I&D is not consistent across current research. The exact procedure used for I&D is well described by Duong et al. (2010) and not specially described by Lee and Lieberman (2006). Barriers, both internal (e.g., lack of experience or skill) and external (e.g., time, resources) to performance of I&D in the primary care setting, have been identified (Hersh et al., 2009). Furthermore, general consensus on wound care does not exist, with questions raised, for example, about the necessity for routine packing of simple cutaneous abscesses. Whereas some maintain that wound packing averts dead space and wicks drainage from the wound to prevent new abscess formation, others assert that packing is painful to the patient and is not associated with improved healing outcomes (O'Malley, Fowler, & Ilyas, 2009).

Compliance with treatment was defined in one randomized controlled trial (Duong et al., 2010) as taking 50% or more of prescribed medication. The researchers verified the amount of medication taken by quantifying study medication on the return visit or parental report over the telephone (Duong et al., 2010). Although there is no specific percentage that signifies adequate adherence to medications, 80% is commonly seen in the literature as acceptable (Andrade, Kahler, Frech, & Chan, 2006).

Follow-up duration varied across the studies, from 30 (Hyun et al., 2009) to 90 days (Duong et al., 2010), and this impacts understanding of short- and long-term resolution. Liu et al. (2011) discussed treatment of recurrent SSTIs and the possibilities of family education, decolonization, and environmental control measures, and Huang et al. (2009) suggested the use of bleach baths for treating staphylococcus colonization in the atopic pediatric patient. These recurrent infections would require long-term follow-up and intentional examination of treatment effectiveness.

It is essential that that healthcare providers consider these issues with respect to their own practice: consistency in identification, classification, and treatment of pediatric CA-MRSA SSTI. In practices with multiple partners, a standardized classification and treatment plan is recommended. Practitioners should agree on the SSTI classification that warrants use of antibiotics to enable continuity of care and allow for follow-up data on efficacy

to be collected. When I&D is provided as treatment, consistency in performance across clinicians is also important. Duration of follow-up for pediatric patients treated for CA-MRSA SSTI needs to be adequate to assess for both short- and long-term resolution of infection. And finally, education to equip families for prevention and early recognition is a key element in the comprehensive management of CA-MRSA.

CONCLUSIONS

Compromised skin integrity in the form of CA-MRSA SSTIs is a major risk for the pediatric population. Intact skin is the first line of defense against many forms of bacteria. However, compromises in skin integrity are normal part of growth and development in the pediatric population. As children learn to walk, ride bikes, skate, and play sports, compromises in skin integrity are commonplace. With CA-MRSA, bacteria that are resistant to antibiotics are taking advantage of the compromises in skin integrity and colonizing the wounds of children.

In the past few decades, beta-lactam and cephalosporins have been the standard empiric treatment for SSTIs that became colonized with bacteria and were not healing spontaneously. With the growing prevalence of CA-MRSA, the beta-lactams and cephalosporins are less effective and, in many cases, ineffective in treating SSTIs. With their ineffectiveness, treatment standards are evolving. Treatment changes are paramount in the fight against CA-MRSA and involve not only the healthcare community but also those involved in the lives of the pediatric population. Practitioners must follow the clinical practice guidelines and begin to utilize I&D more frequently and antibiotics less frequently. Families need to be educated on the recognition, identification, and treatment of CA-MRSA SSTIs. Once families recognize CA-MRSA SSTIs in their early uncomplicated stages, I&D alone will be curative treatment (Liu et al., 2011). Decreasing the use of antibiotics will decrease the bacteria's exposure to antibiotics, slow down the development of bacterial resistance to antibiotics, decrease side effects, decrease medical costs, and reduce the incidence of CA-MRSA. ■

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