Editorial

Practical Management Tips for Methicillin-Resistant *Staphylococcus aureus*

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In this month's issue of *Cutis*®, Kil et al[1,2] focus on the treatment of cutaneous manifestations of methicillin-resistant *Staphylococcus aureus* (MRSA) infections. There is some good news to report. Most cutaneous community-acquired MRSA (CAMRSA) infections are abscesses that respond to drainage. When an oral antibiotic is needed, inexpensive agents such as trimethoprim/sulfamethoxazole (TMP-SMX) and tetracycline retain activity against most strains. Clindamycin is more problematic, as some geographic areas have a high prevalence of inducible resistance. Inducible clindamycin resistance is more common among children with cystic fibrosis, and in this population, clindamycin may not be a reliable choice.[3] Therapeutic failure with vancomycin has been associated with intracellular survival of bacteria within leukocytes. One in vitro study showed that vancomycin killed 99% of extracellular MRSA, but the intracellular survival rate was 33.8%. The addition of rifampin with or without TMP-SMX results in better intracellular killing.[4] Linezolid kills intracellular MRSA much more efficiently than vancomycin and can be effective in the treatment of multidrug-resistant MRSA, even when concentrations at the infection site are compromised by impaired blood flow.[5] The principal drawback of linezolid is that it remains extraordinarily expensive. New agents such as telavancin, tigecycline, and ceftobiprole medocaril appear promising.

Tip 1: Drainage remains the most important intervention for any abscess, which also holds true for CAMRSA abscesses.

Tip 2: Know your local antibiograms. Your local laboratory can identify inexpensive antibiotics that are reliable for CAMRSA in your area as well as the local prevalence of inducible clindamycin resistance. In most areas, TMP-SMX and tetracycline remain excellent choices. Expect inducible clindamycin resistance in children with cystic fibrosis.

Tip 3: Vancomycin failures are often related to survival of intracellular bacteria. The intracellular kill rate can be improved by the addition of rifampin. For serious infections, linezolid appears to be a fairly reliable drug but remains very expensive.

Colonization of wounds can be addressed by debridement or with the use of topical antimicrobials. Debridement alone usually is effective. Topical antimicrobials should be used responsibly to slow the emergence of resistant strains. A topical paste comprised of 70% sugar and 3% povidone-iodine accelerated healing in a diabetic mouse model of MRSA-infected ulcers.[6] Sugar creates a hypertonic environment and was widely used during World War I for the treatment of deep infected wounds (personal communication, Anny Elston, MD [my grandmother]; she treated many such wounds in soldiers returning from prisoner-of-war camps). There is little potential for the development of resistance to sugar paste. The same is true of Dakin solution (bleach at a dilution of 2 tablespoons per bathtub). Because of the potential for development of resistance, it is best to reserve agents such as chlorhexidine and triclosan for decolonization when there is an outbreak of infection, rather than using them widely for prevention of colonization. In contrast, agents such as bleach demonstrate little to no potential for the development of resistance. Bleach baths of 2 tablespoons per tub also are helpful in the management of impetiginized eczema, where it is fair to assume that colonization will persist. Agents such as pyrithione zinc deserve further study. Although zinc has little antimicrobial activity against staphylococci, it interferes with bacterial adherence to tissue and may prove to be a good agent for the cleansing of minor cuts and scrapes among athletes.[7]

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Tip 4: Wound colonization and superficial infection can be addressed with debridement or agents that have little potential for the development of resistance. If we abuse agents like chlorhexidine and triclosan, they will lose their effectiveness.

There is still no international consensus as to when staphylococcal carriage should be treated. Lack of large well-designed trials does not equate to lack of efficacy. It should be noted that the official guidelines from the Netherlands, a country that has maintained an extraordinarily low prevalence of MRSA compared with its neighbors, do not grade the level of evidence.[8] The Dutch were quick to adopt a search-and-destroy policy for facility-based and community outbreaks and colonization. Although the recommendation was not made on high-level evidence, they credit it for their success in preventing widespread outbreaks of MRSA infection.[9]

We do know that MRSA frequently colonizes close contacts, such as family members. In one study, 43% of families (22/51) showed evidence of colonization, with 70% of household contacts (42/60) positive for MRSA within the affected families.[10] There also is a growing body of evidence that decolonization can prevent infections. Five-day perioperative prophylaxis with nasal mupirocin and topical triclosan can reduce the incidence of MRSA infection after orthopedic and vascular surgery.[11] Chlorhexidine baths combined with intranasal mupirocin has been shown to result in a 52% decrease in the infection rate among patients in the intensive care unit.[12] The decrease in the infection rate translates to a reduction in mortality.[13] Intranasal mupirocin alone has been disappointing in preventing CAMRSA infections among military recruits.[14] The failure is most likely related to cutaneous sites of carriage. Both nasal and cutaneous colonization must be addressed to achieve good results. Washing with chlorhexidine gluconate for a week, in addition to intranasal mupirocin, rifampin, and doxycycline, can produce sustained decolonization. Mupirocin resistance correlated with treatment failure in this regimen.[15] One weakness of the above regimen is that doxycycline achieves poor levels in the nares, leaving mupirocin-resistant bacteria exposed to rifampin alone. Minocycline and clindamycin achieve better levels in the nares.

Tip 5: Colonization of skin and nares must be addressed. Moist intertriginous sites and eczematous skin are commonly colonized.

Retapamulin, a new pleuromutilin topical antibacterial labeled for the treatment of skin infections, is effective against staphylococci, including MRSA.[16] This therapeutic modality appears promising for the eradication of MRSA nasal carriage. Triple antibiotic ointment (neomycin, polymyxin B sulfate, and bacitracin) also appears promising for the eradication of nasal carriage and there is little evidence of resistance.[17] Bacitracin, polymyxin B sulfate, and gramicidin ointment is effective in eradicating MRSA colonization in the face of mupirocin resistance.[18] Silver sulfadiazine also appears promising and retains activity against mupirocin-resistant strains.[19] Spread of fusidic acid–resistant *S aureus* is an important problem in countries where the drug is available.[20] Indolmycin generally shows good activity against MRSA, though high-level resistance has been reported.[21] Botanicals deserve further study. Topical application of components of eucalyptus oil has been reported to clear MRSA infection.[22] Tea tree oil products also have shown efficacy. The combination of tea tree oil nasal ointment 4% and tea tree oil body wash 5% eliminated colonization at rates roughly comparable to mupirocin nasal ointment 2% and triclosan body wash.[23]

Recolonization from the environment remains a problem and fomites must be addressed.[24] Sharing bar soap and towels has been identified as an important risk factor for the spread of MRSA among athletes. An affluent family with 4 children is likely to have only 2 towel bars in the children's bathroom, creating the potential for spread of MRSA. Simple maneuvers such as replacing bar soap with liquid soap and having each child take a color-coded towel back to his/her room to dry over a chair can help prevent recolonization. Sports equipment should be wiped down with alcohol. The mechanical action is as important as the antibacterial agent.

Tip 6: Address fomites, including bar soap, towels, and sports equipment.

Effective management of CAMRSA infections requires a comprehensive approach. Individual abscesses respond to drainage. Oral or parenteral antibiotics should be reserved for patients with systemic illness or surrounding soft tissue infection. Elimination of nasal and cutaneous carriage, as well as contaminated fomites, can reduce the spread of disease and the incidence of recurrent infection.

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