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Documentation of vancomycin-resistant Staphylococcus aureus (VRSA) among children with atopic dermatitis in the Qassim region, Saudi Arabia

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Abstract

Introduction: *Staphylococcus aureus* is known as a common pathogen in atopic dermatitis. A methicillin-resistant *S. aureus* strain with reduced susceptibility to vancomycin (VISA/VRSA) is increasing worldwide. The aims of this study were to evaluate the antibiotic-susceptibility pattern of *S. aureus* isolated from children with atopic dermatitis and to identify the occurrence of resistance to glycopeptide antibiotics.

Methods: Swabs were collected from atopic dermatitis skin lesions of 80 children being treated at dermatology clinics whose ages ranged from 6 months to 15 years in the period from March 2009 to February 2010. Isolates were studied with an antibiogram for an antibiotic-susceptibility test. The selected antibiotics were the usually administered antimicrobials at dermatological clinics in Buraydah (Qassim, Saudi Arabia). Results were determined as minimal inhibitory concentration (MIC) using the Vitek system.

Results: Thirty *S. aureus* isolates showed resistance to streptomycin (100%), benzylpenicillin and ampicillin (96.7%), and oxacillin (90%). *S. aureus* resistance to trimethoprim/sulfamethoxazole, tigecycline, and vancomycin was 63.3%, 83.3%, and 53.3%, respectively. Resistance to linezolid was less, at 5.7%.

Conclusions: Strains of MRSA with decreasing susceptibility to vancomycin were documented in the Qassim region of Saudi Arabia. Other studies will be required on VISA/VRSA strains concerning phenotypic and genotypic characterization.

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Introduction

Staphylococcus aureus is known to be the most frequent pathogen in atopic dermatitis (AD) for which antibiotics are a mode of treatment (1). During the past 20 years, these bacteria have developed resistance to commonly prescribed antimicrobial agents. Methicillin-resistant *S. aureus* (MRSA) infection first emerged in the United States in the 1970s, and by the 1990s MRSA was considered to be endemic in most large urban medical centers (2, 3). MRSA has become endemic in hospitals worldwide and it is now an incipient community pathogen in many geographical regions (4). Glycopeptides are the antibiotics of choice for the treatment of infections caused by MRSA. The first strain of *S. aureus* with reduced susceptibility to vancomycin and teicoplanin was reported from Japan, whereas the first isolate of vancomycin-resistant *S. aureus* (VRSA) was reported from the United States in the 2002, Brazil, and Jordan (5–8). The vancomycin minimum inhibitory concentration (MIC) required to inhibit most strains of *S. aureus* is typically between 0.5 and 2 mg/L (9). *S. aureus* isolates for which vancomycin MICs are 8 to 16 mg/L are currently classified as vancomycin-intermediate, and isolates for which vancomycin MICs are ≥ 32 mg/L are classified as vancomycin-resistant (9). However, the Centers for Disease Control and Prevention (CDC) recommendations for infections due to *S. aureus* strains for which the vancomycin MICs are 4 μg/ml are refractory to vancomycin therapy. Patients infected with these strains fail to clinically improve with vancomycin therapy. Recently, MRSA with reduced susceptibility to vancomycin was isolated from a Saudi patient in Riyadh, Saudi Arabia (8).

The aims of this study were to evaluate the antibiotic-susceptibility pattern of *S. aureus* isolated from children with AD and to determine the occurrence of resistance to glycopeptide antibiotics.

Methods

We included a sample of 80 children between 6 months and 15 years old with AD whose diagnosis was based on the criteria of Hanifin and Rajka (11). These patients were being treated at outpatient dermatology clinics at Qassim University–affiliated hospitals from March 2009 to February 2010. A parent's written informed consent was obtained according to the guidelines of the ethical committee of the College of Medicine at Qassim University. Patients being treated with topical steroids in the last 2 weeks, systemic antibiotics in the last 4 weeks, or immune-modulating drugs at any time were excluded. A swab saturated with brain-heart-infusion broth (Oxoid) was carefully rolled over lesions on the limbs or face of patients, tightly sealed, and then immediately transported to the laboratory. These swabs were then cultured on blood agar base (Oxoid), nutrient agar, and mannitol salt agar, and then incubated at 37 °C for 24 to 48 hours (12). The colonies were identified by Gram stain, morphology, and biochemically by a Vitek automated machine (BioMerieux®) at different incubation periods according to the manufacturers' procedures (13). The antibiotic-susceptibility test for S. aureus isolates from patients suffering from AD was determined. These antibiotics were selected as the usually administered antibiotics at dermatological clinics in Buraydah (Qassim, Saudi Arabia). The susceptibility of the *S. aureus* isolate was determined as minimal inhibitory concentration (MIC) by the Vitek automated machine (BioMerieux®). The following antibiotics were tested: benzylpenicillin, ampicillin, cefo-

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taxime, ciprofloxacin, clindamycin, erythromycin, gentamycin, levofloxacin, linezolid, moxifloxacin, nitrofurantoin, oxacillin, quinupristin/dalfopristin, rifampicin, streptomycin, tetracyclin, tigecycline, trimethoprim/sulfamethoxazole, and vancomycin.

Data were entered into and proportions calculated by SPSS statistical software, version 16.0 (SPSS Inc., Chicago, IL).

Results

Thirty *S. aureus* strains were isolated from AD lesions in the total sample of children in this study (N = 80) from March 2009 to February 2010. These isolates showed that 29 (96.7%) S. aureus strains were resistant to benzylpenicillin and the same were resistant to ampicillin, 29 (96.7%) strains were also resistant to third-generation cephalosporin, 27 (90%) to cefotaxime, 18 (60%) to ciprofloxacin, 9 (30%) to vancomycin, 8 (26.6%) to gentamycin, and 5 (16.7%) to nitrofuritin, but the isolates (26, or 86.6%) were highly susceptible to linezolid (Table 1). Moreover, all *S. aureus* strains showed resistance to streptomycin, 29 (96.7%) of them to the penicillin group, 27 (90%) of them to oxacillin, and 26 (86.7%) isolates to quinupristin/dalfopristin (see Table 1 and Fig. 1).

Table 1 | **Antibiogram of *S. aurues* isolated from AD lesions in Saudi children.**

Antibiotic	S. aureus % resistance
Streptomycin	100
Ampicillin	96.7
Benzylpenicillin	96.7
Cefotaxime	90
Oxacyline	90
Quinupristin/Dalfopristin	86.7
Tigecyline	83.3
Co-trimoxazole	83.3
Ciprofloxacine	60
Rifampicin	60
Clindamycin	53.3
Tetracycline	43.3
Moxifloxacin	40
Erythromycin	36.7
Vancomycin	30
Gentamycin	26.7
Nitrofurantoin	16.7
Levofloxacin	10

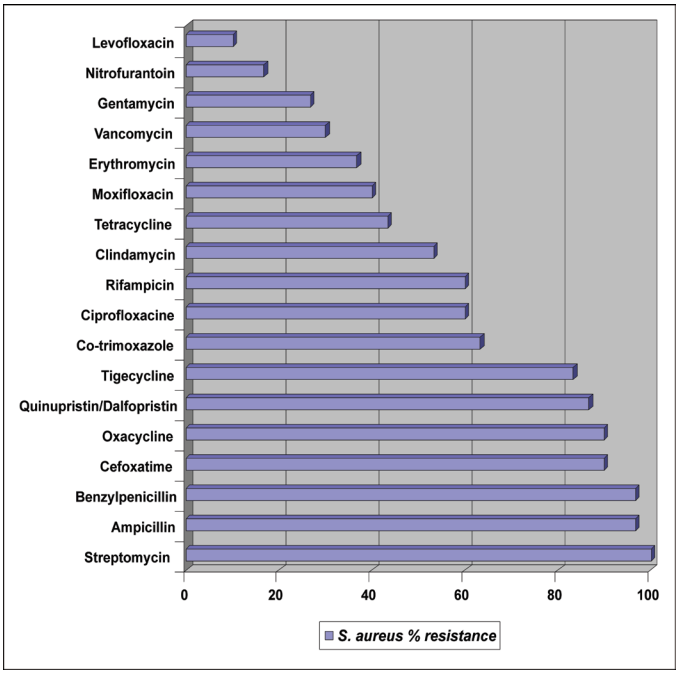

Figure 1 | Antibiotic resistance of *S. aurues* from AD lesions in Saudi Children.

Discussion

The antibiogram of *S. aureus* in this study showed that there was a high percentage of resistance to streptomycin, cefoxitin, and oxacillin (Table 1). Ninety percent of *S. aureus* strains were resistant to methicillin compared to the reported 77.5% MRSA by Baddour et al. in a study conducted for epidemiology of the MRSA from several hospitals in Riyadh, Saudi Arabia. In the same study, with determination of MIC against vancomycin using an E-test, no isolate showed decreased susceptibility to the drug (14). The risk for MRSA increased in general and the prevalence of MRSA among *S. aureus* in Saudi Arabia isolates increased from 2% in 1988 to 33% in 1998. In Jeddah, Saudi Arabia, MRSA comprised 7.5% per year of all *S. aureus* isolates in 2003 (15). All MRSA isolates represented community-acquired MRSA, similar to the findings in other studies (16). There is significantly increased MRSA among all *S. aureus* isolates, with a high prevalence in the United States (17). Glycopeptides such as vancomycin were frequently the antibiotics of choice for the treatment of infections caused by methicillin-resistant *S. aureus* (MRSA). In this study, 16 (53.3%) strains of MRSA had reduced rates of susceptibility to vancomycin (VISA/VRSA); all of them showed MIC > 8 µg/mL according to the National Committee for Clinical Laboratory Standards (NCCLS) (9). Moreover, the first isolation of the strain D958, with methicillin-resistant *S. aureus* with reduced susceptibility to vancomycin, was isolated from a 69-year-old Saudi male (8). Many strains of VISA associated with a clinical infection have been reported worldwide. The first report was described in a 4-month-old infant with a surgical-site infection in Japan in 1996 (5). Subsequently, the CDC has confirmed the presence of VISA in six patients in the United States; two reports were from the CDC [unpublished data] (18). However, the first infection with VISA occurred in France in November 1995 in a 2-year-old girl with leukemia and a central line–associated bacteremia, which was successfully treated with surgical drainage and quinupristin/dalfopristin. There was a good response to quinupristin/dalfopristin (19). In comparison, in this study we found that 86.7% of MRSA was resistant to quinupristin/dalfopristin. Further studies are needed to explain the reason for the reduced susceptibility of MRSA isolates to vancomycin. There is solid evidence to support the exchange of genetic material among VRSA bacteria. Genetic analyses suggest that the in-vivo transfer of vancomycin resistance from *E. faecalis* to an MRSA strain occurred to produce the Michigan VRSA isolate. Acquisition of the van A gene in the Michigan isolate occurred via interspecies transfer of the van A transposon, harbored within a multiresistant conjugative plasmid from co-isolated vancomycin-resistant *E. faecalis* as cited by Appelbaum (20). In this study, the *S. aureus* stain was resistant to trimethoprim/sulfamethoxazole, tigecycline, and streptomycin at 63.3%, 83.3%, and 100% resistance respectively. On the other hand, 86.6% of the isolates were susceptible to linezolid; thus, it may be a potential option for drug-resistant MRSA (21).

In this study, the reasons for decreased susceptibility to vancomycin may be due to exposure to or non-optimal utilization of vancomycin, or due to use of antimicrobial agents in food-producing animals in the Qassim region of Saudi Arabia.

Conclusion

Strains of MRSA with decreasing susceptibility to vancomycin were documented in the Qassim region of Saudi Arabia. Linezolid can be used as an alternative safer drug for strains of VISA/VRSA. Further studies will be required on the VISA/VRSA strains con-

cerning phenotypic and genotypic characterization, particularly on the van A gene.

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