Antibiotic Resistance: MRSA in Dentistry

Dr. Pramod Tadakamalla 1 BDS, (MPH)  
Dr. Joseph Evans 2 DDS  
1,2 Department of Dental Hygiene, Western Kentucky University, Kentucky, USA

Corresponding Author  
Pramod Tadakamalla  
1350, Center Street, Apt.2  
Bowling Green, Kentucky 42101  
Phone: 678 – 983 – 2196  
Email: pramodtadak@gmail.com

Access this Article Online

www.idjsr.com
Use the QR Code scanner to access this article online in our database
Article Code: IDJSR 0071

Abstract
Use of antibiotics in dentistry is a common scenario for treatment and prophylactic measures. Maximized use of these antibiotics augmented the outbreak of resistant bacterial infections caused by new strains like Methicillin-Resistant Staphylococcus aureus (MRSA) and Vancomycin Resistant Staphylococcus aureus (VRSA). Increased prescripations of antibiotics in dental treatments have posed a major threat of infectious diseases in patients leading to serious health concerns. This article reviews the history of MRSA and the mechanism of forming resistance. It also focuses on the clinical implications, management, and complications of these resistant Staphylococcal infections in dentistry. This article spotlights the preventive measures to be taken to prevent these infections and thereby supporting the rational use of antibiotics in dentistry.

Key Words: Methicillin Resistance Staphylococcal Infection, MRSA, MecA gene, resistance, clinical manifestations, management, prevention, complications.

Introduction
Use of broad spectrum antibiotics in the dental setting has increased for therapeutic and prophylactic purposes in an alarming fashion. This is leading to the development of resistance to drugs and has become inefficient in curing infections. Studies throughout the world have shown that the prescription of antimicrobials by dentists is more prophylactic rather than treating a disease. Therefore, the inappropriate prescribing of antibiotics by dental practitioners is playing a significant role in the emergence of resistant microbial strains.

Bacterial Resistance
Antibiotic coverage and microbial resistance have a complex relationship. One of the studies demonstrated the volume of drugs used influences the selection of antibiotics. However, a quantitative relationship between antibiotic resistance and volume of drug could not be explained. A decrease in antibiotic resistance can be noticed after a significant reduction in antibiotic use. Exposure of oral microbial flora to low doses of drugs (ex: minocycline) resulted in emergence of strains which have reduced susceptibility to those drugs.

History of MRSA
The term MRSA stands for Methicillin-Resistant Staphylococcus aureus. It causes a staphylococcus infection resistant to methicillin, oxacillin, penicillin, amoxicillin, etc. For decades, MRSA has affected immune compromised patients in hospitals and other health care centers. MRSA is a type of staphylococcus bacteria resistant to the beta lactam group of antibiotics. The important timelines in the development of MRSA are listed below:

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1941</td>
<td>Introduction of Penicillin into treatment of infectious diseases</td>
</tr>
<tr>
<td>1944</td>
<td>S.aureus Penicillin resistant</td>
</tr>
<tr>
<td>1960</td>
<td>New penicillin-resistant drugs used to fight against staph infection(i.e., Methicillin)</td>
</tr>
<tr>
<td>1968-1970</td>
<td>MRSA causing severe hospital outbreaks in Europe and USA.</td>
</tr>
<tr>
<td>1968</td>
<td>Vancomycin introduced into MRSA therapy.</td>
</tr>
<tr>
<td>1996</td>
<td>S.aureus strain with intermediate vancomycin resistance reported in Japan</td>
</tr>
</tbody>
</table>
Mechanism of Resistance
S. aureus resistance developed due to chromosomal & plasmid mediated β-lactamases. The resistance to methicillin is mediated by mecA gene, a part of mobile genomic element of the staph chromosome. This mecA gene expression produces an altered penicillin binding protein (PBP 2a). When PBP is altered, then the antibiotic cannot inhibit cell wall formation and hence resistance is rendered. The mecA gene is a part of mobile genetic element in MRSA strains, called SCC mec. There are 5 different types of SCC mec elements, which integrate at the same time in the chromosome by a mechanism involving site-specific recombination. Each of the SCC mec has a varying degree of drug resistance. SCC mec II & III are found in many nosocomial MRSA strains. These chromosomes harbor other antibiotic-resistance genes conferring resistance to aminoglycosides, tetracyclines, erythromycin, and clindamycin. CA-MRSA carries SCC mec IV which only carries the mecA gene. This mecA gene encodes a new β-lactam insensitive to penicillin.

Horizontal gene transfer is another mechanism by which MRSA develops & acquires resistance. In horizontal gene transfer, plasmids inside the cytoplasm of bacteria have the ability to transfer resistance genes between the same and different species. 3 different mechanisms involved are 1) Conjugation, 2) Transformation & 3) Transduction. Conjugation is a procedure of cell-to-cell contact by which resistant genes transfer occur. Transformation is where a bacterial gene from the external environment is acquired. Transduction involves bacteriophages transferring DNA between two closely related bacteria.

MRSA expresses many virulence factors like surface proteins that promote colonization of host tissues, invasions that promote bacterial spread in tissues with leukocidin, kinases, hyaluronidase, and surface factors like capsule which inhibits phagocytic engulfment. Other virulence factors include biochemical properties like carotenoids, catalases that enhance the survival in phagocytes, membrane damaging toxins that can lyse the cell membranes like hemolysins, leukotoxins, leukocidins, etc. and exotoxins that damage host tissues and increase the symptoms of diseases.

Transmission of MRSA
Most of the MRSA infections are of skin origin in the community. Its main mode of transmission is through the hands i.e., of the health care workers. So, hand washing is the most important factor in preventing the spread of infection. In a treatment area, the dental chair including the seat and arm rest, floor beneath the chair, sink, towel dispenser, counter top, and suction chamber remain the sources of infection. These usually are not directly contacted with the patient. MRSA was isolated from various surfaces in health care facilities. However, these surfaces and objects are likely to play a minor role in its transmission. Other routes of transmission of MRSA include body fluid exposure to non-intact skin of health care personnel, mucous membranes, or through the sharp or percutaneous injuries. In dentistry, MRSA is known to colonize the saliva and so considered as potentially infected material and often contains blood.

Skin injury after trauma, burns and surgeries can often lead to serious infection by MRSA, especially if the patient has a history of chronic bacterial infection and when treated with multiple doses of
Clinical Manifestations of MRSA

Clinical manifestations of MRSA include abscess or invasion by lymphatics, blood, and major organs. These lesions range from a simple abrasion to a large draining abscess. Even a most common and benign abrasion can turn as a source for a huge, disseminated, and devastating MRSA infection that can be systemic in nature and may not respond to multiple antibiotics in combination. Carbuncles, painful lesions that can cause fever, are increased in WBC counts with an ineffective drainage site as a result of infection due to MRSA. It serves as a reservoir for recolonization and cross-infection between different body sites, different patients, and health care associates. The most frequent symptoms associated are erythema, inflammation and swelling, pain, or burning sensation of mucosa. Persistent MRSA infection can result in a more severe form of illness called “nonmenstrual Toxic Shock Syndrome” and “Scalded Skin Syndrome”. These can present with hypotension, erythema, fever, and multi-organ dysfunction. Nonmenstrual toxic shock syndrome commonly occurs in newborn and post-operative patients. These lesions usually start as a superficial pustule, rupture, and form a yellow honey to brown red crust. These lesions spread and transform into vesicles and bullae. Multi system dysfunction includes gastrointestinal disturbances like vomiting or diarrhea, musculoskeletal disturbances like myalgias; hyperemic mucous membranes; increased blood urea and creatinine levels in renal system with pyuria; hepatic disturbances like increased bilirubin, aspartate and alanine transferase levels; neurologic findings like changes in mental status. Improving hygiene levels and preventing postoperative cross infection helps in preventing this type of infection in children. Major organ failures are considered as a final phase in MRSA toxic shock syndrome with systemic invasion.

Management of MRSA

As the rate of infection due to MRSA is increasing, the management of bacteremia associated with it is a clinical challenge. Establishment of the extent of infection is the most important part of management. A single positive culture report should initiate empirical therapy and lead to obtaining follow-up blood culture reports for prognosis and so as to determine the extent of MRSA infection. The removal of intravascular material along with prosthetic replacement is also required in the management of staphylococcus aureus bacteremia because of high recurrence rates. Failure to remove the device increases the risk of recurrence of MRSA bacteremia or death. It has a mortality rate of 54.2% with removal of the device when compared to 25% without removal. Duration of antimicrobial therapy depends on the extent of infection. Empirical drug therapy of skin and soft tissue infections caused by MRSA in outpatients include clindamycin, trimethoprim – sulfamethoxazole, tetracycline (doxycycline, minocycline), and Linezolid. If the therapy also requires covering beta-hemolytic streptococci, beta-lactam antibiotics should also be included in the combination with the above drugs. Use of rifampicin as a single agent or as an adjunctive therapy is not recommended. In hospitalized patients, surgical debridement along with broad spectrum antibiotic coverage should be considered. The other options include IV vancomycin, oral or IV linezolid 600mg BID, daptomycin 4mg/kg/dose IV OD, telavancin 10mg/kg/dose IV OD, and clindamycin 600mg IV TID. In patients with non-purulent cellulitis, beta-lactam antibiotics like cefazolin should be considered as modification to MRSA active therapy. 7-14 days of therapy is recommended depending on the patient’s clinical response. Other potential antimicrobial agents include quinupristin-dalfopristin, a streptogramin antibiotic, ceftibiprole and ceftaroline which are broad spectrum cephalosporins. Pediatric considerations are likely to include mupirocin 2% ointment applied topically along with empirical therapy of clindamycin 10-13mg/kg/dose IV for every 6-8 hours to be administered. Linezolid 600mg IV is advised BID for children greater than 12 years age and IV of 10mg/kg/dose for every 8 hours for less than 12 years of age as an alternative. For neonates with MRSA sepsis, topical mupirocin, IV vancomycin, or clindamycin are recommended for non-endovascular infections, linezolid, and clindamycin are better alternatives. Recurrent MRSI infections should be treated with proper environmental hygiene and decolonization measures including nasal decolonization with mupirocin twice daily for 5-10 days and topical body decolonization with antiseptics like chlorhexidine for 5-14 days.
Prevention of MRSA

Preventing MRSA infection is the key to infection control in health care. To protect dental patients, dental health care workers and dentists must follow certain strict infection control practices, as enumerated by CDC\(^1\). New guidelines have been prescribed by the CDC and are divided into 7 categories listed in the table below. These guidelines are given for all health care settings including dental environments. The CDC also makes an additional recommendation to get a flu vaccine in addition to routine hepatitis B vaccination\(^7\).

The American Dental Association (ADA) advises dental practitioners to prevent the MRSA infection by washing hands and keeping cuts and scrapes clean and covered with bandage until healed\(^6\). Avoid contact with wounds or bandages or other patients; avoid sharing personal items such as towels, razors, clothes or washcloths. Washing clothes with bleach and hot water then drying them in a hot dryer is a safe method of preventing the infection\(^3\).

Complications of MRSA

Patients suffering with bacteremia caused by S. aureus are likely to develop metastatic complications resulting from the hematogenous spread of a distant site of a local infection site, involving one site more frequently. The common sites of metastatic infections are bone and joints (especially if prosthetic material is used)\(^6\). A wide range of complications can be caused by MRSA which include SSTIs, septicemias, bacteraemia, endocarditis, pneumonia, bone and joint infections, toxic shock syndrome, and CNS disorders. Vertebral complications can also occur which include epidural abscess, vertebral osteomyelitis, and spondylodiscitis\(^6\).

Conclusion

Increasing antibiotic resistance in the world with the emergence of varied infections of MRSA, NDM-1, etc. should be seriously considered. The extensive use of antibiotics and improper health care settings are involved in the development of such strains. The diagnosis and management of these infections should be considered with care to prevent any further complications arising from it. Extensive research should be initiated in this aspect to develop a new range of antimicrobial agents and control these infections. At the same time, proper precautionary measures are to be advised and inspected by the surveillance departments of the entire medical, dental, and other health care associations keeping in view the rising morbidity due to these infections globally. The use of antibiotics needs to be set up with proper guidelines and certain parameters for their prescription.

ACKNOWLEDGEMENTS

Durga Sreenivas. S. MDS
Former Professor and Head of Department,
Department of Oral Surgery
MNR Dental College, Hyderabad, India.

References