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Methicillin-Resistant Staphylococcus Aureus Infections-A Review

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Abstract

Methicillin-resistant Staphylococcus aureus (MRSA) is an infection caused by a gram-positive bacterium. This type of bacteria is resistant to many different antibiotics. The MRSA-related hospital -acquired infection in a surgical patient is a challenge to treat and is usually associated with high morbidity, mortality and prolonged hospital course. We have made an attempt to review and update the knowledge and information related to the MRSA infections with reference to preventive measures and treatment options for better patient management and outcomes. We believe that it will help in better understanding of the pathology and formulate effective treatment options for overall benefit to the community and the organizations.

Keywords: mrsa; infection; antibiotics; surgery; decolonization; cardiac; endocarditis

Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) is an infection caused by a gram-positive bacterium. This type of bacteria is resistant to many different antibiotics. The MRSA-related hospital -acquired infection in a surgical patient is a challenge to treat and usually associated with high morbidity, mortality and prolonged hospital course. The bacterium can be carried on the skin or in the nose without the person showing any signs of infection (carrier). On the other hand, the same pathogen exposes the patients to infections and complications involving tissues and organs during or before surgical interventions or in the hospital stay [1-2]. Therefore, hospital or community acquired infection is of paramount importance to the health care workers not only to prevent severe infections but also prevent transmission. The guidelines for the prevention and management of the MRSA infections are available in the literature and prepared by various organizations [2]. The most widely recognized and used recommendations are from the Infectious Diseases Society of America. In the context of MRSA, the resistance to antibiotic is defined as an oxacillin minimum inhibitory concentration (MIC) of greater than or equal to 4 micrograms/mL. Mutation of a penicillin-binding protein, a chromosome-encoded protein present in the bacteria, is the basic reason of resistance [3]. At molecular level, the MRSA resistance to beta-lactam antibiotics is due to the presence of the mecA gene sequence, which is known to generate transpeptidase PB2a that reduces the affinity of the bacterium to bind to beta-lactam antibiotics [3]. The MRSA infection is one of the leading causes of hospital-acquired infections and inflicting a financial burden. These infections can be further divided into hospital-associated infections and community-associated infections.

Preventive measures

The most important factor to consider when dealing with MRSA-related problems is to identify and treat the risk factors for Hospital Acquired-MRSA.

These risk factors are:

- Patients with surgical wound/ intravenous line/ventilator/intubation/injections
- Prolonged hospitalization
- Recent use of antibiotics
- Immunocompromised state
- Being in close proximity to other patients, family members, or health care workers who are colonized with MRSA

Screening and diagnosis

Appropriate screening for the MRSA in the patients in the hospital settings includes bacterial culture from the skin, nasal mucosa and from the skin folds such as axilla, groin or surgical sites. In some situations, an infected wound may harbor MRSA and wound culture with "Levine's" method is appropriate to get specimen. The gram stain and then study of the colony in the pathology laboratory is required through culture of the bacterial flora. Now a days, immunological, histopathological, and chemical tests are also available as advanced diagnostic methods for the diagnosis. Culture and sensitivity tests reveal resistance to Methicillin but may show sensitivity to other broad-spectrum agents such as Vancomycin.

Hand washing and contact precautions

Hand hygiene and cleaning of the instruments, surfaces and proper part preparation during the procedures such as line insertions, catheterization or surgery is crucial to prevent MRSA infections.

Community acquired MRSA

The MRSA infection spreads by sharing clothes, instruments, touching and working in a crowded place such as nurseries, barber shops, swimming pools or beaches. Therefore, suggested precautions include hand wash, use of sanitizers, proper disposals of used items, avoidance of overcrowding and environmental sanitization including cleaning measures.

Once diagnosed, a decolonization strategy is followed as per individual hospital's policy.

Clinical presentations of MRSA infections

The MRSA is associated with gram-positive cocci and any systems of the body can be involved from the skin and soft tissue to a severe infection like endocarditis, septicemia, pneumonia, urinary tract infections, bone and joint infections, central nervous systems and surgical site infections [1-2]. The coagulase positive and negative nature of the MRSA is the cause of the resistance and virulence related to this pathogen.

Appropriate investigations are dependent upon body systems involved. However, the basic recognition of the organism on the gram staining and culture is crucial. Results of the wound, tissue or blood test are usually available in 24-72 hours. People with infections of the lung, bone, joint, or other body systems usually require laboratory tests as well as imaging studies (x-ray, CT scan, echocardiogram, MRI, radionuclide scan).

Treatment strategies

The treatment of the MRSA depends upon the system and organ involved and the place of treatment (home or hospital) and also depend upon the severity and the comorbidities.

The following recommendations are primarily applicable to the hospital settings and are based on the guidelines of the Infectious Diseases Society of America [2-4]. Antibiotic treatment and local management (wound, abscess or lesion and associated complications) are the main stays of the treatment. The current literature review indicates following management options for various MRSA infections based on the nature of tissue involvement:

Skin and soft-tissue infections in community-associated MRSA

Simple abscesses or boils may be managed with incision and drainage alone. Those with moderate severity or extensive lesions require 7-10 days of oral empirical therapy including clindamycin, trimethoprim/ sulfamethoxazole, a tetracycline (doxycycline or minocycline), and linezolid [2-4]. Recently, the FDA has approved Delafloxacin for the treatment of skin infection caused by MRSA in adult patients using following regimens: Oral: 450 mg every 12 hours for 5 to 14 days and intravenous 300 mg every 12 hours for 5 to 14 days [5]. Delafloxacin belongs to the Fluoroquinolones group of antibiotics. Peculiarity about this drug is that it can be used for any degree of severity of MRSA infection as it is available in both oral and intravenous formulation. It can be used as alternative to Linezolid in patients, where Linezolid cannot be used either due to contra-indications or patients with thrombocytopenia.

Recurrent MRSA skin and soft-tissue infections

Decolonization may be considered if a patient develops a recurrent infection despite good personal hygiene and wound care. Strategies for decolonization include nasal decolonization with Mupirocin twice per day for five to 10 days, or nasal decolonization with Mupirocin twice per day for five to 10 days plus topical body decolonization with Chlorhexidine for five to 14 days. An oral antibiotic in combination with rifampin may be indicated for moderate infection [2,6].

MRSA bacteremia and infective endocarditis of the native cardiac valves

Recommended treatment for adults with uncomplicated bacteremia includes vancomycin or daptomycin at a dosage of 6 mg per kg intravenously

once per day for at least two weeks. For adults with complicated bacteremia (positive blood culture results without meeting criteria for uncomplicated bacteremia), four to six weeks of therapy is recommended, depending on the extent of infection. Emergency valve replacement is indicated in destroyed valve with severe regurgitations, hemodynamic deterioration, vegetation in the valve and embolization [2,3,6,7].

Prosthetic Valve Endocarditis

Patients with prosthetic valve endocarditis are sick patients and have poor prognosis. They should be treated urgently with intravenous vancomycin and rifampin (300 mg orally or intravenously every eight hours for at least six weeks), plus gentamicin (1 mg per kg intravenously every eight hours for two weeks). A need for replacement of the valve is required as an emergency as per above-described indications for the native valve [6,7].

MRSA Pneumonia

Treatment options for hospital acquired MRSA or community acquired MRSA pneumonia include 7-21 days of intravenous vancomycin or linezolid, or clindamycin (600 mg orally or intravenously three times per day), if the strain is susceptible. A complicated pneumonia leading to pleural effusion or empyema requires appropriate surgical intervention and also need for ventilator support [2-4].

MRSA Bone and Joint Infections

Debridement, drainage or excision of the involved bone segment may be indicated for bone and joint involvement. However, intravenous antibiotics vancomycin and daptomycin (6 mg per kg intravenously once per day) is advised. Antibiotic options for oral route include Bactrim-4 mg per kg twice per day) in combination with rifampin (600 mg once per day), linezolid, and clindamycin (600 mg every eight hours). Therapy usually lasts for 8-12 weeks [2-3].

Persistent MRSA bacteremia and vancomycin treatment failures in adults

Persistent bacteremia needs a search for a focus of infection and it may require drainage of abscess or surgical debridement as necessary. High-dose daptomycin (10 mg per kg per day), if the isolate is susceptible, in combination with another agent (e.g., gentamicin, rifampin, linezolid) should be considered.

Vancomycin therapy in the MRSA infections

Traditionally, vancomycin is indicated and used for most of the MRSA infections. The route of administration is intravenous and dosage or frequency is usually dependent on the plasma levels and co-morbidities. Frequent drug levels monitoring is good to maintain an effective concentration in the blood. Use of trough vancomycin concentrations is the most accurate and practical method to guide vancomycin dosing. Serum trough concentrations should be obtained at steady state conditions. Vancomycin trough concentrations of 15 to 20 mcg per mL have been historically recommended in patients with serious infections [2]. However, latest guidelines issued jointly by American society of health system Pharmacists and Infectious diseases society of America for vancomycin therapy recommend the use of multifaceted approach with a target AUC/MIC ratio 400 to 600 (assuming MIC 1 mg/L by Broth Microdilution) [8].

MRSA infections in children

More or less, management of the MRSA in the pediatric population is based on the same principles as adults. The choice of the antibiotic treatment including role of surgery is also not different. However, a careful dose scheduling and drug level monitoring is important in children.

Cardiac surgery and MRSA

As per published data, the MRSA carriers who undergo cardiac surgeries are not associated with higher mortality or surgical site infections and have similar outcomes comparable to those of no-carriers. However, higher rates of MRSA infections or septicemia or device -related complications are found in carriers. This signifies the role of preoperative screening or prophylaxis in such patients [4]. Surgical Infections in cardiac surgical patients have been associated with higher mortality and morbidities in cardiac surgery. Postoperative surgical site infection is a grave concern and usually associated with Staphylococcus aureus or Staphylococcus epidermidis. Therefore, preoperative screening and routine antibiotic prophylaxis of less than 48 hours is recommended to prevent infection. However, prolonged use of prophylactic antibiotics, 48-hours after surgery is not shown to be effective and in fact correlated with an increased risk of acquired antibiotic resistance [6-7].

Decolonization strategies for MRSA

A need for identification and decolonization of treatment of MRSA infection is mandatory to avoid

adverse effect of MRSA [3]. It is preventable and we should know that MRSA is a virulent and drug resistant infection. The decolonization is a process to remove the bacterial flora from the body sites (usually nasal passage and body surface) using antibacterial agents. As per 'REDUCE MRSA' trial that involved multicenter study to compare various strategies of decolonization, it is important to decolonize every patient in the hospital settings and this is relevant more in the ICU and surgical settings where body cavities and surface is exposed and vulnerable due to weak host defense and multi-pathogen invasions [2-3]. The purpose of decolonization is to reduce transmission and disease caused by the MRSA. The surgical site infection, ventilator associated pneumonia and catheter related infections are common due to the MRSA. The 'REDUCE MRSA' was largest randomized trial and had compared three groups of patients: Target decolonization (Patient screening, isolation and decolonization), screening and isolation only and universal decolonization- no screening but decolonization) for all the patients included in the study.

Findings of the trials concluded that in the intensive care settings, a universal decolonization regime helps significantly in the reduction of blood stream infection rates for all kind of bacteria as compared to the targeted decolonization or screening only group of the patients [1-2]. They mentioned that there was reduction of infection per 54 patients. In addition, the MRSA infection in the blood was also reduced, although statistically not significant [2]. The recommended protocol of universal decolonization consisted of multi-dose regimen of intra nasal Mupirocin and Chlorhexidine bath. The local application of Mupirocin three times a day, intra nasal and once daily body bath using cloth socked with Chlordixine for 5 days is given to all the patients irrespective of their screening or reports. It has been reported that universal decolonization is most effective in reducing MRSA colonization by 37% and all infections in the blood by 44% [2,6]. The advantage of universal regimen is that there is no need for MRSA surveillance test and no need for contact precaution. This will eliminate cost and manpower issues and also avoid delays. However, it is not clear yet, whether Mupirocin alone or combined with Chlorhexidine is better. Chlorhexidine not only cleans MRSA but many other organisms and therefore effective in a broader way. Another issue is development of resistance. The application of these agents might cause development of resistance to the medications and the regimen and therefore, intermittently, it is important to screen the patients for resistance in a setting with universal regimen [2,6]. The targeted decolonization is also one way that is used by many institutions. For example, in most of the adult cardiac surgical units, the nasal, axillary and groin MRSA swabs (3- swabs- each) are taken for all surgical patients upon admissions before surgery. Any positive case needs decolonization. The decolonization procedure is beneficial for the control of MRSA, prevention of transmission, prevention of complications and reduction in the need for treatment of a drug resistance pathogen that leads to a cost burden, prolonged hospitalization and waste of resources in the health care systems.

Conclusion

Prevention, decolonization, early recognition of infection and appropriate use of antibiotics in timely manner is crucial to manage established MRSA infection. Such strategy limits morbidity and mortalities during medical or surgical management of the patients and helps achieving better outcomes. Moreover, a successful MRSA infection prevention or treatment has positive effect on hospital stay and cost of treatment for the patients and the hospitals.

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