Implications Of Methicillin-Resistant *Staphylococcus aureus* On Nursing Home Practice

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Abstract: ***Background:*** **Methicillin-resistant *Staphylococcus aureus* (MRSA) is being isolated with increasingly frequency from nursing home patients. There is a limited choice of antibiotics available to treat infections caused by the organism. Control measures for nursing homes have not been well established.**

Methods: **Using the key words "methicillin," "homes for the aged," and "long-term care," and also using the text term "MRSA," the MEDLINE files were searched from 1966 to 1989 using a CD ROM system. Articles occurring subsequent to this search, until the manuscript was submitted, were accessed using a monthly update from the MEDLINE database using the same key words.**

Results: **MRSA prevalence rates as high as 34 percent have been reported from long-term care settings. Risk factors for developing MRSA include being sick, debilitated, and functionally impaired. Frequent use of antibiotics and invasive devices, such as catheters, are also identified risk factors. The implication of MRSA colonization on patient outcomes is not clear. Vancomycin remains the drug of choice for treating MRSA infections. Control measures include surveillance of new and established cases and the introduction of isolation procedures. Patients colonized with MRSA should not be refused admission to a nursing home because of their MRSA status.**

Conclusions: **MRSA in nursing homes will continue to increase. There are resulting implications for patient care, health care costs, and admission and discharge policies. Research should first establish what effect MRSA colonization has on clinical outcomes in this setting and, if necessary, go on to develop clinical and cost effective methods of prevention and control. (J Am Board Fam Pract 1992; 5:193-200.)**

An outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) in a local teaching nursing home stimulated our interest in this subject. On reviewing the literature, we noted that MRSA is being increasingly recognized in long-term care institutions but that its microbiologic and epidemiologic importance and means of control in this setting have not been fully investigated. The purpose of this review is to outline the knowledge that exists, to give some guidelines for the control of MRSA in nursing homes, and to highlight areas requiring future research.

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S. aureus resistant to methicillin has been identified in the United States since the early 1960s; the first major institutional outbreak was reported from Boston City Hospital in 1968.[1] The index case was identified as coming from a local nursing home. Another hospital report in 1970 described isolation of MRSA from 8 patients.[2] Three of the patients had recently been admitted from local nursing homes. Cultures from patients residing in the nursing homes uncovered only 1 other resident with MRSA. A much higher rate of MRSA isolation was reported from a Missouri nursing home in 1987.[3] Following five cases of MRSA pneumonia occurring in quick succession, a survey sampling nursing home residents and staff showed that 12 percent of residents and 7 percent of staff had cultures positive for MRSA. Six of the 9 residents found to have MRSA had not been out of the nursing home in the 6 months before its isolation, suggesting that they were infected with the organism while in the nursing home. An additional report in 1988 indicated that more than 50

percent of *S. aureus* isolated from patients admitted to an acute care facility from local nursing homes was resistant to methicillin.[4] MRSA was isolated from patients admitted from 18 different nursing homes in a 2-year period.

Epidemiology

Prevalence

A prevalence rate as high as 34 percent has been recorded for infection or colonization with MRSA among residents of a Veterans Association (VA)-affiliated, long-term care facility.[5] A nasal colonization rate of 7 percent for staff was found in the course of the same study. Serial nasal cultures conducted in a community nursing home showed that many of the patients would fluctuate between being culture positive and culture negative at different times without having been treated in the interim.[6] Prevalence rates should be reported as point prevalence, and prevalence surveys should report serial measures for this organism. Prevalence rates for MRSA at other body sites other than the nares have not been well described.

Risk Factors

The explanation for the increasing numbers of MRSA cases being reported from nursing homes is very likely multifactorial. Risks include serious or chronic underlying disease, prior hospitalization, repeated transfers between acute and chronic care facilities, and prior surgery. Patients who are more debilitated and who have greater functional impairment and greater nursing needs appear to be at greater risk of becoming colonized or infected with MRSA.[6] Invasive devices often play a critical role, especially in MRSA nosocomial infections. Examples include central venous catheters that can lead to bacteremia, indwelling bladder catheters that can lead to urinary tract infections, and endotracheal tube access that leads to tracheobronchitis or pneumonia. A critical factor, perhaps more important in chronic care, is prolonged antibiotic use. Earlier use of oral broad-spectrum antibiotics can predispose to the development of MRSA.[7]

Transmission

High rates of nasal colonization have been found among staff working in facilities experiencing outbreaks of MRSA.[6,8,9] The most common mode of transmission of resistant strains is direct patient contact. Medical staff, particularly nurses and physicians, can be important vectors, mostly by hand-to-hand contact.[9-11] Those investigating an MRSA outbreak in a surgical intensive care unit found that 8 percent of nurses working in the intensive care unit had positive nares cultures; one more heavily colonized nurse was suspected of being responsible for the majority of the cases.[12] Because some investigators report lower colonization rates in health care workers,[13] it could be that transient hand carriage of MRSA also can play a role in transmission. In addition, MRSA has been cultured successfully from inanimate objects in facilities where there were outbreaks, including floors, hydrotherapy tubs, lamps, light switches, and curtains. Many of these fomites, however, might not play an important role in transmissions because investigators have shown varying experience with environmental contamination during outbreaks. While some researchers documented extensive MRSA contamination of the environment, others could find little, if any, documentable involvement.[14] Most investigators have not found environmental sampling useful.[15] MRSA has also grown on plates exposed to the air in units with high MRSA infection rates, but the relative contribution of air transmission is unclear, and air is thought not to be a major mechanism of spread. Transmission among roommates has been found to be infrequent for nasal colonization with MRSA.[6]

Sites Affected

MRSA can infect or colonize virtually any body site. It can be isolated readily from the skin, in particular the axillary region, where there can be relatively high bacterial counts. MRSA is most commonly isolated from the upper airway, including the nares.[1,2] MRSA can also frequently be isolated from open wounds, such as burns and pressure sores.[2,3,8] The urinary tract is a site for MRSA involvement as well. Two of the 18 cases reported from Boston City Hospital had MRSA in their urine[1]; in another study, 11 of 41 patients with positive MRSA cultures had the organism isolated from their urine.[16] In a teaching nursing home affiliated with the University of Connecticut, where there were 35 new cases of MRSA positive cultures in a 2-year period, 15 patients had MRSA isolated from their urine.[17] The ma-

jority of these patients had indwelling urinary catheters at least temporarily and had received multiple courses of antibiotics before becoming MRSA positive. Storch, et al.[3] found that 2 of 25 patients in a nursing home with positive MRSA cultures grew it from their urine, and both had chronic indwelling urinary catheters.

Virulence

The virulence of MRSA in the nursing home environment is uncertain. In three different hospital outbreaks of MRSA, Thompson, et al.[18] found that the overall mortality caused by methicillin-resistant infections was no different compared with mortality of case-matched controls with sensitive strains of *S. aureus*. In a study conducted in a long-term care Veterans Administration facility, 25 percent of patients who were nasal carriers of MRSA went on to develop staphylococcal infections within a 3-year period, compared with 4 percent of patients who had nasal *S. aureus* sensitive to methicillin.[19] Only one death was reported during the course of a staphylococcal infection. As already described, chronic illness, functional impairment, and debilitation are risk factors for developing MRSA colonization or infections. MRSA colonization could prove to be a marker for degree of illness and functional impairment rather than an independent risk factor for a poor outcome. This area in particular needs further investigation.

Antibiotic Sensitivity and Methods of Culturing

S. aureus can be divided into four major categories: (1) penicillin susceptible, (2) penicillin-resistant strains that are susceptible to methicillin (as well as oxacillin, nafcillin, and the first-generation cephalosporins), (3) strains with "borderline" resistance, and (4) methicillin-resistant *S. aureus* (MRSA).

MRSA is not only resistant to methicillin, as its name implies, but is also resistant to other semisynthetic penicillins such as nafcillin and oxacillin. It is important to remember that MRSA should also be considered resistant to the other major classes of β-lactam agents, including the cephalosporins. Actually, many strains of MRSA are also resistant to aminoglycosides, erythromycin, clindamycin, and tetracyclines. Although most strains of methicillin-resistant *S. aureus* produce β-lactamase, the β-lactamase does not appear to contribute much to their level of resistance to methicillin, oxacillin, or nafcillin. Low-affinity penicillin-binding proteins (PBP-2a or PBP-2') seem to be the more important determinants of resistance.[20]

Widespread quinolone resistance among MRSA has been reported from a general hospital in Israel. In this hospital, after the introduction of routine testing for quinolone resistance in 1987, 90 percent of MRSA strains isolated have been resistant to both ofloxacin and ciprofloxacin.[21] In a similar report from New York City, large-scale quinolone resistance was found among MRSA isolates from both hospital and nursing home patients.[22] Interestingly, the nursing home isolates of methicillin-sensitive strain of *S. aureus* also had a high rate of quinolone resistance. In both instances, the data suggest an independent selection of quinolone resistance rather than an isolated mutant variety of the organism. The emergence of ciprofloxacin resistance during an outbreak of MRSA in a VA-affiliate nursing home has recently been reported.[5] By the end of the study period, 100 percent of MRSA isolates were resistant to ciprofloxacin. Vancomycin is an effective agent for the treatment of established MRSA infections, and resistance to it has not yet been reported.

Laboratories where routine antibiotic sensitivity testing is done should not have difficulty detecting these strains of *S. aureus* if plates are incubated at 35°C for at least 24 hours on a medium with a high sodium chloride (NaCl) content.[23] A more detailed review on laboratory detection of MRSA than is warranted here is provided by Jorgensen.[24]

Management of MRSA in a Nursing Facility

Management of MRSA can be divided into two sections: Management of acute infections, and control measures to reduce infections and colonization.

Treatment of Acute Infections

Vancomycin is still the drug of choice for the treatment of MRSA infections. As it can be given only intravenously and most nursing homes do not administer intravenous antibiotics, patients usually will be transferred to an acute care hospital for treatment. When, because of patient or

family wishes, a nursing home resident cannot be transferred to an acute care hospital, treatment in a nursing home might be necessary. In the event of an acute MRSA infection, trimethoprim-sulfamethoxazole combined with rifampin can be effective when the organism is sensitive, the patient is not allergic, and the clinical situation allows oral therapy.[14,25] Ciprofloxacin, an oral fluroquinolone, combined with rifampin, has been used in such a situation.[26] It should be emphasized, however, that these alternatives to vancomycin have not been validated in controlled trials, and their use to treat MRSA infection should be limited to the specific situation described. High rates of ciprofloxacin-resistant MRSA from several studies[5,6,27] suggest that ciprofloxacin is now of limited value in treating MRSA infections.

In many cases of acute infection, especially pneumonia, the physician caring for the nursing home patient will frequently need to institute antimicrobial therapy without knowing what organisms are responsible. The empiric choice of antibiotic coverage must be made on the basis of the organisms most likely to produce infection at that site and the sensitivities of those organisms in that institution. The history of clinical events leading up to the infection, (e.g., a history of vomiting with a high likelihood of aspiration), the degree of illness, the possibility of bacteremia, and the results of laboratory investigation will all influence the choice of antibiotics. In an institution in which MRSA is endemic, and certainly in a patient known to be colonized with MRSA, the use of vancomycin for initial treatment of acute infections needs to be seriously considered, especially when the patient is very ill or bacteremia is suspected. The vancomycin can be coupled with a broad-spectrum antibiotic, such as a second- or third-generation cephalosporin for gram-negative coverage, until the results of cultures are known.

Control Measures

Guidelines have been published for control measures in hospital outbreaks of MRSA,[28-30] but not for nursing homes. Because data are lacking, it is impossible at this time to make definitive recommendations on the control of MRSA in nursing homes. Nevertheless, the problem exists now for many long-term care institutions and the physicians who take care of patients in them. The following recommendations are based on a review of the data that already exist. They are offered as advice to help physicians who manage patients in nursing homes where MRSA is present to develop their own control measures. Controversy will continue on this subject until such time as the effectiveness of various control measures is proved in long-term care settings.

Control measures for MRSA in nursing homes can be divided into three components: surveillance, isolation, and management of the carrier state.

Surveillance

Surveillance is the monitoring of cases of bacterial involvement that occurs during a specific time. Colonization and the identification of clinical infections in patients can be included. It is important at this stage to attempt to differentiate between colonization and infection. When an organism is isolated from a body site, such as the nares, and there are no signs or symptoms of inflammation, then that organism is considered to be colonizing the area. If there are signs or symptoms of inflammation, then the organism is causing an infection. Unfortunately, the clinical differentiation is not always that clear.

The efficacy of conducting surveillance for MRSA in residents of nursing homes or those being admitted to the nursing home has never been established. Surveillance can encompass keeping a record of all cases of MRSA discovered in the course of routine clinical practice. It can be expanded to include spot surveillance of patients, such as nasal swab taken from all new patients admitted to the nursing home from a hospital where MRSA is present. Staff members can occasionally be included in the surveillance process. The antibiotic resistance patterns of MRSA from different patients can be recorded to assess whether the same strain of MRSA is responsible for all the cases being identified. Phage typing of MRSA can also be conducted for the same purpose. For those interested in pursuing identification methods in more detail, guidelines are provided by Mulligan and Arbeit[31] in a review on the subject.

Given our current knowledge, we would recommend that nursing homes keep a record of all cases of MRSA identified in the facility. We would

suggest culturing at-risk sites in these patients (e.g., nares, open wounds, or urine of patients who are catheterized). A record should be kept of the antibiotic sensitivities for each isolate. The person's location in the home should also be recorded. At this time there is insufficient evidence to support culturing specimens taken from all other residents or staff in the institution. Spot surveillance of patients being admitted from hospitals known to harbor MRSA or of patients previously known to be MRSA positive should be considered. This information will help in introducing and monitoring the next control step, which is isolation.

Isolation

Isolation of cases and the use of universal precautions have proved to be the most effective means of controlling the spread of MRSA in acute care hospitals.[9,28] Dedicated isolation areas, with a separate room for each patient, are especially helpful, but few hospitals and no nursing homes have such units. Where single rooms for the isolation of MRSA are not available, patients with positive isolates can be grouped in the same rooms. This strategy was used with apparent success in one institution experiencing a high rate of MRSA, but a control group was not used, and the causal relation between grouping and a decreased prevalence of MRSA was not proved.[11] When to stop isolation of paired patients after one becomes culture negative for MRSA can present a dilemma. If transferred too soon, a patient can be a reservoir of infection for other noncolonized patients. If kept together too long, a culture-negative patient can become recolonized from the roommate if breaks occur in the precautions being used to contain spread of the organism.

The implications for isolating patients in nursing homes and in hospitals are different. A review on control measures for MRSA in the hospital setting states that an effective and cost-saving means of managing patients with MRSA is to discharge them as soon as possible. This option is rare for nursing home patients who are in need of long-term care. Many nursing home residents will stay in the nursing home for the rest of their lives, and they could be intermittently or continuously colonized with MRSA. Should they be isolated indefinitely? Should they be allowed to go to the physical therapy department or attend social events with other residents?

Given the environmental constraints in nursing homes and the limited information now available on the efficacy of isolation, what should be done? Patients known to be infected or colonized with MRSA at sites from which the organism can easily be spread, such as open wounds, sputum in a patient with a tracheostomy or acute cough, or in a patient's urine, should, where possible, be placed in a single room.[32] When a single room is not available, patients should be roomed with other patients known to have MRSA. All patients with MRSA preferably should be in one unit or one part of the institution, as grouping has had some success in minimizing new cases elsewhere.[33-37] Personnel having contact with these patients should wear gloves and gowns or aprons as part of universal precaution guidelines. Using a mask when suctioning is done or when increased respiratory secretions are present is reasonable. Staff should also wear a mask when caring for colonized patients with respiratory infections or an active cough. Good hand washing is imperative, and contaminated materials, such as urinary drainage bags, catheters, and dressings, should be properly discarded. When patient colonization persists, physical and occupational therapy that can be performed in the patient's room should be provided there. Mandatory visits, if absolutely necessary, to the physical therapy department should be planned well in advance with adequate information given to those workers who will have contact with the patient (including transport personnel, and therapists). The severity of the infection, the location of colonization, and the needs of the patient should be carefully weighed when making a decision about moving the patient to another part of the facility. Taking these factors into account will help indicate whether attendance at social events in the nursing home can be allowed as well. Rarely should visits from family and close friends be curtailed.

Management of Carriers

The appropriate management of identified carriers of MRSA in nursing homes is also far from clear. Most of the efforts so far have been directed at the elimination of nasal carriage of MRSA. Many agents have been used both topically and systemically, including topical bacitracin,[37] a com-

bination of oral rifampin and trimethoprim-sulfamethoxazole[25] with or without a topical agent, ciprofloxacin alone,[38] and ciprofloxacin in combination with rifampin.[26] In all these reports the rates of eradication were poor, the rates of recolonization were high, or the period of follow-up was short. Mupirocin (Bactroban™), a topical antibiotic now available in the United States, has been studied as a means of eradicating the MRSA carrier state in patients with the organism isolated from the nares.[39,40] Rates of initial eradication were impressively high, but rates of recolonization were also high. There have now been several reports of MRSA resistant to mupirocin.[41,42] In addition to antimicrobial therapy, an easy and reasonable approach is to attempt to decrease skin bacterial counts by daily bathing with an agent such as chlorhexidine (Hibiclens™).

Does successful eradication of MRSA carriage control an outbreak? The answer is, again, unclear. Yu, et al.[43] showed that with patients on dialysis the eradication of nasal *S. aureus* decreased the frequency of staphylococcal infections of access site, skin, and soft tissue. Dacre, et al.[44] and Hill, et al.[39] each reported that the elimination of nasal carriage of MRSA with mupirocin had a positive impact on the control of hospital outbreaks, though no control groups were used. On the other hand, Bacon, et al.[10] found that the eradication of nasal MRSA from personnel in a VA hospital did not have any impact on the emergence or spread of nosocomial MRSA.

Matters are further complicated when considering other body sites as areas of MRSA colonization. Sapico, et al.[16] found 11 of 41 patients with positive MRSA cultures in an acute care hospital had MRSA in their urine, yet only 1 of these patients had symptoms of a urinary tract infection. Attempts at eradication with antibiotics were reported to be successful, but the conversion to MRSA-negative status in urine samples was no greater in the treated than in the untreated group. If urine should prove to be a common site of MRSA colonization in nursing home patients, as our own data would suggest,[17] urine may become an important vector for the spread of MRSA.

The best approach at the moment is to resist the temptation to eradicate MRSA colonization with antibiotics. This path could prove to be difficult to follow in the face of increasing MRSA isolates or MRSA-related infections. If compelled to attempt an eradication program, we would recommend 10 days of oral trimethoprim-sulfamethoxazole and rifampin for nasal, skin, or urine colonization with the addition of nasal applications of muprocin three times a day for 10 days for nasal colonization.

Interinstitutional Relations

Hospitals and nursing homes might be reluctant or refuse to accept patients known to harbor MRSA.[3] One can blame the other for being responsible for their MRSA problem. The energy that can be directed toward accusations of substandard care and poor infection control practices between hospitals and nursing homes should be directed toward collaboration to manage the problem. Open lines of communication are needed between hospitals and nursing homes when transferring patients known to be infected or colonized with MRSA. Patients known to be MRSA positive should not be refused admission to a hospital or nursing home because of it. The nursing home might find it useful to identify an infectious disease specialist or hospital epidemiologist with an interest in the area to act as a consultant on control measures. Joint education programs for hospital and nursing home staff, especially the nursing aides who provide most of the hands-on care, should be instituted. Physicians also need to be educated about MRSA and what it means for their patients' care.

Conclusion

Increases in the nursing home population in this country, earlier discharge of sicker patients from acute care hospitals, and the introduction of increasingly broad spectrum antibiotics into nursing home practice will lead to the emergence of more resistant strains of bacteria in addition to MRSA. Research priorities include identifying the impact of MRSA colonization on patient outcomes in nursing homes, elucidating the risk factors contributing to the emergence of MRSA, and analyzing the effect of control measures.

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