Spring 2009

MRSA RESOURCE LINE

A QUARTERLY SUMMARY OF PEER-REVIEWED PUBLISHED LITERATURE

MRSA an important cause of bacteremia in Calgary Health Region

Laupland et al. Staphylococcus aureus *bloodstream infections: risk factors outcomes, and the influence of methicillin resistance in Calgary, Canada, 2000-2006.* J Infect Dis *2008;198(3):336-43.*

Methicillin-resistant *Staphylococcus aureus* (MRSA) is emerging as an important cause of *S. aureus* bacteremia infections in the Calgary Health Region, according to Canadian surveillance data.

Dr. Kevin Laupland, University of Calgary, Alberta, and colleagues carried out a population-based study in the Calgary Health Region (CHR) between 2000 and 2006 to define the epidemiological profile of *S. aureus* bacteremia in the region and to assess whether the incidence and severity of the bacteremia, as well as the rates of antimicrobial resistance, were increasing. "Surveillance for bacteremia *S. aureus* infections was conducted by Calgary Laboratory Services, a regional laboratory system that receives >95% of all blood samples submitted for culture from hospitals, nursing homes and clinics in the CHR," the authors noted.

Of the 1542 incident bacteremia *S. aureus* infections documented over the seven-year study, 599 (39%) were nosocomial cases, 561 (36%) were healthcare-associated community-onset infections and 382 (25%) were community-acquired. The great majority of the bacteremic *S. aureus* infections were caused by methicillin-susceptible *S. aureus* (MSSA) organisms, researchers added. However, 169 infections were identified as MRSA infections, 88% of these were either nosocomial or healthcare-associated community-onset infections and 11% were community-acquired. The overall annual incidence of *S. aureus* bacteremia due to MRSA was 2.2 cases per 100,000 population/year. Of interest, rates of both healthcare-associated community-onset infections and nosocomial MSSA bacteremia did not differ significantly throughout the duration of the study while rates of community-acquired MSSA bacteremia gradually decreased.

Yet as the authors observed, "Rates of MRSA bacteremia dramatically increased"—a finding they believed was principally attributable to major increases in nosocomial and healthcare-associated community-onset disease. Risk factors for both MSSA and MRSA bacteremia included advancing age and significant chronic comorbid illnesses or alcoholism or both. However, by far the most significant risk factor for both MSSA- and MRSA-associated *S. aureus* bacteremia was hemodialysis, which carried a relative risk of 364 for MSSA infections and 330 for MRSA infections. The case-fatality rate for the cohort overall was 25% and was highest for patients with nosocomial infections (35%), followed by those with healthcare-associated infections (21%) and community-acquired infections (16%). For those with MRSA-associated bacteremia, the case-fatality rate was significantly higher at 39% than for those with MSSA bacteremia at 24%.

Rates of resistance to various antimicrobials over the course of the study were relatively reassuring. During the latter part of the study, MRSA strains showed a high but stable rate of resistance to ciprofloxacin, and rates of resistance to trimethoprim-sulfamethoxazole were low for both MSSA and MRSA strains. Two out of 1483 isolates were resistant to rifampin, one of 1491 isolates had reduced susceptibility to vancomycin and none of the 174 isolates tested against linezolid demonstrated reduced susceptibility.

"Before we conducted this study, the clinical impression in our region was that *S. aureus* bacteremias were increasing at an alarming rate," the authors stated. Although this turned out to be true for MRSA bacteremia, it was not the case for MSSA bacteremia, they added. Given that MRSA infections were rare both prior to surveillance onset and early on in the study, it is especially noteworthy that MRSA infections were responsible for one in five incident *S. aureus* bacteremias in 2005 to 2006. The authors concluded that this latter finding clearly has "important implications for empirical antimicrobial therapy for patients with suspected *S. aureus* infections."

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Prevalence of CA-MRSA increasing in Canada

Barton et al. Guidelines for the prevention and management of community-associated methicillin-resistant Staphylococcus aureus*: A perspective for Canadian health care practitioners.* Can J Infect Dis Med Microbiol *2006;17:(Suppl C:)4C-24C.*

Front-line physicians need to be aware that the prevalence of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections is increasing in Canada, as is their potential to cause severe skin and soft tissue infections.

Such was the prevailing sentiment to emerge from guidelines published in 2006 for Canadian healthcare practitioners under co-authors Drs. Michelle Barton and Michael Hawkes, University of Toronto, Ontario. The authors were reporting on behalf of the Writing Group of the Expert Panel of Canadian Infectious Disease, Infection Prevention and Control and Public Health Specialists. As they pointed out, the current prevalence of CA-MRSA in Canada is unknown but thought to be low, based on the collective clinical experience of infectious disease experts across the country. "However," they added, "as the prevalence of CA-MRSA increases, clinicians may need to change their approach to the management of presumed *S. aureus* infections."

Furthermore, they warned, vigilance and determined control efforts are needed if Canada is to limit the emergence of CA-MRSA in its communities; such an outbreak occurred in 2004 in the Calgary Health Region. As later reported by Gilbert et al. (*CMAJ* 2006;175(2):149-54), the cause of the outbreak was determined to be the USA300 strain of CA-MRSA—the first reported Canadian outbreak caused by this particular strain—that was disseminated into a marginalized population in the Calgary Health Region, notably among people with a history of illicit drug use, the homeless and those who had been recently incarcerated.

This outbreak has important public health implications for Canada. As editorialized by Dr. Upton Allen, also of the University of Toronto, in the same issue of the *CMAJ*, those at highest risk for CA-MRSA could act as vectors and readily spread the infection to other urban areas including healthcare facilities, prisons and shelters. How best to prevent the spread of MRSA in the community setting has yet to be established.

In a later commentary, Dr. Hawkes (*CMAJ* 2007; 176(1):54-6) reminded physicians that the "five Cs" involved in CA-MRSA transmission include:

- crowding
- frequent skin contact
- compromised skin
- sharing contaminated personal care items
- lack of cleanliness.

Thus, a pivotal strategy to prevent the spread of CA-MRSA in the community is good hygiene, consistent hand washing, covering any draining skin lesions and not sharing potentially contaminated personal articles. "Physicians have a role to play in preventing the spread of CA-MRSA as well," Dr. Hawkes added, "by educating their patients… notifying public health authorities in the case of a suspected outbreak and by restricting the unnecessary use of antibiotics because this drives the selection of antibiotic-resistant organisms."

Physicians may consult the guidelines for more complete information on the epidemiology, treatment and prevention of CA-MRSA in Canada.

Canadian infection control programs continue to fall short of expert recommendations

Zoutman D, Ford BD. A comparison of infection control program resources, activities, and antibiotic resistant organism rates in Canadian acute care hospitals in 1999 and 2005: Pre-and post-severe acute respiratory syndrome. Am J Infect Control *2008;36(10):711-7.*

Canadian infection control programs continue to fall short of expert recommendations even after critical outbreaks such as the severe acute respiratory syndrome (SARS) crisis, according to a Canadian report. Meanwhile, nosocomial rates of antibiotic-resistant "superbugs" including MRSA have increased dramatically since 1999, when the survey was first initiated.

Drs. Dick Zoutman and Douglas Ford, Department of Pathology and Molecular Medicine, Queen's University, Kingston, Ontario, and Infection Control Service, Kingston General Hospital, examined the extent to which infection control program resources and activities had improved between 1999, when the Resources for Infection Control in Hospitals (RICH) first surveyed the state of infection control programs in Canadian acute care hospitals, and again in 2005. They simultaneously examined whether rates of various antibiotic-resistant organisms had changed over the same time interval. "In March of 2006, all acute care hospitals in Canada with 80 or more beds were mailed a bilingual cover letter and the 2005 version of the RICH survey regarding the state of infection control in their facility," the authors indicated.

Approximately 60% of the hospitals responded, representing 140 out of 233 eligible facilities. Results showed that the mean MRSA rate had increased to 5.2 per 1000 admissions in 2005 from a mean of 2.0 per 1000 admissions in 1999—more than double the rate over the six-year interval. "Hospitals reporting new nosocomial vancomycin-resistant *Enterococcus* [VRE] cases increased 77% over the same period," the authors added, while rates of *Clostridium difficile*-associated diarrhea (CDAD) trended upwards to a mean of 4.7 per 1000 hospital admissions in 2005 from a mean of 3.8 per 1000 admissions in 1999. Sixty-one per cent of the surveyed hospitals also reported having new nosocomial VRE cases in 2005 compared with 34.5% in 1999.

Interestingly, the proportion of hospitals in Quebec reporting new nosocomial VRE cases increased the most: in 2005, over 72% of Quebec hospitals had new cases of nosocomial VRE vs. 21.1% in 1999. Actual mean VRE rates across Canada were 1.0 per 1000 admissions in

2005 compared with 0.4 per 1000 admissions in 1999. Infection control professionals or full-time equivalents also increased to a mean of 0.8 per 100 beds in 2005 from a mean of 0.5 per 100 beds in 1999.

Paradoxically, the proportion of infection control professionals in hospitals approved by the Certification Board of Infection Control decreased over the two survey points to 38% in 2005 from 53% in 1999. As the authors pointed out, both the SARS outbreak in 2003 in Toronto and the CDAD outbreak in several cities in Quebec between 2002 and 2004 brought hospital infection prevention and control programs under very high public scrutiny. Because of these two events, the SARS Commission in Ontario and the National Advisory Committee on SARS and Public Health, among others, placed considerable emphasis on resources being funnelled into infection prevention and control programs in Canadian hospitals, they added.

"Despite these crises-motivated influxes of resources, Canadian infection control programs in 2005 continue to fall short of expert recommendations with respect to the intensity of surveillance and control activities and infection control program human resources," the authors concluded. Taking into consideration the emergence of hypervirulent *C. difficile* strains, the predicted influenza pandemic and increasing rates of both MRSA and VRE, "there continues to be great need for ongoing investment in infection control programs," they added.

Identifying patients at high risk for MRSA carriage on hospital admission

Evans et al. Rapid identification of hospitalized patients at high risk for MRSA carriage. J Am Med Inform Assoc *2008;15(4):506-12.*

An alternative method to rapidly identify patients at high risk for MRSA carriage on hospital admission has been validated by a multicentre study under American investigators.

Recommendations from the Society for Healthcare Epidemiology of America advise hospitals to obtain surveillance cultures for MRSA on all patients on hospital admission. As an alternative approach, Scott Evans, PhD, LDS Hospital, Intermountain Healthcare, Salt Lake City, Utah, and multicentre colleagues tested a computer-based alerting system developed to facilitate rapid, targeted surveillance of adult inpatients for MRSA carriage at admission and during hospitalization. "We automated an MRSA risk stratification algorithm and computer-based alerting system to notify nurses and infection control practitioners when high-risk patients needed to be tested for MRSA carriage," the authors explained.

The alert served as a standing order to obtain a nasal swab for rapid polymerase chain reaction (PCR) testing to document MRSA carriage status. During the evaluation period, 31 out of 153 (20.3%) patients identified by computer criteria to be at high risk for MRSA carriage had positive PCR tests compared to only 12 out of 293 patients (4.1%) identified by computer criteria to be low-risk patients. "Overall, 20% of patients were classified as high risk at the time of admission," investigators reported.

Among the newly admitted patients, the sensitivity of the high-risk alerts was 55.9%, its specificity was 82.4%, the positive predictive value was 20.3% and the negative predictive value was 95.9%. No single risk factor could identify all the patients with MRSA carriage, investigators observed, but the criterion with the highest positive predictive value was previous MRSA colonization or infection. The average total time to identify MRSA carriage was 19.2 hours, "soon enough to help reduce potential self-infection to MRSA or transmission to other patients," the authors stated.

A cost-effective alternative to vancomycin for cSSTI due to suspected MRSA

Schurmann et al. Cost-effectiveness of linezolid versus vancomycin for hospitalized patients with complicated skin and soft-tissue infections in Germany. Eur J Health Econ *2009;10:65-79.*

As demonstrated in a German hospital setting, results generated from an economic model indicate that linezolid is a cost-effective alternative to vancomycin for the empirical treatment of patients with complicated skin and soft-tissue infection (cSSTI) due to suspected MRSA.

Dr. Dirk Schurmann, Department of Internal Medicine/Infectious Diseases and Pulmonary Medicine, Charité Medical University, Berlin, and multicentre colleagues estimated the cost of empirically treating cSSTI with linezolid vs. vancomycin in hospitalized patients in Germany. Costs were observed from both a hospital and healthcare system perspective. "From the hospital perspective, empirical treatment with linezolid was estimated to be €1326 less costly than empirical treatment with vancomycin," the authors stated, at €6714 for linezolid vs. €8040 for vancomycin. Empiric treatment with linezolid was also €973 less costly from the healthcare system perspective, which includes post-discharge costs—specifically, €8232 for linezolid vs. €9206 for vancomycin. Differences in the cost of the two strategies were largely due to shorter hospital stays for linezolid-treated patients. The total estimated length of hospital stay for successful first-line treatment for linezolid was 10.5 days compared with 15.9 days for vancomycin, a difference of 4.5 days, investigators observed.

Cure rates were similar between the two groups. Overall, 98.4% of patients who started on linezolid were cured vs. 98.1% of those who were started on vancomycin. However, when only cure rates due to first-line therapy were considered, 90.1% of patients beginning treatment with linezolid were cured compared with 85.5% of patients who began treatment with vancomycin. Of those patients who failed first-line treatment with linezolid, 84% were cured

on second-line therapy (the equivalent of 8.4% of patients starting treatment on linezolid) compared with 87% of patients who failed treatment on vancomycin being cured on second-line linezolid treatment (the equivalent of 12.6% of all patients starting treatment on vancomycin).

"The results of the model indicate that empirical treatment with linezolid was associated with a higher estimated percentage of patients cured [both over two lines of treatment and at the conclusion of first-line treatment] and a lower average cost when compared with empirical treatment beginning with vancomycin," the authors concluded.

High failure rates in MSRA infections following recommended treatment course

Dombrowski J, Winston L. Clinical failures of appropriately-treated methicillin-resistant Staphylococcus aureus *infections.* J Infect *2008;57(2):110-5.*

Based on results of a single-centre study, researchers have observed a high rate of treatment failure in an urban patient population with MRSA infections despite the cohort having completed a recommended course of therapy, largely with vancomycin monotherapy.

Drs. Julia Dombrowski and Lisa Winston, University of California, San Francisco, studied the epidemiology of clinical failures among patients with MRSA infections who completed appropriate antibiotic therapy at the San Francisco General Hospital over a seven-year period. "Appropriate treatment was defined as intravenous treatment with an antibiotic to which the infecting bacterial strain was susceptible for at least one week in pneumonia, two weeks in bloodstream infections, four weeks in endocarditis, epidural abscess and joint infection and six weeks in osteomyelitis," the authors noted.

Some 214 cases were included in the final analysis. Vancomycin was used as monotherapy in 73% of the infections and in combination with another antibiotic (most commonly rifampin or gentamicin) in the rest. Failures were defined as those patients who had culture, radiographic or clinical evidence of infection within 60 days of completion of antibiotic therapy. Patients who were treated again for an MRSA infection at the same site as the original infection, endocarditis being the one exception, were also considered to be unsuccessful.

The overall failure rate was 25%. By infection site, failure in cases of osteomyelitis was particularly common at 46%. Failure rates were also high among those with epidural abscess at 28%, surgical wounds at 27% and pneumonia at 18%. Sixteen per cent of endocarditis infections also resulted in failure as did 12% of bloodstream infections and 4% of joint infections.

The hospital's recommendations for antibiotic treatment of MRSA osteomyelitis have now been changed so that parenteral vancomycin/rifampin, vancomycin/clindamycin or oral linezolid are now recommended for six weeks, followed by two to three months of consolidation therapy with rifampin/levofloxacin, clindamycin, trimethoprim-sulfamethoxazole or doxycycline, however, if linezolid was used initially, this course of treatment was continued. ❑

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