Management of Methicillin-Resistant Staphylococcus aureus Colonization in Children Undergoing Open Airway Surgery

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Introduction

The overuse of antibiotics has been a major contributing factor in the development of resistant strains of bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA).[1] These resistant bacterial strains have lead to increased healthcare costs and contribute to morbidity and mortality in the general population as well as in hospital-based populations. This phenomenon is well documented and accepted in the international medical community. Numerous epidemiologic studies conducted over the past decade indicate an increasing incidence of MRSA colonization and infection.[2-8] The peer-reviewed literature reflects general consensus that this increase is associated with a concomitant increase in morbidity and mortality rates in both the general population and in hospital-based populations. Increased patient morbidity and mortality rates have in turn led to increased healthcare costs. Specifically, a study conducted by Anderson et al on MRSA surgical site infections estimates that the associated additional per patient cost of hospitalization at approximately 62,000 US dollars.[10] As reported by Song et al, some strains of MRSA were associated with a 40% increase in mortality risk in neonatal intensive care units (NICUs).[9] Furthermore, neonatal MRSA infection was independently associated with a 40-day increase in NICU stay.[9]

In view of such findings, an advisory statement issued by the National Surgical Infection Prevention Project in 2005 recommended that all patients with known MRSA colonization receive prophylactic treatment with vancomycin.[11] A recent randomized, double-blind, placebo-controlled multi-center trial of pre-operative nasal screening for *Staphylococcus aureus* and treatment in adult patients undergoing surgical procedures found the number of acquired nosocomial infections can be significantly reduced by screening and treating nasal carriers of *S. aureus*. [17] In the field of otolaryngology, Polubothu et al advised that an antibiotic prophylactic protocol for airway reconstruction should include intraoperative as well as postoperative antibiotic therapy, and should be carried out on all patients known to be colonized with MRSA.[12]

Risk factors for MRSA colonization or infection are still being elucidated in children. A recent prospective study of children with community-acquired MRSA infection failed to establish links among risk factors, demographics,

underlying medical conditions, or prior antibiotic exposure with risk of acquiring community-acquired MRSA.[14] Other studies in adults have identified risk factors for community-acquired MRSA, which include immunocompromised disease states, long-term antibiotic use, and patients living in communal housing.[1,15] And though MRSA has historically been considered a nosocomial infection present in high-risk populations, recent studies of community-acquired MRSA in pediatric neck abscesses report an increasing incidence ranging from 21.6 to 40%.[2,7,8] In addition, pediatric patients referred for open airway surgery, by in large, are a group at high-risk for MRSA-colonization. Many of these patients have complicated medical histories and have had multiple hospital admissions, a history of prior operative procedures, and have been exposed to multiple systemic antibiotics.

In our experience at Cincinnati Children's Hospital Medical Center, MRSA infection in open airway procedures can be a devastating complication, resulting in dehiscence, graft loss, and weakening of the cartilaginous structure of the laryngotracheal complex. Given our high index of suspicion for MRSA in patients undergoing open airway surgery, our group developed and instituted a screening and treatment antibiotic protocol. We recently reviewed the results of this protocol for a group of patients undergoing open airway surgery between 2007 and 2009.

MRSA Screening Protocol

A MRSA screening and treatment protocol was developed and implemented by the otolaryngology service in consultation with the director of infectious diseases at our institution. All pediatric candidates for open airway procedures underwent initial MRSA screening according to the protocol. MRSA surveillance cultures were obtained on initial airway evaluation in patients deemed appropriate candidates for open airway procedures. The nares, perianal/perirectal area, axilla, gastrostomy tube site (if present), and tracheotomy tube aspirate (if present) were all cultured for MRSA.

MRSA Treatment protocol

Patients with known MRSA-colonization or with a history of MRSA infection without evidence of negative culture status were considered to be colonized and were treated with our protocol.

Preoperatively MRSA colonized patients were treated with double-strength trimethoprim/sulfamethoxazole (DSTS) at 6–12 mg/kg, divided twice daily, for 72 hours prior to surgery. Patients with positive nasal cultures also received intranasal mupirocin twice daily for 72 hours before surgery. Perioperatively intravenous vancomycin admistered approximately one hour prior to skin incision and then every 6–8 hours until the surgical site drains were removed. Patients with an allergy to vancomycin and or sulfa drugs received clindamycin as an alternative. Postoperatively MRSA colonized patients received oral DSTS or clindamycin for a total of 14 days. Otherwise, culture-directed antibiotics were administered instead of vancomycin if sensitivities were obtained respiratory aspirates.

Patients who tested MRSA-negative and those for whom a second culture prior to surgery was unavailable received intravenous cefazolin to address potential infection with skin flora.

Postoperative protocol

Patients who tested positive for MRSA were treated for 14 days postoperatively with the same antibiotic regimen that was used preoperatively.

Criteria for transition from MRSA-positive to MRSA-negative

For MRSA-positive patients to be considered MRSA negative, three negative cultures were required. In addition, patients had to remain off systemic antibiotics for two weeks preoperatively prior to being cultured again.

Pediatric Study Population

One hundred eighty patients underwent 201 open airway operations, however only 197 operations were included in the protocol. There were no significant differences between MRSA-positive patients and MRSA-negative patients with regard to age at surgery, gender, gestational age at birth, or co-morbidities. Additionally, there were no significant differences between these two groups with regard to the percentage of patients who underwent two-stage vs single-stage procedures or the percentage of those with a history of tracheotomy placement.

Colonization and MRSA Prevalence

As anticipated, the prevalence of MRSA was high (31.5%). This result is considerably higher than prevalence reports recently reported in patients undergoing surgery.[6, 13] The high MRSA prevalence is attributed largely to the characteristics of the study population. Specifically, 62% of the children were premature, 87.8% had been tracheotomized, and many had serious co-morbidities such as pulmonary, gastrointestinal, and cardiac disease. These factors can be considered proxies for frequent hospitalization and exposure to antibiotics. This is consistent with reports that ORSA colonization may be greater in patients who have previously spent more than five days in an institutional setting and have had frequent exposure to antibiotics.[4, 14, 15]

MRSA treatment and postoperative infection

Postoperative infection was defined as any infection documented and treated during the postoperative period. Infections were categorized as: MRSA vs non-MRSA, deep wound (neck abscess), graft failure associated with infection, ventilator-associated pneumonia, urinary tract infection, and parotitis.

Corroborating findings in previous studies,[16, 17] we found that treatment of MRSA-positive patients per our protocol resulted in rates (16.4%) of postoperative infections that were similar to those found in MRSA-negative patients (17.2%), p=0.79. No statistically significant difference was noted for any MRSA infections, deep wound infections, or graft failures when comparing MRSA-negative and MRSA-positive patients treated per protocol. There were three cases of postoperative MRSA infection which occurred in patients who were previously MRSA negative, indicating that MRSA was acquired during hospitalization. None of the MRSA-positive patients developed a MRSA-associated infection postoperatively. Two laryngotracheal reconstruction cartilage graft failures and one anastomotic dehiscence occurred in non-MRSA patients. None of these events occurred in MRSA-positive patients. The occurrence of graft loss and anastomotic dehiscence suggests that despite a screening and treatment protocol, there is still an inherent risk of acquiring postoperative infections.

Conclusion

Our findings strongly suggest that screening and treatment of pediatric MRSA-colonized patients undergoing airway surgery decreases MRSA-associated infections. In view of these results, we strongly advise instituting screening and treatment protocols for MRSA for children undergoing open airway surgery.

References

1. Grundmann H, Aires-de-Sousa M, Boyce J, Tiemersma E. Emergence and resurgence of meticillin-resistant *Staphylococcus aureus* as a public-health threat. Lancet. Sep 2 2006;368(9538):874-885.
2. Inman JC, Rowe M, Ghostine M, Fleck T. Pediatric neck abscesses: changing organisms and empiric therapies. Laryngoscope. Dec 2008;118(12):2111-2114.
3. Kaoutar B, Joly C, L'Heriteau F, et al. Nosocomial infections and hospital mortality: a multicentre epidemiology study. J Hosp Infect. Dec 2004;58(4):268-275.
4. Kuehnert MJ, Hill HA, Kupronis BA, Tokars JI, Solomon SL, Jernigan DB. Methicillin-resistant-*Staphylococcus aureus* hospitalizations, United States. Emerg Infect Dis. Jun 2005;11(6):868-872.
5. Kuehnert MJ, Kruszon-Moran D, Hill HA, et al. Prevalence of *Staphylococcus aureus* nasal colonization in the United States, 2001-2002. J Infect Dis. Jan 15 2006;193(2):172-179.
6. Merrer J, Pisica-Donose G, Leneveu M, Pauthier F. Prevalence of methicillin-resistant *Staphylococcus aureus* nasal carriage among patients with femoral neck fractures: implication for antibiotic prophylaxis. Infect Control Hosp Epidemiol. Jun 2004;25(6):515-517.
7. Naseri I, Jerris RC, Sobol SE. Nationwide trends in pediatric *Staphylococcus aureus* head and neck infections. Arch Otolaryngol Head Neck Surg. Jan 2009;135(1):14-16.
8. Thomason TS, Brenski A, McClay J, Ehmer D. The rising incidence of methicillin-resistant *Staphylococcus aureus* in pediatric neck abscesses. Otolaryngol Head Neck Surg. Sep 2007;137(3):459-464.
9. Song X, Perencevich E, Campos J, Short BL, Singh N. Clinical and economic impact of methicillin-resistant *Staphylococcus aureus* colonization or infection on neonates in intensive care units. Infect Control Hosp Epidemiol. Feb 2010;31(2):177-182.
10. Anderson DJ. Prevention of surgical-site infections. N Engl J Med. Apr 22 2010;362(16):1540; author reply 1542-1543.

11. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Am J Infect Control. Apr 1999;27(2):97-132; quiz 133-134; discussion 196.
12. Polubothu S, Harrison S, Clement A, Kubba H. An audit of prophylactic antibiotic use in laryngeal reconstruction surgery. Int J Pediatr Otorhinolaryngol. Aug 2009;73(8):1157-1159.
13. Murthy A, De Angelis G, Pittet D, Schrenzel J, Uckay I, Harbarth S. Cost-Effectiveness of Universal MRSA Screening on Admission to Surgery. Clin Microbiol Infect. Mar 20 2010.
14. Sattler CA, Mason EO, Jr., Kaplan SL. Prospective comparison of risk factors and demographic and clinical characteristics of community-acquired, methicillin-resistant versus methicillin-susceptible *Staphylococcus aureus* infection in children. Pediatr Infect Dis J. Oct 2002;21(10):910-917.
15. Drinka PJ, Stemper ME, Gauerke CD, Miller JE, Goodman BM, Reed KD. Clustering of multiple endemic strains of methicillin-resistant *Staphylococcus aureus* in a nursing home: an 8-year study. Infect Control Hosp Epidemiol. Feb 2005;26(2):215-218.
16. Merrer J, Desbouchages L, Serazin V, Razafimamonjy J, Pauthier F, Leneveu M. Comparison of routine prophylaxis with vancomycin or cefazolin for femoral neck fracture surgery: microbiological and clinical outcomes. Infect Control Hosp Epidemiol. Dec 2006;27(12):1366-1371.
17. Bode LG, Kluytmans JA, Wertheim HF, et al. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. N Engl J Med. Jan 7 2010;362(1):9-17.
18. Statham, MM, Rutter MJ, Germann JN, Tabangin ME, Cohen AP, deAlarcon A, Screening and Treatment of Methicillin-Resistant *Staphylococcus aureus* in Children Undergoing Open Airway Surgery. Unpublished data.