Commentary

Can mupirocin prevent methicillin-resistant *Staphylococcus aureus* infections?

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See related research by Muller *et al.* in this issue [http://ccforum.com/content/9/3/R246]

Abstract

In a retrospective study, Dr Muller and colleagues have assessed the efficacy of mupirocin nasal ointment alongside hygienic measures in methicillin-resistant *Staphylococcus aureus* (MRSA)-positive patients admitted to the intensive care unit (ICU). Their findings, which suggest that intranasal mupirocin can prevent ICU-related MRSA infections, need confirmation in a well-designed clinical trial. In general: early identification, isolation and treatment of all MRSA carriers, including health care workers, and disinfection of contaminated environments, are the main 'ingredients' of an effective MRSA 'search and destroy' program.

In this issue of *Critical Care*, AA Muller and colleagues present a study in which they assessed the efficacy of mupirocin nasal ointment in preventing methicillin-resistant *Staphylococcus aureus* (MRSA) infections in an intensive care unit (ICU) [1]. MRSA constitutes a special problem with regard to the prevention and treatment of infection. Studies show that MRSA carriers have a higher risk of nosocomial infection with this microorganism, and that those infected with MRSA have a greater morbidity and mortality than those infected with susceptible strains [2,3]. It is therefore important to keep the prevalence of MRSA carriage and MRSA infections low. Efforts to achieve this should be supported.

Muller and colleagues performed a retrospective study in which they compared a 2-year MRSA control program with intranasal application of mupirocin, with a 2-year program in which mupirocin was not used. The MRSA control program consisted of screening for MRSA carriage at admission, and, in the event of MRSA carriage, hygienic measures to prevent cross-transmission were intensified. This study is clinically relevant, but the study design used is very susceptible to many biases and their results should therefore be interpreted with caution. Their findings, which suggest that intranasal mupirocin can prevent ICU-related MRSA infections, need confirmation in a well-designed clinical trial.

Results from recent clinical trials that studied the efficacy of mupirocin nasal ointment in preventing methicillin-susceptible *S. aureus* (MSSA) infections can be extrapolated to MRSA infections. MSSA and MRSA are essentially the same microorganism, except that the latter is more difficult to treat with antibiotics. Several double-blind randomized placebo-controlled trials with mupirocin nasal ointment have been performed in both surgical and non-surgical patients, with *S. aureus* infection as the outcome measurement [4-7]. The results of these trials have been disappointing. So far, there is only evidence that mupirocin is beneficial for dialysis patients and general surgery patients [4,7]. But can mupirocin nasal ointment prevent MRSA infections in ICUs?

In comparison with non-ICU patients, critically ill patients admitted to ICUs may receive more benefit from mupirocin, even when moderately efficacious, because the rate of *S. aureus* infections in ICU patients is much higher. Corbella and colleagues reported a relative risk of acquiring nosocomial *S. aureus* bacteremia of 59.6 (95% confidence interval 20.4 to 184.3) for nasal carriers after 14 days of ICU stay, compared with non-carriers [8]. Another study found a relative risk for *S. aureus* bacteremia of 3.9 (95% confidence interval 1.6 to 9.8) for MRSA carriers compared with MSSA carriers [2]. These risk estimates in ICUs are significantly higher than a recently reported threefold increased risk for *S. aureus* nasal carriers of acquiring nosocomial *S. aureus* bacteremia in a general hospital population [9]. Although the clinical trials described above may not be extrapolated to a high-risk setting, they do warn us not to have too high expectations of this drug.

ICU = intensive care unit; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *Staphylococcus aureus*.

Muller and colleagues also report the use of other preventive measures in the event of MRSA carriage. The extra hygienic precautions they implemented for this should, in our view, be standard care for any patient admitted to an ICU, irrespective of MRSA carriage. Currently there is a debate about whether infection control policies in an ICU can prevent cross-transmission of MRSA [10,11]. However, history teaches us that MRSA prevalence is still low in countries where strict infection control policies were implemented soon after the first MRSA strains were detected [12]. These policies also include health care workers and the environment, besides patients, as potential reservoirs of MRSA. Early identification, isolation and treatment of all MRSA carriers, including health care workers, and disinfection of contaminated environments are the main 'ingredients' of an effective 'search and destroy' program. The current study focuses only on the eradication of MRSA from colonized patients, which is just one part of an effective MRSA control program.

Since 2002, the first three vancomycin-resistant MRSA strains have been isolated in the USA [13-15]. Preventing the spread of MRSA and preventing staphylococcal infections are therefore essential. The high usage of vancomycin in ICUs should alert us to the possibility of vancomycin-resistant strains. Effective strategies that can prevent the spread of MRSA and the development of MRSA infections still need to be developed. The use of mupirocin nasal ointment alone will not be sufficient. Increased usage of mupirocin in an MRSA endemic situation, such as ICUs, will lead to the selection of mupirocin-resistant strains [16]. This may hamper the beneficial effects of mupirocin in other patient categories in the long term. There is no evidence yet that mupirocin is effective in preventing MRSA or MSSA infections in ICUs. An international MRSA prevention task force should be set up, with sufficient funding and expertise to develop the right strategies and validate these strategies in clinical trials. We still have a long way to go.

Competing interests

The author(s) declare that they have no competing interests.

References

1. Muller AA, Talon D, Potier A, Belle A, Cappelier G, Bertrand X: **Use of intranasal mupirocin to prevent MRSA infection in intensive care units.** *Crit Care* 2005, **9:**R246-R250.
2. Pujol M, Pena C, Pallares R, Ariza J, Ayats J, Dominguez MA, Gudiol F: **Nosocomial *Staphylococcus aureus* bacteremia among nasal carriers of methicillin-resistant and methicillin-susceptible strains.** *Am J Med* 1996, **100:**509-516.
3. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y: **Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis.** *Clin Infect Dis* 2003, **36:**53-59.
4. Perl TM, Cullen JJ, Wenzel RP, Zimmerman MB, Pfaller MA, Sheppard D, Twombley J, French PP, Herwaldt LA: **Intranasal mupirocin to prevent postoperative *Staphylococcus aureus* infections.** *N Engl J Med* 2002, **346:**1871-1877.
5. Kalmeijer MD, Coertjens H, Van Nieuwland-Bollen PM, Bogaers-Hofman D, De Baere GA, Stuurman A, Van Belkum A, Kluytmans JA: **Surgical site infections in orthopedic surgery: the effect of mupirocin nasal ointment in a double-blind, randomized, placebo-controlled study.** *Clin Infect Dis* 2002, **35:**353-358.
6. Wertheim HF, Vos MC, Ott A, Voss A, Kluytmans JA, Vandenbroucke-Grauls CM, Meester MH, van Keulen PH, Verbrugh HA: **Mupirocin prophylaxis against nosocomial *Staphylococcus aureus* infections in nonsurgical patients: a randomized study.** *Ann Intern Med* 2004, **140:**419-425.
7. Boelaert JR, De Smedt RA, De Baere YA, Godard CA, Matthys EG, Schurgers ML, Daneels RF, Gordts BZ, Van Landuyt HW: **The influence of calcium mupirocin nasal ointment on the incidence of *Staphylococcus aureus* infections in haemodialysis patients.** *Nephrol Dial Transplant* 1989, **4:**278-281.
8. Corbella X, Dominguez MA, Pujol M, Ayats J, Sendra M, Pallares R, Ariza J, Gudiol F: ***Staphylococcus aureus* nasal carriage as a marker for subsequent staphylococcal infections in intensive care unit patients.** *Eur J Clin Microbiol Infect Dis* 1997, **16:**351-357.
9. Wertheim HF, Vos MC, Ott A, van Belkum A, Voss A, Kluytmans JA, van Keulen PH, Vandenbroucke-Grauls CM, Meester MH, Verbrugh HA: **Risk and outcome of nosocomial *Staphylococcus aureus* bacteraemia in nasal carriers versus non-carriers.** *Lancet* 2004, **364:**703-705.
10. Nijssen S, Bonten MJ, Weinstein RA: **Are active microbiological surveillance and subsequent isolation needed to prevent the spread of methicillin-resistant *Staphylococcus aureus*?** *Clin Infect Dis* 2005, **40:**405-409.
11. Cepeda JA, Whitehouse T, Cooper B, Hails J, Jones K, Kwaku F, Taylor L, Hayman S, Cookson B, Shaw S, *et al.*: **Isolation of patients in single rooms or cohorts to reduce spread of MRSA in intensive-care units: prospective two-centre study.** *Lancet* 2005, **365:**295-304.
12. Voss A: **Preventing the spread of MRSA.** *BMJ* 2004, **329:**521.
13. Miller D, Urdaneta V, Weltman A: **Public Health Dispatch: vancomycin-resistant *Staphylococcus aureus* – Pennsylvania, 2002.** *MMWR* 2002, **51:**902.
14. Chang S, Sievert DM, Hageman JC, Boulton ML, Tenover FC, Downes FP, Shah S, Rudrik JT, Pupp GR, Brown WJ, *et al.*: **Infection with vancomycin-resistant *Staphylococcus aureus* containing the vanA resistance gene.** *N Engl J Med* 2003, **348:**1342-1347.
15. Kacica M, McDonald LC: **Brief report: vancomycin-resistant *Staphylococcus aureus* – New York, 2004.** *MMWR* 2004, **53:**322-323.
16. Cookson BD: **The emergence of mupirocin resistance: a challenge to infection control and antibiotic prescribing practice.** *J Antimicrob Chemother* 1998, **41:**11-18.