National Essential Medicine List Adult Hospital Level
Medication Review Process
Component: ENT

Date: June 2015

Medication: Mupirocin, topical nasal

Indication: Reduction in the rate of nosocomial *S. aureus* infections.

Executive summary:

Staphylococcus aureus (*S. aureus*) is the leading organism to cause nosocomial infections. Nasal carriage of *S. aureus* is a risk factor for infection in hospitalized patients. Nasal mupirocin reduces the infection rate in surgical, non-surgical and dialysis patients. However, the effect is diminished when looking at surgical site infections (SSIs) only. Identification of nasal carriers and determining the risk for infection remains a challenge.

Introduction:

The reviewer of the Ear, Nose and Throat (ENT) chapter was requested to evaluate the evidence for the use of nasal mupirocin. Currently nasal mupirocin is not one of the agents listed on the Essential Medicines List (EML). However, it has been used by various institutions around the country. The 2013-2014 National ABC analysis (excluding Mpumalanga) showed that 11595 units were consumed at a value of R239466.

The clinical question was developed by using PICO (**P**roblem, **I**ntervention, **C**omparison and **O**utcome).

P	Adults attending hospital, high risk groups (e.g. diabetes, renal dialysis), *S. aureus* nasal carriers
I	Mupirocin nasal
C	No treatment or placebo or alternative nasal treatment
O	Prevention of infection, reduced hospital stay, need for re-treatment, mortality, harm (e.g. increased resistance)

The question lends itself to best be answered by randomized-controlled trials (RCTs) or controlled clinical trials.

Search strategy:

In the initial scoping for this review the Cochrane Library was searched for relevant reports.
The following broad search strategy was used to search the Cochrane Library:

#1 mupirocin
#2 staph aureus*
#3 (#1 AND #2)

The TRIP Database was also searched using the following relevant terms into the PICO section of the database: mupirocin AND staphylococcus aureus and the following results were obtained (11 results of which 6 were irrelevant):

- Two guidelines
- Two systematic reviews on clinical and cost effectiveness of screening for MRSA
- One primary research trial

Selection of studies:
One Cochrane review was identified which addressed the current question. The Cochrane search was conducted in 2008 and reviewed and assessed as up to date in 2010. As such an additional search for trials, using the same strategy described in the Cochrane review can be used to identify additional trials published since then.

Evidence quality:
Cochrane review: AMSTAR was used to assess the degree to which the review methods avoided bias by evaluating methods reported against 11 distinct criteria. When applied to the review under investigation a score of 10 was obtained. The review is considered to be of good quality. See AMSTAR tool and scoring attached.

Summary:
One review was found that directly addressed the PICO requirements outlined above. It included 9 RCTs involving 3396 participants.[1] The patient population varied and several types of nosocomial *S. aurues* infections were described, e.g. bacteraemia, exit-site infections, peritonitis, respiratory tract infections, skin infections, surgical site infections and urinary tract infections.

The primary outcome of *S. aureus* infection rate was reported in all 9. The secondary outcomes reported varied between the papers. Time to infection was described in one paper. Mortality was described in five papers. Six papers described the adverse events and the infection rate caused by other micro-organisms than *S. aureus* was described in four papers.

Nasal mupirocin reduced the overall *S. aureus* infection rate in nasal carriers. This included surgical, non-surgical and dialysis patients. Pooling of 8 RCTs of low to high quality (n=3374) demonstrated an effect size RR 0.55, 95% CI 0.43 to 0.70; I^2=3%; of these 8 RCTs, the 4 high quality RCTs (n=2909) were analysed and showed a RR 0.69, 95% CI 0.47 to 1.00; I^2=13% when mupirocin topical was compared to control (placebo/no treatment). Although there was a statistically significant reduction in *S. aureus* infection rate, patient populations (surgical, non-surgical, haemodialysis & CAPD patients) and range of types of *S. aureus* infections reported were diverse.

[1] van Rijen M, Bonten M, Wenzel R, Kluytmans J. Mupirocin ointment for preventing Staphylococcus aureus infections in nasal carriers. *Cochrane Database Syst Rev*. 2008 Oct 8;(4):CD006216. Review content assessed as up-to-date: 26 September 2010.

Patients who were proven carriers before surgery had a significant reduction in post-operative *S. aureus* infection when given mupirocin. When the surgical site infections (SSIs) are analysed as primary outcome, instead of all nosocomial infections, no statistically significant effect was found.

No reduction in SSI rate was seen in randomized general surgery trials. In non-general surgery, e.g. cardiothoracic and orthopaedic surgery, randomized trials showed a trend towards the reduction of the SSI incidence. These results indicate that mupirocin is effective in clean high-risk surgical procedures, where the risk of *S. aureus* infection is high. More studies are needed to select the surgical procedures, in which mupirocin is most effective.

Mupirocin reduces the post-operative *S. aureus* infection rate in carriers, but the overall effects in carriers are not clear. It is unclear what effect mupirocin application in nasal *S. aureus* carriers has on the quality of life, length of hospital stay and mortality. It is possible that infections with other microorganisms might have occurred. Short-term use of mupirocin nasal does not carry a high risk for the development of resistance in surgical or dialysis patients.

Recommendation:

It is not recommend using mupirocin nasal in all patients admitted to hospital. The effectiveness of mupirocin is related to carriers only. An important factor to consider is the actual diagnosis of patients who are carriers. A carrier can only be identified once microbiological culture testing was performed, which is often delayed and results are not available prior to surgery. Therefore, if nasal carriage can be determined in a timely manner, then mupirocin is indicated and is likely to reduce the number of *S. aureus* infections.