AN INEXPENSIVE TREATMENT FOR DEEP STERNAL WOUND INFECTION

Fazle Rabbi Imran Adeeb Arain Nadeem A. Fahmi

Mupirocin (Bactroban, GSK) cream is now available in Pakistan. As it is not expensive (Retail price Rs. 140) and it significantly reduce the incidence of sternal wound infection, this review article highlight the importance of applying it intranasally pre and postoperatively.

Sternal wound infections are an infrequent but alarming complication for the cardiac surgeon, and even more so for the patient. About 20% of surgical site infections are caused by *Staphylococcus aureus*.[1] Most *S aureus* infections are due to strains of bacteria that are part of a person's endogenous flora, and not due to exogenously acquired infection.[2] Persons with nasal colonization with *S aureus* (carriers) are at higher risk for subsequent postoperative *S aureus* infections.[3] Nasal and cutaneous carriage of *S aureus* can be eradicated by intranasal application of Mupirocin.[4-6]

Over 45 years ago, William and Weinstein noted the correlation between the presence of nasal carriage of *S aureus* and wound infection after surgery, and recently, Kluytmans reported that nasal carriage of *S aureus* was highly correlated with sternal wound infections.[6-9]

Numerous attempts have been made to eradicate *S aureus* from the nasal carriage with the use of antibiotic ointments, local irrigations and systemic antibiotics. Until the development, however, of a relatively new topical antibiotic, Mupirocin Calcium ointment, these prior treatments were basically ineffective and involved the use of systemic antibiotics to control a topical nasal problem.[9]

There was a well published prospective study by Cimochowski and associates at Wilkes-Barre General Hospital, Pennsylvania. This study was designed to determine whether decreasing nasal bacterial colonization by applying Mupirocin intranasally decreases sternal wound infection.[5]

This study comprises 1,846 patients over a 3-year period. There were two groups of patients. In group 1, the control group, who underwent open heart surgery from Jan 1, 1995 through Oct 31, 1996 was comprised of 992 patients who received no specific prophylaxis other than pre and postoperative intravenous antibiotics (intravenous Cefuroxime 1.5 g. every 12 hours). In group 2, from Dec 1, 1997 through Mar 31, 1999, consisted of 854 patients who received intranasal Mupirocin prophylaxis both preoperatively and postoperatively in addition to the routine intravenous antibiotics. The Mupirocin ointment was applied via a Q-tip swab to each nostril. The first dose was applied the night before surgery, and the second dose was given the morning of surgery. Treatment was continued twice a day for 5 consecutive days postoperatively.

The surgical wound infection rate in the control group was 2.7% (27 of 992) versus 0.9% (8 of 854) in the Mupirocin intervention group ($p = 0.005$) or in other words 66.6& reduction in sternal wound infection rate (2.7& versus 0.9%). When the results were further evaluated the break-down of the deep and the superficial sternal wound infections, there were again a statistically significant difference between the control group and the Mupirocin group, with 1.2% (12 of 992) deep sternal wound infections in the control group versus 0.4% (3 of 854) in the intervention ($p = 0.04$), and finally, 1.5% (15 of 992) superficial wound infections in the control group versus 0.6% (5 of 854) in the intervention group ($p = 0.05$). The results were also analyzed patients with and without diabetes mellitus. Again, there was a significant reduction of sternal wound infection in both groups, with diabetics, patient shaving an overall wound infection rate of 5.1% in the control group compared with 1.9% in the treated group. The incidence of *S aureus* in both the groups was around 20%. Diabetics, however, showed a nasal carriage rate *S aureus* of 33.1%. The increased incidence of *S aureus* in the diabetic group is

* *Address for correspondence:*
Department of Cardiac Surgery
National Institute of Cardiovascular Diseases
Karachi

postulated as a cause for the increase in *S aureus* wound infection in diabetic patients undergoing surgery.

Kluytmans and associates in 1996 published a paper related to the use of intranasal Mupirocin prophylactically to reduce surgical wound infection in cardiac surgery.[9] 928 patients were compared with an intervention group of 752 patients. The surgical site infection was significantly reduced from 7.3% to 2.8%. They did not, however, determine whether the reduction was due to deep sternal infections, superficial wound infections, diabetics, or nondiabetics. Nevertheless, their reduction of surgical site infection from 7.3% to 2.8% (61.1%) was remarkably close to previous study showing 66% reduction.

Mupirocin is produced by a fermentation of pseudomonas bacteria, resulting in a naturally occurring antibiotic that is very active against Staphylococcus, including methicillin resistant strains and streptococcus. According to review by Hudson and associates Mupirocin is structurally unrelated to any other clinically used antibiotic and, in addition, can only be used topically. Intranasal Mupirocin has been reported to be extremely effective in the short-term eradication of *S aureus* persisting up to 1 year. The short-term effectiveness has been reported anywhere from 91% to 100%.[11] Subsequently, there is a regrowth of *S aureus* in the patient's nasal reservoir. However, the time frame reported in the literature is variable, up to 22 weeks in 56% of the patients after a simple short-term course of treatment.[4] Furthermore, its benefit is not only the reduction of nasal *S aureus* reservoirs but also in eliminating positive hand cultures, which has been reported by Reagan and associates.[4] They also noted in their study that 97% of Staphylococcus hand cultures exactly matched the patients current phage type.[4] One possibility of the aetiology of wound points to the patients' own nasal reservoir with subsequent spread to the hands or skin and thus to the wound.[12] No one knows the exact means by which nares *S aureus* is transmitted to the wounds, but it is postulated that one or more of the following explanations are applicatble.[1] The trauma from the endotracheal tube spread *S aureus* from the nose haematogenously to the wound.[2] *S aureus* from the nose is transmitted into the operating air and thus the wound.[3] The *S aureus* from the nose is transmitted to the patient's own skin and is not eradicated completely by the preoperative techniques used to sterilize the operative site.[13]

There was another study by Shrestha and associates at Cleveland Clinic. They conducted a retrospective cohort study examining incidence of postoperative infection in patients undergoing cardiac surgery after introduction of a screening test for nasal *S aureus* carriage, and avoiding Mupirocin treatment of noncarriers. This study was undertaken to evaluate whether avoiding mupirocin in non carriers places them at increased risk for subsequent postoperative infection. It was a retrospective cohort study examining incidence of postoperative infection in patients undergoing cardiac surgery at the Cleveland Clinic after introduction of protocol of polymerase chain reaction screening for nasal *S aureus* carriage and avoiding mupirocin treatment of noncarriers. Between August 2002 and May 2004, 6,334 patients were screened for nasal carriage of *S aureus* before undergoing cardiac surgery. There was no significant difference in infection rates between carriers and noncariers when examining the incidence of all infections (5.6% and 5%), infection caused specifically by *S aureus* (1.04% and 0.80%), any surgical site infection 3.1% and 3.2%), *S aureus* surgical site infection (0.82% and 0.58%), any bloodstream infection 3.1% and 2.5%), and *S aureus* bloodstream infection (0.37% and 0.48%). Mupirocin use declined substantially after introduction of protocol. There conclusion was a strategy of targeting preoperative Mupirocin treatment to carriers leads to significant reduction in Mupirocin use without increasing early postoperative infectious complications in carriers.

There are good reasons to avoid unnecessary Mupirocin use. Although initial studies suggested that long-term use of Mupirocin in patients on peritoneal dialysis did not lead to emergence of Mupirocin resistance, longer term follow-up of the same patients revealed development of resistance.[14-15] At the end of 7 years, 25% of the strains of *S aureus* isolated from these patients were Mupirocin-resistant, the majority (75%) demonstrating high-level resistance.[16] These rates are much higher than in the general population, for whom rates of 2% to 6% have been reported.[17] A Mupirocin-resistance rate of 25% in *S aureus* was also found in another study a median of 15 months after initiating treatment

with Mupirocin in peritoneal dialysis patients.[18] Eradication of colonization has been shown to be far less in patients colonized with Mupirocin-susceptible strains.[19] Patients colonized with Mupirocin-resistant strains had a higher incidence of infectious complications when Mupirocin was used to prevent peritoneal dialysis catheter-associated infections.[18] Extensive use of Mupirocin for nasal decolonization has also been reported to correlate with increasing rates of Mupirocin resistance among methicillin-resistant *S aureus* isolates from 2.7% to 65% over a three year period.[20] Thus, there are compelling reasons to avoid unnecessary use of Mupirocin.

There is huge cost saving by avoiding prolonged intravenous use of antibiotics and surgical procedures for wound debridements. A deep sternal wound carries a cost in US of around $82,000 as compared with the treatment cost of only $12 for intranasal Mupirocin.

In conclusion, the use of intranasal Mupirocin was extremely effective, easy to apply, had no complications, and reduced sternal wound infections in both diabetics and nondiabetic patients. The cost of treatment is minimal but there should be guidelines to avoid resistance to Mupirocin.

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