Enferm Infecc Microbiol Clin. 2020;38(10):463–465

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Editorial

Decolonisation of nasal carriers of *S. aureus* in patients undergoing complex surgeries: from clinical evidence to healthcare practice☆

Descolonización de portadores nasales de *S. aureus*: De la evidencia a la práctica clínica

Healthcare-associated infections (HAIs) continue to be a very serious public health problem. This is because of their incidence, their morbidity and mortality and their high impact on associated costs[1], but they are particularly relevant primarily because many of them are avoidable.

Surgical site infections (SSIs) are the most prevalent of all HAIs and give rise to frequent readmissions with long hospital stays.[2]

The most important risk factors for SSIs are: the expertise of the surgeon, the degree of contamination defined by the type of surgery (clean, clean-contaminated or dirty) and the patient's previous situation in terms of pre-existing concomitant diseases and whether or not they are a carrier of *S. aureus*.[3]

S. aureus is a commensal bacterium of the skin and mucosa that colonises between 16% and 36% of the population.[4] Of these, it is estimated that 60% are persistent carriers and 40% are intermittent carriers.[5] *S. aureus* can colonise different parts of the skin and mucosa, but it is generally accepted that the main reservoir in humans are the nasal passages. Nasal colonisation by *S. aureus* is a well-documented risk factor for SSIs and several published studies have estimated that it can give rise to a twofold to twelvefold increase in the risk of SSIs caused by *S. aureus*, depending on the population and type of surgical procedure.[4,6]

S. aureus is the most common cause of SSIs[2,4] and the second most common pathogen of all HAIs[2]. The vast majority of HAIs caused by *S. aureus* are endogenous and therefore the strains identified in the nasal passages and at the site of surgical infection are usually identical.

In the prevention of nosocomial infections, two different strategies are identified: horizontal and vertical.[7] Horizontal strategies are those applied to the entire population at risk, while vertical strategies are implemented when microbiological studies are able to identify a part of the population that has an increased risk of a particular HAI, and the strategy only targets that part of the population.

Preoperative skin antisepsis with alcoholic chlorhexidine is an example of a horizontal prevention strategy that is applied to the entire population undergoing clean-contaminated or clean surgery, its superiority over povidone-iodine having been demonstrated in a well-designed clinical trial by Darouiche *et al.*[8] In this study, it was observed that chlorhexidine globally reduced the incidence of SSIs in that population by 40%, with this reduction increasing to 50% for infections caused by *S. aureus*.

In 2002, Trish Perl et al. published a clinical trial in the *New England Journal of Medicine* in which nasal carriers of *S. aureus* who were going to undergo elective surgery were first identified and then administered intranasal mupirocin or placebo, while the non-*S. aureus*-carrying population was not administered any treatment. This study, which is an example of a vertical strategy in the prevention of nosocomial infections, failed to demonstrate a reduction in the incidence of SSIs caused by *S. aureus*, but it did show a reduction in the incidence of the other HAIs caused by this microorganism.[9]

In 2010, Bode et al.[10] managed to demonstrate a reduction in SSIs caused by *S. aureus* with a trial that was quite similar to the above study. In this study, nasal carriers were identified by PCR, and instead of being limited to the administration of intranasal mupirocin twice a day, the decolonisation regimen also added a daily bath with chlorhexidine for five days in an attempt to act on other potential colonisation points of the skin. The main objective of the study was to reduce the incidence of all *S. aureus* infections in the population undergoing preventive treatment. The study successfully fulfilled this objective, but it also found the reduction to be even more striking in deep SSIs caused by this bacterium.[10] This study has subsequently been replicated[4,7] and the recommendation for this strategy has been included in most clinical guidelines.[11] In the recent WHO recommendations, identifying *S. aureus* carriers prior to surgery, and then decolonising with mupirocin and chlorhexidine for five days, is presented as a strongly recommended strategy with a moderate level of evidence in cardiothoracic surgery and prosthetic orthopaedic surgery.[11] Since then, this strategy has become the "standard of care" in many cardiac surgery units[7,12–14] and prosthetic orthopaedic surgery units[7,13,14]. For *S. aureus* carriers who are to undergo other types of surgery, the panellists of the latest WHO recommendations make a conditional recommendation with a moderate level of evidence.[11]

In this issue of Enfermedades Infecciosas y Microbiología Clínica [Infectious Diseases and Clinical Microbiology], Bouza and his group[12] present a quasi-experimental study in which they compare identifying *S. aureus* carriers by means of a type of PCR with doing so from a culture in patients who are going to undergo heart surgery. Sampling is performed just before surgery and decolonisation begins with intranasal mupirocin administered immediately

DOI of original article: https://doi.org/10.1016/j.eimc.2020.11.001

☆ Please cite this article as: Gonzalez JL-C, Solchaga VP. Descolonización de portadores nasales de *S. aureus*: De la evidencia a la práctica clínica. 2020;38:463–465.

after the surgery and maintained for five days. It was a real-world study carried out in a single hospital, in which the authors invited all consecutive patients who were to undergo a heart surgery procedure to participate, regardless of whether or not they had undergone prior decolonisation treatment. A total of 200 patients were enrolled. Nasal colonisation was defined as the presence of *S. aureus* in the culture or by PCR positivity. The authors found that 28.5% of patients met this criterion, but 42% of these only met the PCR positivity criterion and had a negative culture. The rest were positive by both culture and PCR.

Of the 33 concordant patients for whom both results were positive, almost 85% had not received any type of decolonisation treatment prior to the study. In the group with positive PCR and negative culture, 29% had received at least one previous round of decolonisation (median of 9 days prior to surgery) but 71% had not received any prior decolonisation treatment.

In their study, the authors found a good correlation between the Ct of the PCR and the number of CFUs in the culture. They also determined that a Ct of 32 has a sensitivity of 99.7% with respect to the positivity of the culture.

All the patients identified as colonised by culture or by PCR underwent decolonisation treatment with mupirocin for five days, starting immediately after surgery. Only three patients (1.5%) with *S. aureus* infections were identified during follow-up (two organ-space SSIs and one ventilator-associated pneumonia). Two of these had received decolonisation treatment after surgery and the other had tested negative in the screening and therefore had not received treatment.

This study reveals some uncertainties and the great difficulties implementing a strategy that has demonstrated significant and objective benefits in the prevention of SSIs caused by *S. aureus*, under the conditions in which these trials were conducted.

First, there is still uncertainty about the best time to take nasal samples prior to surgery. Assuming that the decolonisation treatment should be administered in its entirety before surgery and as close as possible to the date of the procedure, there are real logistical difficulties in being able to carry it out successfully. Pre-operative assessment appointments often take place well in advance of the surgery date, so applying these measures at that time would surely put many patients at risk of colonising again before surgery. On the other hand, surgery schedules are often made insufficiently in advance to allow time to schedule an appointment with the patient, collect samples, wait for the results and perform a five-day mupirocin +/- chlorhexidine treatment. This is probably the reason why a very large proportion of the population analysed had not been screened for colonisation by *S. aureus* and therefore had not received decolonisation treatment before surgery. Moreover, the planned and apparently optimal way to apply this strategy by definition deprives all patients who require emergency surgery of the benefit, which in this study would have been 12.3%. There are some data that suggest immediate postoperative administration may also be beneficial, although it is less quantified, and this is what the authors rely on to implement their strategy.[9]

The second big question posed by this study is which should be the method of choice to identify carriers – PCR or culture. The most robust trial, better targeted and with a greater benefit, was performed with PCR[9], but no cultures were performed. As such, and given the interpretation difficulties that are well described by the authors in their article, it is not known whether those patients with positive PCR and negative culture benefit from this intervention to the same extent. In real life, it must also be borne in mind that the number of patients currently undergoing heart surgery or elective prosthetic orthopaedic surgery in developed countries is extremely high, and will most likely continue to increase in the coming years. In these cases in which there is no urgency to identify and start treatment, the global economic impact of performing the rapid test on all patients must be taken into account, given the possible lower sensitivity of cultures and the logistical difficulties involved in scheduling appointments with patients again and the risk it may entail of depriving those less compliant of the benefits of the measure. This fact is especially relevant as it has been shown that the success of this intervention correlates well with the degree of compliance and with the concentration of mupirocin in nasal secretions.[4] All this suggests that the appointment in which the patient must be informed of their condition as a nasal carrier of *S. aureus*, of the increased risk of SSIs and their serious consequences, and in which they will also have to be instructed on the decolonisation methodology, will be a conscientious and prolonged visit that can hardly be substituted by other non face-to-face ways of giving information. Compliance with the instructions, and ultimately the benefit of the intervention, will largely depend on the effectiveness of this communication process.

Given the logistical difficulty in applying this vertical SSI prevention measure, some authors have postulated turning it into a horizontal strategy and applying it to the entire candidate population for these surgeries in which a greater benefit has been observed. There are some non-comparative data on the degree of acceptance shown by patients in the face of universal decolonisation[15], but there are no studies that demonstrate that this strategy, when implemented in a generalised way, obtains better clinical results than that based on the prior identification of carriers. Generally, the teams that have implemented this type of generalised measure have relied on the organisational difficulty for its implementation, on the fact that induction of resistance to mupirocin and chlorhexidine administered in short periods of time is low[7,16], and on the fact that toxicity to these two active ingredients is uncommon and is usually mild[7]. In any case, for the advocates of this approach it must be remembered that around 80% of the population undergoing surgery would not obtain any benefit from it.

In the pragmatic study by Schweizer et al.[14] in which, in addition to decolonisation, an adaptation of pre-operative antibiotic prophylaxis was administered to patients with methicillin-resistant *S. aureus*, a significant but more modest effect was observed in reducing complex SSIs caused by *S. aureus*. It should be borne in mind that it was a pragmatic study that included patients undergoing emergency surgery who had been excluded from other trials, as was the case in the study by Bouza[12], but in which a reduction in the incidence of SSIs due to *S aureus* associated with the operation performed was not an objective of the study. The study by Schweizer et al.[14] also showed that the degree of compliance with the *bundle* had a clear impact on the final outcomes.

All of the above suggests that, pending new studies to resolve these uncertainties, it would be reasonable for us to adapt our action protocols to our local reality in a possibilist manner. The most efficient way to detect carriers in our setting and for each group of patients must be determined, as must the time of nasal and cutaneous decolonisation. It is also important to determine in which patients a test of cure may be indicated after decolonisation, in order to give them a second chance.

Conflicts of interest

We declare that we have no potential conflicts of interest in relation to this article.

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