International Orthopaedics (SICOT) (2004) 28:16–20
DOI 10.1007/s00264-003-0460-y

ORIGINAL PAPER

J. C. De Lucas-Villarrubia · M. Lopez-Franco
J. J. Granizo · J. C. De Lucas-Garcia
E. Gomez-Barrena

Strategy to control methicillin-resistant *Staphylococcus aureus* post-operative infection in orthopaedic surgery

Accepted: 19 February 2003 / Published online: 15 May 2003

Abstract In the year 2000 the rate of infection after arthroplasty in our hospital was 9.75% and methicillin-resistant *Staphylococcus aureus* (MRSA) was the organism in 33% of the infected joints. In an attempt to overcome this unacceptable situation, we changed our prophylaxis regime over a period of 6 months. This involved modifying the precautionary measures for preventing surgical infections, active prophylaxis against any nasal reservoir of infection in joint implant patients, the control of health care personnel, the strict application of standard and contact precautions in all patients with MRSA, and the use of teicoplanin as prophylaxis during this 6-month period. This resulted in a definite decrease in the incidence of orthopaedic wound infections by MRSA, while the level of MRSA infection elsewhere in the hospital remained constant. Only one infection was detected during this 6-month trial, and this beneficial effect was maintained during the following 6 months. Since then, only sporadic new infections have been detected. Patients with arthroplasties performed during the study were followed for 12 months, and no new cases of MRSA infection were detected.

Résumé Dans l'année 2000 le taux d'infection après arthroplastie dans notre Hôpital fût de 9.75% et le Staphylocoque aureus methicilline – résistant (MRSA) était le germe en cause dans 33% des articulations infectées. Dans le but d'améliorer cette situation inacceptable nous avons changé notre méthode de prophylaxie pendant une période de 6 mois. Cela a impliqué de modifier les mesures pour prévenir les infections chirurgicales : prophylaxie active contre tout réservoir nasal d'infection chez les malades devant avoir un implant; contrôle du personnel de soins; stricte application des règles et des précautions de contact chez tous les malades porteurs de MRSA; usage de teicoplanine comme prophylaxie pendant cette période de 6 mois. Le résultat a été une baisse catégorique de la fréquence des infections opératoires orthopédiques par MRSA, tandis que le niveau d'infection MRSA est resté constant ailleurs dans l'hôpital. Une seule infection a été détectée pendant cet essai de 6 mois, et cet effet salutaire a été maintenu pendant les 6 mois suivants. Depuis lors, seules de nouvelles infections sporadiques ont été détectées. Les malades opérés d'arthroplastie pendant l'étude ont été suivis pendant 12 mois et aucun nouveau cas d'infection MRSA n'a été détecté.

J. C. De Lucas-Villarrubia · M. Lopez-Franco
J. C. De Lucas-Garcia · E. Gomez-Barrena (✉)
Department of Orthopaedic Surgery, Fundacion Jimenez Diaz,
Universidad Autonoma de Madrid,
Avda Reyes Catolicos 2, 28040 Madrid, Spain
e-mail: egomez@fjd.es
Tel.: +34-91-5504827, Fax: +34-91-5494764

J. J. Granizo
Epidemiology Unit, Fundacion Jimenez Diaz,
Universidad Autonoma de Madrid,
Madrid, Spain

Introduction

We report our experience in a situation where there had been a high incidence of post-operative infection with methicillin-resistant *Staphylococcus aureus* (MRSA) after joint replacements, and we report the efficacy of the preventive methods that we implemented.

Materials and methods

During the year 2000, there was an increase in the incidence of post-operative infections in the orthopaedic wards at the University Hospital, and our criteria for defining a surgical site infection followed the 1999 Centers for Disease Control (CDC) Guidelines for the Prevention of Surgical Site Infection [16].

In an 6-month period (January–June 2000), 43 of 721 operated patients developed an infection (rate of infection = 5.9%), and in nine of these, MRSA was found to be the responsible organism. There were 12 infections among the 123 joint replacements (rate of infection = 9.7%) included in the grand total of 721, and in four of these, MRSA was isolated. All the infections were clinically and microbiologically detected before patient discharge and required early surgical debridement. They were thus considered to be "failures" of the prophylactic regime in use with orthopaedic patients at our institution during 2000. This regime consisted of

Table 1 Microbiological data from orthopaedic samples during year 2000

	Wound	Joint arthroplasty	Bone biopsy	Synovial biopsy	Articular fluid	Hemocultures
Total samples	261	32	28	9	58	506
Positive samples (%)	243 (93)	9 (28.1)	8 (28.6)	2 (22.2)	11 (19)	41 (8.1)
Agents						
S. aureus (%)	48 (18.4)	–	1 (3.6)		2 (3.5)	10 (2)
S. coagulase-negative (%)	25 (9.6)	9 (28.1)	4 (14.3)	2 (22.2)	8 (13.8)	18 (3.6)
Gram-negative (%)	61 (23.4)	–	–	–	1 (1.7)	6 (1.2)
Cutaneous flora (%)	18 (6.9)	–	–	–	–	1 (0.2)
Anaerobic (%)	17 (6.5)	–	–	–	–	–
Other (%)	–	–	3 (10.7)	–	–	6 (1.2)

Table 2 Number of cases, infection rate, and prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in different departments, year 2000

Departments	No. cases	Infection rate/100 days of hospital stay	Prevalence/100 admittances (CI 95%)
Urology	3	0.045	0.27 (0.03–0.79)
Cardiac surgery	0	0	0 (0.00–0.30)
Internal medicine A	6	0.047	0.30 (0.11–0.66)
Infectious diseases	10	0.111	0.64 (0.31–1.17)
Internal medicine B	1	0.014	0.08 (0.00–0.45)
Orthopaedic surgery	20	0.153	1.16 (0.71–1.78)
Intensive care	12	0.337	1.24 (1.01–2.16)

cefonicid 1 g intravenously 15–30 min pre-operatively and 1 g intravenously 24 h post-operatively, in addition to the standard precautions used with surgical patients.

In view of the size of this problem, microbiological data were collected in order to discover the micro-organisms present in orthopaedic patients during 2000 (Table 1). These included ward cultures (blood cultures, wound cultures) and "surgical" cultures obtained during operation (cultures from the wound, articular fluid, open bone biopsy, open synovial biopsy and fibrous peri-prosthetic membranes).

Epidemiological data was also obtained in 2000 on the prevalence of MRSA (with 95% confidence interval) for the orthopaedic wards, and this allowed for a comparison with other units at risk in the hospital—particularly the intensive care and infectious disease units.

Nasal carriers were sought among all members of staff. Those who were colonised with MRSA were treated with Mupirocin nasal ointment and were excluded from any clinical activity until cultures for MRSA were negative. In addition, random checks were made for nasal carriers among all orthopaedic in-patients.

As a result, the orthopaedic department and the infections committee at our hospital decided to change the prophylactic regime used in orthopaedic implant surgery during the 6 months from the end of April to the end of October 2001. Firstly, it was confirmed that the surgical procedure was being performed following the general guidelines for the prevention of infection in surgical technique and post-operative incision care [12, 14, 15]. Secondly, every patient who was in the hospital for longer than 24 h before surgery underwent prophylaxis against being a nasal carrier by using topical Mupirocin every 8 h over 3 days, beginning the day before operation. Thirdly, all patients diagnosed as either "colonised" or infected with MRSA were isolated outside the orthopaedic wards, and "contact precautions" were strictly applied [5, 6, 16]. Finally, it was decided to add teicoplanin to the anti-microbial prophylaxis for a controlled period of 6 months. Teicoplanin 200 mgm intravenously was administered during the anaesthetic induction, with a second dose of 200 mgm 24 h later. Cefonicid continued to be given in doses of 1 g pre-operatively and a single dose of 1 g 24 h later.

To assess the efficacy of this new regime, clinical data was collected from 599 patients in this 6-month period (April–October 2001). In addition, the incidence of wound infection by MRSA was measured monthly, and 95% confidence intervals were calculated by exact methods for the orthopaedic department for the rest of the hospital. A comparison between these groups was performed using the chi-square test or the Fisher exact test.

Results

In the year 2000, there were 20 MRSA infections among 1,228 in-patients in the orthopaedic department (prevalence = 1.6%). In the entire hospital, there were 64 MRSA infections out of 21,220 in-patients (prevalence = 0.3%). Thus, of a total of 64 MRSA infections in the hospital, 20 (31%) were in orthopaedic patients. The difference between the prevalence in the orthopaedic department and the rest of the hospital was statistically significant in a Fischer's *t*-test ($p<0.01$), and the odds ratio was 5.15 (CI 95%=3.94–8.98).

The number of MRSA infections in the orthopaedic department was much greater than in any other unit (Table 2), including the intensive care unit. The infection rate (number of infections per 100 days of stay) in the orthopaedic department, although lower than in the intensive care unit, was higher than in any other medical or surgical unit. The prevalence (number of infections per 100 patients) of orthopaedic MRSA infection was significantly higher ($p<0.01$) than the prevalence found in the cardiac surgery, internal medicine and geriatric units.

In the search for a "reservoir", 51 staff members of the orthopaedic department were examined, and we identified 15 (29%) nasal carriers of *S. aureus* and two (3.9%) nasal carriers of MRSA. Methicillin-resistant strains accounted for 13% of nasally detected *S. aureus.*

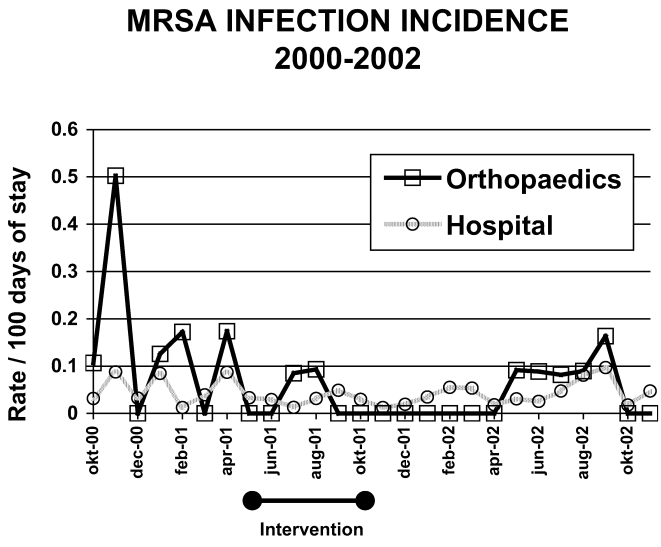

Fig. 1

Orthopaedic in-patients were also examined at random, and we found 41 (24%) nasal carriers of *S. aureus* and nine nasal carriers of MRSA (21.9% of the nasal carriers of *S. aureus* were of methicillin-resistant strains). In other locations, such as ulcers and catheters, we found another four MRSA carriers, and among the 13 MRSA carriers, four also presented with an orthopaedic infection with MRSA.

When using the "new regime", 18 orthopaedic in-patients developed an orthopaedic infection, although this included patients that were admitted for re-operation and who had a previously recognised infection. Of these 18, MRSA was the responsible organism in two. In the series of 96 patients who underwent an arthroplasty there were two infections, one with MRSA. These figures represent a decrease in the orthopaedic infection rate from 5.9% to 3%, and 0.5% of the infections were with MRSA.

The MRSA infection rate per 100 days of stay during the trial of the new regime was 0.029. The prevalence of MRSA infection in the orthopaedic department during the same period was 0.2% (CI=0.02–0.70), which is a significant decrease.

The incidence of infection (new MRSA cases as a percent of days of stay) was obtained monthly from the orthopaedic department and from the rest of the hospital. These showed a decrease in the incidence of MRSA infections in orthopaedic patients, while the hospital incidence remained almost the same (Fig. 1).

The prophylactic use of teicoplanin stopped after the trial, and from then on only sporadic new infections were detected, none due to MRSA. The arthroplasties performed during the trial were followed for a period of 12 months and no further infections appeared.

Discussion

There is growing concern about the increase of post-operative infections due to antibiotic-resistant organisms [6], and this is particularly important in orthopaedics where the increasing incidence of antibiotic-resistant staphylococci threatens the outcome of implant surgery. As the control of infection weakens, so surgical infections increase, and this situation becomes unacceptable. This is what happened at our hospital, and its control required an epidemiological investigation and a clinical trial after discussion between the orthopaedic department and the infectious disease control committee.

Hayley et al. [8] have shown that a useful decrease in infection can be associated with a greater involvement of the medical staff. Our trial was aimed at strengthening the entire infection prophylaxis in orthopaedic surgery, paying particular attention to implant surgery. We first focused on the routine precautions recommended by the CDC and the Healthcare Infection Control Practices (HICPAC) for the prevention of surgical site infections [16]. We found no major violations of these recommendations, but our adherence to these precautionary measures was tightened.

During the epidemiological investigation, we found a reservoir of MRSA in two members of the auxiliary nursing staff, and this required both treatment and separation from our department. However, no surgeons, residents or staff nurses were colonised. The prevalence of the presence of *S. aureus* carriers in hospital personnel has been reported at around 17% with 8.5% being of methicillin-resistant strains [3]. Our data showed a higher prevalence (29% nasal carriage of *S. aureus*) and also a higher percentage of methicillin-resistant strains (13%). Although it is considered that *S. aureus* carriage in hospital personnel is similar in different geographical areas [3], our findings revealed a higher rate than in the published data. Also, among orthopaedic in-patients, the prevalence of *S. aureus* carriers was high (24%). This is well over the prevalence reported for non-hospitalised patients (10%) [3].

Methicillin-resistant strains of *S. aureus* in otherwise healthy people remain uncommon in the community (3%) [3] but were common in our patients (21%). Our patients included both previous day admittances for programmed implant surgery and hip fracture patients with long post-operative stays. This diversity may be the reason for the possible reservoir that was generated, and this was suspected to be a contribution to our epidemiological outbreak of infection. The trial included separation of infected and colonised patients from the orthopaedic wards and contact precautions to control the spread of MRSA [10]. Treatment with Mupirocin nasal ointment in nasal carriers is not as controversial as its prophylactic use [1]. A recent double-blind, randomised placebo-controlled study has shown the effectiveness of this measure in eradicating nasal carriage in orthopaedic patients (rate 83.5% versus 27.8% placebo) [12]. However, in this same study, it proved impossible to reduce

surgical site infections of *S. aureus* by this single measure. These data support our combined use of prophylactic measures instead of relying only on nasal carriage control.

The use of pre-operative antibiotic prophylaxis has been for some time the most efficient weapon to control orthopaedic infection [9, 15, 17]. This is even more important with implants, as the presence of material contributes to bacterial infections [7]. The selection of antibiotics in prophylaxis is of the utmost importance. But nowadays, resistance to methicillin and to most betalactamics and cephalosporins leave few options. Glycopeptides and rifampicin could be useful, but rifampicin is given ovally and glycopeptides are currently considered to be "the last defence" against infection. Therefore, the use of antibiotics is controversial, as inappropriate antibiotic prescribing with the increasing number of antibiotic-resistant strains further decreases its effectiveness [10]. In the controversy involving glycopeptides for prophylaxis, most authors agree that their use should be restricted [6, 9, 20] due to the increasing prevalence of vancomycin intermediately-resistant *S. aureus* (VISA) and vancomycin-resistant enterococci (VRE) [2] in the USA and Japan, in turn related to vancomycin overuse [6].

In Europe, other authors [20] reviewing four available comparative trials of the efficacy and safety of teicoplanin in orthopaedic surgery prophylaxis conclude that teicoplanin 400 mg pre-operatively may be a reasonable choice for use in orthopaedic surgery when there is a high risk of infection with MRSA. Teicoplanin is tolerated better than vancomycin and is comparable to the cephalosporins [18]. Its pharmacological properties and bone concentration also support its use [18]. Others [19] prefer the use of teicoplanin as giving safe and effective antibiotic prophylaxis in hip joint replacement, particularly when methicillin-resistant bacteria are present. However, these statements disregard the fact that if teicoplanin is used widely for antibiotic prophylaxis, bacterial resistance may appear and therefore there will be no effective treatment for MRSA infections.

Despite the controversy of the prophylactic use of glycopeptide, it appears that the increasing number of troublesome methicillin-resistant infections may require a change in the prophylactic regime [21]. Teicoplanin might have to be used to control infections due to flora that have become practically impossible to eradicate in tertiary institutions. If this is not feasible, it might be necessary to consider stopping elective implant surgery at a particular unit. In this situation, where there is a very high incidence of MRSA, the use of teicoplanin in prophylaxis might be justified. However, different circumstances in different institutions make it very difficult to propose a comprehensive plan.

It is interesting that there are only a few reports of outbreaks of MRSA orthopaedic infections in the literature [1, 4, 11, 13]. These reports include 38 patients with proven MRSA infections in 3 years [11]; an outbreak of 17 patients with MRSA infections in an orthopaedic septic care unit [4] with 30% MRSA in 618 cultures taken from patients, personnel and the environment; and finally, an outbreak in six patients and one nurse that occurred within a month [13]. Thus, there is great variability of the incidence of MRSA epidemiology in orthopaedic units. We had an arthroplasty infection rate of 10%, and MRSA strains were detected in 33% of the patients.

Our trial was followed 12 months, and there were no further examples of MRSA infection in our arthroplasties. Therefore, this period seems adequate to ascertain the long-term efficacy of any prophylactic regime to avoid infections related to orthopaedic surgery. No example of vancomycin or intermediate resistant *S. aureus* has been detected at our institution.

In summary, we think that our preventive strategy has been very effective in controlling the rate of post-operative infection, particularly that related to MRSA. In order to maintain this relatively satisfactory situation, any improvement in prophylactic regimes must include many factors. This is why, although we discourage the general use of teicoplanin in prophylaxis even in implant orthopaedic surgery, we encourage the use of combined prophylactic measures in orthopaedic joint replacements in locations where there is a high prevalence of resistant organisms. This could be done for a short period under epidemiological control in a tertiary hospital and where there is a general awareness of the potential risks associated with using glycopeptides.

Acknowledgements The authors are grateful to Val Acebron, RN, from the infection control unit, and to Dr. J. Esteban from the microbiology service for their help.

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