Eradication of methicillin-resistant Staphylococcus aureus with an antiseptic soap and nasal mupirocin among colonized patients – an open uncontrolled clinical trial

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Abstract

Background: Aim of the study was to determine the clinical efficacy of a new antiseptic liquid soap (Stellisept® scrub), based on the combination of undecylenamidopropyltrimonium methosulphate (4%) and phenoxyethanol (2%), for eradication of MRSA among colonized patients who do not receive antibiotic therapy.

Methods: Over two years 50 MRSA patients in 6 hospitals were observed. Treatment was defined as the daily application of Stellisept scrub for the antiseptic body and hair wash (at least 60 s) in combination with nasal mupirocin. A treatment cycle was a minimum of 5 days treatment. Screening was carried out at least 48 h after the treatment cycle was finished, with 24 h between each of the requested three or more samplings, which included the nasopharynx, groin, axilla, perineum and other MRSA-positive skin areas.

Results: Fifteen cases were retrospectively excluded (lack of outcome documentation, concomitant antibiotic therapy, open wounds). All 35 patients had colonization with MRSA before antiseptic treatment on the skin, in the groin (80%), the axilla (25.7%), the perineum (20%) or other skin areas (14.3%). Colonization at more than one skin sites was found in 34.3%. Nasal colonization was found in 21 of 28 patients (75%), 7 patients were without nasal screening prior to the antiseptic treatment. After one treatment cycle MRSA was eradicated in 25 patients (71.4%), after a second cycle the total eradication rate was 91.4%, after a third cycle the rate increased to 94.2%. No patient discontinued the antiseptic treatment due to dermal intolerance of the product.

Conclusions: Progressive eradication of MRSA carriage was observed with the antiseptic soap and mupirocin. The eradication rate was not biased by concomitant antibiotic treatment, screening during treatment or lack of evidence for colonization in contrast to other studies with other preparations.

Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) continues to be a global problem in infection control. For many years it has been a major cause for nosocomial infections in many countries [1,2]. The proportion of methicillin resistance among clinical isolates of S. aureus is still increasing. In southern European countries, the proportion may be as high as 55% [3,4]. MRSA now even
becomes an increasing problem in the community [5,6]. Transmission of MRSA in community has been shown to be as high as 60% [7]. Family members who are living with MRSA carriers are in danger of MRSA transmission [7]. Dermal colonization with MRSA may be persistent, especially in the groin [8]. That is why attempts are often undertaken to treat colonized MRSA patients [9]. Antibiotics were shown to be effective in uncontrolled and controlled trials with eradication rates between 33% and 85% [10-12]. But antibiotics are considered to be inappropriate for patients who are only colonized and not infected with MRSA [13]. One reason is their potential to cause adverse effects, especially allergy, which can not be justified for patients who do not have an infection. More important is the risk of emergence of vancomycin-resistance in S. aureus [14]. Topical antiseptic measures, however, are normally employed [15]. The nasal cavity is usually treated with mupirocin or with tolerable antiseptics [16]. Dermal colonization is eradicated with antiseptic liquid soaps [13] Only few studies have addressed the question of MRSA eradication among colonized patients with liquid soaps in combination with nasal treatment. All of them are uncontrolled trials and most of them have different types of biases.

Aim of our study was to determine the efficacy of the antiseptic soap Stellisept scrub in combination with mupirocin for eradication of MRSA among colonized patients with evidence of dermal colonization (no selection bias), without concomitant antibiotic therapy (no treatment bias) and with regular screening investigations (no outcome bias).

**Methods**

**Study design**

An open clinical trial was chosen as a study design.

**Determination of MRSA carriage**

The MRSA carrier status was determined before and after treatment of the patients. Swabs were taken at least from the following body sites: nasopharynx, axilla, groin and perineum. Any patient with at least one MRSA positive skin site was regarded as a patient with evidence for dermal colonization irrespective of the nasal colonization status.

All swabs were processed on the same day. Briefly, swabs were plated directly on blood agar, oxacillin resistance screening agar base (Oxoid, UK), and dextrose broth for enrichment. After incubation of plates and broth at 37°C for 18 to 24 h, colonies resembling S. aureus were identified and tested for oxacillin resistance. This was done in two steps: disk diffusion with a 5 µg oxacillin disk on Mueller-Hinton agar (incubation at 30°C for 18 – 24 h) and agar screening on Mueller-Hinton agar supplemented with 6 mg/ml oxacillin and 4% saline (Oxa Screen Test Agar, bioMérieux, France; incubation at 35°C for 24 h). Isolates growing within 14 mm around the oxacillin disk and growing on the MRSA screening plates were regarded as oxacillin resistant.

**Treatment of patients**

Definition of treatment and treatment cycle: Treatment was defined as the daily application of Stellisept scrub for the antiseptic body and hair wash (at least 60 s) in combination with nasal mupirocin. A treatment cycle was defined as a minimum of 5 days treatment.

**Treatment of the nasal cavity**

The nasal cavity was treated with mupirocin which was applied twice per day as recommended by the manufacturer (Turixin®, GlaxoSmithKline, Munich, Germany).

**Treatment of the skin**

The skin and hair was treated once a day with the antiseptic liquid soap (Stellisept scrub, Bode Chemie GmbH & Co., Hamburg, Germany) which is based on two active ingredients: 4% (w/w) undecylenamidopropyltrimonium methosulphate and 2% (w/w) phenoxyethanol. The minimum duration of antiseptic skin treatment was 60 s. This application time is derived from in vitro data on the activity of the product against various epidemic MRSA strains and various clinical MRSA isolates [17].

For body washing the skin was moistened with tap water and the liquid soap applied without dilution. Mobile patients washed themselves under supervision of a healthcare worker. Immobile patients were washed by healthcare workers. After the 60 s application residual soap had to be rinsed or washed off with tap water. Linen and clothes were changed during the antiseptic treatment and the surrounding surfaces treated with a surface disinfectant [13].

**Patient selection and data**

Six hospitals participated in the study. The local infection control nurse of a hospital was responsible for data collection. Patients were included

- if there was evidence for dermal colonization with MRSA irrespective of the colonized body site (minimum screening of axilla, groin and perineum) and
- if they did not receive antibiotics at the beginning of the treatment and
- if they had no signs of a clinical infection and
- if compliance with the treatment could be expected for the anticipated duration of hospital stay.
Patients were excluded

• if antibiotics were given during the treatment or during
  the surveillance culture interval or

• antiseptic treatment was initiated for treatment of colo-
  nized or infected wounds and

• if patients were discharged before screening cultures
  could be obtained after treatment.

The following data were collected for each patient: gender,
hospital, MRSA positive body sites before and after the
antiseptic treatment (nasopharynx, axilla, groin, peri-
neum, other body sites) and additional information if rel-
vant for the outcome assessment. The microbiological
method in each hospital for identification of MRSA from
initial and follow-up swabs was not evaluated for its sen-
sitivity and specificity since it has become routine in Ger-
man laboratories.

**Post treatment screening**

Post treatment screening was done according to the Ger-
man recommendation on MRSA patients issued by the
Robert-Koch Institut [13]. A minimum wash-out period
of 48 h was required between the last treatment and the
first set of screening swabs. Screening swabs had to be
taken for three consecutive days and at least from the fol-
lowing sampling sites: nasopharynx, axilla, groin and
perineum. Additional body sites were included if they
were found to be MRSA positive before antiseptic
treatment.

**Results**

Fifty patients were treated between 2001 and 2002 in the
6 hospitals, mainly in surgery, internal medicine, inten-
sive care or other departments such as gynecology (n = 2),
neurology (n = 2), urology (n = 1) or dermatology (n = 1;
Table 1). Four of the 50 patients were discharged early
resulting in a lack of information on the outcome (coloni-
zation with MRSA after antiseptic treatment). Eight
patients received concomitant systemic antibiotic therapy
initiated after inclusion in the study. Three patients had a
colonized or infected wound which was treated during the
study. All of them were excluded resulting in a total of 35
cases with proven dermal MRSA colonization and without
concomitant systemic antibiotic therapy.

21 of the 35 patients were male (60%), the mean age was
69.1 years (minimum 27 years, maximum 91 years). Nasal colonization was found in 21 of 28 patients (75%),
7 patients were without nasal screening prior to the anti-
septic treatment. Dermal colonization was documented
mainly in the groin (80%), followed by axilla (25.7%),
perineum (20%), forehead (5.7%), umbilicus (5.7%) and
upper leg (2.9%; Table 2). Multiple colonization of the
skin was found in 34.3% of the patients.

After one cycle of antiseptic body wash and concomitant
nasal antisepsis with mupirocin, 25 of the 35 patients
were found to be MRSA free (71.4%; Table 2). The mean
duration of treatment was 6.7 ± 2.5 days. Successful erad-
ication of MRSA was confirmed with three negative con-
secutive series of swabs in 16 patients (64%). Two
consecutive series of swabs were negative in five patients
(20%) and one series of swabs was negative in four
patients (16%) which was explained by early discharge of
the patient. Treatment failures after the first cycle were due
to persistent colonization of the same skin area (5 of 10),
colonization of another skin area (4 of 10) and persistent
colonization of the nasopharynx (1 of 10). Of the remain-
ing 10 patients, two were not treated any further due to
discharge and 8 underwent a second treatment cycle with
seven of them being MRSA negative afterwards (total of
91.4% being MRSA negative). The mean duration of treat-
ment in the second cycle was 6.4 ± 2.1 days. In order to
confirm successful eradication of MRSA after the second
cycle, three consecutive series of swabs were negative in six
patients (85.7%) and two consecutive series of swabs were
negative in one patient (14.3%). The one patient
remained colonized on the same skin area without nasal
 carriage and underwent a third treatment cycle resulting in
dermal MRSA eradication (total of 94.2% being MRSA
negative; Table 2). Three series of consecutive swabs were
negative to confirm successful eradication of MRSA.

### Table 1: Number of patients per hospital and the type of unit of all included patients.

| Hospital | Internal medicine | Surgery | Intensive care unit | Other departments | All departments |
|----------|-------------------|---------|---------------------|-------------------|----------------|
| 1        | 1                 | 0       | 4                   | 4                 | 9              |
| 2        | 6                 | 5       | 0                   | 1                 | 12             |
| 3        | 6                 | 2       | 0                   | 0                 | 4              |
| 4        | 4                 | 3       | 0                   | 1                 | 8              |
| 5        | 0                 | 1       | 1                   | 3                 | 5              |
| 6        | 6                 | 5       | 1                   | 0                 | 11             |
| All      | 18                | 20      | 6                   | 6                 | 50             |

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No patient had to discontinue the antiseptic body wash due to dermal intolerance or uncomfortable perception of the product.

**Discussion**

Although eradication of MRSA from colonized patients is regarded as a key element in prevention of transmission in a hospital, so far only few studies have addressed the clinical efficacy of antiseptic soaps in combination with a nasal antiseptic for that purpose. No study was found with a positive or negative control for the antiseptic skin treatment, only one study was found with a negative control for nasal mupirocin (Table 3). In addition, most of the uncontrolled trials contain substantial biases which limit or even diminish the value of them.

In our study, we found an eradication rate after one treatment cycle of 71.4% which is comparable to antibiotic treatment [10,18]. After two treatment cycles, the rate was 91.4% and came up to 94.2% after a third treatment cycle. With no other antiseptic soap we were able to find comparable data which are not confounded by a lack of evidence for initial MRSA colonization, concomitant antibiotic therapy or screening cultures during antiseptic treatment.

One limitation of our study is the lack of a control. We can not exclude that washing with plain soap and water or doing nothing would not have had a similar effect regarding the eradication of MRSA, although it is very unlikely based the persistence of MRSA colonization in the groin [8]. It would have been much more interesting to compare Stellisept scrub with either a non-medicated soap (negative control) or another antiseptic soap (e.g. based on chlorhexidine). But the use of non-medicated liquid soap would have been acting against the German recommendation for MRSA patients (antiseptic soaps or liquid preparations should be used for treatment of the skin) [13]. The use of medicated soap, however, would have been an interesting option, ideally in a double-blind randomized design. But chlorhexidine as the most common active agent for this type of treatment has been described in recent studies with artificial contamination of fingers with MRSA to have no advantage compared with non-medicated liquid soap [19,20]. It was therefore not considered to be suitable as a positive control [21]. That is why an open uncontrolled design was chosen.

Another limitation is the rather short follow-up of 5 days after termination of the treatment (2 days wash-out and 3 days screening cultures). Most patients stayed as long in their hospital as it was necessary to complete the screening cultures. The main reason for even shorter follow-up is discharge of the patient from a hospital. Continuation of hospital stay with the only aim to complete screening cultures was not possible in our study. Follow-up was unknown in some studies [22,23], shorter in others [24] or longer [10,18], but in some studies not for all patients [8,25].

| Localisation of MRSA colonization | Before treatment (n = 35) | After treatment cycle 1 (n = 35) | After treatment cycle 2 (n = 8) | After treatment cycle 3 (n = 1) |
|----------------------------------|--------------------------|---------------------------------|-------------------------------|--------------------------------|
| Nasopharynx                      | 21                       | 1                               | 0                             | 0                              |
| Any skin site                    | 35                       | 7                               | 1                             | 0                              |
|   • Groin                        | 28                       | 5                               | 1                             | 0                              |
|   • Axilla                       | 9                        | 3                               | 1                             | 0                              |
|   • Perineum                     | 7                        | 2                               | 0                             | 0                              |
|   • Forehead                     | 2                        | 1                               | 0                             | 0                              |
|   • Umbilicus                    | 2                        | 0                               | 0                             | 0                              |
|   • Upper leg                    | 1                        | 0                               | 0                             | 0                              |

Identification of MRSA was not carried out for all screening swabs in one laboratory but with the same test method. Differences in the sensitivity and specificity have been described [28-30] which may have an impact on the identification of a MRSA patient. But it is unlikely to have
an impact on the result of the antiseptic treatment because the method would have been the same before and after treatment of the same patient. That is why it was justified not to carry out the identification of MRSA in one specific laboratory especially because recent data indicate that determination of phenotypic resistance may largely underestimate the genotypic resistance in MRSA [31].

Another finding is the good dermal tolerance of the antiseptic soap. All 35 patients tolerated repetitive use of the preparation very well, even more than one treatment cycle. Another preparation (Octenisept) has been described to lead to skin redness in 4 of 28 patients resulting in termination of the treatment [25]. The excellent dermal tolerance of Stellisept scrub on intact and scarified skin has been described before [32].

**Conclusions**

Stellisept scrub in combination with nasal mupirocin was found to effectively and progressively eradicate MRSA from colonized patients. Antiseptic treatment may have to be repeated.

**Authors’ contributions**

GK designed the study, organized the participating hospitals, collected the data and analyzed them. AK participated in the design of the study and in the analysis of data. Both authors read and approved the final manuscript.

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