Effect of antibiotics for eradication of MRSA-carriage

Version 2

Author: Sally Radwan
Supervisor: Dr. Jan Källman
Department of Clinical infection
University Hospital of Örebro
Abbreviations

MRSA  Methicillinresistent Staphylococcus aureus
S.aureus  Staphylococcus aureus
HA - MRSA  Hospital acquired
CA - MRSA  Community acquired.
SSTI  Skin and soft-tissue infections
SCCmec  staphylococcal cassette chromosome mec
PVL  Panton-Valentine leukocidin
PMN  human polymorphonuclear neutrophils
TSS  Toxic shock syndrom
PCR  Polymerase chain reaction
PBPs  Penicillin-binding proteins
MGE  Mobile Genetic Elements
MIC  Minimal Inhibitory Concentration
ODD  Oxacillin Disk Diffusion
MHA  Muller-Hinton agar
CDD  Cefoxitin Disk Diffusion
Fig.  Figure
NaCl  Sodium Chloride
μg  Microgram
Hb  Hemoglobin
Abstract:
MRSA are isolates of S.aureus which are not susceptible to the antibiotic Methicillin, which used to be the first line therapy of treating S.aureus infection. Resistance to methicillin implies resistance to all β-lactam antibiotics. The objective of this descriptive retrospective observational study was to understand the outcome of the given treatment for eradication of MRSA carriage, by revealing the percentage of re-colonization and eradication, as well as compare the increase of HA and CA- MRSA infection during a period of October 2010-October 2013. Investigations were made on a total of 105 MRSA positive individuals who have been in contact with the care system within Örebro municipal. It was performed by reading through their medical records and mainly focusing on the site of colonization, outcome effect of the used antibiotics and focusing on the trend of HA - and CA- MRSA. Both the pharynx and nasal sites were preferable colonization site of MRSA. The antibiotic Dalacin and the nasal salvage, Bactroban nasal, showed a total result of 70% and 100% respectively of eradicating MRSA- carriage. Other comparable antibiotics as Fucidin and Eusaprim showed an eradication result of, 50% and 33% respectively. It was shown that combined treatments, showed a higher incidence of re-colonization. The source of HA-MRSA and CA-MRSA is increasing with the years and there is a three- fold increase of HA-MRSA, while double fold increase of CA-MRSA. In conclusion, the preferable colonization site was both the pharynx and nares. Bactroban Nasal and Dalacin showed most promising result for eradication of MRSA carriage in contrast to the rest of the treatments, including combined treatments. The both sources of HA- MRSA and CA- MRSA showed an increasing trend with years. Further studies that primarily include a greater number of patients would facilitate more accurate results.

Key words: MRSA, β-lactam, HA-MRSA, CA-MRSA, S.aureus Dalacin, Bactroban Nasal, re-colonization, eradication, colonization.
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Introduction

**Microbial characteristics of S. aureus**

S. aureus is a species that taxonomically belongs to the genus Staphylococcus as well as the family Staphylococcaceae. They are classified as gram-positive spherical bacteria, forming clusters, which microscopically resembles grapes. They are 1 micrometer in diameter. S. aureus colonizes mainly the nasal passages. It can additionally be found in the skin, pharynx, hair follicles, and perineum. They may cause a wide range of infections and intoxications. The have the capacity to ferment Mannitol. The species forms a fairly large yellow colony on rich medium and it is often hemolytic on blood agar. Staphylococci are facultative anaerobes. This indicates the growth either by aerobic respiration or by fermentation that yields mainly lactic acid. They can grow at temperature range of 15 to 45 degrees. The bacterium is catalase-positive, coagulase-positive and oxidase-negative. This species are non-motile as well as non-spore forming.

S. aureus strain has potential to cause diseases and hence called pathogenic. Specific strains of S. aureus can cause range of diseases via its virulence determinants of its structure, biochemical or/and its genetic features. They can for instance cause septicemia, food intoxication, and toxic shock syndrome but mostly pus and wounds infections. Since it occurs in human flora, it ensures the capacity for transmission from one individual to another.

**Colonization**

Colonization refers to the presence of a high concentration of bacteria at a site that they can be detected, without causing any signs of illness or infections. However, it is a risk factor for consequent clinical infection, if colonized MRSA on the skin invades an open passage as wound or cut in the skin [1, 2]. In case of infections, bacterias were not initially present in the site from which it has been detected, but was introduced either from another source or from contamination. [3, 4]. It can be clinically identified as wound infections, surgical site infection, abscesses, though, many organs can also be effected and give rise to life threatening status [4]. Patients involved in the hospital care have a risk factor to develop MRSA infection if they have weakened immune system, because of a certain medical condition or treatment (e.g. chemotherapy), recent use of antibiotics, hospitalized for a longer period or having a surgical wound and/or intravenous line. Patients which have hemodialysis have a significant high risk to become infected [2]. Community associated risk factors to become infected includes usually healthy individuals with skin issues as eczema, or have an opening site for
the passage of MRSA as in the case of having tattoos or body piercing. Athletes are also included in this category as they are usually exposed to physical contact [2].

The most preferable condition for growth and survival of MRSA is 25°C and 11-33% relative humidity. The higher relative humidity the less ideal environment, leading to less MRSA survival [5]. The most frequent site of colonization is the anterior part of the nostrils, but, it also colonizes in the pharynx and perineum/ groin [6, 7]. They way to get colonized by MRSA can occur via physical contact, by touching the skin of another individual who is an MRSA carrier. Another way is to touch contaminated surfaces as door handle or phone) [2]. Studies have shown three different types of MRSA carriage, which are: persistent, intermittent carriers, and non- carriers [8-10]. The persistent carriers have a greater prevalence of colonization of other body sites in addition to the nostrils and rarely alter their strains in contrast to the intermittent bacteria [11].Transient colonization is referred to individuals who are temporarily colonized by MRSA for instance in nostrils or pharynx, without establishment of bacterias. Hence, MRSA positive result will only be shown during the occasional screening [11].

**Virulence and toxins of S.aureus**

Several virulence characteristics are responsible for the pathogenesis of S.aureus infection. The most important virulence factors and associated clinical syndromes are listed in table 1.

**Table 1.** Virulence factors of S.aureus and their clinical effects [12-16].

<table>
<thead>
<tr>
<th>Involved virulence factors in:</th>
<th>Involved factors:</th>
<th>Accompanying clinical effect:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attachment</td>
<td>Fibronectin- binding proteins and collagen</td>
<td>Endocarditis, osteomyelitis, catheter infection</td>
</tr>
<tr>
<td>Host devastation</td>
<td>Leucocidins, PSM</td>
<td>Invasive skin infections and necrotizing pneumonia</td>
</tr>
<tr>
<td>Tissue invasion/ penetration</td>
<td>Phospholipase C, hyaluronate</td>
<td>Tissue destruction and metastatic infection</td>
</tr>
<tr>
<td>Toxin- mediated disease or sepsis</td>
<td>Alfa-toxin, lipotichoic acid,</td>
<td>Food poisoning, TSS</td>
</tr>
</tbody>
</table>
S.aureus has the ability to produce a plethora of toxins and some are mentioned below:

**Panton-Valentine leukocidin**

PVL is a staphylococcal leukocidin (cytotoxic to white blood cells) which belongs to the pore-forming toxin family, β-barrel molecular complex. It also comprises other toxins as γ-toxin, and α-toxin. It induces lysis of host defense cells as PMNs, monocytes and macrophages [13]. It is encoded by lukS-PV and lukF genes-PV, which in turn encodes the pore the cytolytic activity, LukS-PV and LukF-PV. Clinically, they are responsible for skin abscesses [16].

**Phenol-soluble modulins**

PSMs are a family of amphipathic, α-helical peptides produced by staphylococci. They are peptide toxins, which are known to attract and lyse neutrophils and erythrocytes [15].

**Alpha-toxin**

Most S.aureus strains produce α-toxin, which has a cytolytic property. It is not cytolytic to neutrophils but it lyases macrophages and erythrocytes and has pro-inflammatory effects. Finally, alpha-toxin has been shown to contribute to the penetration of the epithelial barrier during skin infection with the MRSA strain USA300 [16].

**Methicillin-Resistant Staphylococcus aureus**

MRSA are defined as isolates of S.aureus which are not susceptible to antibiotics methicillin, which used to be the first line therapy of treating S.aureus infection. Resistance to methicillin implies resistance to all β-lactam antibiotics [17, 18]. Therefore, precision and swiftness with detection of methicillin resistance is of key importance to ensure correct antibiotic treatment in infected patients, as well as control of HA- MRSA isolates in hospital to avoid spreading. The phenomenon was first reported 1961 and became a major problem to take into consideration in many parts of the world in the late 1970s and early 1980 [2, 17].

The first MRSA was isolated by Patricia Jevons. From 1980s new strains of MRSA appeared and led to uninterrupted pandemic infections of MRSA globally [17]. Since this bacterium is able to produce series of toxins and cause harm [12, 13], the continuous emergence of mutations of the specific genes responsible for the resistance of treatment, leads to difficulty to prevent and control MRSA. MRSA infections were initially confined to the health care
environment, but have also been found in the community [19, 20]. Both HA- MRSA and CA- MRSA share some strains but differs in antimicrobial susceptibility and potential virulence [19, 20]. Contaminated devices, medical waste as well as medical staffs that carry MRSA is considered as an infection source [2, 4, 21].

**Genetics of MRSA**

MRSA has a group of MGE genes, which is mobile within the genome and plays a significant role in the spread of virulence factors. It is a fragment of DNA which transfers into the host cell where it can either replicate or integrate in host DNA. The genetic component responsible for resistance, meca, is not native to the S.aureus genome. The MecA gene located on SCCmec is characterized as a mobile resistance element. There are 5 SCCmec subtypes, I- V. Subtype I, IV and V have a small size and encode recombinase genes as well as structural and regulatory genes for resistance to methicillin [14].

MRSA have the ability to produce PBP2a protein, altered penicillin- binding protein, encoded by the meca gene. It has a property of low affinity for β-lactam antibiotics, and hence minimizing its target effect [15]. This gene is regulated by two genes located upstream of the meca gene, called mecR1 and mecl. Together they are mentioned as mec complex. The mecR1 gene encodes a transmembrane inducer of meca consisting of membrane- spanning and penicillin binding domains, while the other gene, mecl, encodes a strong repressor of meca [17, 22]. The resistance level differs in a spectrum from phenotypically susceptible to highly resistant. This is dependent on the PBP2a production, which is affected by chromosomal factors. That’s why all meca clones are not resistant to methicillin [14].

**Difference in characteristics between HA - and CA - MRSA**

HA-infection is defined as an infection that occurs for a patient who was not admitted to the hospital or other health care setting for that reason, neither was it incubating at the time of admission [20, 23]. The infection can occur 48 hours of hospital entrance as well as three days of discharge, as well as 30 days after an operation [23, 24]. It is known that CA- MRSA occurs in a person with no previous history of health care exposure [20, 23, 24]. However, the definition can be misleading. Since time- based definition regarding hospital discharge can be ambiguous since S. aureus has the characteristics to persist as a colonizer for months or years and the onset of CA- infection may be caused by HA- strains [19,22, 24-27]. People who were not hospitalized but were detected with SSTI were reported to have CA- MRSA [27]. The
strains of CA-MRSA are often resistant to fewer antibiotics, compared to the HA-MRSA strains, owing to the pressure of antibiotics that have been within hospitals [19, 22]. It usually has IV and V subtypes of SCCmec unit and type IV usually contain the gene encoding for PVL. They are classified as more virulent. HA-MRSA isolates classically have the subtypes’ I-III and rarely carry the gene encoding for PVL [19].

From a prospective study, it was found that CA-MRSA isolates were in a higher extent, compared to HA-MRSA susceptible to ciprofloxacin, clindamycin, erythromycin and Gentamicin [19]. Since the two isolates have SCCmec types which can carry various additional genetic information, it is possible for them two develop resistance to several antibiotic classes, which commonly occurs in HA-MRSA [19].

MIC values of HA-MRSA clones are usually higher than those of CA-MRSA clones [19].

**Molecular techniques for detection of MRSA**

There are many techniques available for detection of MRSA. It can for instance be performed by either amplification of genes by the usage of PCR alternatively by phenotypic testing. Then phenotype of resistance can vary even though genetic homogeneity depending on culture conditions (temperature and osmolarity of the medium) [28]. This in turn can be difficult for detection of MRSA with phenotypic susceptibility methods. Oxacillin disk diffusion is one of the traditional methods for MRSA screening, but lately cefoxitin disks as well as PBP2a latex agglutination have also been used as it yields high precision [29]. These methods are categorized as antibiotic susceptibility tests, which work as culture screening method. It works by collecting culture from colonized area as pharynx, nares and perineum and inoculate on a MRSA-selective chromogenic agar. Most of the methods yield a result of presumptive MRSA colonies the next day, while the method of using latex agglutination can confirm the result after 10 min. In this method, antibodies are used against PBP2a, which are extracted from suspensions of colonies and the detection is made by agglutination with latex particles coated with monoclonal antibodies to PBP2a. This test may not be reliable for colonies grown on media containing NaCl [22]. ODD test works by inoculating the suspected MRSA colony onto MHA. 1 μg Oxacillin disks is applied and then get incubated at 35 °C for 24 h. An inhibition zone <10 mm in diameter indicates oxacillin resistance. In comparison to CDD method, 30 μg disks are applied and the suspected MRSA isolates are inserted onto MHA plates. The plates are then incubated at 37 °C for 18 h to allow the bacteria to grow.
Diameters of inhibition zone ≤21 mm indicated oxacillin resistance, and diameters ≥22 mm are considered to indicate sensitivity [22].

PCR-based molecular methods is used by the aid of primers designed to amplify species-specific targets. These targets are nuclease (nuc), coagulase (coa), protein A and surface-associated fibrinogen- binding protein genes. However, lately, this method is mainly used for detecting the mecA gene. It is a very efficient way to yield result quickly but yet expensive method of choice [19].

The screening duration vary from every county council in Sweden. Positive MRSA patients who have been in contact with the University Hospital of Örebro are screened once again after one month after the first detection. The second screening opportunity is three months after the first screening. If the patient continues to be positive, a new screening opportunity will be offered again after 3 months, but if negative after 6th months. Four negative screenings in a row defines no longer as a carrier. MRSA screenings can be performed either by DNA testing or by investigating bacterial culture by taking samples from for instance nares, pharynx, wounds, perineum/ groin and urine.

**β- lactam antibiotics**

β- lactams are widely prescribed antibacterial drugs which is capable to lyse dividing bacteria and therefore considered as bactericidal. Drugs within this class share the same mechanism of action, as they all contain a β-lactam ring in their structure. Their principal function is to inhibit the cell wall synthesis of bacteria by binding to PBPs located in their cell wall. The conjugation leads to cell death by inhibition of peptidoglycan synthesis, and inactivating an inhibitor of an autolytic enzyme that crosslink the peptide chains, attached to the peptidoglycan. However, their chemical structures vary for the different agents and therefore differ in the spectrum of action [18, 30, 31].

S. aureus has the ability to produce four PBPs which are susceptible to modification by beta-lactam antibiotics, which allows the antibiotics to be considered bactericidal. The MRSA bacteria additionally contain the mecA gene. A mutation in this gene produces an alternative type of the four standard PBP, called PBP2a. This enzyme provides transpeptidase activity to allow cell wall synthesis at beta-lactam concentrations that inhibit the β- lactam-sensitive PBPs, and thus bestows resistance [18, 30, 31].
There are four subclasses of β-lactam agents named penicillins, cephalosporins (which are subdivided into four generations), monobactams and carbapenems. Those vary structurally except having the same β-lactam ring. Broad spectrum antibiotics are noted to have a broader effect against both gram positive as well as negative bacteria while the narrow spectrum is typically effective against Gram positive bacteria. The spectrum of action is dependent upon two factors. Firstly, it concerns the degree of penetration of cell wall and the outer membrane, as well as the binding ability to specific transpeptidases. Both hydrophobic and hydrophilic β-lactams are capable to diffuse through the murein layer of gram positive bacteria. The hydrophilic agents are additionally capable to diffuse readily through the gram negative bacteria’s outer membrane pores in comparison to hydrophobic agents. Secondly, is the extent to which the drug inhibits a specific transpeptidases, after accessing the periplasmic space. Penicillin has a short plasma half-life and the elimination of most penicillin occurs via renal elimination, 90% through tubular secretion [28, 32].

**Medications for eradication of MRSA**

The antibiotic Dalacin, trade brand for Clindamycin shows in some studies an appealing result of MRSA eradication [33, 34]. However, many strains of MRSA are also resistant to it and it should not be used when treating systemic or bacteremic infections where MRSA is the suspected pathogen [35, 36, 37]. Rimactan which is the brand name for Rifampicin works as bactericidal in vitro activity against MRSA [37]. Studies have proved that using this drug in monotherapy will contribute to a rapid emergence of resistance [38, 39]. Rimactan is rather suggested to be used in combined therapy, because it has shown to result with a synergistic activity against staphylococci [40]. Studies have shown that Rimactan in combination with Clindamycin yields a successful eradication of MRSA carriage [20, 41, 42]. Combined therapy of topical antibiotics as nasal salvage and systemic antibiotic has shown to result in good eradication result of MRSA-carriage too [43]. Nasal salvage in monotherapy has also shown to eradicate MRSA-carriage efficiently as well as result in minimal toxicity and approved for MRSA outbreaks [45, 46].
**Aim**

The aim of this research is principally to understand the outcome effect of the given treatment for eradication of MRSA carriage by revealing the percentage of re-colonization and eradication, as well as compare the increase of HA and CA-MRSA during a period of October 2010- October 2013.

**Material and Methods**

*Materials*

The main material used was “Klinisk Portal”. It is a systemic computer program which can only be used within health care settings, to view medical records. It saves information regarding patients who have been in contact with the health care system only in Örebro County. From this program it is possible to search patients who were positive for MRSA from October 2010 till October 2013. In advance to the initiation, an outburst-list of all positive patients at different time interval with their identity number was received; it was a total of 105 patients.

*Method*

From the outburst list received, positive patients within the time interval October 2010-October 2013 were selected. Information regarding their medical status of MRSA and the treatments was looked up in Klinisk portal. While reading through the patients’ medical records, I focused on points regarding the amount of patients infected during the time interval, source of MRSA, CA-MRSA or HA-MRSA and the sites of colonization, where MRSA screenings from nares, pharynx, wounds, perineum/groin showed positive result. Screenings were performed on patients with SSTI, tracking of infected family members, adopted (during adoption screening), wound infections, postoperative infections, patients who have been treated abroad. Any patient with at least one MRSA positive colonization site was regarded as MRSA positive. The screened patient that is a carrier in more than one site, have all their positive sites included in the study too, as the preferable site of colonization. I also focused on treatments for eradication of carriage. Different treatments were tested on different colonized patients. However, only 70 patients out of 105 MRSA positive were treated with antibiotics (especially short term carriers). A patient is considered to be eradicated from MRSA when four negative MRSA screenings is resulted. Some patients that continue as MRSA carriers after treated infection are considered re-colonized. They are included in the study as recolonization after given treatment. After collecting the needed data, I used the program
Excel, where I could set up the data into charts. I had three charts in total for every year. First chart represents the site and source of infection correlated with the number. The second chart explained the given treatment correlated with the number given. The last chart represented the reinfection site correlated with the treatment used. These charts were then converted into bar graphs, for a visual comparison between the different years, starting from October 2010 – October 2013. The charts referring to the site of colonization for all the three years were fused together into one bar graph. The numbers of patients with a source of infection from CA-MRSA and HA-MRSA or other (adoption screening or abroad stay) were made into a single graph, and the three different years were distinctive, with its number. Patients considered as HA-infected were those who had a post-operative infection, infected staff within the health care setting, infected patients in the hospital. CA-MRSA infected patients are those who appeared at the primary care and had a wound or SSTI and got screened for MRSA. Family members who were infected were included in the category of CA-MRSA. The third graph made was referring to the efficacy of medication given to treat patients with colonized MRSA with topical ointment or together with antiseptics, Hibiscrub, while the severely colonized yielded systemic antibiotic combined with antiseptic solution and topical ointment. Systemic antibiotic refers to treating the whole body with tablets and capsules with Dalacin combined with Rimactan per os. The infected individuals also received solely systemic antibiotic as Dalacin and Eusaprim.

Individuals who were solely visitors in Sweden or asylum-seeking, and got in contact with the health care system in Örebro were also registered as MRSA positive. They become a part of the obtained data concerning the County. Frequently, the asylum-seeking patients does not have a prolonged valid personal date of birth, which in turn restricts additional searching regarding the points to be considered for the investigation. Therefore, those people were excluded from this study. Registered MRSA positive patients that deceased and does no longer have an accessible medical record, were also excluded from this study. However, individuals who were settled in another city prior to Örebro, and were already MRSA positive and later came in contact with the hospital care in Örebro were included in the study.

**Ethical considerations**

This study is approved from the operation manager of the infection center of University Hospital of Örebro. No personal records from patients will be revealed in the academic
presentation, and I am personally well informed regarding the confidentiality within healthcare, when reviewing medical records.

**Results**

*Site of colonization*

A total of 105 MRSA positive patients, were found during October 2010 and were investigated. The preferable site of MRSA colonization in the Örebro County was principally pharynx, followed by the nares and lastly groin or perineum. Many patients that were colonized with MRSA in the pharynx were also colonized at other sites (perineum/ groin or nasal part). These sites were as well included in the investigation of preferable colonization site.

![Figure 1](image.png)

**Figure 1.** From a total of 105 investigated MRSA positive patients from October 2010-October 2013 the preferable MRSA colonization site in the Örebro County was pharynx followed by nares, nasal part. The individual, who were colonized in more than one colonization site, had their additional colonization sites included too.
Source of infection

Patients with both CA- and HA- MRSA showed an increasing trend of MRSA through the investigated time interval. However, the dominating source of MRSA infection showed to be CA-MRSA. There is an approximate doubling of CA- MRSA infections in comparison to HA- MRSA, which has a threefold increase from October 2010- October 2013. The increase of HA- MRSA is alarming and causes concerns. Other sources of MRSA infection did not show to be a leading source (fig 2).

Figure 2. From a total of 105 patients, an increasing trend of both HA and CA- MRSA infections during the different time intervals can be seen. Pattern of other sources of MRSA can also be distinguished.

Tested treatments on MRSA positive patients, showed various outcome effects. The outcome effect of the given treatment to both infected and colonized MRSA patients are elucidated by the relation between re-colonized and eradicated MRSA carriers after given treatment. Re-colonization is referred to MRSA colonization at any specific site after a treatment, while eradicated refers to a total of four negative MRSA screenings in a row after given treatment. The highest incidence of recolonization with MRSA was shown after treatment with Hibiscrub, Bactroban nasal and systemic antibiotic. Only 25% were eradicated while 75% were re-colonized at a colonization site. However, a minor difference was noted without the use of systemic antibiotic. The number of eradication showed a total of 52% while re-colonization of 47%. Bactroban Nasal demonstrated a successful result of 100% eradication.
However, Dalacin illustrated a higher percentage of eradication in contrast to re-colonization, 70% and 30% respectively and had a lot more tries. Fucidin and Eusaprim have a percentage of re-colonization of a minimum 50%. In total, a comparison of eradication and re-colonization after giving all the treatments yielded a result of 59% and 41% respectively. Only 70 patients from a total of 105 MRSA positive patients were treated.

**Fig 3.** This figure shows different treatment options used in the study and its outcome effect. Patients that still tend to be colonized after treatment were classified as recolonized. While the eradicated MRSA carriers showed a total of four negative MRSA screenings in a row and considered no longer contagious. From a total of 105 MRSA positive patients in the study, only 70 patients were treated. The effectiveness of the treatment can be seen by the relation between re-colonization and eradication after given treatment.
Discussion
The aim of this study was to investigate the outcome of the given treatment for eradication of MRSA carriage by revealing the percentage of re-colonization and eradication, as well as compare the increase of HA and CA-MRSA during a period of October 2010-October 2013. Out of 105 MRSA positive patients, only 70 people were treated with various medications. A total of 31 trials with the antibiotic Dalacin were made on MRSA carriers and 70% were eradicated from the bacteria. Dalacin showed to be the most effective drug per os with a lower incidence of re-colonization in contrast to the other given treatments (figure 3). However, it still demonstrates a high percentage of re-colonization. A hypothesis regarding the susceptibility to antibiotics and the type of MRSA strain can be considered. Another study has also showed an appealing result when using Dalacin for eradication of MRSA and yet a lesser recolonization incidence was obtained [33]. Nevertheless, other studies also showed a lesser recolonization incidence when using combined therapy with Rimactan rather than solely monotherapy [38-40] which was not in this case, where a total of recolonization incidence showed a total of 75%. Rimactan is considered as an effective drug which effectively eradicates MRSA from mucosal surfaces [38]. Bactroban Nasal, the local ointment, also used for eradication, showed a total of 100% successful result. Several studies have also indicated similar pleasing result [40-42]. Nonetheless, in this study, the combination of Hibiscrub and Bactroban nasal did not yield as tempting results as many studies have shown its efficacy to eradicate a high number of colonized MRSA [46-48]. In this investigation it rather showed the next highest recolonization incidence after giving this combined treatment. Probable reason can be regarded as confusion on misunderstanding about the scrub or nasal salvage as personal items [2, 3, 47]. Since other studies have shown to give an appealing result [46-48], more tries with this treatment has to be tested on the carriers in order to get a more reliable result.

The fundamental threefold increase of HA-MRSA (fig.2) is most probably due to scamp with hygiene as many studies also indicates [49, 50]. The increase of CA-MRSA incidence leads to increased proportion of patients who will be hospitalized, (due to MRSA-carriage). Comparing this result to another study made in United States of America, the number of CA-MRSA and HA-MRSA infected are also increasing. CA-MRSA is considered as the most common pathogen for causing wound infections [50]. The hypothesis regarding the downward slope of other sources of MRSA (fig 2) could possibly depend on more people who tend to be more cautious while traveling abroad. The cautious note is probably due to the
increased awareness of getting bacterial infections while traveling abroad, which is well described in the traveling brochures etc.

Many studies show the target site of MRSA colonization is in the anterior nares [29, 44] and an insignificant distinguish can also be seen in this study between the amount of patients colonized with MRSA in nares and in the pharynx. These preferable sites of colonization are due to the appropriate environment; temperature and humidity that appear to be a possible source of growth, and multiplication [2]. This can also be associated with the fact that these parts of the human body are nearly always exposed to contagion. Touching contaminated surfaces (with MRSA) or having physical contact with someone who is colonized with MRSA assists colonization. Additionally, individuals practically always use hands to itch the nose or grabbing eatable materials, which are also contributing factors [38-40].

Before starting the investigation, several points were supposed to be considered as: the site of colonization, amount of patients infected during the investigated time interval, source of infection, treatments for eradication of MRSA carriage as well as the outcome effect of the treatments used by analyzing the relation between the eradicated and recolonized. The eradicated MRSA individuals are those who have showed four negative screenings in a row. Nevertheless, several factors were excluded from the study including the age, gender, socioeconomic status, comorbidities, individuals who have ceased and does not have an available medical record and the asylum-seeking patients who have been in contact with the health care setting but does no longer have a valid personal identification number for looking through their medical records. Visitors to Sweden who were positive for MRSA after the first screening were excluded too. People who were settled in Örebro and were positive for MRSA and moved to another city were also excluded from the study.

The weakness of this retrospective observational study mainly includes too few tries of different medications on the limited number of patients. The lesser tries, the less reliable results and thus, an improvement can be made by for instance extending the time interval that was investigated, in order to get more available medical records, which could influence the obtained results. Additional improvements can also be made by including a control group that indicates whether a decrease of MRSA carriage occurs after received topical or systemic treatment. Furthermore, verification of eradicated MRSA carriage by clinical investigation including white blood cell count and Hb, could possibly influence the view of eradication
result differently. Another weakness concerns the irregular screening schedule for some patients due to their case and the duration of their given treatment for eradication of MRSA. Usually, screening routines are performed in the following manner that after detection of MRSA after the first time, the second screening opportunity is after three months. If the patient continues to be positive, a new screening opportunity is maintained again after 3 months, but if negative after 6th months. Four negative screenings in a row defines as eradicated MRSA. Changes in the standard screening routine can yield a different result and therefore not a concrete result can be made regarding the treatment options and the results can be misleading too. Additionally, some patients are already on other antibiotics for some other infections and the outcome of the screening can influence the verification of eradication. People who are having wounds or skin issues cannot start treatment without their issue being solved, and since not many confirmed information regarding healing process was mentioned in the medical record, the result of the eradication after the treatments could have been different. Improvement can be done by enlightening information about healed bodily issues as wounds in advance to a treatment. This would possibly contribute to more accurate answer regarding eradicated number.

This retrospective study showed an increased colonization of MRSA at the pharynx, however, a slight difference was found in the nasal part. Many studies have shown that nares are the preferable site of colonization [9, 29, 44]. Moreover this study also showed an increased trend amongst a source of infection from CA-MRSA as well as HA-MRSA during the time interval from October 2010- October 2013. The threat of the rising number of infected MRSA within a population of a county is alarming. The increasing trend occurs possibly due to the increased number of immigrants to Örebro County, and the lack of knowledge regarding bacterias as well as misunderstanding information received from the care systems. Another possible point of view concerning the increased number of CA- MRSA is due to the lack of knowledge on how to prevent the spreading of bacterias in the society amongst different communities that are not associated with health care settings, which include athletes, intravenous drug users and prisoners [2, 51]. The increasing amount of HA- MRSA carriage is most likely multifactorial. The increase of CA-MRSA incidence leads to increased proportion of patients who will be hospitalized, (due to MRSA- carriage). Lack of compliance with hygiene routines amongst the staff also induces an increased number of HA-MRSA [49, 50]. However, the most preferable drug shown to effectively eradicate MRSA carriage is by the use of Dalacin per os and/ or the local ointment Bactroban nasal. Many studies have also
confirmed that conclusion [43, 45, 46]. Studies have also revealed the effectiveness of Dalacin in combination with Rimactan per os [20, 40-42], which in this study was not the case. Informing carriers as well as their next of kin thoroughly regarding MRSA, the spread and its resistance pattern, might increase the attention of the topic which is required for a joint effort to prevent the inclination.

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References


