Management of Sinonasal Methicillin-Resistant Staphylococcus Aureus Infection

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Staphylococcus Aureus

- The Gram-positive aerobe S. aureus is one of the most important pathogens.
- It causes a variety of infections in both pediatric and adult patients, from generally minor skin infections (boils and cellulitis) to life-threatening infections (endocarditis and sepsis).
- Because of its virulence and the widespread use of broad-spectrum antibiotics, S. aureus has developed resistance to many topical, oral and parenteral antibiotics.
Methicillin-Resistant Staphylococcus Aureus

Methicillin resistance is mediated by PBP-2a, a penicillin-binding protein encoded by the mecA gene that permits the organism to grow and divide in the presence of methicillin and other beta-lactam antibiotics.
MRSA...

- Involved in a wide range of community-acquired and nosocomial infections.

- The first isolates of MRSA were identified in hospitalized patients and hospital nursing staff in the early 1960s.

- Community-associated MRSA has become the most frequent cause of skin and soft tissue infections seen in emergency departments in the United States.
MRSA

It has become especially important in recent years because of its increasing prevalence in patients with **acute and chronic sinusitis** as well as its presence in the nasal mucosa of normal individuals.
Treatment options for MRSA sinonasal infections

- Topical antibiotics
- Oral antibiotics
- Intravenous antibiotics
Topical Antibiotics

- The topical route offers high local levels of drug with minimal systemic absorption, lower costs, and decreased morbidity.

- For MRSA rhinosinusitis, topical antibiotic therapy with mupirocin appears to be both safe and effective, and may replace oral and intravenous treatments in some patients.
MUPIROCIN.

- It is a topical anti-staphylococcal agent that inhibits RNA and protein synthesis.
- No known drug interactions and side effects are minimal (burning, pain, and stinging).
- The only contraindication to its use is a known hypersensitivity reaction.
- Prolonged use of the drug can lead to overgrowth of resistant organisms and superinfection.
Topical Mupirocin

- Solares and colleagues have shown encouraging data supporting the use of topical mupirocin nasal irrigations as an alternative to intravenous antibiotics in the treatment of acute exacerbations of CRS due to MRSA.

- Patients using mupirocin in sinus irrigations showed improved symptoms and reduced MRSA recovery on subsequent cultures.
Treatment of chronic rhinosinusitis exacerbations due to methicillin-resistant *Staphylococcus aureus* with mupirocin irrigations

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Abstract

**Introduction:** Chronic rhinosinusitis (CRS) exacerbations due to methicillin-resistant *Staphylococcus aureus* (MRSA) are routinely encountered. Treatment often involves intravenous antibiotics that provide only transient benefits. Mupirocin has well-recognized antistaphylococcal activity, and its nasal formulation is approved by the Food and Drug Administration for the eradication of nasal colonization with MRSA.

**Objective:** The aim of this study was to describe the use of mupirocin nasal irrigations for the treatment of CRS exacerbations due to MRSA.

**Materials and methods:** Charts of patients who received mupirocin nasal irrigations for MRSA exacerbations of CRS between January 2000 and October 2003 were reviewed.

**Results:** Forty-two MRSA-positive cultures were obtained from 24 patients (mean age, 61 years; range, 38–92 years; 15 women and 6 men). Twenty-eight episodes were treated with mupirocin nasal irrigations and doxycycline; 4 were treated with mupirocin nasal irrigations and trimethoprim-sulfamethoxazole, and 7 episodes were treated with mupirocin nasal irrigations alone. Patients were reevaluated at approximately 4 to 6 weeks. Repeat cultures were not obtained in 12 patients (because of clinical and endoscopic resolution). Adequate follow-up was unavailable for 3 patients, and of the 27 repeat cultures, only 1 grew MRSA. Twelve patients had at least one recurrence, with a mean number of episodes of 1.75 (range, 1–8 episodes). The mean follow-up was 11.8 months (range, 3–27 months).

**Conclusions:** Mupirocin nasal irrigations may avoid the need for intravenous antibiotics, which often provide temporary benefits and entail greater cost and morbidity. Thus, mupirocin nasal irrigations may provide a relatively simple means for the management of MRSA exacerbations of CRS.
Methodology..

- The results of endoscopic sinus cultures for CRS exacerbations performed in the clinic between January 2000 and October 2003 were reviewed.

- Patients with MRSA-positive sinus cultures obtained under endoscopic visualization in the outpatient rhinology clinic were identified.

- The charts of patients who received mupirocin nasal irrigations, either alone or in combination with either TMP/SMX or doxycycline were reviewed further.
Method..

- **42** MRSA-positive cultures were obtained from 24 patients
- **28** episodes were treated with mupirocin nasal irrigations and doxycycline (100 mg po bid, 4 weeks)
- **4** episodes were treated with mupirocin nasal irrigations and TMP/SMX DS (1 tablet po bid, 4 weeks)
- **7** episodes were treated with mupirocin nasal irrigations alone.
- **3** episodes were excluded from the analysis because of insufficient follow-up.
- Patients were reevaluated approximately **4 to 6** weeks after commencing treatment.
Result...

MRSA-positive cultures (n = 42)

- Insufficient follow-up (n = 3)
- Clinical & endoscopic resolution (n = 12)
- Symptomatic improvement
  - Endoscopic evidence of disease (n = 13)

  - Repeat cultures obtained
    - Negative (n = 5)
      - P. aeruginosa (n = 3)
      - S. maltophilia (n = 2)
      - MSSA (n = 2)
      - H. influenzae (n = 1)
    - Negative (n = 1)
      - Other (n = 9)
  - No repeat culture

- No improvement (n = 14)
  - Repeat cultures obtained
    - MRSA (n = 1)
The average length of follow-up was 11.8 months (range, 3–27 months).

12 patients had at least 1 recurrence of MRSA exacerbation, with a mean number of episodes of 1.75 (range, 1–8 episodes) for the overall series.

At the end of the study, only 1 patient remained MRSA-positive.
Oral antibiotics

- A study demonstrated that a 92% rate of resolution of MRSA sinusitis when treated with culture-directed oral and topical medications.

- Oral antibiotic choices are guided by susceptibility data, but typically include trimethoprim/sulfamethoxazole or clindamycin.
Successful outpatient treatment of sinusitis exacerbations caused by community-acquired methicillin-resistant Staphylococcus aureus

Roland Z. Gerencer

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Abstract

OBJECTIVE: To determine whether community-acquired MRSA sinusitis can be adequately treated on an outpatient basis without the need for intravenous antibiotics.

STUDY DESIGN AND SETTING: Retrospective review of all cases of community-acquired MRSA sinusitis encountered by the author over a 36-month period.

RESULTS: Of 29 patients who tested positive for MRSA sinusitis, 26 patients had follow-up information available and were retrospectively reviewed. The average follow-up period was 12.0 months (range: 1–36 mo). Twelve infectious episodes of MRSA were treated with oral antibiotics alone and 16 were treated with a combination of oral and topical antibiotics. The mean time to clinical resolution with these regimens was 5.7 weeks (range: 3–8 wks). Two patients experienced recurrent MRSA infections resulting in a recurrence rate of 7.7% and an overall resolution rate of 92.3%.

CONCLUSIONS: Community-acquired MRSA sinusitis can be very adequately treated on an outpatient basis with culture-directed oral and topical antibiotics.
OBJECTIVE:
To determine whether community-acquired MRSA sinusitis can be adequately treated on an outpatient basis without the need for intravenous antibiotics.

STUDY DESIGN AND SETTING:
- Retrospective review of all cases of community-acquired MRSA sinusitis encountered by the author over a 36-month period.

- There were 29 chronic sinusitis patients

- 3 patients were lost to follow-up, leaving 26 patients for inclusion in this study.
All cultures were obtained in the office setting or at one of 2 community outpatient surgery centers.

Office endoscopic cultures

(continued to display purulence on endoscopy after failing an empiric trial of at least 3 weeks of an appropriate oral antibiotic)

(Patients who were already on a broad-spectrum antibiotic at the time of presentation and who displayed symptoms of sinusitis)

All patients who displayed frank purulence at the time of endoscopic sinus surgery (ESS) underwent endoscopic intraoperative cultures.
RESULT..

- 32 community-acquired MRSA isolates from 29 patients during the review period.
- All except 1 of the 32 isolates of MRSA came from patients who had at least 1 endoscopic sinus operation in the past.
- An average of nearly 2 endoscopic sinus surgery procedures before the diagnosis of MRSA.
- 12 isolates of MRSA were encountered intra-operatively.
- 20 isolates were identified in the outpatient setting.
MRSA sinusitis was encountered throughout the postoperative period.

11 of the 26 (42%) patients followed were diagnosed with MRSA at or within 90 days of ESS.

The median time for detection postoperatively was 8 months.
Clinical resolution of MRSA sinusitis was determined by the patient’s symptoms and verified by in-office endoscopy.

Overall, the patients fared very well, with a mean time to clinical resolution of 5.7 weeks (range, 3-8 weeks).

All except 1 patient in this population was able to clinically clear the sinusitis exacerbation with a combination of oral and topical antibiotics.

There were no patients who failed this therapy for whom intravenous vancomycin would have been considered.
Result..

- Two patients experienced recurrent MRSA sinusitis
- An overall recurrence rate of 7.7%
- A clinical cure rate of 92.3%.
**Intravenous Antibiotics**

- Intravenous antibiotics are guided by susceptibility data.

- Chosen only in severe situations, as their efficacy in sinonasal situations is unclear, and long-term administration of parenteral antibiotics is associated with a moderate amount of morbidity.

- Tabaee et al. showed that 67% of patients experienced adverse events when treated with parenteral antibiotics for sinonasal MRSA infections.

**Outpatient intravenous antibiotics for methicillin-resistant Staphylococcus aureus sinusitis.**

Tabaei A¹, Anand VK, Yoon C.

[Author information]

**Abstract**

**BACKGROUND:** The widespread use of broad-spectrum antibiotics has resulted in an increase in the prevalence of methicillin-resistant Staphylococcus aureus (MRSA). Its presence in sinonasal cultures in patients with sinusitis suggests its pathogenicity. However, the efficacy and safety of treatment modalities for MRSA sinusitis remain incompletely described.

**METHODS:** A retrospective chart review of six patients treated for MRSA sinusitis with outpatient intravenous (i.v.) antibiotics was performed for patient demographics, history of antibiotic use, history of prior sinus surgery, and treatment-related complications. A quality-of-life survey and endoscopically guided cultures before and after therapy were used to measure treatment outcomes.

**RESULTS:** The cohort consisted of five women and one man with a mean age of 50.8 years. All patients had undergone multiple sinus procedures with a mean number of 2.7 procedures per patient (range, 1-6 procedures). Five patients (83.3%) experienced negative cultures after outpatient i.v. antibiotics. The single patient who had persistent cultures experienced clinical and endoscopic improvement in her symptoms. The quality-of-life scores improved in five of the six patients (83.3%) after therapy. Four patients (66.7%) experienced five adverse events including allergic reaction (four events) and neutropenia (one event), all of which resolved with a change in medication.

**CONCLUSION:** Outpatient i.v. antibiotics may be an effective therapy for the treatment of MRSA sinusitis. The occurrence of adverse events requires a dedicated protocol to therapy. Future studies are required to investigate long-term efficacy.
A retrospective review and quality-of-life survey was performed for patients who had undergone intravenous (IV) antibiotics November 2000 and September 2005. The diagnosis was based on a combination of clinical, endoscopic, radiographic, and culture findings.
METHODOLOGY..

- Endoscopically guided cultures were taken from the middle meatus in patients with mucopurulent discharge.

(1) In the office if the subjective symptoms and endoscopic findings persisted after a course of empiric oral antibiotics.

(2) At surgery if mucopurulent discharge was identified.
The cohort consisted of five women and one man with a mean age of 50.8 years.

All patients had undergone multiple sinus procedures with a mean number of 2.7 procedures per patient (range 1–6 procedures).

Based on sensitivities, patients received a **6- to 8-week** course of outpatient I.V antibiotic therapy.
- 5 patients (83.3%) experienced negative cultures after outpatient i.v. antibiotics.

- 1 patient had persistent cultures experienced clinical and endoscopic improvement in her symptoms.

- The quality-of-life scores improved in five of the six patients (83.3%) after therapy.

- 4 patients (66.7%) experienced 5 adverse events including allergic reaction (4 events) and neutropenia (1 event), all resolved with a change in medication.
Methicillin-Resistant Staphylococcus aureus Sinusitis in Nonhospitalized Patients: A Systematic Review of Prevalence and Treatment Outcomes

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METHODOLOGY

- MEDLINE, Embase, and Cochrane databases
- English-language..
- Studies published between 1942 and 2012...
- Studies were excluded (did not provide quantitative data on the prevalence or treatment of ARS or CRS with MRSA-positive cultures)..
The principal summary measures were prevalence of MRSA sinusitis and rate of resolution of MRSA after medical treatment.
Methodology.

409 records identified by search criteria; abstracts screened

349 records excluded (irrelevant to prevalence or treatment of MRSA sinusitis in non-hospitalized patients)

60 full-text articles assessed for eligibility

49 records excluded (did not report quantitative data)

1 article included from reference lists

12 studies included in qualitative synthesis
## Results

<table>
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<th>Study</th>
<th>Inclusion Criteria</th>
<th>Ages Included</th>
<th>Culture Site</th>
<th>MRSA-Positive Cases, n (%)</th>
<th>Prevalence of MRSA Among All Staphylococcus aureus Isolates, n (%)</th>
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</thead>
<tbody>
<tr>
<td>Brook et al., 2008</td>
<td>ARS, outpatient</td>
<td>Adults</td>
<td>MM</td>
<td>12/244 (4.9)</td>
<td>12/23 (52.1)</td>
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<tr>
<td>Huang and Hung, 2006</td>
<td>ARS, outpatient</td>
<td>All ages</td>
<td>MM</td>
<td>16/446 (3.6)</td>
<td>16/53 (30.2)</td>
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<td>Lin et al., 2012</td>
<td>ARS, outpatient</td>
<td>Children</td>
<td>Nasal cavity</td>
<td>11/69 (15.9)</td>
<td>11/16 (68.8)</td>
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<td>Tellez et al., 2006</td>
<td>ARS, outpatient</td>
<td>All ages</td>
<td>MM</td>
<td>0/136 (0)</td>
<td>0/9 (0)</td>
</tr>
<tr>
<td>Whitby et al., 2011</td>
<td>CA-SA positive culture at the time of ESS</td>
<td>Children</td>
<td>Sinus during ESS</td>
<td>—</td>
<td>12/56 (21.4)</td>
</tr>
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<tr>
<td>Brook et al., 2008</td>
<td>CRS, outpatient</td>
<td>Adults</td>
<td>MM</td>
<td>18/214 (4.4)</td>
<td>18/38 (47.4)</td>
</tr>
<tr>
<td>Damm et al., 2004</td>
<td>CRS, outpatient</td>
<td>Adults</td>
<td>MM</td>
<td>33/190 (17.4)</td>
<td>33/45 (73.8)</td>
</tr>
<tr>
<td>Genoway et al., 2011</td>
<td>CRS, outpatient</td>
<td>Adults</td>
<td>Nasal cavity or sinus</td>
<td>3/168 (1.8)</td>
<td>3/65 (4.6)</td>
</tr>
<tr>
<td>Jiang et al., 1999</td>
<td>CRS, prior ESS, outpatient</td>
<td>Adults</td>
<td>MM</td>
<td>17/82 (20.7)</td>
<td>13/30 (43.3)</td>
</tr>
<tr>
<td>Manarey et al., 2004</td>
<td>CRS, prior nasal culture, outpatient</td>
<td>Adults</td>
<td>MM</td>
<td>13/141 (9.2)</td>
<td>13/67 (19.4)</td>
</tr>
</tbody>
</table>

MRSA = methicillin-resistant Staphylococcus aureus; CRS = chronic rhinosinusitis; MM = middle meatus; ESS = endoscopic sinus surgery.

*Denominator is the number of positive cultures for any bacterium.
Treatment outcomes of MRSA Sinusitis

- 6 studies were identified
- 4 reported the treatment of CRS and 2 reported treatment of ARS.
- The percentage of infections that resolved with medical treatment ranged from 58.3% to 100%.
- Duration of treatment ranged from 2 to 7 weeks.
1 study limited the treatment to intravenous antibiotics.

3 studies used oral antibiotics alone.

2 studies used a combination of oral and topical antibiotics.

A range of antibiotics were utilized, most commonly including doxycycline, clindamycin, and sulfamethoxazole-trimethoprim.

Topical agents included mupirocin or aminoglycoside agents.
# Treatment outcomes of MRSA Sinusitis

<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion Criteria</th>
<th>Culture Site</th>
<th>Antibiotic</th>
<th>Route</th>
<th>Duration of Treatment</th>
<th>Outcome Measure</th>
<th>Resolution of Infection, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gerencer, 2005</td>
<td>CRS, adults, MRSA-positive culture, outpatient</td>
<td>Sinus in office or during ESS</td>
<td>Doxycycline, minocycline, TMP-SMX; gentamicin, tobramycin, mupirocin</td>
<td>Oral, topical</td>
<td>1–42 days</td>
<td>Clinical symptoms, endoscopy</td>
<td>24/26 (92.3), three lost to follow-up</td>
</tr>
<tr>
<td>Huang and Hung, 2006</td>
<td>ARS, outpatient</td>
<td>MM</td>
<td>Fusidic acid, cerfuroxime, TMP-SMX, amoxicillin-clavulanate, levofloxacin, clindamycin, pefloxacin</td>
<td>Oral</td>
<td>Not given</td>
<td>Clinical symptoms</td>
<td>14/14 (100), two lost to follow-up</td>
</tr>
<tr>
<td>Jiang et al., 1999</td>
<td>CRS, adults, prior ESS</td>
<td>MM</td>
<td>Pefloxacin, chloromycin, ofloxacin, clindamycin, amoxicillin</td>
<td>Oral</td>
<td>2–7 weeks</td>
<td>Clinical symptoms</td>
<td>13/17 (76.7)</td>
</tr>
<tr>
<td>Solares et al., 2006</td>
<td>CRS, MRSA-positive culture</td>
<td>Sinus in office</td>
<td>Mupirocin, doxycycline, TMP-SMX</td>
<td>Oral, topical</td>
<td>4 weeks</td>
<td>Culture, symptoms, endoscopy</td>
<td>25/39 (64.1), three lost to follow-up</td>
</tr>
<tr>
<td>Tabaei et al., 2007</td>
<td>CRS, adults, MRSA-positive culture, intravenous antibiotics</td>
<td>MM</td>
<td>Vancomycin + cefepime, vancomycin + levofloxacin, inezolid</td>
<td>Intravenous</td>
<td>Not given</td>
<td>Culture, SNOT-20</td>
<td>6/6 (100)</td>
</tr>
<tr>
<td>Whitby et al., 2011</td>
<td>Non-hospital-acquired sinusitis, children, <em>Staphylococcus aureus</em>-positive culture at the time of ESS</td>
<td>Sinus during ESS</td>
<td>Not given</td>
<td>Oral</td>
<td>Mean 11.3 days (SD 4.6 days)</td>
<td>Culture, symptoms, imaging</td>
<td>7/12 (58.3)</td>
</tr>
</tbody>
</table>
A potential new antibiotic to combat MRSA

Andreas Peschel and colleagues at the University of Tübingen, Germany. report:

- The potential new soldier in the fight against MRSA is a molecule called lugdunin.
- Produced by the bacterium *Staphylococcus lugdunensis*.
- They screened 90 bacteria from the human nose, and found that only *S. lugdunensis* killed MRSA.
Lugdunin
In a sampling of 187 hospital patients, people whose noses naturally contained *S. lugdunensis* were six times less likely to have *S. aureus* than people whose noses lacked *S. lugdunensis*.

This suggests that *S. lugdunensis* is able to combat the growth of the problematic bacterium.
Peschel’s team infected the skin of mice with *S. aureus*

Lugdunin ointment killed the infection both on the surface and in deeper layers of the skin.

*S. lugdunensis* also reduced the amount of *S. aureus* when squirted into the noses of cotton rats.

They are currently talking to companies interested in developing lugdunin as a drug for human use..
Conclusion..

Aggressive medical measures on an outpatient basis combining oral and topical antibiotics for (2-8 weeks) with serial endoscopy and cultures can provide very satisfactory outcomes.
Thank you for your attention!