Tea Tree Oil as an Agent for MRSA Decolonization

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Abstract
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**First Advisor**
Annjanette Sommers

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Tea Tree Oil as an Agent for MRSA Decolonization

Andrea Kremsreiter

A Clinical Graduate Project Submitted to the Faculty of the
School of Physician Assistant Studies
Pacific University
Hillsboro, OR
For the Masters of Science Degree, August 13, 2016

Faculty Advisor: Brent Norris, PA-C, MS
Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS
Biography

[Redacted for privacy]
Abstract

Background: MRSA infections are a significant cause of morbidity and mortality worldwide. Due to concerns about increasing antibiotic resistance, alternative therapies are being considered to prevent and treat MRSA infections. Tea tree oil preparations have been shown to have antimicrobial properties, including against MRSA, in in vitro studies. The purpose of this review is to investigate the effects of topical tea tree oil preparations as an eradication agent for patients colonized with MRSA.

Methods: An exhaustive online medical literature search was conducted using MEDLINE-Ovid, Web of Science, and CINAHL using the keywords: MRSA and tea tree oil. Eligible studies were assessed using the GRADE system.

Results: Two randomized controlled trials met inclusion criteria for this systematic review. One RCT (N=224) found that tea tree oil preparations were effective as MRSA eradication regimens, although slightly less effective than the routine treatment regimen. Another study (N=30) found that topical tea tree oil preparations were more effective than routine treatment regimens in decolonizing patients with MRSA, although the results were not statistically significant due to small patient sample size.

Conclusion: Tea tree oil has been shown to have activity against MRSA both in vivo and in vitro. However, studies investigating the use of tea tree oil as agent for MRSA decolonization do not provide strong enough evidence for its induction into universally used treatment regimens. Tea tree oil is safe and well tolerated by patients and can be considered as an alternative agent to eradicate MRSA from patients who are unable or unwilling to follow current standard of care treatment regimens.

Keywords: MRSA, tea tree oil
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Table I: Summary of Findings
Table II: Quality Assessment of Reviewed Articles

List of Abbreviations

MRSA……………………………………..Methicillin resistant Staphylococcus aureus
MSSA……………………………………Methicillin susceptible Staphylococcus aureus
HA-MRSA……………Healthcare-associated methicillin resistant Staphylococcus aureus
HA-MSSA………..Healthcare-associated methicillin susceptible Staphylococcus aureus
Tea Tree Oil as an Agent for Decolonization of MRSA

BACKGROUND

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a significant pathogen causing considerable morbidity and mortality worldwide. A 2011 report from the United States Center for Disease Control (CDC) estimates that there were 80 461 invasive MRSA infections and 11 285 MRSA related deaths annually.¹ These numbers, coupled with concerns about increasing antibiotic resistance, have led researchers to consider alternative agents including plant derived oils, like tea tree oil, in the fight against MRSA.

*Staphylococcus spp.* are common colonizers of human skin. Of those species, *S. aureus* is the most virulent.² *S. aureus* can cause skin and soft tissue infections, such as furuncles, but can also cause more invasive illnesses such as osteomyelitis, pneumonia, urinary tract infections, bacteremia, and sepsis which can lead to death.¹ It is estimated that 10-30% of the general population carries *S. aureus* in the anterior nares² and 7% of US hospital patients are colonized with MRSA.³ Many carriers are asymptomatic but are at a higher risk of invasive infection due to autoinoculation. These carriers many also unknowingly spread the bacteria to those they are in direct contact with. Moreover, *S. aureus* can survive periods of drying.² As such, people are at risk of colonization if they come in contact with contaminated fomites.

Strains of *S. aureus* developed resistance to methicillin shortly after its induction in use in the 1960s.⁴ The term MRSA is now used to describe strains of *S. aureus* that are resistant to beta lactam antibiotics, including methicillin, oxacillin, nafcillin, and
dicloxacillin, as well as cephalosporins. It is this continuously developing antibiotic resistance that makes MRSA a public health threat worldwide.

Healthcare-associated MRSA (HA-MRSA) is a particularly heavy burden for both patients and the healthcare system alike. A meta-analysis found patients with HA-MRSA bacteremia had a twofold greater risk of death compared to patients with healthcare-associated methicillin susceptible S. aureus (HA-MSSA) bacteremia. Further studies have concluded that patients infected with MRSA require longer intensive care stays and have increased ventilator dependency. In addition to increased patient morbidity and mortality, HA-MRSA infections are of concern due to the financial burden it places on healthcare systems. Patients afflicted with MRSA bacteremia have a 1.29 fold increase in length of hospitalization and a 1.36 fold increase in hospital charges compared to patients with MSSA bacteremia.

The increasing concern about antibiotic resistance has cultivated interest in the use of complementary medicines, such as plant-derived oils like tea tree oil. Tea tree oil is a volatile essential oil produced by the Australian plant Melaleuca alternifolia. Tea tree oil has been shown to have a number of antimicrobial effects in vitro, which are mainly attributed to the compound terpinen-4-ol. This in vitro research has led some to consider its application as an agent for the eradication of MRSA in patients colonized with the pathogen.

The intent of this review is to determine whether tea tree oil products can be used as an effective means for decolonizing MRSA carriers. Due to the very serious threat antibiotic resistant organisms place on public health, new drugs and treatments must be
sought if we wish to prevent transmission and improve associated morbidity and mortality.

**METHODS**

An exhaustive literature search using MEDLINE-Ovid, Web of Science, and CINAHL was performed and used the following search terms: “MRSA” and “tea tree oil.” Inclusion/exclusion criteria was applied. Included were human studies evaluating tea tree oil as an agent for MRSA decolonization compared to standard of care decolonization regimens. Studies focusing on tea tree oil as an agent of decolonization of MRSA wounds were further excluded, as the purpose of this review is to evaluate its effect on the carriage of MRSA. Studies were excluded if they were not published in the English language. Studies meeting these eligibility criteria were analyzed for quality using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system.⁹

**RESULTS**

The initial search of the abovementioned databases yielded 78 articles for review. After applying the eligibility criteria, two relevant articles were identified. These articles are randomized controlled trials assessing the use of tea tree oil as a decolonization agent for MRSA.¹⁰,¹¹ See Table I.

**Dryden et al**

Dryden et al¹⁰ published their randomized controlled trial evaluating the application of tea tree oil in the eradication of MRSA colonization. Patients at the participating hospital who were colonized with MRSA were considered for this study. Those excluded from the study included patients unable to give informed consent,
sensitive to tea tree oil, under the age of 16, pregnant, or breastfeeding. Two hundred thirty six patients were enrolled in the study, but 12 were lost to follow-up. Thus, 224 patients were evaluated. Study participants were randomly allocated to receive routine care or intervention care. The routine care regimen was defined by Dryden et al as mupirocin 2% nasal ointment applied to the anterior nares three times a day for five days, chlorhexidine gluconate 4% soap applied all over the body at least once a day for five days, silver sulfadiazine 1% cream to skin lesions, wounds, leg ulcers once a day for five days. The intervention care regimen was defined by Dryden et al as tea tree 10% cream applied to the anterior nostrils three times a day for five days; tea tree 5% body wash all over the body at least once a day for five days; tea tree 10% cream to skin lesions, wounds and ulcers, and also to axillae or groins as an alternative to the body wash. MRSA detection was accomplished with swabs of the nose, throat, axillae, groin creases, and open skin lesions prior to treatment, day 2 post treatment, and day 14 post treatment. Positive detection of MRSA in any site was defined as failure to clear MRSA. Upon completion of the trial, 56 (49%) patients in the routine care group and 46 (41%) patients in the tea tree oil treatment group were decolonized of MRSA. No significant difference between treatment regimens was present (P=0.0286 Fisher’s exact test). The effects of the respective treatment regimens on nasal carriage were analyzed separately. Dryden et al determined that mupirocin 2% nasal ointment is significantly more effective at clearing nasal carriage of MRSA than tea tree 10% cream (P=0.0001
Fisher’s exact test). Fifty eight (78%) of the 74 routine care patients with nasal MRSA colonization were cleared with the mupirocin treatment. Thirty six (47.3%) of the 76 tea tree oil intervention patients with nasal MRSA colonization were cleared with the tea tree cream treatment.  

**Caelli et al**

This randomized controlled trial was undertaken as a pilot study to determine the efficacy of tea tree oil in the decolonization of MRSA. In this study, 30 adult inpatients either infected or colonized with MRSA were randomly allocated to receive routine care or intervention care. Routine care was defined as 2% mupirocin nasal ointment and triclosan bodywash. Intervention care was defined as 4% tea tree oil nasal ointment and 5% tea tree oil body wash. IV vancomycin was administered to all infected patients. Study participants were instructed to follow their prescribed regimen for a minimum of three days. Screening samples were obtained at 48 and 96 hours post completion of the treatment regimen from patients’ nares, perianal region, and any site known to be previously MRSA positive.

In this study, the tea tree oil intervention was more effective in clearing MRSA than the routine care regimen. Five patients (33%) in the tea tree oil treatment group were cleared of MRSA compared to two patients (13%) in the routine care regimen. Due to the limited size of this study, these results do not indicate a significant difference in outcomes. Seven patients (47%) in the tea tree oil treatment group and 5 patients (33%) in the routine care regimen failed to complete this trial for unspecified reasons.
DISCUSSION

Increasing resistance to current antibiotics has led to the consideration of alternative therapies to control and prevent MRSA infections. *In vitro* studies have demonstrated the bactericidal activity of tea tree oil against MRSA. The next step in identifying the utility of tea tree oil as an agent for decolonization of MRSA would be *in vivo* human randomized controlled trials. This review analyzed two such randomized controlled trials.\textsuperscript{10,11} Although the overall quality of these two studies is low (see Table II), there is some evidence of efficacy of tea tree oil as an agent for decolonization of MRSA and further studies are warranted.

**Limitations of Study – Dryden et al**

Dryden et al\textsuperscript{10} published a randomized controlled trial comparing a tea tree oil intervention regimen with a routine care treatment regimen as described above. This study had some limitations that should be kept in consideration when analyzing the outcomes. This study had an adequate sample size and well-described, comparable treatment regimens. However, compliance to the treatment regimen was not closely monitored and relied on nursing staff and patients to report any problems with delivery of the treatment regimen.

**Limitations of Study – Caelli et al**

The randomized controlled trial published by Caelli et al\textsuperscript{11} determined that 4% tea tree nasal ointment and 5% tea tree body wash was more effective at eradicating MRSA than the routine care regimen of 2% mupirocin nasal ointment and triclosan body wash. However, the population size (N=30) was inadequate to determine statistical significance. Further lowering this quality of evidence was significant loss to follow-up. Seven patients
(47%) in the tea tree oil treatment group and 5 patients (33%) in the routine care regimen failed to complete this trial for unspecified reasons. It is unclear whether blinding was utilized for this study, but because discrete endpoints (eradication of MRSA) were used, this does not greatly impact the quality of evidence. Also of note, this study was sponsored in part by Australian Bodycare Pty Ltd; this company manufactured the tea tree oil products used in the study. Because the endpoints of the study are discrete, the risk of bias from this factor is limited and of little concern. Further aspects to consider when evaluating the quality of evidence from this study include the disparity in treatment days. All patients were instructed to use their prescribed treatment regimen for a minimum of three days, but the endpoint varies considerably. The average number of treatment days in the routine care group was 5.6 days (range = 2-14). The average number of treatment days in the tea tree oil intervention group was 10.7 days (range = 1-34). Compliance monitoring protocol was omitted from this article.11

**Further discussion**

Due to the low quality of evidence presented in these studies, tea tree oil treatment regimens should not replace the current routine care interventions. However, these studies do demonstrate that tea tree oil topical preparations may have similar efficacy to routine care regimens in eradicating MRSA colonization. The tea tree oil treatment regimens were well tolerated among participants in both studies and no adverse reactions were observed.10,11 Based on this evidence, tea tree oil preparations may be appropriate for patients unable or unwilling to use routine care regimens (mupirocin, triclosan, chlorhexidine gluconate, and/or silver sulfadiazine).
Due to the limitations of these studies, further research is required to establish tea tree oil’s place as an agent of decolonization of MRSA. Large scale, randomized controlled trials with explicit treatment protocols and compliance monitoring would be ideal in order to definitively identify tea tree oil as an agent for the eradication of MRSA colonization.

Currently mupirocin and chlorhexidine gluconate are the current standard agents for MRSA decolonization. However, in the United States, MRSA decolonization is not routinely recommended in asymptomatic carriers with low risk of transmission due to concerns of efficacy and growing antibiotic resistance. Studies have demonstrated evidence of MRSA strains that have developed resistance to mupirocin and chlorhexidine gluconate. These concerns justify further studies on the efficacy of tea tree oil as an agent of MRSA decolonization. It is evident that new treatments must be sought and established if we wish to quell the onslaught of MRSA carriage and infection.

CONCLUSION

Due to the significant burden antimicrobial resistant pathogens place on individuals’ health and our healthcare system as a whole, new drugs and therapies must be explored and implemented into standards of care. Tea tree oil has been shown to have bactericidal activity against MRSA in in vitro studies. This review analyzed data from randomized controlled trials conducted in human patients colonized or infected with MRSA. Based on the data in those trials, tea tree oil may be considered as an alternative agent for the decolonization of MRSA. However, the low quality of evidence in those trials necessitates the need for further studies to determine the efficacy of the tea tree oil based treatment regimen.
References


### Table I: Summary of Findings

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study Design</th>
<th>Patient Population</th>
<th>Group</th>
<th>Number of Patients</th>
<th>Number of Patients with Nasal Carriage of MRSA</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Dryden et al</td>
<td>Randomized Controlled Trial</td>
<td>Inpatients 16 years or older infected or colonized with MRSA</td>
<td>5, Tea tree oil treatment regimen</td>
<td>110</td>
<td>46 (41%)</td>
<td>Patients cleared of MRSA carriage</td>
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<tr>
<td></td>
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<td>76</td>
<td>36 (47.3%)</td>
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<td>Patients cleared of nasal carriage of MRSA</td>
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<td></td>
<td>Routine care treatment regimen</td>
<td>114</td>
<td>56 (49%)</td>
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<td>74</td>
<td>58 (78%)</td>
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<td>P = 0.0286</td>
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<td>P = 0.0001</td>
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<table>
<thead>
<tr>
<th>Authors</th>
<th>Study Design</th>
<th>Patient Population</th>
<th>Group</th>
<th>Number of Patients</th>
<th>Average patient age (years)</th>
<th>Average Treatment Duration (days)</th>
<th>Outcomes</th>
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<td>Adult inpatients infected or colonized with MRSA</td>
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<td>58 (range = 28-82)</td>
<td>10.7 (range = 1-34)</td>
<td>Patients cleared of MRSA carriage</td>
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<td>Routine care treatment regimen</td>
<td>15</td>
<td>74 (range = 45-87)</td>
<td>5.6 (range = 2-14)</td>
<td>Patient loss to follow up</td>
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*P*-value

- *P* = 0.0286
- *P* = 0.0001
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<td>Indirectness</td>
<td>Inconsistency</td>
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<td>Dryden et al\textsuperscript{10}</td>
<td>RCT</td>
<td>Serious\textsuperscript{a}</td>
<td>Not Serious</td>
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<td>RCT</td>
<td>Very Serious\textsuperscript{c,e}</td>
<td>Not Serious</td>
<td>Not Serious\textsuperscript{d}</td>
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\textsuperscript{a}Blinding procedure not mentioned.  
\textsuperscript{b}Tea tree oil preparations by Ord River Tea Tree Oil Ptd Ltd.  
\textsuperscript{c}Large loss to followup.  
\textsuperscript{d}Confidence intervals were not calculated for this article.  
\textsuperscript{e}Small sample size  
\textsuperscript{f}This study was sponsored in part by Australian Bodycare Pty Ltd