Is Tea Tree Oil Preparation an Effective Topical Therapy for Patients with MSRA Colonized Wounds?

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Is tea tree oil preparation an effective topical therapy for patients with MRSA colonized wounds?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW
In Partial Fulfillment of the Requirements for
The Degree of Master of Science
In
Health Sciences-Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

December 16, 2016
ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not tea tree oil preparation an effective topical therapy for patients with MRSA colonized wounds.

STUDY DESIGN: This review is based on three randomized controlled trials (RCTs) published in 2004, 2013, and 2014. These studies compared the efficacy of tea tree oil (TTO) topical preparations in MRSA colonized wounds.

DATA SOURCES: All articles used were published in English, in peer-reviewed journals, and found using PubMed and Cochrane Review databases.

OUTCOMES MEASURED: The efficacy of tea tree oil preparations on MRSA colonized wounds were evaluated by using data from conventional wound cultures and wound measurements during and post treatments.

RESULTS: Dryden et al. (2004) found no significant difference between the two treatment regimens (TTO vs Standard Treatment) when all patients and colonized sites were taken into consideration. Blackwood et al. (2013) determined that washing patients with 5% TTO body wash had no significant effect on the incidence of MRSA colonization in comparison to Johnson’s Baby Wash. On the contrary, Lee et al. (2014) found 10% TTO preparation was successful in eliminating MRSA from colonized wounds. It was also determined that 10% TTO preparation was successful in the recovery of chronic wounds that showed a delay in healing.

CONCLUSIONS: Results from two of the three studies demonstrate that there is no significant difference in wound outcome for patients treated with TTO preparations versus standard treatment methods. To further investigate whether TTO results is an effective topical therapy for MRSA colonized wounds comparative studies with a larger sample size are needed.

KEY WORDS: Tea tree oil, MRSA, wounds, colonization, eradication, humans
Introduction

Over the past three decades, tea tree oil (TTO) has claimed to have an antibacterial, analgesic, and anti-inflammatory effects against Methicillin-resistant Staphylococcus aureus (MRSA).\(^1\) At a concentration of 5%, reflecting the typical concentration of available solutions, TTO is known to kill MRSA.\(^2\) TTO is also a popular “natural” antiseptic, suggesting that this agent may be useful for skin antisepsis.\(^3\) It is standard practice to attempt to clear MRSA with topical antimicrobials and antiseptics, however, with an increase in usage of these agents, patients are becoming more resistant to typical treatments.\(^3\)

This topic is relevant to patients and the PA practice because wound colonization with MRSA is associated with high mortality in critically ill adults.\(^2\) Of these critically ill adults with MRSA colonized wounds, 60% subsequently develop a MRSA infection in the ICU setting.\(^2\) As a health care provider, it is our role to provide clinical interventions that will decrease the mortality of patients. With a vast majority of ICU patients being affected with MRSA, it is imperative to provide treatments that will decrease the likelihood of infecting other patients and providers within the hospital setting.

The clinical spectrum of MRSA infection can range from asymptomatic colonization, to skin and soft tissue infection, to life-threatening invasive infection.\(^4\) Patients affected by colonization serve as a reservoir for transmission to others. Colonization can occur from contact with contaminated wounds or dressing of infected individuals, contact with another individual’s colonized intact skin, contact with contaminated inanimate objects, and inhalation of aerosolized droplets from chronic nasal carriers.\(^4\) MRSA can also be transmissible though contact with medical equipment such as tourniquets, stethoscopes, and blood pressure cuffs.\(^4\) As a future PA
this is imperative because it illustrates how health care providers could inadvertently contribute to the colonization of MRSA in patients they provide care to.

As the field of healthcare expands the cost of clinical interventions for patients continue to rise. National data indicate that hospitalizations for MRSA infection have increased 119% from 1999 through 2005. The median 6 months unadjusted cost for patients infected with MRSA was $34,657 in 2005. Patients infected with MRSA spent more days hospitalized, received more laboratory tests, imaging tests, physical medicine and rehabilitation services which lead to increased medical bills.

Staphylococcus Aureus bacteria is one of the most common causes of skin infections in the United States. In 2014, the CDC reported 72,444 incidents of invasive MRSA infections. MRSA refers to types of staph that are resistant to a type of antibiotic methicillin. MRSA can disrupt normal wound healing process, leading to prolonged wound healing. Staph and MRSA can cause an assortment of problems such as skin infections, sepsis, pneumonia, and bloodstream infections.

The methods used to treat MRSA colonized wounds depend on the institution, but frequently include combinations of the following: nasal mupirocin, chlorhexidine body wash, Johnson’s Baby Softwash, silver sulfadiazine 1% cream, and saline gauze dressing. TTO preparations are being proposed as a treatment method for MRSA-colonized wounds because of its known effectiveness as an antimicrobial and skin antiseptic. TTO has been used for decades for other skin conditions such as furuncles, superficial fungal infections, anaerobic vaginitis, and eradication of head lice. Due to the success TTO had with other medical conditions and proven ability to kill MRSA, it is hypothesized that TTO can have the same success with MRSA colonized wounds. MRSA is known to be resistant to numerous antibiotics, so providing an
alternative method that is not resistant such as TTO could offer an improved treatment for wounds.6

Objective

The objective of this selective EBM review is to determine whether or not tea tree oil preparation is an effective topical therapy for patients with MRSA colonized wounds.

Methods

Three randomized controlled trials were included in this systematic review. Articles for this review were selected based on the population studied, TTO as the primary intervention, and outcomes measured. In all three studies, the population consisted on men and women 16 and older who had wounds colonized with MRSA. These studies all used TTO preparations at varying concentrations to intervene against MRSA colonized wounds. Dryden et al. (2004) selected a TTO regimen which consisted of 10% tea tree cream and 5% tea tree body wash compared to the standard treatment regimen. The standard regimen comprised 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, and silver sulfadiazine 1% cream to skin lesions, wounds, leg ulcers once a day for five days.3 The TTO regimen comprised 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.3 Blackwood et al. (2013) utilized 5% TTO body wash (Novabac skin wash) compared to Johnson’s Baby Softwash where patients had at least one full bed bath daily with the allotted wash.2 Lee et al. (2014) utilized 10% TTO preparation compared to standard non-adhesive dressings. In the TTO group, the wound was cleansed gently with 0.9% normal saline
to remove any debris and loose necrotic tissue, then 10% topical tea tree preparation applied onto the wound surface.\textsuperscript{1} In the comparison group, wounds were cleansed with 0.9% normal saline before they were covered by a non-adhesive pad.\textsuperscript{1}

Articles were researched via Pubmed and Cochrane Review databases. Selection of articles was based on relevance to the clinical question, randomized controlled trials format, and included patient-oriented outcomes (POEMS). Keywords entered included “MRSA,” “colonized wounds,” “tea tree oil,” and “humans.” All selected studies were English language peer-reviewed journal articles published in 2004-2014. Inclusion criteria for this systematic review include primary literature published between 2000-present, addressed outcomes that matter to patients (POEMS), and evaluated the efficacy of TTO as a topical therapy for MRSA-colonized wounds as a measured outcome. Exclusion criteria included previous Cochrane reviews, previous students published systematic reviews, and wounds that were not MRSA colonized. Specific exclusion criteria for each study is listed below in Table 1. Statistics reported in the Dryden et al. (2004) and Lee et al. (2014) study include RBI, ABI, NNT, and p-value. Statistics for Blackwood et al. (2013) include standard deviation, t-test values, and p-value. See Table 1 below for Demographics and Characteristics of Included Studies.
### Table 1 - Demographics & Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th># Patients</th>
<th>Age (years)</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
<th>Withdrawal</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee ¹ (2014)</td>
<td>RCT, single-blind study</td>
<td>32</td>
<td>Mean age of control pt 79.4 yo (+/- 6.9) Mean age to TTO group 81 yo (+/- 7.6)</td>
<td>All patients with open chronic wounds with positivity in MRSA wound culture. If the pt had multiple wounds, the largest wound was used.</td>
<td>Patients suffering from peripheral vascular disease, using systemic or topical antimicrobial treatment, having clinical signs of infection, and more than 105 MRSA bacteria per gram of wound tissue being detected from the MRSA wound surface culture. Wounds with undermining or tunneling and known sensitivity to tea tree oil.</td>
<td>0</td>
<td>10% Topical tea tree oil preparation dressing vs. standard non-adhesive dressings</td>
</tr>
<tr>
<td>Blackwood ² (2013)</td>
<td>RCT</td>
<td>445</td>
<td>18+</td>
<td>All patients colonized with MRSA were eligible for inclusion</td>
<td>Patients who were less than 18 years of age; were pregnant; were known to be colonized with MRSA on admission; were unlikely to remain in the ICU for at least 48h; were known to have sensitivity to TTO; declined consent; were readmissions; or were enrolled in another trial of an Investigate Medicinal Product (or within the previous 30 days)</td>
<td>54</td>
<td>5% tea tree oil body wash (Novabac 5% Skin wash) vs. Johnson’s Baby Softwash</td>
</tr>
<tr>
<td>Dryden ³ (2004)</td>
<td>RCT</td>
<td>224</td>
<td>16+</td>
<td>All patients colonized with MRSA were eligible for inclusion</td>
<td>Patients who were unable to give informed consent; known to be sensitive to tea tree oil; under the age of 16; pregnant or breastfeeding.</td>
<td>0</td>
<td>Mupirocin 2% nasal ointment, chlorhexidine gluconate 4% soap, and silver sulfadiazine 1% cream vs. tea tree oil regimen of tea tree 10% cream and tea tree 5% body wash</td>
</tr>
</tbody>
</table>
Outcomes Measured

The outcome measured in this study was the efficacy of TTO preparation for the eradication of MRSA.\textsuperscript{1,2,3} Dryden et al. (2004) measured this outcome via swab for MRSA detection collected from the nose, throat, axillae, groin creases, and any open skin lesions before starting treatment, after the second day, and day 14 post treatment.\textsuperscript{3} Lee et al. (2014) achieved the outcome by taking 5 measurements for MRSA bacterial count and wound healing condition at baseline and 1 week intervals during the 4 week intervention period.\textsuperscript{1} Wounds were measured via the Pressure Ulcer Scale for Healing (PUSH) tool 3.0 and MRSA colonization determined via wound culture with a sterile swab stick on the surface of wounds.\textsuperscript{1} Blackwood et al. (2013) study used new MRSA colonization during the inpatient episode in ICU, defined as detection of MRSA by conventional culture methods in screening swabs of nose and groin, or in clinical specimens processed by the laboratory during clinical care to measure the efficacy of TTO preparations.\textsuperscript{2} Blackwood et al. (2013) also examined the incidence of MRSA bacteremia and maximum increase in sequential organ failure assessment (SOFA) score with reference to baseline assessment to determine the efficacy of TTO preparation for MRSA-colonized wounds.\textsuperscript{2}

Results

All three studies were performed using the methods previously outlined. Dryden et al. (2004) study consisted of 224 participants in a hospital setting.\textsuperscript{3} Non-eligible participants included those unable to give informed consent, known to be sensitive to TTO, under age of 16, pregnant or breastfeeding.\textsuperscript{3} Treatment regimens and participant compliance were not closely monitored by the investigating team.\textsuperscript{3} Of the 114 participants that received standard treatment, 56 (49%) were cleared of MRSA.\textsuperscript{3} The remaining 110 participants that received TTO regimen 46 (41%) were cleared of MRSA.\textsuperscript{3} For both groups the p-value was 0.0286, meaning both treatment group has
statistically significant results. Mupirocin nasal ointment performed better than 10% tea tree oil in nasal decolonization, while tea tree oil performed better than chlorhexidine in decolonizing the skin lesions.\(^3\) There were no incidents of adverse effects or treatment intolerance reports for the nurses or patients. Table 2 summarize the results and efficacy of the Dryden et al. (2004) study.

Lee et al. (2014) study consisted of 32 participants recruited from two non-government nursing homes.\(^1\) Participants excluded from the study included those with known sensitivity to TTO or its major components, peripheral vascular disease, using systemic or topical antimicrobial treatment, having sign of clinical infection, and more than 105 MRSA bacteria per gram of wound tissue being detected from the surface culture.\(^1\) Investigators did not report compliance within the study. Throughout the five week duration of the study, TTO group had a decrease in the mean viable count of MRSA.\(^1\) Compared with the baseline, viable MRSA in wounds at the first, second, third, and fourth weeks was reduced by 36%, 66%, 93% and 98%, respectively.\(^1\) In contrast, an increase in the mean viable count of MRSA was noted in the control group.\(^1\) Compared with the baseline control group result, viable MRSA at the first, second, third, and fourth measurements was increased by 26%, 39%, 53% and 60%, respectively.\(^1\) To identify the significant difference in MRSA eradication between the treatment groups one-way ANOVA was used which revealed a statistically significant difference in treatment methods.\(^1\) (See Table 3)

To determine the outcome of wound measurement, PUSH scores were used. A decline in PUSH scores was noted in the TTO group with complete wound healing observed at week four. Compared with baseline the percentage decreased at the first, second, third, and fourth measurements were 30.4%, 31.6%, 87%, and 100% respectively.\(^1\) Within the control group, complete wound healing did not occur, but PUSH scores decreased. Compared to the baseline
control group measurement, the wound size decreased 6.2%, 8.6%, 17.3%, and 43.2% respectively.¹ To identify the significant difference in wound healing between the treatment groups one-way ANOVA was used which revealed a statistically significant difference in treatment methods.¹ (See Table 4). Table 2 summarizes the results and efficacy of the Lee et al. (2014) study. There were no adverse effects reported throughout the study.

Table 2: Efficacy of TTO preparation on MRSA colonized wounds

<table>
<thead>
<tr>
<th>Study</th>
<th>Proportion of patients having improvement on standard treatment (CER)</th>
<th>Proportion of patients having improvement on TTO preparations (EER)</th>
<th>Relative benefit increase (RBI)</th>
<th>Absolute benefit increase (ABI)</th>
<th>Number needed to treat (NNT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dryden</td>
<td>31%</td>
<td>47%</td>
<td>51.6%</td>
<td>16%</td>
<td>7</td>
</tr>
<tr>
<td>Lee</td>
<td>60%</td>
<td>98%</td>
<td>0.633%</td>
<td>38%</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 3: One-way ANOVA comparing the control and TTO groups regarding quantity of MRSA

<table>
<thead>
<tr>
<th>Date recorded</th>
<th>F (1,30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>2.08</td>
<td>0.159</td>
</tr>
<tr>
<td>Week 1</td>
<td>31.8</td>
<td>≤0.001</td>
</tr>
<tr>
<td>Week 2</td>
<td>108</td>
<td>≤0.001</td>
</tr>
<tr>
<td>Week 3</td>
<td>197.6</td>
<td>≤0.001</td>
</tr>
<tr>
<td>Week 4</td>
<td>178.3</td>
<td>≤0.001</td>
</tr>
</tbody>
</table>

Table 4: One-way ANOVA comparing the control and TTO groups regarding quantity of MRSA

<table>
<thead>
<tr>
<th>Date recorded</th>
<th>F (1,30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.59</td>
<td>0.810</td>
</tr>
<tr>
<td>Week 1</td>
<td>9.37</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Week 2</td>
<td>40.81</td>
<td>0.000</td>
</tr>
<tr>
<td>Week 3</td>
<td>80.67</td>
<td>0.000</td>
</tr>
<tr>
<td>Week 4</td>
<td>71.60</td>
<td>0.000</td>
</tr>
</tbody>
</table>
Blackwood et al. (2013) study consisted of 391 patients, 196 assigned to JBS group and 195 in the TTO group. All patients were eligible for inclusion except those who: were less than 18 years of age, were pregnant, were known to be colonized with MRSA on admission, were unlikely to remain in the ICU for at least 48 hours, were known to have sensitivity to TTO, declined consent, were readmissions, or were enrolled in another trial of Investigative Medicinal Product (or within the previous 30 days). At admission 445 patients were eligible for inclusion, however 30 patients withdrew because of positive MRSA screen, 9 legal representatives declined consent, and 11 patients were inappropriately randomized to the study. Throughout the study, two additional patients were withdrawn due to adverse events, a rash that was determined to be unrelated to body wash, and two patients declined consent. The study settings were two ICUs and the patients presented with negative MRSA screening at admission. Investigators did not follow compliance within the study. To determine the variance in MRSA colonization between the TTO and Johnson’s Body Softwash groups the investigators calculated the percentage difference using Fisher’s exact test and 95% confidence intervals. Throughout the study, a total of 39 patients, 22 JBS participants, and 17 TTO participants developed new MRSA colonization. The difference in the percentage colonized was determined to be insignificant (see Table 3). There was no significant difference in the mean maximum increase in SOFA score between groups, and no participants developed MRSA bacteremia. (See table 4)

Table 3: New MRSA Colonization

<table>
<thead>
<tr>
<th>Patients with new MRSA colonization</th>
<th>Percentage Difference TTO vs. JBS group</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5%</td>
<td>(-8.95, 3.94)</td>
<td>0.50</td>
<td></td>
</tr>
</tbody>
</table>
Table 4: SOFA Scores

<table>
<thead>
<tr>
<th></th>
<th>Sofa Score</th>
<th>Standard Deviation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>JBS Group</td>
<td>1.44</td>
<td>1.92</td>
<td>0.85</td>
</tr>
<tr>
<td>TTO Group</td>
<td>1.28</td>
<td>1.79</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

TTO is a known antimicrobial, antisepsis, and anti-inflammatory product used for skin disorders. However, there is limited published evidence on the value and use of TTO in a contemporary medical setting. Common limitations to all three studies were the small sample sizes, compliance not being measured throughout the studies, and short length of the clinical trials. For example in the Blackwood et al. (2013) study, it would have taken investigators 9 years to recruit the desired sample size because the average accrual rate was only 19 patients per month. Due to the limited sample size of this study investigators were unable to answer the question of the effectiveness or TTO in preventing MRSA colonization. Only Lee et al. (2014) study found statistical significance for the use of TTO preparations on MRSA colonized wounds. This could perhaps be contributed to the use of 10% TTO preparation, higher concentration than other studies, or the low sample size of 32 participants. Treatment blinding could not be applied to the studies because of the distinctive smell of TTO preparations.

**Conclusion**

Based on this systematic review, evidence is inconclusive to prove that TTO is an effective topical therapy for MRSA-colonized wounds. Even though TTO has been incorporated in a wide variety of domestic products such as soaps, shampoo, and antiseptic creams to provide antifungal and antibacterial protection it could not be concluded that TTO preparations were effective on MRSA wounds. Resistance to standard treatment regimens such as mupirocin and antibiotics are
increasing so it is imperative to find an alternative treatment for MRSA colonization. In this review 5% and 10% TTO products were used which failed to provide complete eradication of the MRSA wounds. Future studies should examine the use TTO preparations at higher concentrations to see if MRSA eradication will occur since the ideal strength of TTO preparations for MRSA eradication is unknown.
References


