Prophylactic Use of Permethrin in Tick Infested Areas

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Abstract

Background: The prevalence of tick-borne diseases in the U.S. continues to escalate causing a major public health concern. Due to challenges that providers are faced with when diagnosing and treating tick-borne diseases, such as Lyme Disease, preventative methods are critical. This is a systematic review on the EPA-approved use of permethrin-treated clothing and its efficacy in the reduction of tick bites.

Methods: An exhaustive medical literature review was conducted utilizing PubMed-MEDLINE, Web of Science, and CINAHL using keywords: permethrin and tick bites.

Results: The search produced 44 studies with 4 pertaining to the clinical question. One study was excluded, due to its completion in a clinical setting versus the outdoors. Two of three studies revealed a statistical difference between the treatment and control groups and were considered to be of moderate quality.

Conclusion: Statistically significant findings between groups, who wore permethrin-treated clothing, and those who did not, indicates that permethrin is an efficacious preventative method for tick bite reduction.

Keywords: Permethrin, permethrin-treated clothing, tick bites, vector-borne diseases, tick-borne diseases, Lyme Disease, Rocky Mountain Spotted Fever

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Prophylactic Use of Permethrin in Tick Infested Areas

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A Clinical Graduate Project Submitted to the Faculty of the

School of Physician Assistant Studies

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For the Masters of Science Degree, August 11, 2019

Faculty Advisor: Annjanette Sommers, PA-C, MS

Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS
Biography

[Redacted]
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Acknowledgements

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List of Abbreviations

CDC  Centers for Disease Control and Prevention
EPA  Environmental Protection Agency
LD   Lyme Disease
RMSF Rocky Mountain Spotted Fever
Prophylactic Use of Permethrin in Tick Infested Areas

BACKGROUND

Vector-borne diseases are transmitted by humans or animals carrying infectious organisms that have resulted in 700,000 deaths annually worldwide.¹ Common infectious offenders include mosquitoes and ticks that have resulted in public health dilemmas that include malaria, yellow fever, Zika, and Lyme disease (LD).¹,² According to a report by the Centers for Disease Control and Prevention (CDC) that reviewed U.S. trends in vector-borne diseases from 2004-2016, 650,000 vector-borne cases were reported with the majority as result of tickborne transmission. Of those, LD is the most prevalent.² Since 1991, the annual incidence of LD (*Borrelia burgdorferi*) has been reported to have doubled, particularly in the northeastern region of the U.S.²,³ Other tickborne diseases that are becoming more prevalent yearly include Anaplasmosis, Ehrlichiosis, Babesiosis, and Rocky Mountain Spotted Fever.²

Early diagnosis of tick-borne diseases is critical in reducing mortality and to appropriately manage long-term complications for those that are infected.⁴–⁶ Early identification, however, can be cumbersome if hallmark signs, such as erythema migrans, characteristic to LD,⁷ are missed.⁵,⁸ Patients may present with non-specific, viral-like symptoms that can generate an ambiguous differential diagnosis that can delay treatment and increase healthcare costs.⁴,⁸,⁹ Patients may also experience long term complications associated with tick-borne diseases that can include fatigue, musculoskeletal pain, and neurological symptoms. In addition, a retrospective study⁴ evaluating medical claims from 2006-2010
indicated that LD was associated with significantly higher total health care costs compared to their matched controls. Their findings estimated costs that were $2968 higher and required more outpatient interactions within a 12-month period.\textsuperscript{4} Another study\textsuperscript{10} pertaining to medical and indirect costs associated with an epidemic of Rocky Mountain Spotted Fever (RMSF) in Arizona, estimated $1.3 million in medical costs and $181100 in acute productivity loss.\textsuperscript{10} With the prevalence increasing annually for tick-borne diseases,\textsuperscript{2} it is crucial to ascertain how to control these diseases so that mortality, co-morbidities, and costs can all be minimized.

Due to the diagnostic challenges associated with the diagnosis of vector-borne diseases,\textsuperscript{3,9} a preventative approach is another meaningful measure to consider. The CDC and the Environmental Protection Agency (EPA) recommend using long-sleeved shirts and long pants in addition to EPA-registered insect repellants.\textsuperscript{3,11} The CDC also advocates for permethrin-treated clothing for the prevention of tick and mosquito bites.\textsuperscript{11} Known as an acaricide, permethrin, has been a widely used treatment applied to uniforms of those, who work outdoors in tick-infested areas, namely National Park Service employees and the U.S. military.\textsuperscript{12,13} Although permethrin is the only EPA-approved pesticide recommended for the prevention of tick bites, research related to its effectiveness in tick bite reduction is limited.\textsuperscript{13–16} A systematic review of studies that utilized permethrin as a prophylactic treatment for tick bite reduction was completed to assess its efficacy.
METHODS

An extensive search was performed utilizing PubMed-MEDLINE, Web of Science, and CINAHL using the terms "permethrin" and tick bites”. Inclusion criteria included: human-only studies, randomized controlled trials, observational studies, exposure to permethrin treatment only, and outcomes related to tick exposure (tick bites). Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group guidelines7 was utilized to assess the quality of each study reviewed.

RESULTS

The search produced 44 studies with 4 pertaining to the clinical question. All 4 studies were collected from PubMed-MEDLINE, due to duplicates found in Web of Science and CINAHL. The articles reviewed consisted of 1 observational study, 1 single-blinded study, and 1 randomized controlled trial. The fourth study was excluded, due to the design consisting of a clinical environment versus an outdoor setting. Research participants were comprised of civilians and military personnel wearing either permethrin-treated clothing or non-treated clothing and exposed to tick infested environments. (See Table 1.)

Faulde et al

This was a preliminary observational study14 to assess the efficacy of permethrin-treated uniforms among German military personnel, training in areas noted for dense tick populations and increased tick bite incidence. Tick bite incidences from 2009, before implementation of permethrin-treated uniforms,
were compared to incidence reports from 2010 and 2011, after treated uniforms had been distributed to military personnel. Data pertaining to tick bites was collected using self-reported questionnaires, containing details such as the location of the bite, environmental conditions at the time, and whether permethrin-treated attire had been worn.\textsuperscript{14}

Of the 2977 military personnel followed in 2009, a total of 262 tick bites associated with non-treated uniforms were reported by military personnel, indicating an incidence of 8.8\% per person (see Table 2).\textsuperscript{14} In comparison, of the 2885 military personnel followed in 2010, only 53 tick bites were reported. Of those, 49 were associated with military personnel donning either non-treated uniforms, administered prior to 2010, or uniforms consisting of a combination of non-treated and permethrin-treated items. Three of the tick bite incidences were associated with permethrin-treated clothing, however, personnel had combined non-treated items, such as parkas, with their uniforms.\textsuperscript{14} Only one incidence report consisted of personnel donning only permethrin-treated clothing. In 2011, Faulde et al\textsuperscript{14} followed 1289 military personnel and found that 15 out of 18 tick bite incidences consisted of personnel using a combination of non-treated and permethrin-treated clothing. Again, only one incidence report was associated with only permethrin-treated items. Tick bite incidences for 2010 and 2011 were 0.035\% and 0.078\%, respectively. In addition, Faulde et al took into account the total number of days pertaining to tick exposure at each training site and found no significant difference between the sites. This implies that all 3 sites had the same degree of tick exposure.\textsuperscript{17}
To affirm potential tick exposure among the training sites of interest, Faulde et al assessed tick frequency utilizing a tick dragging method, which consisted of dragging blankets through exposure sites for tick collection. Samples collected from 2009-2011 indicated high tick densities in all 4 areas with no significant difference between areas. This finding validated these training sites as appropriate places to examine the efficacy of permethrin treatment for military personnel.\(^\text{17}\)

Findings from the Faulde et al\(^\text{17}\) study revealed a distinct difference regarding tick bite incidence between 2009 and 2010-2011. The decrease in incidence rates indicates that permethrin can potentially be an effective preventative method for tick bites. It was also noted by Faulde et al\(^\text{14}\) that there was an increase in incidence rates from 2010-2011. Taking into consideration the findings from the Vaughn et al study\(^\text{13}\) which was of similar design, the authors suspected that there could be decrease in the effectiveness of permethrin-treated clothing due to a lesser amount of permethrin remaining on the uniforms. Reduced permethrin residuals could be attributed to how often uniforms were laundered, or from environmental conditions the uniforms were exposed to.\(^\text{13,14}\) Another factor to consider is that although the authors were successful in affirming that each site was densely tick-populated, self-reports from military personnel lacked information related to the tick species that they had been afflicted by. It is possible that certain species of ticks may be more tolerant to permethrin treatment compared to others.
Richards et al

Richards et al\textsuperscript{15} examined permethrin-treated clothing on its preventative performance for tick bites in participants employed with the forestry services within the central Appalachian region. This was a single-blinded study that had recruited participants via email request, who were $\geq 18$ years old. Twenty-one participants were assigned to the treatment group and 13 to the control in a stratified fashion, according to the state they resided in. Uniforms for both groups were mailed to InsectShield\textsuperscript{®}, proprietors of a permethrin formulation for commercial use, who either treated clothing items, or performed a sham treatment for those assigned to the control group. Participants provided Richards et al\textsuperscript{15} with log books consisting of information such as clothing worn, application of repellants, hours spent outdoors, and number of tick bites. Also, ticks found attached to participants were mailed to the researchers for identification purposes and for future research.\textsuperscript{15}

Of the 34 participants, 15 from the treatment group and 9 from the control submitted data to Richards et al,\textsuperscript{15} that indicated a difference in the frequency of tick bites between groups (see Table 3). Data showed that the treatment group experienced a higher frequency of bites per person, but a higher number of people in the control experienced a minimum of one tick bite. However, the authors noted that the participant logs revealed heterogeneity within groups with regards to prevention methods used during tick exposure. There was also no
significant difference in the number of tick samples submitted to researchers from both groups.¹⁵

Limitations were apparent in the Richards et al.¹⁵ study most notably the sample size, which impacted its statistical power. This most likely resulted in the authors being unable to identify clear differences between the treatment and control group. The number of hours logged by participants (see Table 3) also suggests that participants might not have been followed long enough to gather a sufficient amount of data for analysis. There was also the lack of standardization with regards to preventative methods, utilized by both groups that likely led to heterogeneity within groups, which possibly produced confounding variables making it more difficult for data to be assessed. This study also was unable to determine relative risk associated with the size of tick habitations at each location that participants were employed at. This would have validated the potential risk that participants had with regards to tick exposure and bolstered the effectiveness of permethrin treatment for prevention. Additionally, there was no mention of a randomization strategy for treatment assignment, which implies that selection bias for the study may have occurred. Attrition bias also seems probable, due to the lack of participant logs submitted from each group. These biases could result in the study sample not necessarily being representative of the actual central Appalachian region.¹⁵
A randomized double-blind controlled trial conducted by Vaughn et al\textsuperscript{13} assessed the efficacy of permethrin-treated uniforms of those employed in forestry, parks and recreation, and wildlife services in North Carolina. Sixty-seven participants were randomly assigned to the treatment group and 66 to the control, all were ≥ 18 years old and spent ≥ 10 hours outdoors, per inclusion criteria. All uniforms were sent to InsectShield\textsuperscript{®}, who either treated clothing items with permethrin or provided a placebo treatment, consisting of merely washing items for those assigned to the control group. Participants provided Vaughn et al\textsuperscript{13} with tick bite logs that included information such as tick bite location, number of bites, and if any repellent was used in addition to wearing their uniform. In the event that a tick was found still attached to the participant, vials were provided so that they could submit the specimens to researchers for identification purposes.\textsuperscript{13}

According to the incidence rates calculated by Vaughn et al\textsuperscript{13} those in the treatment group had a significantly lower tick bite occurrence (0.24 bites per 100 work hours) compared to the control group (1.37 per 100 work hours) in the first year of follow-up (see Table 4). Incidence rates differed between the groups in the second year of follow-up, although these values were not statistically significant (p=0.38). There was loss-to-follow up in each group during both years, however, the numbers were roughly the same. A higher number of tick samples
were submitted by the control group to Vaughn et al\textsuperscript{13}; however, whether this was statistically significant was not mentioned in the article.\textsuperscript{13}

Vaughn et al\textsuperscript{13} revealed that permethrin-treated clothing can be significantly more effective in the prevention of tick bites compared to untreated clothing and repellant alone. Due to the incidence rate, however, being higher the following year for the treatment group, Vaughn et al\textsuperscript{13} suspected that permethrin residuals on clothing items may not have been as effective the following year possibly due to environmental factors, or simply due to items being over worn. Another factor considered by the authors was that there may have been inconsistencies with how the interventional method was implemented among treatment group participants. This could have made it harder to control for confounding, thus influencing the data. More stringent instruction to how the interventional group might dress prior to working outdoors, may have permitted the intervention to be more standardized.\textsuperscript{13}

**DISCUSSION**

With tick-borne diseases on the rise in the U.S., they are becoming a heightened public health concern.\textsuperscript{2,17,18} While initial treatment for some diseases, such as LD, can be simply managed with the use of antibiotics, diagnosis can be arduous for some individuals, who present with vague symptoms.\textsuperscript{8} There are also long-term health complications related to tick-borne diseases, which can be difficult to manage as well.\textsuperscript{19} Due to the challenges that many providers are faced with regarding diagnosis and treatment, prevention is a more practical
approach to alleviate the incidence of tick-borne disease.\textsuperscript{19,20} This systematic review explored an EPA-approved preventative method by examining three studies using permethrin as prophylaxis for tick bites.

All three studies demonstrated permethrin-treated clothing as an effective method for repelling various tick species, however, only 2 of the 3 studies were successful in gathering statistically significant data that indicated there was a difference between the treatment and control groups. The third study\textsuperscript{10} had difficulties with recruiting participants and thus experienced a small sample size, which as previously mentioned, negatively impacted the study’s statistical power. Additionally, heterogeneity existed within groups, which Richards et al\textsuperscript{15} implied was likely due to a variety of ways the participants may have worn their permethrin-treated items that led to a lack of a standardized intervention. This may have also made it difficult for the authors to determine if there was a difference between their treatment and control groups. The other 2 studies likely faced inconsistencies regarding what treated garments were worn and how, but they had large enough sample sizes where this might not have been detrimental to their data.

Another potential inconsistency for all 3 studies was that all participants and personnel examined could wear another kind of insect repellent in addition to the treated clothing they were administered. Although, 2 of the 3 studies were able to detect a difference between the treatment and control groups, there is the possibility that insect repellent may have served as a confounding variable. Utilizing insect repellent may have influenced the number and types of garments
worn that were thought to be permethrin-treated. This could have resulted in data being slightly skewed.\textsuperscript{15}

All 3 studies mainly collected data from self-reported questionnaires, which consisted of information related to the tick bites, types of clothing worn, and if additional insect repellant was used. The study authors may have been confronted with self-reporting bias,\textsuperscript{21} depending on the length of time between a tick bite occurrence and when the individual recorded the event. This can be considered recall bias, which is a type of self-reporting bias\textsuperscript{21} that can negatively influence the reliability of the data. There was no mention of this being contemplated in any of the studies and whether adjustments were made to control for it in their statistical analyses.

An advantage of the Faulde et al\textsuperscript{14} study was the capacity to perform tick drags that exhibited the degree of tick infestation at each training site of interest. The authors were able to calculate mean values for tick densities and determined that there was no significant difference between the sites.\textsuperscript{14} This finding validated that there was an actual risk to tick exposure and that it was the same at each site of interest, which supported the reliability of their findings. The other 2 studies had collected tick samples from their participants, although neither indicated whether there was statistical difference between their control and treatment groups regarding the number of ticks submitted. It was also unclear whether participants in these 2 studies had the same degree of tick exposure. This questioned whether those wearing permethrin-treated clothing were in areas
at sufficient risk for tick exposure. Again, the Faulde et al\textsuperscript{14} study was able to convey this.

Regardless of the limitations for all 3 studies, collectively, permethrin-treated clothing was determined to be effective. Another aspect that was considered by 2 of the 3 studies was the long-term effectiveness of permethrin-treated clothing.\textsuperscript{13,14} Findings from the Faulde et al\textsuperscript{14} study revealed that although treated items had an effective impact on tick bite reduction in 2010, the incidence rate slightly increased the following year. Results from the Vaughn et al\textsuperscript{13} study depicted similar results when comparing their incidence rates between year 1 and year 2. Both studies considered factors that might have influenced the concentration of permethrin remaining on clothing, such as the number of times the garment had be worn and washed, as well as environmental factors.\textsuperscript{13,14} It had been concluded that further research was required to learn what factors may be related to the diminished effectiveness of permethrin-treated clothing.\textsuperscript{13,14}

**CONCLUSION**

To conclude, permethrin-treated clothing for tick bite reduction can be a useful preventive method.\textsuperscript{13–15} The EPA has approved its use and in 2009, risk assessments were evaluated that determined the insect repellent to be safe when applied to clothing.\textsuperscript{22} Although deemed safe for commercial use, public perceptions concerning pesticides in general may have an impact on it being regularly used.\textsuperscript{23,24} Identifying popular concerns and educating the public regarding the risks and benefits of permethrin, may be advantageous in preventing the increasing trend of vector-borne diseases.
References


<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Downgrade Criteria</th>
<th>Upgrade Criteria</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faulde et al^14</td>
<td>Cohort</td>
<td>Not Serious a</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Richard et al^15</td>
<td>Single-Blinded</td>
<td>Very Serious a,b,c,d,e</td>
<td>Likely g</td>
<td>Very Low</td>
</tr>
<tr>
<td>Vaughn et al^13</td>
<td>RCT</td>
<td>Not Serious</td>
<td>Likely g</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

- a Confidence Intervals not provided
- b Lack of blinding by data collectors
- c No mention of randomization methods during treatment assignment
- d Risk of selection bias and attrition bias
- e Heterogeneity within groups
- f Small sample size
- g Permethrin treatment provided by proprietors of a permethrin formula
### Table II. Faulde et al\textsuperscript{14}

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Tick Bites Reported</th>
<th>Total Tick Bites Using Treated and Non-treated Items</th>
<th>Total Tick Bites Using Treated Items</th>
<th>Incidence Rate Per Person</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009 (n=2977)</td>
<td>262</td>
<td>--</td>
<td>--</td>
<td>8.8%</td>
</tr>
<tr>
<td>2010 (n=2885)</td>
<td>53</td>
<td>52</td>
<td>1</td>
<td>0.035%\textsuperscript{1}</td>
</tr>
<tr>
<td>2011 (n=1289)</td>
<td>18</td>
<td>17</td>
<td>1</td>
<td>0.078%\textsuperscript{1}</td>
</tr>
</tbody>
</table>

\textsuperscript{1}Rate associated with permethrin-treated uniforms worn correctly

### Table III. Richards et al\textsuperscript{15}

<table>
<thead>
<tr>
<th>Group</th>
<th>Total Number of Tick Bites</th>
<th>Total Number of Hours Outdoors Per Group</th>
<th>Tick Bite Incidence Per Person</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Group (n=15)</td>
<td>314</td>
<td>1149</td>
<td>21</td>
</tr>
<tr>
<td>Control Group (n=9)</td>
<td>116</td>
<td>765</td>
<td>13</td>
</tr>
</tbody>
</table>
### Table IV. Vaughn et al\textsuperscript{13}

<table>
<thead>
<tr>
<th></th>
<th>Total Tick Bites</th>
<th>Tick Bite Incidence Per 100 Work Hours</th>
<th>Incidence Rate Difference (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Year 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=64)</td>
<td>84</td>
<td>0.24</td>
<td>-1.13 (CI=1.78, -0.50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Control Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=63)</td>
<td>493\textsuperscript{a}</td>
<td>1.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Year 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=53)</td>
<td>181\textsuperscript{b}</td>
<td>0.69</td>
<td>-0.36 (CI= -1.12, 0.40)</td>
<td>0.38</td>
</tr>
<tr>
<td>Control Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=48)</td>
<td>287</td>
<td>1.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a} One participant reported 102 tick bites in 1 week and was considered an outlier

\textsuperscript{b} One participant reported 50 tick bites in 1 week and was considered an outlier