Effect of Permethrin-Impregnated Underwear on Body Lice in Sheltered Homeless Persons
A Randomized Controlled Trial

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IMPORTANCE The control of body lice in homeless persons remains a challenge.

OBJECTIVE To determine whether the use of long-lasting insecticide-treated underwear provides effective long-term protection against body lice in homeless persons.

DESIGN, SETTING, AND PARTICIPANTS A randomized, double-blind, placebo-controlled trial was conducted in February and December 2011 in 2 homeless shelters (Madrague Ville and Forbin) in Marseille, France. Of the 125 homeless persons screened for eligibility, 73 body lice-infested homeless persons, 18 years or older, were enrolled.

INTERVENTIONS Body lice-infested homeless persons were randomly assigned to receive 0.4% permethrin-impregnated underwear or an identical-appearing placebo for 45 days, in a 1:1 ratio, with a permuted block size of 10. Visits were scheduled at days 14 and 45. Data regarding the presence or absence of live body lice were collected.

MAIN OUTCOMES AND MEASURES The primary and secondary end points were the proportions of homeless persons free of body lice on days 14 and 45, respectively. Mutations associated with permethrin resistance in the body lice were also identified.

RESULTS Significantly more homeless persons receiving permethrin-impregnated underwear than homeless persons receiving the placebo were free of body lice on day 14 in the intent-to-treat population (28% vs 9%; \( P = .04 \)), with a between-group difference of 18.4 percentage points (95% CI, 1.4-35.4), and in the per-protocol population (34% vs 11%; \( P = .03 \)), with a between-group difference of 23.7 percentage points (95% CI, 3.6-43.7). This difference was not sustained on day 45. At baseline, the prevalence of the permethrin-resistant haplotype was 51% in the permethrin group and 44% in the placebo group. On day 45, the permethrin-resistant haplotype was significantly more frequent in the permethrin group than in the placebo group (73% vs 45%, \( P < .001 \)).

CONCLUSION AND RELEVANCE Permethrin-impregnated underwear is more efficient than placebo at eliminating body louse infestations by day 14; however, this difference was not sustained on day 45. The use of permethrin may have increased the resistance to permethrin in body lice and thus must be avoided.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01287663
Homelessness is a major social and public health problem worldwide. The prevalence of body lice in sheltered homeless persons varies from 7% to 22%. Body lice are known vectors of Bartonella quintana, Rickettsia prowazekii, and Borrelia recurrentis, which cause trench fever, epidemic typhus, and relapsing fever, respectively. Consequently, all measures that can be used to decrease the burden of body lice infestation in homeless persons, and more generally in persons living in crowded and unhygienic environments, are warranted to avoid the spread and/or outbreak of these diseases.

Pediculus humanus humanus, the human body louse, is a host-specific hematophagous ectoparasite that lives in the clothes. Body lice are extremely contagious and can be spread through body contact, shared clothing, or shared bedding in overcrowded conditions. The classic therapeutic measures for body lice infestations are the frequent changing or washing of the infected person’s clothes and blankets at 50°C and the frequent treatment of bedding with insecticides. However, in our experience with the sheltered homeless persons in Marseille, France, these measures have had little success. Oral ivermectin reduces the prevalence of body lice infestations and pruritus in homeless persons, but the effect is transient. These findings suggest that the complete eradication of this ectoparasite in homeless persons remains a challenge.

The pyrethroids are the major commercially available pediculicides. All World Health Organization–recommended insecticide-treated mosquito nets are pyrethroid based. The impregnation of clothing with a pyrethroid emulsion has been reported to eradicate body lice after a single application to military uniforms, even after 20 washes, and may provide long-lasting protection. The clinical safety and effectiveness of topical permethrin in humans have been reported previously.

We conducted our randomized, double-blind, placebo-controlled study to determine whether the use of long-lasting permethrin–treated underwear provides long-term protection against louse proliferation in sheltered homeless persons. Our secondary aim was to assess the mutations associated with permethrin resistance in the body lice.

Methods

Study Design

Our study was a double-center, double-blind, randomized, placebo-controlled intervention trial. Homeless persons were given underwear treated with permethrin or an identical-appearing placebo for 45 days. The protocol was approved by our institutional review board (January 24, 2011; reference 2010-A01406-33), and the study was performed in accordance with the good clinical practices recommended by the Declaration of Helsinki and its amendments. All participants provided written informed consent. This study is registered with clinicaltrials.gov (identifier NCT01287663).

Underwear Preparation

An 8% (8-g/L) permethrin formulation for impregnation, which is commercially available under the label Barrage Insect (S.P.C.I., S.A., Paris, France), was prepared as a 1:20 emulsion in water as recommended by the manufacturer. The impregnation was performed by an independent person in the Public Hospitals of Marseille laundry. Sets of underwear (T-shirt, underpants, and socks) were placed into the emulsion for 15 minutes, completely saturated, removed, and allowed to dry. Once dry, the underwear was odorless. According to the manufacturer’s instructions, the permethrin–impregnated underwear is effective up to 6 months and even after 6 washes. Other sets of underwear were treated identically but without the permethrin formulation. The permethrin-impregnated and placebo underwear were identical in appearance but were labeled discreetly and then stored in 2 separate boxes until use.

Participants

To recruit a sufficient number of participants, 2 independent study cohorts of homeless persons were performed. In study A, homeless persons were recruited in February 2011 from 2 shelters (Madrague Ville and Forbin) in the city of Marseille. In study B, different homeless persons were recruited in December 2011 from the same 2 shelters. Each facility provides nighttime shelter for a mean of 300 homeless persons who stay in the shelter overnight and leave it in the morning. Homeless persons with a self-reported diagnosis of pruritus and/or with body lice were screened. Homeless persons were eligible for inclusion in the study if they were 18 years or older, were able to provide consent, declared that they slept at least 3 nights per week in 1 of the 2 shelters, and had at least 1 live body louse recovered on examination. The exclusion criteria were the presence of cutaneous superinfection or intravenous drug use.

Randomization and Interventions

Homeless persons were randomly assigned to the intervention group with sealed, opaque envelopes in a 1:1 ratio with a permuted block size of 10. Participants and investigators were unaware of the treatment assignments throughout the study. Visits were scheduled on days 14 and 45. Data on the presence or absence of live body lice, whether the clothes had been changed between visits, and the occurrence of adverse events were collected.

All participants received their protocol underwear on day 1 (baseline) and at each follow-up visit (on days 14 and 45) under the supervision of the investigators. The underwear could also be changed between the follow-up visits in the shelters at the request of the individual (with respect to the assigned group). The used underwear was collected by the same entomologist for detailed visual inspection. This evaluator was trained in the technique for detecting and counting live body lice from the infested underwear. Dead and living lice were differentiated; lice were considered to be dead if they were not moving. Homeless persons were excluded from further study if they had any manifestations suggesting adverse effects, and specific treatment was given as needed. The final visit on day 45 was regarded as the end of the study for every participant.

If persistent live body lice were found at this visit, homeless persons were offered a single dose of oral ivermectin (12 mg).
Outcome Measures and Safety End Points

The primary efficacy end point was the proportion of homeless persons free of body lice (defined as absence of living body lice in the underwear) 14 days after treatment. The secondary efficacy end point was the same assessment 45 days after treatment. End points were assessed on the basis of the exhaustive examination of live body lice in all collected underwear.

The pruritus that normally accompanies body lice infestation may be exacerbated temporarily after dermal exposure to permethrin. Physical examinations were performed at scheduled visits, and adverse events were recorded during the 45-day study period. The prevalence and severity of pruritus, graded from 0 to 3 (0, none; 1, mild; 2, moderate; and 3, severe), were assessed at each visit.

Another objective was to investigate the evolution of permethrin resistance in the body lice. The permethrin resistance of body lice was determined in a representative random sample of body lice collected from all body lice-infested homeless persons and stratified by the level of infestation of the homeless persons (see eTable 1 in the Supplement). A melting curve analysis genotyping method, based on a previously reported real-time polymerase chain reaction using hybridization probes, was used to detect the 3 mutations (M815I, T917I, and L920F), identified in the voltage-sensitive sodium channel α-subunit gene, responsible for knockdown resistance (kdr). According to the literature, these 3 mutations define the RRR haplotype, which confers permethrin resistance in head lice.

Statistical Analysis

We estimated that approximately 60 body lice-infested homeless persons (30 in each group) would need to be enrolled to provide 90% power to detect a difference of 40 percentage points between the permethrin and placebo groups when calculating the proportion of homeless persons free of body lice on day 14 with a 2-sided α = .05, assuming an anticipated effect between 20 and 40 percentage points in the placebo group. In our experience, approximately 70% of pruritus symptoms are due to body lice infestations, and presuming that the rate of individuals lost to follow-up could be up to 30%, we predicted that we would need to screen 122 homeless persons. Analyses were conducted in accordance with the intent-to-treat and per-protocol principles. In the intent-to-treat analysis, only the homeless persons who were present at the scheduled follow-up visits were included. For the intent-to-treat analysis, loss to follow-up was considered a treatment failure. The Pearson χ² test and Fisher exact test, as appropriate, were applied to analyze the primary and secondary end points of efficacy, and 95% CIs for the difference between the success rates in the study groups were calculated. The t test for independent groups and Mann-Whitney test, as appropriate, were used to investigate the safety end point of mean pruritus score and the continuous variables. P ≤ .05 (2-tailed test) was established as the level of significance for all tests. Statistical analyses were performed using SPSS statistical software, version 17.2 (SPSS Inc).

Results

Participants

The trial profile is summarized in the Figure. Of the 125 homeless persons screened for eligibility in February and December 2011, 73 (58%) were eligible on the basis of the presence of live body lice (40 in the permethrin group and 33 in the placebo group) and were consequently randomized...
into the control and treatment groups (Figure). They were predominantly male (96%), were mostly from the Madrague Ville shelter (92%), and had a mean (SD) age of 56.9 (13.3) years (age range, 20-79 years). Approximately 45% reported being homeless for less than or equal to 24 months. Baseline characteristics were similar between the treatment groups (Table 1).

**Primary and Secondary Outcomes**

In the intent-to-treat population, 11 of 40 homeless persons (28%) were free of live body lice on day 14 (primary endpoint) in the permethrin group compared with 3 of 33 (9%) in the placebo group ($P = .04$), with a between-group difference of 18.4 percentage points (95% CI, 1.4 to 35.4) (Table 2). This proportion was also significantly greater in the permethrin group than in the placebo group in the per-protocol population (34% vs 11%; $P = .03$), with a between-group difference of 23.7 percentage points (95% CI, 3.6 to 43.7).

With respect to the secondary efficacy endpoint, in the intent-to-treat population, 11 of 40 homeless persons (28%) were free of live body lice on day 45 in the permethrin group compared with 9 of 33 (27%) in the placebo group (28% vs 27%; $P = .98$), with a between-group difference of 0.2 percentage points (95% CI, -0.3 to 0.8). In addition, no significant difference was found between the 2 proportions in the per-protocol population (41% vs 38%; $P = .81$), with a between-group difference of 3.2 percentage points (95% CI, -23.6 to 30.0) (Table 2).

Significant reductions from the baseline in the mean number of body lice were observed on day 14 and day 45 in the permethrin and placebo groups (see eTable 2 in the Supplement). However, no significant difference was found between the 2 groups on day 14 (mean [SD], 176.1 in the permethrin group vs 202.1 in the placebo group; $P = .18$) or on day 45 (mean [SD], 148.4 [427.6] in the permethrin group vs 147.6 [272.3] in the placebo group; $P = .68$) (data not shown).

**Adverse Events**

No adverse events were reported in any treated homeless persons. The prevalence of pruritus was reduced in both groups, with no significant differences in the proportion of homeless persons free of pruritus between the permethrin group and the placebo group on day 14 (8 of 32 [25%] vs 6 of 27 [22%]; $P = .80$), with an odds ratio of 1.16 (95% CI, 0.34–3.91), or on day 45 (8 of 27 [30%] vs 8 of 24 [33%]; $P = .77$), with an odds ratio of 0.84 (95% CI, 0.25–2.75) in the per-protocol population. The mean (SD) pruritus score at baseline was 2.53 (0.69) in the permethrin group and 2.24 (0.90) in the placebo group. No significant differences were found in the mean reduction in pruritus score from baseline between the permethrin group and the placebo group on day 14 (−0.68 vs −0.28; 95% CI, −0.97 to 0.17; $P = .17$) and on day 45 (−0.92 vs −0.45; 95% CI, −1.15 to 0.21; $P = .17$).

**Permethrin Resistance of Body Lice**

Of the 34,035 live body lice that were collected, 371 were used to assess permethrin resistance because at least 1 louse per infested homeless persons was selected (see eTable 1 in the Supplement): 187 were collected in study A (91 on day 1 [44 from 18 homeless persons from the permethrin group and 47 from 17 homeless persons from the placebo group]) and 184 in study B (67 on day 1 [32 from 16 homeless persons from the permethrin group and 35 from 7 homeless persons from the placebo group]) and 184 in study B (67 on day 1 [32 from 16 homeless persons from the permethrin group and 35 from 7 homeless persons from the placebo group]) and 184 in study B (67 on day 1 [32 from 16 homeless persons from the permethrin group and 35 from 7 homeless persons from the placebo group]) and 117 on day 45 (56 from 8 homeless persons from the permethrin group and 61 from 8 homeless persons from the placebo group).

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**Table 1. Demographic and Baseline Characteristics of the Study Groups**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%) of Study Participants</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Permethrin (n = 40)</td>
<td>Placebo (n = 33)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>56.4 (14)</td>
<td>57.62 (12)</td>
</tr>
<tr>
<td>Men</td>
<td>37 (92)</td>
<td>33 (100)</td>
</tr>
<tr>
<td>Madrague Ville Shelter</td>
<td>36 (90)</td>
<td>31 (94)</td>
</tr>
<tr>
<td>Marginal homeless$^a$</td>
<td>20 (50)</td>
<td>20 (61)</td>
</tr>
<tr>
<td>Homeless with &gt;50 lice</td>
<td>18 (45)</td>
<td>19 (58)</td>
</tr>
<tr>
<td>Duration of homelessness ≤24 mo</td>
<td>15 (38)</td>
<td>19 (58)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>40 (100)</td>
<td>33 (100)</td>
</tr>
</tbody>
</table>

$^a$ Data are presented as number (percentage) of study participants unless otherwise indicated.

**Table 2. Effect of Treatment on Days 14 and 45 in Study A and Study B Combined**

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>No./Total (%)</th>
<th>Difference, % (95% CI)</th>
<th>$P$ Value</th>
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</thead>
<tbody>
<tr>
<td>Intent-to-treat population</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body lice–free homeless after 14 d</td>
<td>11/40 (28)</td>
<td>3/33 (9)</td>
<td>18.4 (1.4 to 35.4)</td>
</tr>
<tr>
<td>Body lice–free homeless after 45 d</td>
<td>11/40 (28)</td>
<td>9/33 (27)</td>
<td>0.2 (−20.3 to 20.8)</td>
</tr>
<tr>
<td>Per protocol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body lice–free homeless after 14 d</td>
<td>11/32 (34)</td>
<td>3/28 (11)</td>
<td>23.7 (3.6 to 43.7)</td>
</tr>
<tr>
<td>Body lice–free homeless after 45 d</td>
<td>11/27 (41)</td>
<td>9/24 (38)</td>
<td>3.2 (−23.6 to 30.0)</td>
</tr>
</tbody>
</table>
At baseline, the prevalence of the permethrin-resistant haplotype (Table 3) among the lice collected was 51% in the permethrin group and 44% in the placebo group. On day 45, the permethrin-resistant haplotype was significantly more frequent in the permethrin group than in the placebo group (73% vs 45%; \( P < .001 \)).

At baseline, the prevalence of permethrin-resistant mutations (Table 4) was established as 99% for the L920F mutation and 53% for the T917I mutation in the permethrin group and 87% for the L920F mutation and 48% for the T917I mutation in the placebo group. The prevalence of the T917I mutation increased significantly from baseline to day 45 in the permethrin group (from 53% to 77%; \( P = .008 \)) but remained stable in the placebo group (from 48% to 45%; \( P = .69 \)). The prevalence of the L920F mutation increased significantly in the placebo group from baseline to day 45 (from 87% to 100%; \( P < .001 \)). The prevalence of the M815I mutation was established as 100% for all samples.

### Discussion

In this randomized controlled trial, long-lasting permethrin-treated underwear is more efficient in the elimination of body louse infestations than placebo in the short term (ie, on day 14), but the difference with the placebo was not sustained by day 45 and is accompanied by increasing permethrin resistance in body lice collected from homeless persons.

Resistance to permethrin has been reported in the head louse *Pediculus humanus capitis* in many parts of the world.\(^{17-20}\) This is the first trial, to our knowledge, that tests permethrin-impregnated underwear on body lice in sheltered homeless persons, combined with molecular detection of mutations associated with permethrin resistance in body lice. The \( kdr \) allele frequency in the body louse population at baseline was unexpectedly high in study A (averaging 38%). The relative ease with which this group of mutations was identified within the modern body louse population may be related to prior exposure to dichlorodiphenyltrichloroethane, which likely involved \( kdr \)-like mechanisms in some cases, in a manner similar to the rapid increase of permethrin resistance in the head louse populations shortly after the introduction of synthetic pyrethroids in Europe and worldwide.\(^{17-20}\) Resistance of the body louse to dichlorodiphenyltrichloroethane was reported at the end of the 1940s and early 1950s.\(^{21-23}\) This finding could suggest that, although no resistance to permethrin was reported in the body lice in Western Europe before this study, some lice are currently resistant to pyrethroids through dormant cross-resistance attributed to the \( kdr \) mechanism.

In our study, the increase of the prevalence of the T917I mutation interestingly coincided with the loss of permethrin efficacy. This result is coherent with that obtained in a
previous study that concluded that the T917I mutation alone was responsible for most of the target site insensitivity reported in the resistant RRR haplotype. In addition, a recent study reported a prevalence of 5% of the T917I mutation, against 70% for both the M815I and L920F mutations, in an Egyptian head louse population for which selection with pyrethroid-based pediculicides was expected to be low. These findings suggested that head lice may have acquired the M815I and L920F mutations first and then, once these 2 mutations are present, rapidly acquired the T917I mutation, high levels of nerve insensitivity, and resistance after they were again placed under pyrethroid selective pressure, leading to control failure.

Our trial had several limitations that merit consideration. First, we believe that head and body lice are transferred among people when they come in close personal contact in the shelter, and thus the resistance to permethrin is also shared. Indeed, of the 11 homeless persons who were free of live body lice on day 14 in the permethrin group, 2 were reinfected on day 45. Moreover, the frequency of the L920F mutation increased significantly from baseline to day 45 in the permethrin group in study A, suggesting that L920F-mutated lice had been transferred between the permethrin and placebo groups.

In conclusion, this trial clearly demonstrates that the use of permethrin–impregnated underwear had the consequence of increasing the percentage of permethrin-resistant body lice in sheltered homeless persons. These findings lead us to recommend avoiding the use of permethrin to treat body lice infestations, although implementing new strategies is crucial.

Second, recent studies suggest that head and body lice can be mixed in persons infested with both head and body lice. Whether these lice are conspecific remains controversial and although head and body lice do not interbreed in the wild, fertile hybrids that have intermediate morphologic characteristics have been reported under laboratory conditions. Moreover, several observational studies have also suggested that head lice could become body lice when raised under the laboratory conditions.

Third, it appears that only a change of underwear could reduce body lice infestation (equivalent efficiency of placebo at day 45 compared with permethrin). This occurrence would not be expected outside a controlled study. In fact, at the start of this study, the mean number of body lice per homeless person was high (approximately 450 body lice per subject), and despite the availability of the protocol underwear in shelters, most homeless persons changed their clothes only during scheduled follow-up visits and had not washed them between visits.

In conclusion, this trial clearly demonstrates that the use of permethrin-impregnated underwear had the consequence of increasing the percentage of permethrin-resistant body lice in sheltered homeless persons. These findings lead us to recommend avoiding the use of permethrin to treat body lice infestations, although implementing new strategies is crucial.

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Correction: This article was corrected on December 5, 2013, for an error in the first sentence of the Results section of the Abstract.

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