The effect of a single dose of oral ivermectin on pruritus in the homeless

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Background: Homeless people commonly present with ectoparasite-based pruritus. We evaluated the efficacy of a single dose of ivermectin to reduce the pruritus prevalence in a homeless population.

Methods: We conducted a randomized, double-blind, placebo-controlled trial from January 2006 to April 2006 in two homeless shelters in the city of Marseille, France. Homeless people complaining of pruritus were randomized to receive either ivermectin (24 mg) or placebo. Follow-up visits were planned at day 14 and day 28 after the inclusion to assess the outcome of pruritus.

Results: Forty-two subjects with pruritus were randomized to the ivermectin group and 40 to the placebo group. On day 14, pruritus was reported by significantly more subjects in the placebo group than those in the ivermectin group for both the per-protocol (PP) population (91.42% versus 68.57%, \( p < 0.014 \)) and the intention-to-treat (ITT) population (92.5% versus 73.80%, \( p = 0.038 \)). No significant effect was observed at day 28. Ivermectin was the only independent factor associated with the absence of pruritus at day 14 in both PP population [OR: 4.60 (95% CI: 1.13; 18.73), \( p = 0.033 \)] and ITT population [OR: 4.38 (95% CI: 1.07; 17.77), \( p = 0.039 \)].

Conclusions: A single dose of oral ivermectin has a transient beneficial effect on the reduction of the prevalence of pruritus in the homeless population. More studies are required to assess the efficacy of multiple repeated treatments with ivermectin to reduce scabies and body lice endemic among homeless people with pruritus and the impact of such treatment on this population.

Keywords: body louse, scabies, skin infection, infection control, clinical trial
Thus, any additional measures able to decrease the impact of ectoparasite-based pruritus in homeless people may be useful.

Oral ivermectin has become a systemic alternative to topical treatments for scabies and head lice. Its efficacy against the human body louse has been demonstrated in experimental models, and recently in humans by the observation of a reduction in the prevalence of body lice infestation after three doses of oral ivermectin administered at 7 day intervals in a cohort of the homeless from a shelter in Marseille, France. Nevertheless, the effect of ivermectin was transient and the proportion of infested subjects increased at day 45, suggesting that complete eradication of this ectoparasite in homeless people living in poor conditions is impossible. The efficacy of ivermectin in both scabies and body lice infestation yet suggests that this drug could be a good empirical therapy for the treatment of pruritus, the clinical hallmark of these ectoparasitoses. To the best of our knowledge, the efficacy of a single dose of oral ivermectin in homeless people complaining of pruritus has never been assessed in a randomized controlled trial. We therefore conducted a clinical trial in which the primary objective was to test the hypothesis that a single oral dose of ivermectin was effective in significantly reducing the prevalence of pruritus in a sheltered homeless population.

Materials and methods

Study setting and population

This study was conducted from January 2006 to April 2006 in two town shelters designated for accommodating homeless people in the city of Marseilles, France. Each of the two shelters offers about 300 beds as well as showers, a washing service free of charge, clothes and food in addition to a general practitioner and a registered nurse who are available on a daily basis. The study population was homeless people with a complaint of pruritus. The study was performed in accordance with the good clinical practices recommended by the Declaration of Helsinki and its amendments. The study protocol was reviewed and approved by our Institutional Review Board. The study was registered in the clinical trial register in France as PHRC national 2005-Ivermectin monodose et SDF-Brouqui. All enrolled persons gave written informed consent.

Study design and protocol

The study was designed and monitored by a committee including P. B., C. R., S. B., C. F. and D. R. in accordance with the medical staff and authorities of the homeless shelters. It was a randomized, double-blinded, parallel-grouped, placebo-controlled trial evaluating the effect of a single dose of oral ivermectin on the prevalence of pruritus in the sheltered homeless. Criteria for inclusion in the study were a complaint of pruritus, age ≥18 years, male gender, absence of concomitant use of any other drugs, and absence of contraindication with ivermectin therapy (hypersensitivity to ivermectin), ability to provide written informed consent and self-declaration to sleep regularly in one of the two shelters.

Eligible subjects were randomly assigned to receive either oral ivermectin (a single administration of four 6 mg capsules) or placebo (four capsules). Capsules of ivermectin and placebo were identical in appearance and had been previously prepared and placed by the pharmacist (P. C.) into two boxes, labelled A and B. Subjects were randomly assigned by one of the authors (S. B., C. F. or P. B.) using previously prepared envelopes containing five tickets for treatment A and five for treatment B. Each participant chose one ticket in the envelope himself. Then, he received four capsules of treatment A or B according to the letter (A or B) noted on his ticket. Treatments were administered under the supervision of the investigators. All persons involved in conducting the study were blinded to the trial drug codes.

Upon inclusion, demographic information (age, weight and duration of homelessness) and clinical findings (magnitude of pruritus, surface area of itchy lesions and presence or absence of body lice) were collected from the participants and recorded on a standardized questionnaire. The magnitude of pruritus was estimated by a visual analogue scale consisting of a 10 cm line drawn upon the questionnaire (zero was considered as absence of pruritus and 10 cm as severe pruritus); the surface area of itchy lesions was estimated as a percentage of the body surface area as for body surface area estimation of burn patients; and body lice were carefully searched for in the clothes of participants. A presumptive diagnosis of scabies and/or body lice infestation was made for typical pruritus with characteristic dermatological lesions and distribution. An established diagnosis of pediculosis corporis was made on finding body lice in the clothes.

Two follow-up visits were planned at day 14 and day 28 after inclusion in order to assess the outcome of pruritus, the change in the surface area of itchy lesions, the presence of adverse events and a change of clothes in-between visits. The primary efficacy assessment was a change in the prevalence of pruritus from baseline. Secondary efficacy assessments included a change in the magnitude of pruritus in persons with persistent pruritus and a change in the surface area of itchy lesions.

At follow-up visits, observation of any manifestations suggesting adverse events lead to exclusion of the subject from the study and treatment of their conditions. At day 28 after inclusion, any subject always complaining of pruritus received a single dose of 12 mg of oral ivermectin. Statistical analysis

In our experience with the sheltered homeless population of Marseilles, we estimated that 90% of the complaints of pruritus were due to ectoparasitism (body lice infestation and scabies) and that 30% of these pruritus cases could be cured within 28 days with insecticides and/or change of clothes; however, rarely without any therapeutic measures. The proportions of pruritus cases cured in the placebo and ivermectin groups were estimated to be 27% and 72%, respectively; those that were not cured in the two groups were estimated to be 73% and 28%, respectively. Therefore, the therapeutic efficacy of ivermectin was estimated at 62% (1 – 0.28/0.73).

The sample size was calculated to document a 62% reduction in complaint of pruritus in the ivermectin group, compared with the placebo group at follow-up visits in accordance with a type I error (α = 0.05) and a type II error (β = 0.20), and considering that the rate of subjects lost to follow-up could be up to 30%, the total number of subjects we aimed to recruit was estimated to be at least 96 (48 in each group).

Data were recorded by using a standardized questionnaire, entered into the Excel software (Microsoft©) and analysed by using the STATA® version 9 software. The Kruskal–Wallis test was used to compare continuous variables. Fisher’s exact test was used to compare differences between proportions. To assess the impact of ivermectin on pruritus treatment and to avoid confounding factors, the multiple logistic regression model adjusting for the changes of clothes (which could influence pruritus disappearance) and the percentage of the body surface area as for body surface area estimation of burn patients; and body lice were carefully searched for in the clothes of participants. A presumptive diagnosis of scabies and/or body lice infestation was made for typical pruritus with characteristic dermatological lesions and distribution. An established diagnosis of pediculosis corporis was made on finding body lice in the clothes.

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duration of homelessness (which was subsequently found to be more frequent in the placebo group) was made. Statistical analysis of data collected at follow-up visits at days 14 and 28 was performed both for the intention-to-treat (ITT) and for the per-protocol (PP) patient populations. For the ITT analysis, loss of patient to follow-up visit was considered as treatment failure.

### Results

#### Study population

A total of 87 subjects were enrolled in the study between January and March 2006; 5 were excluded due to missing randomization codes and 82 were included in the analysis. A presumptive diagnosis of scabies and/or body louse infestation was made in 92.7% of the subjects, and a diagnosis of pediculosis corporis was established in 56.1%; 42 subjects were randomly assigned to the ivermectin group and 40 to the placebo group (Figure 1). The baseline characteristics of the two treatment groups were similar (Table 1).

#### Primary outcome measure

At the day 14 follow-up visit, pruritus was reported by significantly more subjects in the placebo group than those in the ivermectin group for both the PP population (91.42% versus 68.57%, \( P = 0.014 \)) and the ITT population (92.5% versus 73.80%, \( P = 0.038 \)). No significant difference was found at day 28 (Table 2). Among subjects with an established diagnosis of pediculosis corporis, pruritus was reported at the 14 day follow-up visit by significantly more subjects in the placebo group than in the ivermectin group for both the PP population \([24/24 (100\%) \text{ versus } 11/18 (61.1\%), \ P = 0.0012]\) and the ITT population \([24/26 (92.3\%) \text{ versus } 11/20 (55\%), \ P = 0.038]\). No significant difference was found at the day 28 follow-up visit.

#### Secondary outcome measures

Among subjects with persistent pruritus during follow-up visits, the frequency of those who reported a decline in the pruritus intensity was similar in the two treatment groups (Table 2). There was no significant difference between the ivermectin group and the placebo group for the mean decrease in the pruritus intensity from baseline to the 14 day follow-up \([4.87 \pm 6.41 \text{ (range: } –7; +18) \text{ versus } 3.77 \pm 5.89 \text{ (range: } –6; +14), \ P = 0.49]\) and at the 28 day follow-up \([4.4 \pm 6.81 \text{ (range: } –9.5; +17) \text{ versus } 6.06 \pm 5.23 \text{ (range: } –5.5; +14.5), \ P = 0.32]\).

#### Impact of changing clothes on pruritus at day 14 follow-up visit

There was no significant difference between the ivermectin group and the placebo group in reported changing of clothes between day of inclusion and day 14 in the analysis that included the total study population (85.29% versus 68.57%, \( P = 0.132 \)) as well as that including subjects with an established diagnosis of pediculosis corporis \([16/18 (88.9\%) \text{ versus } 12/21 (57.1\%), \ P = 0.065]\).

There was no significant difference between subjects who declared no pruritus and those who reported pruritus in changing of clothes between day of inclusion and day 14 in the analysis that included the total population of both the PP population \([13/14 (92.9\%) \text{ versus } 39/55 (70.9\%), \ P = 0.081]\) and for the ITT population \([13/14 (92.9\%) \text{ versus } 40/56 (71.4\%), \ P = 0.083]\), as well as in that including the subgroup of subjects with an established diagnosis of pediculosis corporis for both the PP population \([6/7 (85.7\%) \text{ versus } 22/32 (68.8\%), \ P = 0.6]\) and the ITT population \([6/9 (66.7\%) \text{ versus } 22/39 (56.4\%), \ P = 0.44]\).

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**Table 1. Demographic and baseline characteristics of the study groups**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Ivermectin (n = 42)</th>
<th>Placebo (n = 40)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>49.87 ± 11.28</td>
<td>51.43 ± 11.78</td>
<td>0.56</td>
</tr>
<tr>
<td>Weight (kg), mean ± SD</td>
<td>69.90 ± 12.55</td>
<td>74.00 ± 14.49</td>
<td>0.24</td>
</tr>
<tr>
<td>Duration of homelessness &gt; 24 months, n/total (%)</td>
<td>22/42 (52.4)</td>
<td>28/40 (70)</td>
<td>0.07</td>
</tr>
<tr>
<td>Magnitude of pruritus (cm), mean ± SD</td>
<td>10.21 ± 5.94</td>
<td>12 ± 4.34</td>
<td>0.39</td>
</tr>
<tr>
<td>Presumptive diagnosis of scabies or pediculosis corporis, n/total (%)</td>
<td>38/42 (90)</td>
<td>38/40 (95)</td>
<td>0.67</td>
</tr>
<tr>
<td>Established diagnosis of pediculosis corporis, n/total (%)</td>
<td>20/42 (47.6)</td>
<td>26/40 (65)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

*Presumptive diagnosis of scabies or pediculosis was based on the characteristics of pruritus and dermatological lesions.

*Established diagnosis of pediculosis corporis was based on the finding of body lice in clothes.*
Impact of ivermectin on pruritus

Among the total population of the study, multiple logistic regression analysis (Table 3) demonstrated that ivermectin was the only independent factor associated with recovery of pruritus at day 14 in both the PP population [OR: 4.60 (95% CI: 1.13; 18.73), \(P = 0.033\)] and for the ITT population [OR: 4.38 (95% CI: 1.07; 17.77), \(P = 0.039\)]. Among subjects with an established diagnosis of pediculosis corporis, ivermectin was found to be strongly associated with recovery of pruritus (\(P = 0.017\)).

Among subjects included in the ivermectin group, there was no significant difference in the rate of recovery of pruritus between individuals for whom body lice were found in clothes and those for whom body lice were not found (\(P = 0.4\)).

### Adverse events

No adverse events were observed at follow-up visits in subjects who received ivermectin as well as those who received placebo.

### Discussion

On day 14 after drug administration, pruritus was less frequently reported by subjects in the ivermectin group than those in the placebo group. Multiple logistic regression analysis found that ivermectin was an independent factor associated with the recovery of pruritus. No significant benefit was found at day 28.

In our study, clinical manifestations including pruritus characteristics and typical itchy lesions suggesting body lice or scabies were found in 92.7% of the subjects; furthermore, pediculosis corporis was established in 56.1% of the participants by the presence of body lice in the clothes. These findings are consistent with previous epidemiological studies that suggest that pruritus reported by homeless people is mainly due to ectoparasites, especially body lice infestation.1,2 The commonly admitted best treatment of body lice infestation is to change the clothes, 1,6 which could influence the prevalence of pruritus. However, analysis with a logistic regression model including ivermectin, change of clothes and duration of homelessness >24 months found that ivermectin was an independent factor associated with the absence of pruritus at day 14. This was observed in the whole homeless population and also in the subpopulation of subjects in whom pediculosis corporis was definitively established.

The failure of ivermectin to reduce the prevalence of pruritus at day 28 is consistent with previous reports on the treatment of scabies and body lice by this drug.5,7,8,10 In several previous publications, it has been reported that a single dose of 12 mg (200 \(\mu g/kg\)) of ivermectin for the treatment of scabies may be effective, but multiple doses are often required to achieve a...
complete cure. In a previous pilot study in humans, we observed that administration of three doses of 12 mg of oral ivermectin, separated by 1 week, resulted in a dramatic reduction of lice at day 14, but was followed by a recrudescence of lice infestation at day 45.

The reasons for the absence of a significant long-term beneficial effect of ivermectin in pruritus could be explained in several ways. First, since all subjects included in this study slept in the same crowded shelter, re-infestation from other untreated subjects is very likely. The transient effect of a single dose of ivermectin on pruritus could also reflect the lack of ovicidal action of the drug and the progressive decrease of drug concentration in blood. When nymphs hatched from the eggs several days after drug administration, the drug concentration may be ineffective. A regimen of two or three doses separated by 1 week was also suggested for the treatment of scabies. However, this regimen is insufficient to completely eradicate body lice. An emergence of resistant strains of lice to ivermectin in this population, who have been exposed to this drug several times, is possible, as has been reported in two subjects with multiple recurrences of crusted scabies, who received 30 and 58 doses of ivermectin, and in head lice.

Limitations of this study must be considered. One concerns the choice of pruritus as the endpoint. Even if characteristics of pruritus and itchy lesions suggested pediculosis and/or scabies in 92.7% of the subjects and that lice were observed in 56%, we are not sure that there are no other conditions including poor cutaneous hygiene and chronic skin conditions leading to pruritus. This may have limited the decrease in the pruritus prevalence. A second area of concern is the proportion of subjects lost to follow-up: 15% at day 14 and 29% at day 28. This was not surprising, because the majority of the population were chronic alcoholic individuals who usually refuse help and healthcare, despite the efforts of the shelter staff. However, it is unlikely that lost to follow-up introduced a substantial bias in the ITT analysis at day 14 because the loss was balanced and non-differential across the study groups (7/42 versus 5/40, P = 0.82). It has been suggested that an optimal regimen can be obtained for the treatment of body lice or scabies, with two or three repeated administrations of ivermectin at 14 or 7 day intervals, respectively. However, this strategy is difficult to achieve in the setting of homelessness. Consequently, based on the fact that larger doses of ivermectin would be efficient for a longer period of time, we decide to use only one high dose (24 mg). However, our results did not support this hypothesis. The lack of sustained efficacy of ivermectin in this study is likely due to the fact that only a small proportion of homeless people living in this shelter were given the treatment. If the treatment has individual benefits, it probably did not reduce significantly and persistently the infestation level of the community, as demonstrated previously. To reduce durably the lice infestation level and consequently the associated pruritus, two options are suggested: the repeated mass treatment of the community or the systematic empirical ivermectin treatment of pruritus in individuals seeking help. The last suggestion might be more easily accepted by the homeless themselves who undoubtedly recognized the efficacy of the ‘6 ivermectin pills’ on pruritus and will probably be easily convinced to seek medical advice to get ‘pills’ when itching occurs.

Despite these limitations, we think that our study provides a useful additional therapeutic option for the management of ectoparasite-based pruritus. The strategy we used in this study does not challenge those previously used for the treatment of ectoparasites in homeless people, including the use of insecticides, washing and change of all clothing and linens. The current study has not compared the efficacy of a single oral dose of ivermectin with these classical therapeutic measures including topical treatments. It has been suggested that ivermectin should be used routinely as a first-line therapy for patients who have not responded to a topical scabicide or those who may be unable to comply with topical therapy. Annual epidemiological surveys of the sheltered homeless in Marseille suggest that this population probably belongs to these categories since classic therapeutic measures have little efficacy in reducing the prevalence of scabies and body lice in homeless people. Thus, the beneficial effect at day 14 suggests that a single dose of oral ivermectin can help to improve, at least transiently, the clinical impact of body lice or scabies in these people. In addition, ivermectin can be used many times without occurrence of serious adverse effects. An increased risk of death has been reported among elderly homeless people who received ivermectin, but has not been confirmed. Randomized trials with ivermectin and clinical experience including millions of people in many countries found no major adverse side effects and suggest that the drug is remarkably safe. Thus, we believe that the repeated use of oral ivermectin on demand at each complaint of pruritus, in association, if possible, with insecticides and changing of clothes, could be a reasonable strategy to control ectoparasite-borne pruritus in homeless people.

Our study demonstrated that a single dose (400 μg/kg) of oral ivermectin has a beneficial effect because it can reduce the prevalence of pruritus in homeless people, but this effect is transient. Our findings suggest that ivermectin may become, in combination with other measures such as changing of clothes and use of topical treatment, the treatment of choice for pruritus in homeless people. The repeated use of this drug in homeless people with pruritus could result in reduced prevalence of pruritus in this population and therefore the prevalence of secondary cutaneous infections resulting in itchy lesions.

Acknowledgements

For their cooperation in the clinical trial, we thank the medical students, interns and fellows (A. Bienaimé, P. Seng, J. C. Lagier, S. Baille, M. Derouin), Dr A. Ménard, Dr H. Gadélius, M. Morlas (a social worker), nurses from the Centre de Formation et de Recherche en Santé Tropicale (Professor J. Delmont) from the infectious diseases services (Professor A. Stein) and from the emergency department (Dr P. Jean); as well as the directors, the general practitioner, the nurses and the personnel of the two shelters, M. Coantic and E. Blisson from Œuvre Antituberculeuse. The manuscript was translated into English with the support from American Journal Experts. A special thanks to Christopher Paddock from the CDC, Atlanta, GA for further English review and suggestions.

Funding

The study was funded by PHRC national 2005 (ivermectine et SDF) and supported by the Œuvre Antituberculeuse des Bouches du Rhône.
Ivermectin for pruritus in the homeless

Transparency declarations

None to declare.

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