Original article

Screening the asymptomatic soldiers after a stay in sub-Saharan Africa. A retrospective observational study

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ABSTRACT

Background: Many tropical clinics offer post-travel screening for parasitic infections in asymptomatic travellers. However, literature on attack rates and incidence rates of parasitic infections is scarce.

Method: All military personnel returning from a tropical region during the year 2018 were tested for the presence of antibodies against Strongyloides stercoralis, Schistosoma and Entamoeba histolytica. Test results were compared with previous results if available to distinguish recent and old infection.

Results: In total, 949 soldiers were included in the study. The median age was years 31 (IQR: 26–41), 96.3% were male. The median duration of stay in the tropics was 35 days (IQR: 14–90). The destination was predominantly central Africa. Serological tests were positive for S. stercoralis in 10 patients (1.1%), Schistosoma in 3 (0.3%), and E. histolytica in 16 (1.7%). The attack rates were 0.84, 0.32 and 1.69 respectively. The incidence rates were 3.99, 1.49 and 7.97 respectively.

Conclusions: The risk for parasitic infection in the asymptomatic returning soldiers is low. However, the potentially serious complications of unrecognised parasitic infection can legitimise systematic screening.

1. Introduction

Although post travel screening is offered by some travel clinics, the diagnostic yield of screening asymptomatic travellers is not well determined. The literature is rather sparse and the Center for Disease Control (CDC) doesn’t have guidelines or recommendations for the screening of asymptomatic international travellers. Some experts even discourage screening [1]. Some evidence based guidance for screening for strongyloidiasis is available, but it focuses on a migrant population [2]. From a theoretical point of view, screening for parasitic infections seems appropriate, since helminth infections, if unrecognised, can lead to serious complications. More particularly, infection with Strongyloides stercoralis and Schistosoma spp. can cause devastating morbidity and mortality later on in life. Mainly immunosuppressed patients can develop severe strongyloidiasis (hyperinfection syndrome or disseminated strongyloidiasis) with high mortality despite treatment [3]. Ectopic egg migration can lead to life-threatening disease in schistosomiasis [4].

Previous studies showed low incidences of helmith infections in (long-term) travellers, arguing against systematic screening [5]. On the other hand, screening for schistosomiasis, limited to travellers with a history of exposure to fresh water in endemic regions seems appropriate [6].

As military activities during deployments in tropical conditions comprise intensive soil and fresh water contact, the risk of being infected with helminths is suspected to be higher compared to the regular traveller [7–9]. A study of Aerssens et al. emphasizes the need for active systematic post-tropical screening in military personnel (n = 197) after deployment to a Schistosoma-endemic region in the Democratic Republic of the Congo, of which 61% of the 49 seropositive cases were asymptomatic. The median time from exposure to diagnosis for the seropositive group in this cohort was 768 days (interquartile range (IQR) 230) [10]. In consequence of the delayed diagnosis and related comorbidities in military personnel, Belgian Defence organises systematic screening of...
all military personnel residing in sub-Saharan Africa for a period of at least one month.

The aim of our study was to determine the usefulness of systematic screening asymptomatic military personnel after a stay in the tropics. More specific, attack rates and incidence rates were calculated for *S. stercoralis*, *Schistosoma* and *Entamoeba histolytica*.

2. Methods

2.1. Design and study population

The study was conducted in the center for infectious diseases (ID4C) at the Queen Astrid Military Hospital in Brussels (QAMH), Belgium. A computer assisted search was performed to identify all military personnel returning from a tropical region (most often sub-Saharan Africa) during a one year period from January 1, 2018 to January 1, 2019. The study was approved by the Medical Ethics Committee of the CHU Brugmann, Brussels, Belgium (CE 2019/80).

Before presenting to the ID4C, all participants filled in a standardized questionnaire containing questions on specific risks (swimming in lakes, rivers or streams, walking barefoot, contacts with ill people, unprotected sexual contact) according to routine practice.

All participants were seen by a medical doctor or (exceptionally) by a nurse who specialized in travel medicine. The data in the questionnaire, complemented with the history and physical examination done by the physician, determined the extent of the screening laboratory investigation.

2.2. Laboratory methods

All participants were tested for the presence of antibodies by Enzyme-Linked Immuno Sorbent Assay (ELISA) against *Entamoeba histolytica* (Entamoeba histolytica, Bordier Affinity Products, Cresier, Switzerland) and *Strongyloides stercoralis* (Strongyloides ratti, Bordier Affinity Products, Cresier, Switzerland). Additionally, testing for Schistosoma antibodies by ELISA (Schistosoma mansoni, Bordier Affinity Products, Crissier, Switzerland) and indirect hemagglutination antibody test (IHA) (ELI.H.A Schistosoma, ELITech Group MICROBIO, Puteaux, France) was done only after fresh water contact. All tests were performed according to the manufacturer’s instructions and were compared with previous results if available to distinguish recent and old infection.

2.3. Data analysis

Attack rates per 100 travelers were calculated by dividing the number of seroconversions by the total number participants at risk. Incidence rates per 1000 person-months were calculated by dividing the number of seroconversions by the total number of months in which participants were at risk for infection. We did not systematically perform baseline serology before leaving to the tropical zone. For calculations of attack rate and incidences we considered unknown serology as negative serology.

Baseline and demographic characteristics were summarized using descriptive statistics. Attack and incidence rates were computed with their 95%CI using normal approximation for attack rates and quadratic approximation to the Poisson log likelihood Function for incidence rates (IR). Fisher Exact’s test, with post-hoc analysis using chi²-tests and Bonferroni’s correction method, was used for the IR difference between regions. Tests are considered significant for a p-value of <0.05. All statistical analyses were performed using STATA®IC 14.1 (StataCorp, College Station, Texas 77845 USA).

3. Results

3.1. Study population

Overall, 949 soldiers were included in the study. The median age was years 31 (IQR: 26–41), 96.3% were male. The median duration of stay in the tropics was 35 days (IQR: 14–90). Country of destination was Gabon in the major part (n = 535, 56.4%) followed by Mali (n = 354, 37.6%) and other countries (comprising Burundi, Central African Republic, Democratic Republic of Congo, Rwanda, Niger). Malaria prophylaxis consisted of doxycycline in n = 766 (80.7%), atovaquone-proguanil (10.4%), mefloquine (2.1%) and a combination of several agents in 4.3%. The majority of the population (59.6%) was compliant with this prophylactic treatment. Fresh-water contact was mentioned in n = 392 (41.3%), mainly in Gabon (as part of their mission activity). Walking barefoot or other intense contact with soil was reported in n = 301 (31.7%), contact with ill people in n = 19 (2%), and sexual contact in n = 10 (1.1%), of which three were unprotected.

3.2. Diagnoses

Overall, serological tests were positive for *S. stercoralis* in 10 patients (1.1%), *Schistosoma* in 3 (0.3%), and *E. histolytica* in 16 (1.7%). Attack rates and incidence rates are described in Table 1.

The 10 patients with a positive serology for Strongyloides were completely asymptomatic. Two of them already demonstrated antibodies on a previous sample. They were considered as having old infections, of whom one was retreated with ivermectin. The other patients had unknown (n = 4) or negative (n = 4) previous serology. Eosinophilia was recorded in only 2 out of 10 patients, with eosinophil counts of respectively 500 10⁹/l (7.2%) and 1200 10⁹/l (15%) (Table 2). Taking into account the previous serology only 8 patients had a recent Strongyloides infection leading to an attack rate (95% CI) of 0.84% (0.26–1.42).

The three patients diagnosed with schistosomiasis (Table 3) were all exposed to fresh water in Africa. Previous serology for schistosomiasis was unknown (n = 2) or negative (n = 1). Two out of this three patients had slightly elevated eosinophilia (600 10⁹/l; 9.5% and 1100 10⁹/l; 13.3% respectively). If only those patients who reported contact with fresh water were considered at risk, the attack rate and incidence rate (95% CI) for schistosomiasis rose slightly from respectively 0.32–0.76% (0.00–1.63) and from 1.49 to 4.48 per 1000 person-months of travel (1.45–13.89).

All 16 patients with a positive serology for *E. histolytica* were considered as having a recent infection, since previous serology was negative (n = 6) or unknown (n = 10). Only 2 out of 16 patients had minor symptoms of diarrhea for which they didn’t look for medical contact before presenting to ID4C (Table 4).

4. Discussion

In this retrospective study the serology based attack rates and incidence rates are low. Recent infections with any of the three parasites was found in 2.8% of soldiers, and disease specific incidences ranged between 1.49 and 7.97 per 1000 person-months of travel.

Since the military activity in Gabon activity comprises jungle training, our data are representative only for non-military travelers in case of adventure travel (which has three main components: physical activity, connection with nature and immersive cultural experience).

Other papers describe variable attack rates and incidence rates in a different population (mainly related to touristic activities and Africa as the travel destination in only about 20%). Recent infection (suggestive by serology) with Schistosoma species and *S. stercoralis* was found in respectively 0.51% and 0.25% of travelers to developing countries (median travel duration of 21 days) with incidence rates of respectively 6.4 and 3.2 per 1000 person-months [5]. In another cohort only one case
Table 1
Attack and incidence rate of different parasitic infections among exposed military personnel.

<table>
<thead>
<tr>
<th>Parasites</th>
<th>Region</th>
<th>Number of seroconversion</th>
<th>Number of person at risk</th>
<th>Person-months of exposition</th>
<th>Attack rate, % (95% CI)</th>
<th>Incidence Rate/1000 person-months (95% CI)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongyloidosis</td>
<td>All regions</td>
<td>8</td>
<td>949</td>
<td>2007</td>
<td>0.84 [0.26–1.42]</td>
<td>3.99 [1.99–7.97]</td>
<td>0.045**</td>
</tr>
<tr>
<td></td>
<td>Gabon</td>
<td>5</td>
<td>535</td>
<td>476</td>
<td>0.93 [0.12–1.74]</td>
<td>10.50 [4.37–25.24]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mali</td>
<td>3</td>
<td>354</td>
<td>1227</td>
<td>0.85 [0.00–1.80]</td>
<td>2.45 [0.79–7.58]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>0</td>
<td>60</td>
<td>304</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>All regions</td>
<td>3</td>
<td>949</td>
<td>2007</td>
<td>0.32 [0.00–0.67]</td>
<td>1.49 [0.48–4.63]</td>
<td>0.506</td>
</tr>
<tr>
<td></td>
<td>Gabon</td>
<td>0</td>
<td>535</td>
<td>476</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mali</td>
<td>2</td>
<td>354</td>
<td>1227</td>
<td>0.56 [0.00–1.35]</td>
<td>1.63 [0.41–6.52]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>1</td>
<td>60</td>
<td>304</td>
<td>1.67 [0.00–4.91]</td>
<td>3.29 [0.46–23.33]</td>
<td></td>
</tr>
<tr>
<td>Entamoeba histolytica</td>
<td>All regions</td>
<td>16</td>
<td>949</td>
<td>2007</td>
<td>1.69 [0.87–2.51]</td>
<td>7.97 [4.88–13.01]</td>
<td>0.004***</td>
</tr>
<tr>
<td></td>
<td>Gabon</td>
<td>9</td>
<td>535</td>
<td>476</td>
<td>1.68 [0.59–2.77]</td>
<td>18.91 [9.84–36.34]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mali</td>
<td>4</td>
<td>354</td>
<td>1227</td>
<td>1.13 [0.03–2.23]</td>
<td>3.26 [1.22–8.69]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>3</td>
<td>60</td>
<td>304</td>
<td>5.00 [0.00–10.51]</td>
<td>9.86 [3.18–30.57]</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher Exact’s test for the IR difference between regions. ** p-value with Bonferroni’s correction for the IR difference between Gabon and Mali = 0.086. *** p-value with Bonferroni’s correction for the IR difference between Gabon and Mali = 0.004.

a One-sided 97.5% CI.

Table 2
Patients with positive serology for Strongyloides.

<table>
<thead>
<tr>
<th>Strongyloides stercoralis</th>
<th>N = 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travel destination</td>
<td>Travel duration (days)</td>
</tr>
<tr>
<td>Mali</td>
<td>90</td>
</tr>
<tr>
<td>Mali</td>
<td>90</td>
</tr>
<tr>
<td>Mali</td>
<td>60</td>
</tr>
<tr>
<td>Gabon</td>
<td>28</td>
</tr>
<tr>
<td>Gabon</td>
<td>25</td>
</tr>
<tr>
<td>Gabon</td>
<td>90</td>
</tr>
<tr>
<td>Gabon</td>
<td>21</td>
</tr>
<tr>
<td>Gabon</td>
<td>30</td>
</tr>
<tr>
<td>Gabon</td>
<td>14</td>
</tr>
<tr>
<td>Gabon</td>
<td>30</td>
</tr>
</tbody>
</table>

* no routine stool or PCR testing.

Table 3
Patients with positive serology for Schistosomiasis.

<table>
<thead>
<tr>
<th>Schistosomiasis</th>
<th>N = 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Destination</td>
<td>Travel duration (days)</td>
</tr>
<tr>
<td>Mali</td>
<td>90</td>
</tr>
<tr>
<td>Rwanda</td>
<td>30</td>
</tr>
<tr>
<td>Mali</td>
<td>120</td>
</tr>
</tbody>
</table>

* no routine stool or PCR testing.
out of 437 (0.2%) was positive (combined stool polymerase chain reaction (PCR) and serology) for *S. stercoralis* in travelers to (sub)tropics (median travel duration of 12 weeks) whereas none of the stool samples obtained two weeks after return was positive for *E. histolytica* [6]. In a large group of long term travelers (median travel duration 20 weeks) Schistosoma and *S. stercoralis* antibodies were detected in respectively 0.61 and 0.17% (incidence rates respectively 1.5 and 0.34 per 1000 person-months) [11].

Our results need to be interpreted very cautiously. Diagnoses were made serologically and no stool microscopy, antigen detection or PCR were performed which may have underestimated the attack and incidence rates. However, appointments at the ID4C were at least 3 months after return, a time frame during which seroconversion in a majority of patients infected with *S. stercoralis* or *Schistosoma* is expected to occur [12]. This may not be true for *E. histolytica* infections that may only become invasive after this time frame [13]. On the other hand, serological cross-reactions between helminths are a well known phenomenon and the majority of test results in our patients was only weakly positive [14]. In addition the low pre-test probability in low prevalence settings such as in our population may have revealed false positive results, and baseline serology was not systematically performed before leaving to a tropical region and we considered unknown serology as negative thereby disregarding pre-existence of antibodies as a consequence of an infection during previous missions. For all these reasons the true attack and incidence rates might be lower than the ones displayed in our results.

Due to known long term risks of strongyloidiasis and schistosomiasis, and as we believe that the benefit of screening outweighs the harms of overdiagnosis and consequent treatment, all patient with positive serology were treated. Strongyloidiasis was treated by ivermectin, schistosomiasis by praziquantel. Patients with *E. histolytica* antibodies were treated by paromomycin and metronidazole added sometimes, because of the potential risk to infect others or to develop (extra-intestinal) disease.

No systematic serological follow-up after treatment was arranged partly due to difficulties in interpreting these results. Some authors suggest the use of serial serologies to assess efficacy of the treatment. A decrease of antibody titer at 6–12 months after treatment could be indicative of eradication of *Strongyloides stercoralis* [15,16].

Eosinophilia is suggested as a marker for helmint infection, and is often recommended for screening of returning travelers. However, differential diagnosis is broad when eosinophilia is detected and this test has several limitations. In a cohort of asymptomatic returning travelers (n = 1605), the sensitivity of the eosinophil count for an eosinophilia-associated parasitic infection was only 27%. The specificity was 91%, with a positive predictive value of 14% [17]. The high false positive rate easily leads to increased costs (additional laboratory investigations) and follow-up visits. The limited value of eosinophilia was recently stressed by the observation that none of the participants with recent helmint infection had eosinophilia >450 mm⁻³ [11]. In our study eosinophilia (>450 10⁹/l) was detected in two out of eight patients with recent *Strongyloides* infection and in two out of three patients with schistosomiasis.

5. Conclusion

Attack rates and incidence rates of strongyloidiasis, schistosomiasis and *E. histolytica* were low in soldiers returning from a mission in a sub-Saharan region. However, the potentially serious complications of unrecognised parasitic infection can legitimise systematic screening.

CRediT authorship contribution statement

**Peter Vanbrabant:** Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization. **Benjamin Damanet:** Software, Validation, Formal analysis, Data curation, Writing - review & editing, Visualization. **Cedric Maussen:** Software, Formal analysis, Data curation. **Marjan Van Esch-Vekel:** Validation, Writing - review & editing, Supervision. **Patrick Soentjens:** Validation, Writing - review & editing, Supervision, Project administration.

Declaration of competing interest

The authors declare that they have no competing interests.

References

[8] Kelley PW, Takafuji ET, Wiener H, Milhous W, Miller RN. An outbreak of hookworm infection associated with military operations in the Saharan region. However, the potentially serious complications of unrecognised parasitic infection can legitimise systematic screening.

CRediT authorship contribution statement

**Peter Vanbrabant:** Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization. **Benjamin Damanet:** Software, Validation, Formal analysis, Data curation, Writing - review & editing, Visualization. **Cedric Maussen:** Software, Formal analysis, Data curation. **Marjan Van Esch-Vekel:** Validation, Writing - review & editing, Supervision. **Patrick Soentjens:** Validation, Writing - review & editing, Supervision, Project administration.

Declaration of competing interest

The authors declare that they have no competing interests.

References


