Vaccinations and malaria prophylaxis for long-term travellers travelling from Greece: A prospective, questionnaire-based analysis

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Received 16 February 2013; received in revised form 14 March 2014; accepted 13 May 2014
Available online 23 May 2014

KEYWORDS
Vaccine; Prophylaxis; Long-term travellers; Typhoid; Malaria

Summary The purpose of this prospective, questionnaire-based study is to assess pre-travel vaccinations and malaria prophylaxis for long-term travellers who receive pre-travel advice in Greece. A total of 4721 travellers were studied from January 1, 2009 through December 31, 2012. Travellers sought pre-travel advice at a mean of 19.7 days (range: 0–349 days) before departure. Long-term travellers (>1 month) accounted for 2205 (46.7%) of all travellers. Long-term travellers had a mean age of 34.5 years. The majority of them were men (79.8%). In terms of destinations, 84% were visiting malaria-endemic countries and sub-Saharan Africa was the most common destination (17.7%). Most long-term travellers pursued trips for work purposes (70%), visited urban areas (79.6%) and stayed in hotels (29.2%). Yellow fever, typhoid fever, hepatitis A and tetanus/diphtheria vaccines were administered to 1647 (74.7%), 741 (33.6%), 652 (29.5%), and 589 (26.7%) travellers, respectively. Yellow fever vaccine was administered to 339 (87%) and 132 (71%) of long-term travellers to sub-Saharan Africa and South America respectively, whereas typhoid vaccine to 119 (90.8%) and 330 (84.6%) of those travelling to the Indian subcontinent and sub-Saharan Africa respectively. Rabies vaccine was administered to 14 (0.6%) of them. Malaria prophylaxis was recommended to 446 (20%) of long-term travellers. Mefloquine was the most commonly (49%) prescribed agent, and was prescribed to 26.7% of long-term travellers to sub-Saharan Africa. In conclusion, this study revealed that recommendations for vaccine and malaria prophylaxis for long-term travellers to developing countries should be more selective, based on the assessment of all travellers’ and travel characteristics, in order to provide adequate pre-travel preparation for this high risk group.
1. Introduction

Long-term travel is defined typically as a travel of ≥1 month duration [1]. Reasons for long-term travels include tourism, diplomatic, missionary, Peace Corps Volunteer and humanitarian aid work, education and research, military operations, and corporate expatriation [2–6]. Long-term travels are associated with significant risk for specific health problems [1,5,7–14]. In particular, long-term travels to the tropics predispose to higher risk for acquisition of a wide range of infectious diseases compared to short-term travels, because of prolonged exposure to pathogens, limited environmental hygiene, close contact with the local population, poorly developed infrastructure for water supply and sewerage disposal, extreme climatic conditions, risk-taking behaviour, and lack of medical facilities [9,10]. The risk of malaria acquisition is higher in long-term compared to short-term travellers due to longer period of exposure to mosquito bites and poor compliance with chemoprophylaxis and preventive measures [5,11,14]. Malaria recommendations have been difficult to standardize due to the diversity of long-term travellers and their itineraries [14]. Furthermore, long-term travellers are at higher risk for vaccine-preventable diseases, including hepatitis A, typhoid fever, rabies, hepatitis B, Japanese encephalitis and meningitis [12]. The aim of this study is to assess vaccinations and malaria prophylaxis in long-term travellers from Greece travelling to tropical and subtropical countries.

2. Methods

In Greece pre-travel services are provided mainly in the 57 Regional Departments of Public Health, which are the solely authorized yellow fever vaccination centres in this country. Rabies, typhoid, tetravalent meningitis A,C,W135,Y, and cholera vaccines are also delivered exclusively through these centres; however other travel and routine vaccines are also administered. Pre-travel services are provided according to the guidelines of the Hellenic Centre for Disease Control and Prevention, the World Health Organization and the United States Centers for Disease Control and Prevention guidelines. Routine vaccines are administered in accordance with the National Vaccination Program of Greece, which include vaccines against: tetanus-diptheria-pertussis, poliomyelitis, Haemophilus influenzae type B, measles–mumps–rubella (MMR), hepatitis A, hepatitis B, pneumococcus, meningococcus serotype C, human papilloma virus, tuberculosis (Bacillus Calmette-Guérin vaccine), influenza (high risk groups), and rotavirus. These vaccines are administered mainly by paediatricians, but also by internal medicine physicians and primary health-care physicians working in the public or private sector.

All international travellers who attended the 57 Regional Public Health Departments from January 1, 2009 through December 31, 2012 were asked to participate in a questionnaire-based study. The questionnaire was completed with the assistance of the health professional. The following data were collected prospectively using one standardized form per traveller: age, gender, nationality, date of departure, travel destination, duration and purpose of travel, type of accommodation, administration of routine and travel vaccines and chemoprophylaxis. Consent was requested from all participants. Approval for the study was given by the Hellenic Center for Disease Control and Prevention.

Long-term travel was defined as a trip of ≥1 month duration, while short-term travel was defined as a trip of <1 month. Urban accommodation was defined as towns with a population of ≥5000 people, whereas rural accommodation was defined as villages of <5000 population or staying in the countryside.

Statistical analysis was performed using the STATA 8.0 statistical package. χ² and t-test were used in order to investigate any possible relation of duration of travel with travellers’ and/or travel characteristics. P-values of <0.05 were considered statistically significant. The statistically significant parameters were used as independent variables in a logistic regression model with duration of travel as a dependant variable.

3. Results

A total of 4721 international travellers participated in the study, with a participation rate ranging from 70% to 80% per Public Health Department. Most (40%) of participants were from the region of Attica. Travellers sought pre-travel advice at a mean of 19.7 days (range: 0–349 days) before departure. Long-term travellers accounted for 46.7% of all travellers. In terms of duration of travel, 600 (12.7%), 602 (12.8%) and 1003 (21.2%) long-term travellers travelled for 1–3, >3–6 months and >6 months, respectively. Travel characteristics and destinations in relation to duration of travel are shown in Table 1. The majority of long-term travellers were men (79.8%). Long-term travellers were younger than short-term travellers (mean age: 34.5 and 40.9, respectively). 84% of long-term travellers were visiting malaria-endemic countries. Sub-Saharan Africa was the most common destination (17.7%) followed by the Middle East (8.9%) and South America (8.4%). Most long-term travellers pursued trips for work purposes (70%) and recreation (26.7%), travel to urban areas (79.6%) and stayed in hotels (29.2%). Possible involvement in outdoor activities
was reported by 184 (8.3%) travellers and possible contact with animals by 103 (4.7%) of them. Table 2 shows vaccine recommendation rates for long-term travellers by vaccine. Yellow fever, typhoid fever, hepatitis A and tetanus vaccines were administered to 1647 (74.7%), 741 (33.6%), 652 (29.5%) and 589 (26.7%) of long-term travellers, respectively. Yellow fever vaccine was administered to 339 (87%) and 132 (71%) of long-term travellers to sub-Saharan Africa and South America, respectively. The vaccination rate was higher than expected (approximately 30%), mainly for long-term travellers to South America. In particular, of 1647 long-term travellers who were vaccinated against yellow fever, 140 (8.5%) and 359 (21.8%) travelled to areas of sub-Saharan Africa and South America, respectively, for whom the vaccine is not or generally not recommended. Of those
long-term travellers who received typhoid vaccine, 119 (90.8%) and 330 (84.6%) travelled to the Indian subcontinent and the sub-Saharan Africa respectively. The majority of long-term travellers to whom meningococcal vaccination was administered travelled to sub-Saharan Africa (389 travellers; 87%).

Malaria prophylaxis was recommended to 446 (20%) long-term travellers. Mefloquine was the most commonly prescribed agent (49%), followed by atovaquone/proguanil (34%), chloroquine (2%) and doxycycline (1.3%). Mefloquine and atovaquone/proguanil were predominantly prescribed for sub-Saharan Africa, whereas chloroquine was prescribed only in few travellers to Central America and the Caribbean. Table 3 describes malaria prophylaxis according to destination. The majority of long-term travellers to whom chemoprophylaxis was prescribed travelled to sub-Saharan Africa, the Indian Subcontinent and South America. For sub-Saharan Africa, 26.7% and 14.1% of long-term travellers were prescribed mefloquine and atovaquone/proguanil respectively.

Statistically significant parameters were used as independent variables in a logistic regression model with duration of travel as a dependant variable. There was a statistically significant association between long duration of travel, and age; short-term travellers were older than long-term travellers (mean age: 40.9 vs 34.5 years (p-value < 0.001)). The association of destination and purpose of travel with duration of travel was statistically significant; long-term travellers travelled more frequently for work, whereas for short-term travellers recreation was the most common purpose of travel (p-value < 0.001). In terms of routine vaccine recommendations, long-term travellers were more frequently vaccinated against MMR compared to short-term travellers (p-value < 0.001), whereas influenza and hepatitis A were more frequently administered to short-term travellers (p-value < 0.001 and 0.006 respectively). Regarding travel vaccines recommendations, Yellow fever, typhoid and cholera vaccine were administered more frequently to long-term travellers than short-term travellers (p-value < 0.002, < 0.001 and < 0.001 respectively). Duration of travel was statistically significant with malaria prophylaxis. In addition, atovaquone/proguanil was more often prescribed to short-term travellers compared to long-term travellers (p-value = 0.036).

4. Discussion

Long-term travellers are at increased risk to exposure to many infections including vaccine-preventable diseases and malaria. In this study, we assess vaccinations and malaria prophylaxis for 2205 long-term international travellers from Greece who sought pre-travel services at Public Health Departments during 2009–2012. The majority of travellers have to seek advice at the Public Health Departments due to the exclusive availability of certain vaccines there. In Greece pre-travel advice, vaccinations, and antimalarial drugs are provided by the 57 Regional Departments of Public Health across the country which are the main travel health providers. Health professionals providing travel health services include physicians specialized in public health or primary care, nurses, and health visitors. However the number of travellers seeking pre-travel advice is very low; according to the National Statistics Authority (EL.STAT), nearly 76,000 travellers from Greece travelled to developing countries during 2009–2010, of whom 6975 (9.1%) were long-term travellers (>1 month) [15]. Of them, approximately 31.6% sought pre-travel advice. This rate was comparable to 31–52% reported in other studies [16–18].

In our study, the proportion of long-term travellers was higher compared to data from the GeoSentinel Surveillance network and a United States study [7,19]. In accordance
with the latter studies [7,19], most long-term travellers were young and mainly men and Africa constituted their prevalent destination. The majority of long-term travellers pursued trips for work purposes, whereas the GeoSentinel analysis showed that most of them travelled for volunteer activities and business [7]; the proportion of VFRs among long-term travellers was lower in the studied population compared to that of a recent French study [20].

Common vaccine-preventable diseases in international travellers include enteric fever, acute hepatitis and influenza [7,21]. In the current study, yellow fever vaccine was the most commonly delivered vaccine to long-term travellers; the difference between “requirement” and “recommendation” for yellow fever vaccination may not be always perceived clearly by travel health consultants [22]. Although, considering the travel destination solely the recommendation of yellow fever vaccination was generally justified, other travel characteristics such as area and place of stay, duration of travel and possible involvement in high risk activities should have been considered [22].

Typhoid vaccine was the second most commonly administered vaccine. In particular, typhoid vaccine was delivered to >90% of long-term travellers travelling to highly endemic areas. In the GeoSentinel study, typhoid fever was a common diagnosis among cases of vaccine-preventable diseases, accounting for 47.6% of them [21]. The analysis from the GeoSentinel Surveillance network demonstrated that the rate of enteric fever was higher in long-term compared to short-term travellers (9/1000 vs 5/1000) [7]. Typhoid vaccination rates in the current study were within expectations.

Hepatitis A vaccine was recommended to less than one third of long-term travellers, although nearly 100% of them travelled to destinations of high or medium endemicity. In contrast, in other studies hepatitis A was the most frequently administered vaccine to international travellers before departure [19]. Data from the GeoSentinel Surveillance network indicate that the rate of hepatitis A is higher in long-term than in short-term travellers (3/1000 vs 2/1000) [7]. Hepatitis A vaccination should be recommended to susceptible people travelling for any purpose, frequency, or duration to countries with high or intermediate hepatitis A endemicity [25–27]. The lower vaccination rates in the current study could be related to possible pre-existing immunity [18], given the fact that almost all long-term travellers were of Greek nationality.

Meningococcal vaccination was recommended to nearly all long-term travellers to sub-Saharan Africa. Tetravalent meningococcal vaccine (A, C, W135, Y) is indicated for long-term travellers, and particularly for those living in close contact with the indigenous population [27], therefore meningococcal vaccination rates in the current study were within expectations.

Hepatitis B vaccine recommendation was lower than expected. In the GeoSentinel study, hepatitis B was also a common cause of vaccine-preventable disease [21]. Unvaccinated people travelling to countries with intermediate to high levels of endemic hepatitis B transmission for long period of time are at higher risk of contracting hepatitis B due to possible exposure to casual and unprotected sexual contact or through medical treatment [25,28]. Previous immunization and poor perception of the risk of hepatitis B infection may be potential reasons for low hepatitis B vaccination rates in our study [15,29,30].

Rabies vaccination was recommended to only a small proportion of our long-term travellers to rabies-endemic areas, which is much lower compared to the results of a recent French (31%) [31] and a United States study (23%)

<table>
<thead>
<tr>
<th>Chemoprophylaxis</th>
<th>Mefloquine</th>
<th>Atovaquone/proguanil</th>
<th>Chloroquine</th>
<th>Doxycycline</th>
<th>p-Value</th>
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<tr>
<td>High malaria endemicity (undisputed indication of malaria prophylaxis)</td>
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<tr>
<td>Sub-Saharan Africa</td>
<td>104 (26.7)</td>
<td>55 (14.1)</td>
<td>2 (0.5)</td>
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<td>Variable malaria transmission (variable indication of malaria prophylaxis)</td>
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<td>North Africa</td>
<td>6 (20.7)</td>
<td>2 (6.9)</td>
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<td>South Africa</td>
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<td>10 (18.9)</td>
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<td>Caribbean</td>
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<td>North America</td>
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<td>p-Value</td>
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<td>North America (1 (2.7) 0 (0) 0 (0) 0 (0))</td>
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<td>Australia (0 (0) 0 (0) 0 (0) 0 (0))</td>
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* These destinations are 2nd or 3rd travel destinations.
Vaccine and malaria prophylaxis for long-term travellers

[19]. Rabies vaccine should be recommended for long-term travellers to areas with a significant risk of exposure [32,33]. In the current study 4.7% of long-term travellers reported potential contact with animals. The low vaccination rates against rabies may be related to travellers’ poor awareness and/or travel health consultants’ lack of knowledge about the risks of rabies exposure, as shown in a recent study from Greece [34].

Long-term travellers living in countries where vaccine-preventable diseases are more prevalent should receive appropriate booster doses of their routine vaccinations [1,11,12]. In the current study, poliomyelitis, MMR, and influenza low vaccination rates may be associated with previous immunization, since these vaccines are provided also by other health providers [15].

An estimated 30,000 cases of travel-associated malaria are imported annually in industrialized countries [35]. Malaria is diagnosed more frequently among long-term travellers compared to short-term travellers (68/1000 vs 39/1000 respectively) [7,11,14], which is attributed to the poor adherence of the former to chemoprophylaxis and personal protection measures. The use of counterfeit drugs is a serious problem for long-term travellers [1,6,11,14].

Mefloquine is the most commonly recommended antimarial by most travel health consultants for long-term travellers travelling to chloroquine-resistant destinations. However, mefloquine may not be well prescribed among long-term travellers, primarily because of the fear of neuropsychiatric side-effects [1,6,11,14]. Recommendations in regards to the continuous use of atovaquone/proguanil depend on the national guidelines of each country [1,11]. According to the Hellenic National Organization for Medicines guidelines, atovaquone/proguanil is only recommended for short-term travellers. Cost could be a limiting factor for long-term prophylaxis also [1,14]. Long-term travellers rarely use doxycycline, mainly because of the fear of side-effects during the extended periods of travel [1,11,14].

In our study, malaria prophylaxis prescription for long-term travellers was lower than expected. In the USA study, this rate was higher; mefloquine and doxycycline were prescribed to 59% and 61% respectively to travellers pursuing trips >28 days [19]. Stand By Emergency Treatments (SBET) and Primaquine as a primary prophylaxis were never recommended in the current study. Retrospective analysis of the data about duration of travel, destination, area and place of stay and possible activities, that malaria prophylaxis was under-prescribed particularly for travellers to sub-Saharan Africa (20% lower than expected). This may be related to inadequate assessment by travel health consultants about risk regarding acquisition of malaria and more selective malaria recommendations [38]. Furthermore travellers may be reluctant to take antimalarials for several months.

The limitations of the current study include lack of data about travellers’ pre-existing immunization status and about those who declined vaccinations or chemoprophylaxis. Furthermore there was no information about destination in 23.9% of long-term travellers. However, the large number of participants gave us the opportunity to study a wide range of travellers’ characteristics and assess travel vaccine and malaria prophylaxis.

In conclusion, our results show that there is a wide variability in vaccination and prescription of malaria chemoprophylaxis for long-term travellers from Greece travelling to tropical and subtropical countries and recommendations should be more selective, based on careful risk assessment. More focused studies are suggested in order to understand the particular needs of long-term travellers. Public health strategies should be developed in order to increase travellers’ awareness in particular of high risk groups such as long-term travellers about travel risks and the importance of pre-travel consultation. Travel health providers should increase their efforts through training-education and regular access to reference resources for updated information and consistent guidance in order to improve their awareness.

Conflict of interest statement

None declared.

References