ORIGINAL ARTICLE

Travellers returning to Sweden with falciparum malaria: Pre-travel advice, behaviour, chemoprophylaxis and diagnostic delay

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Abstract
We have investigated pre-travel advice, behaviour, chemoprophylaxis and diagnostic delay in travellers returning to Sweden with falciparum malaria. Questionnaires were distributed to patients having been notified with falciparum malaria from 1994 to 2001. Of 408 notified patients, 237 (58%) returned the questionnaires; 62% were males and 43% above the age of 45 y. Africa was the travel destination in 90% of the cases, and 27% had travelled to Kenya. 69% had spent more than 1 night in the countryside, and 6% had stayed in modern urban areas only. 40% took an adequate dose of chemoprophylaxis, although this proportion decreased from 55% to 12% during the study period. Nine per cent used both bed nets and mosquito repellents regularly. The median time from onset of symptoms to contact with health care professionals was 2 d, and from that contact to start of malaria treatment the median time was less than 24 h.

Introduction
A large number of international travellers fall ill with malaria each y, while or after visiting endemic countries. In the European Union member states, the annual number of reported cases is 11,000, with 8000 falciparum infections [1]. There has been an increase in travel to tropical countries during recent decades [2], as well as an increasing number of people from malaria endemic areas emigrating to Europe [3]. Available figures reveal an 8-fold increase in officially reported European malaria cases during the last 25 y, and at the same time the percentage of malaria cases attributable to Plasmodium falciparum has risen from 30 to 70% of the total cases [4]. Descriptive data from TropNet Europ indicate that a majority of falciparum infections in Europe are imported from West Africa, and that use of chemoprophylaxis among malaria cases is infrequent both in travellers and immigrants; 60% and 72%, respectively, having travelled without using it [5]. However, malaria is extremely rare as a cause of death in Sweden with less than 1 case per y (personal knowledge). Since 1997, Swedish guidelines for the use of malaria prophylaxis have been published on an annual basis by the National Expert Group on Malaria Prophylaxis at the Swedish Institute for Infectious Disease Control (SMI). In 1998, the recommended medical prophylaxis was changed from chloroquine and proguanil to mefloquine for travellers to malaria endemic areas in Africa, with the exception of those travelling for a shorter stay to tourist resorts, e.g. Gambia. In the 2000 guidelines, mefloquine was recommended for all travellers to malaria endemic areas in Africa, irrespective of type and length of stay. We have recently studied the risk of imported malaria in Sweden [6]. Since pre-travel advice and adherence to recommendations on malaria prophylaxis may differ between countries, the aim of the present study was to investigate these factors in patients

Material and methods

Malaria is a notifiable disease in Sweden under the Communicable Diseases Act. Cases are reported both by the clinician having seen the patient (clinical notification) and by the laboratory having diagnosed the disease (laboratory notification) to the Swedish Institute for Infectious Disease Control (SMI). Using the unique personal identification number issued to all Swedish residents, the two sources of notification can be linked, thus increasing the sensitivity of the notification system [7].

In 1994, SMI started to send questionnaires to patients having recently been notified as a case of malaria falciparum. The objective was to collect information needed to issue guidelines for malaria prophylaxis to Swedish travellers. The questionnaires were distributed with the assistance of the patients’ doctors, and included questions on pre-travel advice, travel route, length of stay, purpose of stay, type of living, use of chemoprophylaxis, prophylaxis against mosquito bites, time span between first symptoms of malaria, contact with the health care and specific malaria treatment. If the first contact with the health care system was by telephone, the patients were also asked what advice they had received.

The questionnaires were distributed every 6 months to patients diagnosed with falciparum malaria from 1 January 1994 to 31 December 2001, following slightly varying routines: in the first year (1994), questionnaires were sent to all patients, whereas in 1995, none were sent out. Since responses from persons of presumed non-Swedish origin were difficult to obtain, the focus was changed, and in the 2 consecutive y questionnaires were only sent to persons with names suggesting a Swedish origin. After an evaluation in 1998, when again no questionnaires were sent, it was decided to again collect information from all patients. One reason was that the proportion of cases of presumed non-Swedish origin was increasing. To improve compliance, the questionnaire was translated into English. During the whole period, 408 questionnaires were distributed.

For evaluation of doses of chemoprophylaxis we followed the published Swedish guidelines [8]. We did not have information about the patients’ weights; hence an adequate dose was considered to be 2 tablets or more of 250 mg chloroquine per week, alone or in combination with (depending on current recommendations) 1 or 2 tablets of 100 mg proguanil per d or 1 tablet of 250 mg mefloquine per week.

Results

Cases

Of the original 408 patients who received a questionnaire, 237 (58%) responded, with a variation in response rate from 39% in 2001 to 77% in 1997. Of the 171 non-responders, data on gender, age and area of infection are available for 150 patients. The non-responders were younger, and had travelled more often to Central Africa than the responders (Table I). We had no information about the country of birth of the patients, or for how long they had been living in Sweden. Thus, we could not draw any conclusions concerning their immunity against malaria.

Country and area of travel

90% of the malaria cases had been infected in Africa; the majority has been diagnosed after travel to Kenya (\( n = 64; 27\% \)), Tanzania (\( n = 35; 15\% \)) or the Gambia (\( n = 33; 14\% \)) (Table I). Some travellers had visited more than 1 country, making it impossible to deduce the country of infection. To further elucidate the origin of the infections, travel destinations were divided into regions (Table I). The 237 responders had been visiting altogether 264 regions, i.e. most of them had been to 1 region only.

Length of travel

The median length of travelling time was 23 d (range 1–545 d). Five persons had stayed for less than 1 week, and 16 persons had stayed for a y or more. Six persons did not answer the question.

Purpose of stay and type of living

56 (32%) of the cases travelled as tourists, 45 (26%) classified their trip as business journey and 37 (21%) had visited friends; 28 cases (16%) had different combination of the alternatives above. Nine of the responders (5%) did not answer this question. This question was not in the questionnaire in 1994, and patients from this y (\( n = 62 \)) were excluded from the analyses. The majority, 163 (69%) of the cases, stayed at least 1 night in the countryside, 14 (6%) spent their time in modern urban areas only and the rest of the travellers had spent their time in the manners set out in Table I. More than 1 alternative was possible with this question.

Pre-travel advice

79 (33%) of the responders had consulted an infectious diseases doctor for pre-travel advice concerning
malaria and prophylaxis, 28 (12%) had been to a general practitioner and 61 (26%) to a vaccination clinic. 100 (42%) of the responders did not receive advice from medical institutions and among them, 20 cases (8%) stated they had been advised by a friend, 3 (1%) by the travel agency, 59 cases (25%) had previous experience as to what to do/take, 10 cases (4%) did not seek advice at all and 8 (3%) had ‘other’ information sources. Some of the cases had received advice from more than 1 source, thus explaining a total sum of more than 100%. Nine did not answer the question.

Use of chemoprophylaxis

A majority of the cases (n = 169; 71%) took chemoprophylaxis during their trip, although this proportion decreased over the study period: 79% in 1994–97 and 56% in 1999–2001. 102 (43%) cases took chemoprophylaxis regularly and after travel. 96 of the cases (40%) took an adequate drug according to the national guidelines, but this figure decreased over the study period, from 86 (55%) in 1994–97 to 10 (12%) in 1999–2001. A combination of chloroquine and proguanil was used by 77 (50%) of the travellers in 1994–97 and by 22 (27%) in 1999–2001 (only travellers to Africa). Chloroquine only, was used by 37 (16%), proguanil only by 9 (3%), and the rest of the cases (n = 20; 8%) used other drugs or did not remember the name of the drug. Despite the changed recommendations in 1998, 23% (n = 19) of the cases in 1999–2001 used the inadequate combination of chloroquine and proguanil when travelling in Africa. A majority of these cases had sought professional pre-travel advice.

Mefloquine was used by 4 cases (1%), but only 2 of them (a 15-y-old boy and a 29-y-old man) took adequate doses regularly, during and after the trip. The boy had travelled for 1 month with his parents,
in the countryside of Tanzania and Kenya, but his questionnaire lacked information on whether or not he was on mefloquine when presenting with symptoms of malaria. The man had travelled for 3 months in the countryside of Uganda, Kenya, Tanzania, Malawi, Zambia, Zimbabwe, Botswana and Namibia. He stopped taking chemoprophylaxis 1 week earlier than prescribed, i.e. 3 weeks after returning to Sweden, and he was not on mefloquine when he fell ill.

Of 102 patients who used chemoprophylaxis regularly during and after the trip, 45 (44%) had been advised by an infectious diseases physician, 31 (30%) at a vaccination clinic, 13 (13%) had been advised by a general practitioner, 10 (10%) by their friends and 19 (19%) had previous knowledge. Women and men used chemoprophylaxis regularly, during and after the trip, to the same extent.

**Prophylaxis against mosquito bites**

As prophylaxis against mosquito bites, 51 patients (21%) had regularly been using bed nets, 43 cases (18%) had regularly been using mosquito repellents, and 22 cases (9%) had been using both bed nets and repellents regularly. Of those using both, 11 (50%) had also used chemoprophylaxis regularly and had been advised by an infectious diseases doctor before the trip.

**Advice and delays after return**

The median time from onset of symptoms to contact with the health care professionals was 2 d (range 0–71 d, response rate 94%) (Figure 1). The median time from that initial contact to start of malaria treatment was less than 24 h (range 0–60 d, response rate 95%) (Figure 2). 70 of the 237 cases (29%) had either contacted a hospital or a community health centre for telephone advice concerning their symptoms due to malaria. 15 of these 70 patients (22%) had not been advised to seek hospital care.

**Discussion**

We have studied 237 out of totally 408 notified patients with falciparum malaria in Sweden between 1994 and 2001. The surveillance system of notifiable diseases in Sweden is well organized, covers the whole country, and the double sources of notifications provide a high sensitivity [7]. Falciparum malaria is a clinically overt disease and microscopy of thick and thin blood smears is a well-defined method. Thus, we consider that most falciparum malaria cases in Sweden are identified in the reporting system and have been considered for this study as described above. A limitation of this study is the fact that the initial aim of sending questionnaires to notified malaria cases was to collect running information needed to issue annual guidelines for malaria prophylaxis. In retrospect it would have been interesting to include core clinical data, e.g. malaria immunity status, adverse advents and severity of disease. However, we still consider that the data collected are of interest to Swedish physicians working in the field of travel medicine.

90% of the cases had been infected in Africa and the median length of travel was 23 d. The cumulative risk of malaria infection increases with the length of stay in a malaria-endemic area [9] which may influence the proportion of cases.
Less than half the cases took malaria chemoprophylaxis regularly during and after their trip, and in only 40% was the dose adequate according to the national guidelines. These data are consistent with other European studies [5,9].

The majority of the responders were men, and a predominance of imported malaria infections in males has been documented before [5,9–11]. Our study did not indicate, as did Philips-Howard et al. [9], that men are less compliant with prophylaxis compared with women. A relatively high proportion (6%) of the responders had been in modern urban areas only, but our study cannot give an estimate of the specific risk, owing to lack of denominator and of the name of the city visited.

The fact that only 9% of the responders used both bed nets and repellents regularly is an indication that the pre-travel advice might not have been adequate since it was not adhered to. Although 70% of the cases had received pre-travel advice from a medical professional (infectious diseases doctor, vaccination clinic or general practitioner), compliance with chemoprophylaxis as well as with bed nets and repellents was low. This indicates the importance of emphasizing the risk of malaria when giving pre-travel advice.

The chemoprophylaxis compliance rate was similar to that of earlier studies [12–14], although the proportion of the cases that took chemoprophylaxis decreased from 1994 to 2001. This should not necessarily be interpreted as a lower proportion of travellers in general taking prophylaxis, but rather that the drugs recommended to travellers to malaria-endemic areas in 1999–2001 were more efficient (less resistance) than in the previous period (mefloquine vs chloroquine). An indication supporting that the recommendation was followed is a more than 4-fold increase in the sale of mefloquine parallel to a decrease in the sale of proguanil in Sweden in 1994–2001 [15]. When properly used, mefloquine is a highly efficient drug against malaria [16], and indeed, in our study 3 out of a total of 4 cases who took this drug did not use it as recommended. Owing to the cases notified in 1994–97 with falciparum malaria from Africa despite adequate chemoprophylaxis with chloroquine and proguanil in accordance with national guidelines, the recommendation changed in 1998 to mefloquine for most travellers to Africa. Since then there has been a decreasing number of cases diagnosed y-on-y with falciparum malaria in Sweden [17]. Despite the amended recommendations in 1998, 23% (n = 19) of the cases in 1999–2001 used the inadequate combination of chloroquine and proguanil when travelling in Africa and a majority of these had sought professional pre-travel advice. This might indicate that the professional advice was not up-to-date with the prophylaxis recommended or it could have been, in a few cases, a medical reason for not using mefloquine. Three cases used a combination of chloroquine/proguanil when going for a short tourist trip to Gambia in 2000, and therefore this y mefloquine was recommended to all African travellers. With regard to alternative drugs, doxycycline was not generally recommended as chemoprophylaxis before 2002 and atovaquone/proguanil was not available for prophylactic prescription before May 2001. These 2 drugs are now more widely used and recommended as an alternative to mefloquine depending on the clinical situation.

The management of malaria once it became symptomatic was mostly swift, even though an unacceptably high proportion was not advised to seek health care immediately.

The main remaining problem is the group of travellers that does not seek medical advice (in our
study 42%), and among them immigrants from malaria-endemic countries visiting relatives in Africa is an important group [4]. This also was demonstrated in a study by van Herck et al. [18] where travellers visiting friends and relatives were less likely to seek health advice than other groups. There is a challenge in reaching this group specifically and we encourage new methods apart from those already existing within the health care system, e.g. contact with organizations for African immigrants.

There is obviously a need for better advice, especially to high-risk travellers to Africa, with prescription of chemoprophylaxis tailored to the local resistance situation. Better training among health staff giving pre-travel advice as well as new methods of reaching risk groups might reduce the numbers of imported falciparum malaria. To better evaluate risk factors, effects of inadequate prophylaxis, drug resistance and pre-travel advice, there is also a need for further studies.

Acknowledgements

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References