CHEMOPROPHYLAXIS ACCORDING TO THE GUIDELINES ON MALARIA PREVENTION FOR JAPANESE OVERSEAS TRAVELERS

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Abstract. Mefloquine has been licensed and registered in Japan for chemoprophylaxis against malaria since 2001. Guidelines for the prevention of malaria for Japanese overseas travelers were published by a group of malaria specialists under the auspices of the Japanese Society of Tropical Medicine and the Ministry of Health, Labor and Welfare, but not until March 2005. We implemented these guidelines in our clinic at the International Medical Center of Japan in Tokyo and, to better understand whether these guidelines are optimally useful, we conducted a study of Japanese travelers who visited our clinic seeking pertinent information and prophylaxis against malaria. The study group comprised 52 individuals who visited our clinic during the period October 2004 through June 2005 prior to travel abroad. On the basis of the above-mentioned guidelines, mefloquine was given to 27 of these individuals, 22 of whom were judged to need regular chemoprophylaxis. Mefloquine was not recommended to the other 25 individuals because their stays abroad would have been too long to avoid possible side effects or too short for symptoms to appear. In fact, some were traveling to malaria-free areas. Of the 27 individuals given mefloquine, 7 (26%) reported side effects, such as headache, vertigo, and nausea, 17 (63%) reported no side-effects, and the other 3 (11%) were unable to be followed. The diversity of destinations and accompanying malaria risks makes it very difficult for us to administer chemoprophylaxis to overseas travelers appropriately. The guidelines proved to be somewhat useful, but further experience in malaria chemoprophylaxis is needed for physicians to provide reliable pre-travel consultation.

INTRODUCTION

Malaria was eradicated in Japan by 1959, and only imported cases are now encountered. The number of Japanese individuals who travel abroad has increased rapidly. Approximately 16.8 million Japanese individuals traveled to international destinations in 2004, according to data from the Japan Association of Travel Agents (2005). Many of these individuals traveled to malaria-endemic areas and became infected. Mefloquine has been licensed and registered in Japan for chemoprophylaxis against malaria since 2001. Although chemoprophylaxis constitutes an important part of the preparation needed for travel to malaria-endemic areas, its significance is not well-recognized in Japan by travelers or by medical practitioners.

Guidelines on the prevention of malaria for Japanese overseas travelers were published in March 2005 by a group of malaria specialists under the auspices of the Japanese Society of Tropical Medicine and the Ministry of Health, Labor and Welfare. Following the draft of these guidelines, we implemented a pre-travel consultation service as a part of the travel clinic program at the International Medical Center of Japan (IMCJ) in Tokyo, in October 1, 2004. We recently conducted a study to evaluate the adequacy of chemoprophylaxis against malaria, particularly that recommended by the newly published guidelines for individuals visiting the IMCJ.

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MATERIALS AND METHODS

Study population

The subjects of our study were 52 individuals who visited our clinic seeking chemoprophylaxis against malaria prior to their departure to a foreign country. The group consisted of 35 men (67.3%) and 17 women (32.7%) with a mean age of 34.8 years (range 18-70 years) (Table 1).

Consultation and follow-up

We interviewed the 52 individuals who visited our clinic seeking prophylaxis against malaria, and elicited information from each individual, including date of departure, purpose of trip, duration of visit, places to be visited, and degree of possible exposure to mosquitoes. On the basis of this information, we decided whether or not to prescribe the anti-malarial drug. Individuals given mefloquine were followed up for adverse effects.

Table 1
Number of travelers per age category.

Age (years)	Men N = 35	Women N = 17	Total N = 52
<20	0	1	1
21-29	16	9	25
30-39	9	3	12
40-49	4	0	4
50-59	1	2	3
>60	5	2	7

Summary of malaria prevention guidelines

The guidelines give both absolute and relative indications for mefloquine prophylaxis. In essence, an absolute indication is a situation in which travelers will be at a high risk of death or serious illness due to malaria. That is, there is a high prevalence of malaria in the region a traveler will visit and there is a lack of adequate medical facilities in the place the traveler will be staying. When both conditions exist, mefloquine prophylaxis is strongly recommended. A relative indication is a situation in which the traveler will visit a region where malaria is prevalent, but an absolute indication does not exist. In this case, travelers should take mefloquine only after they have weighed the risks of infection against the side effects associated with this anti-malarial drug.

According to directions for the use of mefloquine in Japan, it should not be prescribed for more than 3 months at a time because there is little information regarding its long-term use.

RESULTS

Mefloquine was administered to 27 (51.9%) of the 52 individuals, 22 of whom fulfilled the absolute indication criteria. Twenty-five (48.1%) of the 52 were traveling for leisure and 18 (34.6%) for business. Chemoprophylaxis was judged to be unnecessary in a greater number of leisure travelers than business travelers (Table 2).

The majority of individuals (69.3%) planned to stay overseas for < 1 month (Table 2). None traveling > 3 months were given mefloquine, as recommended by the guidelines, but 2 clients who were traveling for > 6 months were advised to take mefloquine along for standby chemoprophylaxis, because they would be visiting endemic areas, not for the entire time but for a few weeks. The most frequently visited areas were in Asia (63.5%), but more than half of the travelers visiting Asia were thought not to need chemoprophylaxis (Table 3).

Table 2
Travel details and mefloquine prophylaxis.

	Total (n=52)	Prophylaxis (n=27)	No prophylaxis (n=25)
Purpose			
Business	18	12	6
Leisure	25	11	14
Volunteer work	5	3	2
Visiting friends and relatives	2	1	1
Study	1	0	1
Accompany another person	1	0	1
Duration (days)			
0- 7	7	5	2
8-30	29	20	9
31-90	10	0	10
91-	6	2[a]	4
Region			
Africa	16	11	5
Asia	33	15	18
South America	3	1	2

[a]standby chemoprophylaxis

One of the main reasons for non-prescription of mefloquine was time of stay. Some trips were too long for the travelers to avoid possible side effects, and others were too short for travelers to show symptoms during the trip. In addition, some of the destinations were free from malaria.

Another important reason for non-prescription of mefloquine was concern about possible side effects for travelers with chronic conditions, such as neurosis, coronary heart disease, and carcinoma. The clients who were advised not to take mefloquine for chemoprophylaxis are shown in Table 3.

Of the 27 travelers given mefloquine, 7 (27%) suffered side effects, such as nausea, dizziness, headache, fatigue, drowsiness, tinnitus, and appetite loss, but no serious complaints were noted (Table 4).

DISCUSSION

Although the number of visits abroad by the Japanese has increased rapidly in recent years, with the exception of the periods following the terrorist attack in the USA in 2001 and the worldwide SARS outbreak in 2003, the total number of imported malaria cases in Japan decreased from 109 in 2001, to 83 in 2002, 78 in 2003, and 73 in 2004 (National Institute of Infectious Diseases, 2005). We believe that this trend may be a result of adequate chemoprophylaxis provided by medical practitioners who have prescribed recently licensed mefloquine for international travelers from Japan. However, because many Japanese physicians are unfamiliar with tropical or travel medicine, guidelines for the prevention of malaria with appropriate drugs were established.

Table 3
Travelers not given mefloquine.

No	Age (years)	Sex	Destination	Reasons for non-prescription					
				Very long stay	Very short stay	Not enough time to see side effects before trip	Travel destination is malaria free	Contraindicated chronic conditions	Fear of side effects
1	29	M	Around Asia			(1 d)			
2	33	M	Worldwide	(2 y)				(Neurosis)	
3	57	M	India			(6 d)			●
4	30	M	Around Asia			(1 d)			
5	27	M	Around Asia			(1 d)			
6	67	M	Sudan					(Heart disease)	●
7	64	F	Sudan						●
8	20	F	Philippines					(Neurosis)	
9	22	M	Vietnam				(Urban)		
10	26	F	Nepal						●
11	61	F	India						●
12	34	M	Uganda	(3 y)					
13	34	F	Around Asia	(4 m)					
14	34	M	Around Asia	(4 m)					
15	24	F	Around Asia	(4 m)			(Urban)		
16	23	F	Around Asia	(4 m)			(Urban)		
17	38	F	Indonesia	(4 m)				(Neurosis)	
18	22	M	Malaysia	(4 y)					
19	30	M	Philippines		(5 d)				
20	32	F	India	(5 y)		(1 d)			
21	22	M	Around Asia	(6 m)					
22	28	F	India			(6 d)	(Urban)		
23	63	M	Belize		(7 d)		(Resort)		
24	59	F	Belize		(7 d)		(Resort)		
25	70	M	West Africa		(7 d)			(Carcinoma)	

y:years, m:months, d:days

Table 4
Side effects of mefloquine chemoprophylaxis.

Traveler No.	Age (years)	Sex	Nausea	Dizziness	Headache	Fatigue	Drowsiness	Tinnitus	Appetite loss
1	27	M				●			●
2	27	F					●		
3	23	M			●				
4	25	M		●				●	
5	30	M	●						
6	28	M			●				
7	21	F	●	●					

Half of our clients were < 30 years of age, and the majority were men in their twenties. Travel purposes, durations, and destinations varied greatly. The diversity of travel plans made it very difficult for us to prescribe chemoprophylactic drugs appropriately. The absolute indication for mefloquine prophylaxis was met for only half of the individuals traveling to tropical countries, mainly because mefloquine cannot be prescribed for > 3 months, according to the guidelines.

Many of our clients were concerned about the side-effects of mefloquine, such as neuropsychiatric reactions, and some refused to take it. Mefloquine prophylaxis was also contraindicated for travelers who suffered from chronic conditions. We advised our clients to start taking mefloquine 2 weeks before departure and to watch for side effects very carefully. Some clients were last-minute travelers and therefore hesitated to begin mefloquine prophylaxis.

Another important indication for mefloquine prophylaxis in some cases was travel destination. Some individuals were traveling to urban areas or resorts, where there would be no mosquitoes to transmit malaria. Other destinations included areas in Asia where multidrug-resistant malaria is prevalent and mefloquine would not be completely effective for prophylaxis. However, because only mefloquine has been licensed and registered as a chemoprophylactic drug in Japan, we have no other option than to advise those traveling to these destinations to avoid mosquito bites while overseas.

In conclusion, we believe that minor changes should be made to the guidelines. First, we should include other useful chemoprophylactic regimens, for instance, atovaquone/proguanil (Malarone™) or doxycycline, as are included in the UK guidelines (Bradley *et al*, 2003). Second, the guidelines should include a profile of the toxicity and adverse effects of long-term use of mefloquine, based on previous reports (Lobel HO *et al*, 1993; Pennie RA *et al*, 1993).

The guidelines proved useful for our clients, and fortunately none suffered from malaria with or without chemoprophylaxis. However, further experience in administering malaria chemoprophylaxis is needed for physicians to provide more reliable pre-travel advice.

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