

Assessment of Adherence to Prophylactic Antimalarials in Taiwanese Travellers – Data from one Medical Centre in Northern Taiwan

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ABSTRACT Background

This study was conducted to assess the adherence behavior of Taiwanese travellers, who were recommended and prescribed one of three antimalarials (mefloquine, atovaquone plus proguanil, or doxycycline) in the travel clinic at a medical centre in Northern Taiwan.

Methods

Data was collected from travellers who visited the travel clinic at a medical centre in Northern Taiwan and were prescribed malaria chemoprophylaxis from January 2009 to December 2010. Each traveller was asked to return a short questionnaire on potential side effects of the chemoprophylaxis. Phone interviews were conducted from July 2011 to September 2011 to collect further data on drug adherence and side effects.

Results

Just over half of the 160 travellers (53.3%) completed the entire prophylactic regimen. The adherence rate was higher in those who received mefloquine (59%) and atovaquone plus proguanil (53.8%) as compared to those who received doxycycline (31.0%). The common reasons for non-adherence to malaria chemoprophylaxis were perception that the risk of getting malaria was low (32.5%), feeling it was unnecessary to complete the regimen after returning home (23.1%) and side effects from the medication (17.9%).

Conclusions

The adherence rate of prophylactic antimalarials for Taiwanese travellers is still not satisfactory. This is of concern especially with an increase in travel to malaria-endemic regions over recent years. Health practitioners and government policy should emphasize the risk of malaria and the importance of prophylactic antimalarials.

Introduction

Taiwan was registered by the World Health Organization in 1965 on its list of countries with successful malaria eradication.¹ Although there has been no indigenous case of malaria in Taiwan, cases have been imported continuously from abroad. With an increasing surge in tourism over the years, more travelers are also travelling to malaria endemic regions. According to Taiwan's Centre of Disease Control, there had been a total of 21, 17, and 12 imported malaria cases in 2010, 2011, and 2012, respectively.²

As seen in previous studies,³⁻⁵ many travellers were not aware of the risk of malaria infection and the importance of taking and completing the entire anti-malarial prophylactic regimen. There have been few studies on this topic in Taiwan. Our study was conducted in one of the twelve health facilities in Taiwan that was registered by Taiwan's Centre of Disease Control for distributing prophylactic antimalarials.⁶ The aim of this study is to assess the adherence behavior of Taiwanese travellers who were recommended and prescribed one of three antimalarials (mefloquine, atovaquone plus proguanil, or doxycycline).

Methods

Data was collected from travellers who visited the travel clinic at a medical centre in Northern Taiwan and were prescribed malaria chemoprophylaxis from January 2009 to December 2010. The travellers were prescribed one of three antimalarials (mefloquine, atovaquone plus proguanil, or doxycycline) after consideration of their travel destination, length and type of travel, medical conditions and personal preferences. Each traveller was asked to return a short questionnaire on a prepaid postcard regarding side effects from the antimalarial drugs. The deadline for collecting the postcards was April of 2011. Telephone calls were made from July 2011 to September 2011 in an attempt to reach the travelers who did not return the postcards. In the telephone interview, we asked about side effects from the antimalarial drugs, drug adherence, and reasons for not completing the malaria chemoprophylaxis. In addition, travellers' opinions on their experience at the travel clinic and on how best to obtain this type of data were also asked

The study was examined and approved by the Human Research Ethics Committee in Mackay Memorial Hospital, and was issued the project research number MMH-I-S-645.

Results

There was a total of 898 travellers who visited the travel clinic at this one Northern Taiwan medical centre and were prescribed malaria chemoprophylaxis from January 2009 to December 2010 (Table 1). Only Eighty-one of 898 travellers (9%) returned the pre-postaged postcard. 306 travellers were contacted by telephone calls. 511 of 898 travellers (56.9%) could not be reached despite several attempts at doing so.

Side Effects of Malaria Chemoprophylaxis

A total of 387 (81 via postcard and 306 via telephone interview) travellers replied the question about side effects from the antimalarial drugs. (Table 2) Three-hundred of 387 (77.5%) travellers received mefloquine as malaria chemoprophylaxis. The majority of the travellers who took mefloquine (221 of 300; 73.7%) did not have any side effects. Common side effects found in those taking mefloquine included headache(4.7%), nausea(4.3%), and loss of appetite(4.3%). Insomnia and depressed mood were found in 2% and 2.3%, respectively, of those who took mefloquine. Sixty-nine of 387 (17.8%) travellers received doxycycline as malaria chemoprophylaxis. Of those that took doxycycline, 62.3% did not have any side effects. However, nausea(13%) and epigastric pain(11.6%) were common side effects noted in those taking doxycycline. One traveller reported having vaginal candidiasis. A small percentage (18 of 387; 4.7%) of travelers received atovaquone plus proguanil as malaria chemoprophylaxis. The majority of them (13 of 18; 72.2%) did not suffer any side effects. A few individuals had headache, dizziness, skin rash, and skin itch after taking the medication.

Adherence of Malaria Chemoprophylaxis

A total of 306 telephone interviews were conducted concerning adherence. Among these, 76.8% were given mefloquine, 20.0%doxycycline, and 4.2% atovaquone plus proguanil, respectively, as malaria chemoprophylaxis. 300 with participants completed the questionnaire regarding adherence and the six not responding being prescribed mefloquine. In table 3, adherence level was divided into three groups—not used at all (did not take any medication); complete (finished all medication); incomplete (finished part of regimen, including prior to trip, whilst away and on return). More than half of the travellers (53.3%) completed the entire prophylactic regimen. The self-reported adherence rate was higher in those who received mefloquine (59%) and atovaquone plus proguanil (53.8%) as compared to those who received doxycycline (31.0%). The percentage of travellers who did not take any medication of the prescribed anti-malarials was 12.3%, with a higher percentage noted in those prescribed doxycycline. 103 (34.3%) travellers took only part of the prophylactic regimen. More travelers chose to discontinue the regimen after returning home (15.7%) and during the middle of the trip (13.7%), as compared to before the trip. In addition, a higher percentage of those who took doxycycline (24.1% vs. 13.5% for mefloquine and 15.4% for atovaquone plus proguanil) for malarial chemoprophylaxis were noted to discontinue the regimen after returning home.

The common reasons for non-adherence to malaria chemoprophylaxis were perception that the risk of getting malaria was low (32.5%), feeling it was unnecessary to complete the regimen after returning home (23.1%) and occurrences of side effects from the medication (17.9%). Some forgot to take the medication or refused to take the medication for other personal reasons. Most travelers felt it was important to report on whether or not side effects had occurred from the anti-malarial drugs (256 of 290, 88.3%). 93 participants gave a reason for non-return of the postcard; 57% because they forgot and 16% felt it was a troublesome process. Some postcards might have been lost in the mail because 15.1% reported that they did mail the postcard. When asked about the preferred reply method, most travelers chose telephone interview and internet survey.

Discussion

Slightly over half of the travellers who were pre-scribed prophylactic antimalarials from our travel clinic completed the entire regimen (160 of 300; 53.3%). This rate is considered fairly high compared with the adherence rate of less than 20% reported in travelers from other countries.^{3,4} Most of the travellers were made aware of our travel clinic from the internet or from family/friends who had visited previously. Our subjects seemed better aware of health-related behaviors, possibly explaining for the higher adherence rate of malaria chemoprophylaxis.

In our study, the adherence rate was higher in those who received mefloquine (59%) and atovaquone plus proguanil (53.8%) as compared to those who received doxycycline (31.0%). The same pattern was seen in a study on UK travellers who were pre-scribed antimalarial prophylaxis. In that study, statistically significantly higher adherence overall and post-travel was seen with atovaquone plus proguanil compared with doxycycline, and adherence to mefloquine appeared similar to or better than doxycycline and similar to atovaquone plus proguanil for categorical

adherence.⁵ Another US study found high adherence rate (89%) for those who were prescribed atovaquone plus proguanil.⁷

The most common reason for non-adherence to malaria chemoprophylaxis was travellers' perception that the risk of getting malaria was low. A study conducted in China found that travellers all carried anti-malarial drugs for self-treatment and not for prophylaxis.³ Travellers' lack of knowledge in the importance of completing the entire course of prophylaxis was another common reason. Of those that started but did not complete the malaria chemoprophylaxis, most travellers chose to discontinue the drug regimen upon returning home. This was seen in other studies³ as well as our own.

In addition, dosing convenience was also of concern to the travellers. The dosing regimen for mefloquine was one tablet weekly, beginning one to two weeks before travel until four weeks after returning home. The dosing regimen for atovaquone plus proguanil was one tablet per day, beginning one to two days before travel until one week after returning home. The dosing regimen for doxycycline was one tablet per day, beginning one to two days before travel until four weeks after returning home. From the dosing regimens, we could see that those taking doxycycline would have to take the greatest number of tablets, which could explain the lower adherence rate.

Some travellers had discontinued their medications due to occurrence of side effects. However, in our study, a high proportion of travellers (60-70%) did not suffer any side effects, regardless of the medication used. In addition, most travellers agreed on the importance of reporting side effects from the medications. The preferred reply methods were using telephone interview and internet survey.

The purpose of travel or those that came to the travel clinic include; leisure, business, volunteer work, and less often, for visiting families and relatives. Studies have shown the knowledge, attitudes, and practices (KAP) of travellers varied greatly among those with different travel purposes.^{3,8-12} Frequent business travellers and humanitarian workers tend to have better KAP.^{8,11} Those visiting families and relatives in their native countries were less aware of the risk of malaria and tend not to seek preventive measures.^{10,12}

Health professionals play an important role in delivering travel-related knowledge to the travellers. The practitioner's recommendation was highly important for 63% of travelers.⁵ A survey conducted in Taiwan revealed significant deficits in travel medicine knowledge among health-care providers.¹³ Another study in Greece also pointed out a need to increase awareness and education in professionals providing travel health services.¹⁴ It can be speculated that practitioner's emphasis on the importance of antimalarial chemoprophylaxis may have a big impact on adherence to the antimalarial drugs.

A limitation of our study was that we were unable to contact more than half of the travellers (511 of 898) who visited our travel clinic from January 2009 to December 2010. There might also be recall bias since telephone interviews were not executed until more than one year after the prescription of malaria chemo-prophylaxis.

Conclusion

Although prevalence of infectious diseases has decreased tremendously over the years, it is still noted in less-developed countries. More and more people are venturing into those territories for adventure and for fun. This raises concern for possible transmission of infectious diseases after they return to their home-lands. Preventive methods for infectious diseases are thus an important concept that must be made known to travellers.

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Table 1
Characteristics of Study Subjects

	Reply Postcard (n=81, 9%)	Telephone Interview (np306, 34.1%)	Unable to be contacted (n=511, 56.9%)	Total (np898)
Gender (n%)				
Female	45 (55.6)	139 (45.4)	278 (54.4)	462 (51.4)
Male	36 (44.4)	167 (54.6)	233 (45.6)	436 (48.6)
Age Y/0, mean \pm SD)	44.8 \pm 15.6	39.1 \pm 13.4	39.3 \pm 14.5	
Age range(Y/0)	19-75	13-81	5-75	
Country of destination (n, %)				
Africa	52 (42.2)	178 (58.2)	288 (56.4)	518 (57.7)
Americas	10 (12.4)	39 (12.8)	75 (14.7)	124 (13.8)
Europe	0 (0.0)	0 (0)	141 (27.6)	141 (15.7)
Asia	18 (22.2)	81 (26.5)	7 (1.4)	106 (11.8)
Pacific	1 (1.2)	8 (2.6)	0	9 (0.01)

Table 2
Side Effects from Anti-Malarial Prophylactic Medications (multiple choices)

Side Effects	Reply Postcard (n=81, 20.9%)	Telephone Interview (np306, 79.1%)	Total (np387)
Mefloquine (n, %)	65 (80.2)	235 (76.8)	300 (77.5)
None	44 (67.7)	177 (75.3)	221 (73.7)
Nausea	3 (4.6)	10 (4.3)	13 (4.3)
Vomiting	3 (4.6)	7 (3.0)	10 (3.3)
Loss of appetite	8 (12.3)	5 (2.1)	13 (4.3)
Headache	3 (4.6)	11 (4.7)	14 (4.7)
Dizziness	2 (3.1)	0 (0.0)	2 (0.7)
Pruritis	4 (6.2)	0 (0.0)	4 (1.3)
Skin rash	6 (9.2)	0 (0.0)	6 (2)
Insomnia	2 (3.1)	4 (1.7)	6 (2)
Depressed mood	5 (7.7)	2 (0.9)	7 (2.3)
Doxycycline	11 (13.6)	58 (20.0)	69 (17.8)
None	4 (36.4)	39 (67.2)	43 (62.3)
Nausea	4 (36.4)	5 (8.6)	9 (13.0)
Epigastric pain	3 (27.3)	5 (8.6)	8 (11.6)
Photosensitivity	2 (18.2)	2 (3.4%)	4 (5.8)
Headache	1 (9.1)	3 (5.2%)	4 (5.8)
Dizziness	1 (9.1)	1 (1.7)	2 (2.9)

Pruritis	i (m.i)	2 (3.4)	3 (4.3)
Skin rash	i (m.i)	0 (0.0)	i (i.4)
Candidiasis	i (m.i)	0 (0.0)	i (i.4)
infection			
torvaquone plus proguanil	5 (6.2)	13 (0.2)	18 (4.7)
None	4 (80.0)	m (em.2)	i3 (72.2)
Nausea	0 (0.0)	0 (0.0)	0 (0)
Vomiting	0 (0.0)	0 (0.0)	0 (0)
Headache	i (20.0)	i (7.7)	2 (ii.i)
Tiredness	i (20.0)	i (7.7)	2 (ii.i)
Pruritis	0 (0.0)	i (7.7)	i 5.5)
Skin rash	0 (0.0)	i (7.7)	i 5.5)

Table 3
Adherence Rate of Malaria Chemoprophylaxis (according to medication)

	Total (n=306)	Mefloquine (n=235, 76.8%)	Doxycycline (n=58, 19.0%)	torvaquone plus proguanil (n=13, 4.2%)
Adherence condition (n, %)				
Total answered (n)	300	229	58	13
No use at all	37 (12.3)	26 (11.4)	10 (17.2)	1 (7.7)
Complete	160 (53.3)	135 (59.0)	18 (31.0)	7 (53.8)
Incomplete, prior to trip	15 (5.0)	9 (3.9)	6 (10.3)	0 (0.0)
Incomplete, middle (trip)	41 (13.7)	28 (12.2)	10 (17.2)	3 (23.1)
Incomplete, returning from trip	47 (15.7)	31 (13.5)	14 (24.1)	2 (15.4)
Reason for nonadherence (n, %)				
Total answered (n)	117	81	30	6
Forgot	18 (15.4)	12 (14.8)	6 (20.0)	0 (0.0)
Worry about side effects	12 (10.3)	11 (13.6)	1 (3.3)	0 (0.0)
Occurrence of side effects	21 (17.9)	12 (14.8)	8 (26.7)	1 (16.7)
Refuse to take medications	1 (0.9)	1 (1.2)	0 (0.0)	0 (0.0)
Low risk of malaria infection	38 (32.5)	26 (32.1)	8 (26.7)	4 (66.7)
No need to complete net prophylactic regimen	27 (23.1)	19 (23.5)	7 (23.3)	1 (16.7)

Table 4
Travellers' Opinions on Preferred Reply Methods and Other Related Issues

	Total (n=306)	Mefloquine (n=235, 76.8%)	Doxycycline (n=58, 19%)	torvaquone plus proguanil (n=13, 4.2%)
Do you feel it is important to report drug side effects?				
Total answered (n)	290	225	52	13
No	34 (11.7)	27 (12.0)	6 (11.5)	1 (7.7)
Yes	256 (88.3)	198 (88.0)	46 (88.5)	12 (92.3)
Reason for not returning postcard				
Total answered (n)	93	73	17	4
Forgot	53 (57.0)	41 (56.2)	11 (64.7)	1 (25.0)
Too troublesome	15 (16.1)	11 (15.1)	4 (23.5)	1 (25.0)
Occurrence of side effects	2 (2.2)	1 (1.4)	1 (5.9)	0 (0.0)
Lost the postcard	2 (2.2)	1 (1.4)	0 (0.0)	1 (25.0)
Felt it was unnecessary	4 (4.3)	4 (5.5)	0 (0.0)	0 (0.0)
Did not take the medication	2 (2.2)	2 (2.7)	0 (0.0)	0 (0.0)
Felt it would not be helpful	1 (1.1)	1 (1.4)	0 (0.0)	0 (0.0)
Postcard lost in mail	14 (15.1)	12 (16.4)	1 (5.9)	1 (25.0)
Preferred reply method (more than one choice)				
Telephone interview	146 (47.7)	116 (49.4)	29 (50.0)	5 (38.5)
Mobile phone message	35 (11.4)	26 (11.1)	5 (8.6)	4 (30.8)
Return postcards	15 (4.9)	11 (4.7)	3 (5.2)	2 (15.4)
Internet survey	82 (26.8)	71 (30.2)	17 (29.3)	2 (15.4)
Free gift upon reply	5 (1.6)	4 (1.7)	0 (0.0)	1 (7.7)



