Compliance with Antimalaria Chemoprophylaxis in a Combat Zone

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Abstract. Compliance with malaria chemoprophylaxis by military service members (MSMs) is notoriously low, ranging from 30% to 56%. Our objective was to determine the rate of compliance and reasons for non-compliance with malaria chemoprophylaxis among healthy US MSMs in Afghanistan. An eight-question, anonymous online survey was used to collect data regarding the compliance of healthy MSMs with malaria chemoprophylaxis. E-mail surveys were sent to 1,200 MSMs; 528 (44%) MSMs completed the survey. One-time daily doxycycline was the most commonly prescribed chemoprophylaxis (90%); 60% ($N = 318$) responded that they were compliant with their chemoprophylaxis as prescribed, whereas 40% ($N = 221$) indicated that they were not compliant. Compliance with daily dosing was 61% and weekly dosing was 38%. The most common reasons for non-compliance were gastrointestinal effects (39%), forgetfulness (31%), and low perception of risk (24%). Malaria chemoprophylaxis compliance by healthy MSMs in Afghanistan is poor. Side effects, forgetfulness, and lack of education are contributing factors. Commanders bear the primary responsibility for the health of their soldiers, and the individual MSM bears personal responsibility; however, additional public health interventions could possibly have a positive impact on prevention.

INTRODUCTION

Over the past decade, the Armed Forces of the United States have been involved in a war in Afghanistan. During that time, nearly 1 million US military service members (MSMs) have been deployed to this remote and hostile environment. Malaria is one of several infectious diseases that threaten the health and life of deployed soldiers in Afghanistan. From 2002 to 2010, MSMs in Afghanistan have accounted for 20–85 cases of malaria per year.¹ In 2010, there were 58 malaria cases in MSMs in Afghanistan, which was higher than in 6 of the past 8 years.¹ Troops serving in Afghanistan are issued oral antimalaria medications before deployment. The Army has chosen doxycycline (100 mg by mouth one time daily) as the primary chemoprophylaxis agent. The efficacy of doxycycline has been found to be 92–99% in the prevention of malaria.^{2,3} Other agents are prescribed when contraindications to doxycycline are present.⁴

Unit commanders, in cooperation with their unit medical officer, are directly responsible for the health and welfare of their soldiers, including compliance with malaria chemoprophylaxis, under the Army policy of Force Health Protection.⁵ Individual MSMs also bear responsibility. They are required to comply with the military chemoprophylaxis program and are subject to discipline under the Uniform Code of Military Justice for non-compliance.⁴

Previous surveys of MSMs have identified compliance rates with chemoprophylaxis of 30–56%. Those surveys were conducted with troops who had contracted the disease or members of their units contracted the disease, possibly affecting the outcome of the surveys.^{6–9} This report of compliance of healthy MSMs with malaria chemoprophylaxis in Afghanistan, including MSM reasons for non-compliance and the effect of daily versus weekly dosing, is the first of its kind.

METHODS

An Institutional Review Board (IRB) exemption was obtained. An online electronic survey was used to collect

data regarding the compliance of healthy MSMs with oral antimalaria chemoprophylaxis while serving in eastern Afghanistan. Piloting of the survey by a team of military and civilian healthcare professionals was used to validate the questions. Questions were also based on similar malaria chemoprophylaxis surveys of MSMs. A number of changes in the survey questions were subsequently made. From December of 2010 to June of 2011, the survey was distributed to 1,200 MSMs who possessed military e-mail accounts while serving in eastern Afghanistan. The survey requested demographic information (one question), compliance information (four questions), and information regarding pre-deployment education (one question), and it asked the MSM when he or she received his or her chemoprophylaxis medications (one question). Compliance was specifically assessed with two questions that were intended to collect quantitative data (yes or no to compliance with their daily or weekly medications). Reasons for non-compliance were assessed with one survey question that was intended to collect quantitative data, presenting six possible reasons for non-compliance, and qualitative data, allowing for an open-ended response. A single question asked when the MSM had received his or her chemoprophylaxis medication. A review of the English literature yielded no results regarding the compliance with malaria chemoprophylaxis by healthy MSMs in Afghanistan.

RESULTS

Online surveys (1,200) were distributed to MSMs by e-mail. Of 530 MSMs that started the online survey, 528 completed it (99.6%). Respondents were 83% ($N = 438$) male and 17% female ($N = 90$). There was about a 2:1 ratio (336/177) of enlisted to officer MSMs; 60% ($N = 318$) of MSMs indicated that they were compliant with their prescribed medication, whereas 40% ($N = 221$) were not. Doxycycline was found to be the most commonly prescribed antimalaria chemoprophylaxis (90.1%, $N = 475$). Other prescribed medications included mefloquine (3.6%, $N = 19$), malarone (0.9%, $N = 5$), and primaquine (0.2%, $N = 1$); 4.4% of MSMs ($N = 23$) indicated that they did not know what type of medication that they were prescribed, if any. In the subgroup of MSMs prescribed one-time daily medications, 61% ($N = 195/302$) were

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compliant. Of those prescribed the one-time weekly medication, 38% ($N = 16/42$) were compliant. Three hundred and thirty-eight MSMs reported 486 reasons for non-compliance. The most commonly reported reasons for non-compliance were gastrointestinal symptoms (upset stomach, nausea, or diarrhea; 39%), forgetfulness (32%), and low perception of risk (no mosquitoes seen or winter months; 22%); 78.1% ($N = 411$) of MSMs indicated that they received specific patient medication information regarding their medication prescription, and 20.0% ($N = 105$) indicated they were prescribed a medication without receiving any specific medication information from a healthcare professional (physician, physician's assistant, or pharmacist).

Four hundred and fifty-six MSMs (86.7%) confirmed that they received Afghanistan-specific malaria educational training before deployment, whereas 64 service members did not (12.2%); 56.1% ($N = 296$) received their antimalaria medication 2 weeks before deployment in accordance with Centers for Disease Control and Prevention standards and US Army policy, and only 3.2% ($N = 17$) received their chemoprophylaxis medication after arriving in Afghanistan.

DISCUSSION

Malaria is a significant health threat to American troops in areas of Afghanistan at altitudes $< 2,000$ m ($< 6,561$ ft). The malaria species present in those areas are 80–90% *Plasmodium vivax* and 10–20% *Plasmodium falciparum*.^{10–13} According to the Afghanistan Ministry of Public Health (AMPH),¹⁴ over one-half of the country's estimated 26.6 million people are vulnerable to malaria, with 14 of the country's 34 provinces identified as high-risk areas. Many people living in endemic areas may have acquired a level of immunity to the disease, although there is currently no clear concept about how this protection works.¹⁵ Visitors to these areas will not have this immunity.

In making decisions concerning the use of chemoprophylaxis, the US military uses multiple sources of information, including the Centers for Disease Control and Prevention and the National Center for Medical Intelligence. The Army has chosen doxycycline as the primary chemoprophylaxis agent. Doxycycline is the only antimalarial drug for which true resistance has not been documented for any malaria-causing plasmodia anywhere.¹⁶ Oral malaria chemoprophylaxis is currently the US Army's major intervention strategy in the prevention of malaria in Afghanistan,⁴ but only 60% of soldiers participating in this survey have reported that they are compliant with chemoprophylaxis as prescribed; 91% of respondents were prescribed medications with one-time daily dosing. Their compliance rate was 61%. Studies in civilian populations have indicated that physicians can expect 73–83% compliance when patients are prescribed one-time daily dosing.^{17,18} The compliance rate for one-time weekly dosing was worse (38%). Army researchers have also reported that MSM compliance with chemoprophylaxis is "notoriously low"¹⁹ but did not cite their evidence. Interestingly, in a policy brief published in 2008 on the subject of military preparedness, the American Society of Tropical Medicine and Hygiene did not mention non-compliance with chemoprophylaxis as a significant contributing factor, but the organization did advocate for increased federal funding for research into new antimalarial drugs and a malaria vaccine.²⁰

There are significant differences between the prevention of malaria in individual travelers and deployed soldiers. In the military, antimalarial education and training is accomplished within the individual units and not directed individually, because the primary goal is mission success. In addition, long deployments in hostile and austere environments become significant barriers to successful chemoprophylaxis. Force Health Protection (FHP) is the Army policy that describes the responsibility of unit commanders for the health and welfare of their soldiers.⁵ The appropriate use of malaria chemoprophylaxis is an aspect of FHP. An intervention available to military commanders includes directly observed therapy (DOT).²¹ The US Navy recommends DOT for all medication regimens. Chain of command support is required to carry out this method. MSMs are directly observed taking their daily or weekly chemoprophylaxis medication. In the authors' combined 30 months of deployment experience in Afghanistan, DOT is an uncommon practice.

Individual MSMs also bear responsibility for the prevention of malaria. Under military policy, MSMs are required to comply with the chemoprophylaxis program, and non-compliance can lead to discipline under the laws of the Uniform Code of Military Justice.⁴ However, disciplinary action against MSMs contracting malaria is exceedingly rare. Of historical interest, World War II British General William Slim became alarmed when malaria rates among his units reached 70%, largely because of non-compliance by his soldiers with the foul-tasting quinine medication. General Slim did not blame his soldiers or medics for this problem but placed the responsibility on his officers, dismissing three of them.²² Administrative discipline is currently confidential.

This report is the first of compliance of healthy MSMs with antimalaria chemoprophylaxis in Afghanistan. All previous survey reports regarding the compliance of American troops with malaria chemoprophylaxis were conducted after the occurrence of malaria infections in the individual MSM or their unit, possibly affecting the outcomes of the surveys. US Marines returning from Liberia with malaria self-reported 52% compliance with chemoprophylaxis. Forgetfulness was the primary reported reason for non-compliance.⁶

After an outbreak of malaria in their unit, US Rangers returning from Afghanistan with malaria reported 55% compliance with chemoprophylaxis. Distractions were the primary reason for non-compliance.⁷ The work by Newton and others⁸ surveyed Marines concerning compliance with chemoprophylaxis when returning from Somalia with malaria and found 56% compliance. The work by Barrett and others⁹ reported 30% compliance in soldiers returning from Vietnam. Surveying MSMs after they or members of their unit contracted the disease may affect the survey outcome. This manuscript is the first statistical report on compliance of healthy MSMs in Afghanistan with malaria chemoprophylaxis and includes reasons for non-compliance.

In this survey, the three most reported reasons for non-compliance were gastrointestinal complaints, forgetfulness, and low perception of risk. Gastrointestinal complaints included nausea, vomiting, and diarrhea. Forgetfulness was primarily attributed to a very busy work schedule. The MSMs' perceptions of risks of malaria infection were heavily influenced by the lack of visualization of mosquitoes, high-altitude work environment, and winter months. Neither the

low rate of compliance nor the respondents' reasons for non-compliance are unexpected based on previous surveys.

In attempting to understand the poor compliance rate for healthy MSMs, it is certainly likely that American troops working in a combat zone are not comparable with American civilians. Troops in a combat zone possibly have many priorities that outweigh or distract them from the taking of a daily or even weekly medication, including activities and duties intended to protect life and limb.

In this survey, 80 MSMs mistakenly reported that their risk of contracting malaria was diminished when mosquitoes were not visualized and during the winter months. Although not specifically mentioned in the survey, it is very unlikely that an MSM in Afghanistan has witnessed another soldier with a confirmed case of malaria. Therefore, the perception of the risk of contracting malaria would likely be low. In addition, the two large outbreaks of malaria in MSMs had occurred quite remotely from the time of this survey (2002 and 2003).^{6,7} Although the numbers are small, one-time weekly medication dosing did not improve compliance over daily dosing (38% versus 61%).

Malaria threatens not only the health and life of MSMs but also the overall combat power of the US Armed Forces. A suspected or confirmed diagnosis of malaria leads to evacuation from the combat zone to the United States, possibly threatening the mission of that soldier's unit. In addition, the cost of an MSM evacuation to the United States can exceed \$113,000.¹⁹

There are limitations to this study. Because of operation security restrictions, more specific data regarding the location and number of troops present in certain areas could not be provided.

Another limitation of our study is that the sample of MSMs who responded to the survey was assigned to a regional command of Afghanistan and may not be representative of soldiers assigned to the other provinces. In addition, our sample population is likely not representative of the US military as a whole. The ratio of enlisted soldiers to officers in the US military ranges from 10:1 in the Marines to 5:1 in the Army.²³ In this survey, the ratio of enlisted respondents to officers was approximately 2:1.

Because military policy requires MSMs to take their chemoprophylaxis as prescribed and because MSMs are subject to discipline for non-compliance, it is possible that some MSMs who responded to the survey may not have been completely honest in reporting their compliance. Despite the anonymity of the survey, there still may have been some fear of discipline. Therefore, it is possible that the non-compliance rate is actually higher than reported.

It may have been valuable to investigate compliance with other malaria prevention measures, such as vector control and insect repellent. A report²⁴ in 2006 indicated that the US government provides "treated uniforms" and "repellent" as part of its non-drug malaria prevention measures to troops deployed to Afghanistan. Also, survey information concerning MSMs participation in DOT programs would also have provided additional insight into compliance.

Strengths of the study include simple quantitative questions that were validated by healthcare professionals. The response rate (44%) was higher than the 30% rate that would be expected for an online survey.²⁵ The 60% compliance in healthy MSMs identified in this survey is supported

by other studies that have reported poor compliance of MSMs (30–55%) in deployed environments, although those surveys were after malaria infections in their units. In addition, we are reporting the perceived adverse events in a true effectiveness setting.

The following four recommendations are for improving MSMs compliance with antimalarial chemoprophylaxis. (1) DOT is an intervention available to commanders and other unit leadership. Increased use of DOT is a public health intervention that would probably have the greatest impact on improving compliance. In absence of or addition to DOT, there are other possible interventions. (2) Gastrointestinal complaints were the most common survey response (39%) as the reason for non-compliance. Follow-up with a healthcare professional should be mandatory during the first month of deployment to identify non-compliant MSMs and allow an opportunity for a healthcare professional to make alternate recommendations. (3) Forgetfulness was the second most common survey response (31%) by MSMs as the reason for non-compliance. Almost all MSMs in Afghanistan attend a group meeting on a daily basis, including morning reports, briefings, and formations. Reminders about oral malaria prophylaxis should be added to the agenda for those meetings. (4) Twenty-two percent of the subgroup of non-compliant MSMs mistakenly reported that their non-compliance was based on no visualization of mosquitoes, winter months, and working at altitudes. These responses reveal a possible deficiency in pre-deployment training on malaria. This specific information concerning risk should be added to pre-deployment training, and because there are many training and education activities conducted for the benefit of MSMs during their deployment to Afghanistan, malaria awareness and prophylaxis could be added as required training during deployment.

The primary strategy of the US military for the prevention of malaria in Afghanistan is chemoprophylaxis. The recommended medications are effective in preventing malaria. Despite strong incentives, compliance by healthy deployed MSMs is poor. One-time weekly dosing did not improve compliance over one-time daily dosing. There are vector control measures available to MSMs, but their use was not evaluated in this survey. The frequency of DOT was also not evaluated. Gastrointestinal side effects, forgetfulness, and low perception of risk are the primary self-reported reasons for non-compliance. Increased use of DOT and various low-cost public health interventions could possibly have a positive impact on prevention.

Despite the potential limitations, this study adds both new and supportive data to the body of knowledge on the topic of MSMs compliance with malarial chemoprophylaxis in a combat zone and reasons for non-compliance. The chemoprophylaxis compliance rate by healthy MSMs is essential information in planning and evaluating new public health interventions intended to improve compliance.

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