Malaria Prophylaxis Adherence Among Aircrew Members

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INTRODUCTION: Joint Base Charleston's C-17 Globemaster III mission is executed by 400 active-duty members from three operational and support wings. Aircrew and mission-essential personnel travel to locations with endemic diseases which are mostly eradicated in the United States. Recently, two members contracted malaria after missions in Africa which required advanced hospital care. Personnel were provided chemoprophylaxis, but the members who contracted malaria were among several who chose not to take it. This preliminary survey assessed aircrew malaria prophylaxis adherence and examined potential factors contributing to nonadherence.

METHODS: JB Charleston aircrew members who visited the Flight and Operational Medicine Clinic between January and April 2018 were administered a retrospective, online survey. Researchers performed descriptive statistics and Chi-squared analysis.

RESULTS: Most respondents were pilots under 30 yr of age and were prescribed malaria chemoprophylaxis while on a mission. More than two-thirds of respondent aircrew members did not take the medication as prescribed or did not take it at all. Of those, over half of respondents stated too many pills/too many days and medication side effects as the main reasons for nonadherence. Furthermore, almost 70% of adherent members experienced negative medication side effects such as nausea and heightened dreams. There was no statistical relationship between crew position, age, side effects, and prophylaxis adherence.

DISCUSSION: Numerous factors contribute to poor prophylaxis regimen compliance among aircrew members. This study highlighted the need for risk-based policy validation, improved patient education, prophylaxis enforcement, process improvements to facilitate adherence, and evaluation of perceived vs. actual risk.

KEYWORDS: chemoprophylaxis, military, flyers, C-17 Globemaster III, Africa.

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Joint Base (JB) Charleston's mobility mission is supported by C-17 Globemaster III capabilities executed by 400 active-duty members across 10 squadrons. Aircrew and mission-essential personnel often travel to parts of the world where diseases exist that have largely been eradicated in the United States. One such disease of concern is malaria.

Malaria is transmitted by mosquitoes and caused by the *plasmodium* parasite.[2] Department of Defense guidance mandates the structured approach Military Treatment Facilities (MTFs) will take with respect to communicable diseases. Malaria prevention is comprised of three main measures per Department of Defense (DoD) Directive 6200.04:[6] 1) personal protective measures,[5,7] which include the use of bed nets, permethrin-treated uniforms, insect repellants, proper wear of the uniform, etc.; 2) vector control by integrated pest management methods;[7] and 3) chemoprophylaxis.[5,6,8]

When members are tasked to leave the country in support of operations, they undergo a thorough process of medical and administrative preparation. As a general rule, areas with malaria attack rates less than or equal to 0.1% per month do not require chemoprophylaxis.[9] Based on attack rates and duration of mission, malaria prophylaxis may be issued. Members must be issued sufficient antimalarial medications for the length of deployment as determined by the appropriate Geographic Combatant Command. First-line prophylactic medications

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include atovaquone-proguanil (Malarone) and doxycycline, but mefloquine may also be used if the member presents with contraindications to the first-line agents.[1] Chemoprophylaxis is considered a force health protection measure and the responsibility for compliance is shared by line commanders and the member.

In 2016, after a multicountry mission in Africa, a service member was diagnosed with malaria; the member was assigned to another base but flying with a local crew. The member's medical intervention involved several months of hospital care, including 1 mo of ventilator-dependent intensive care. More recently, in September of 2018, an aircrew comprised of members from several bases embarked on a mission outside the continental United States for which malaria prophylaxis was directed and provided. Upon return, two members exhibited malaria symptoms. The members presented to the Flight and Operational Medicine Clinic (FOMC) for evaluation and were immediately referred to an inpatient facility and hospitalized. Laboratory testing revealed that one member was positive for *P. falciparum*, while the other member tested negative. Medical history for both patients was notable for noncompliance with the prescribed chemoprophylaxis regimen.

The FOMC's primary purpose is to optimize aircrew health to support operational readiness. To this end, the FOMC team strives to equip aircrew members with knowledge and chemoprevention to prevent malaria contraction.[5] In 2017, JB Charleston FOMC revamped the education of mosquito-borne vector prevention as well as chemoprophylaxis education. However, through outreach within the squadrons, FOMC personnel became aware that many aircrew members take chemoprophylaxis incorrectly or not at all. The goal of this preliminary survey was to assess aircrew malaria prophylaxis adherence as well as to understand potential factors that contribute to nonadherence.

While ample literature discusses prescription compliance, very little exists on chemoprophylaxis adherence, especially among aircrew members. Many effective medications are only beneficial if patients closely follow prescription regimens; however, many aircrew members either do not take the prophylaxis as prescribed or avoid it completely, thereby hindering prophylaxis effectiveness and increasing the relative risk of malaria contraction. Adherence comprises both dose taking, taking the correct number of pills per day for the entire length of the prescription, and dose timing, ingesting the pills at the correct time each day.[4] Proper adherence is further challenging for aircrew members as they fly complex, often lengthy missions across different time zones. Compliance with causal malaria prophylaxis regimens is often poor, particularly among those who frequently travel abroad for short time periods.[3] Predictors of poor medication adherence that pertain to aircrew members may include poor provider-patient relationships, missed appointments, inadequate follow-up, negative side effects, patient's lack of belief in prophylaxis benefits, patient's lack of insight into the illness, and the complexity of treatment.[4]

Research Questions

1. Does aircrew position influence malaria prophylaxis adherence?
   a. H_0: Aircrew position does NOT influence malaria prophylaxis adherence.
   b. H_A: Aircrew position does influence malaria prophylaxis adherence.
2. Does age influence malaria prophylaxis adherence?
   a. H_0: Member's age does NOT influence malaria prophylaxis adherence.
   b. H_A: Member's age does influence malaria prophylaxis adherence.
3. Does malaria prophylaxis prescription on previous missions influence malaria prophylaxis adherence?
   a. H_0: Having been prescribed malaria prophylaxis on previous missions does NOT influence malaria prophylaxis adherence.
   b. H_A: Having been prescribed malaria prophylaxis on previous missions does influence malaria prophylaxis adherence.
4. Do moderating factors (such as number of pills or previously experiencing side effects) influence malaria prophylaxis adherence?
   a. H_0: Moderating factors do NOT influence malaria prophylaxis adherence.
   b. H_A: Moderating factors do influence malaria prophylaxis adherence.

METHODS

Due to the nature of this study, the protocol was found to be exempt from Institutional Review Board evaluation, which was confirmed by the hospital ethics function via the Chief of the Medical Staff. A retrospective, online survey was offered to aircrew members who visited FOMC (convenience sample) between January and April 2018; as contact was made in the clinic, members were confined to patients on active-duty orders and empaneled to the FOMC. Members were explained the purpose, risks, and benefits of the survey and provided a link to review and perform the survey at their convenience. Of the approximately 400 aircrew members at JB Charleston, 142 members completed the survey, ensuring a 35.5% response rate. Independent variables examined in the survey included crew position, age, and malaria prophylaxis prescription while on a previous mission. Moderator variables included factors influencing nonadherence and previous side effects of malaria prophylaxis experienced by members. These variables were examined in relation to the dependent variable of malaria prophylaxis adherence. Descriptive statistics were employed on the survey results ($N = 142$). Variables were measured at the categorical level and consisted of two or more independent groups, which satisfied required assumptions, and a Chi-squared analysis was then performed.

RESULTS

Descriptive Statistics

The majority of respondents were pilots (60.6%), followed by loadmasters (31.7%), then other positions (7.7%). Most respondents were between 24 to 29 yr old (43.7%), and 71.8% (102 members) had previously been prescribed malaria chemoprophylaxis in the form of Malarone or doxycycline while on a mission (**Fig. 1**). What is most concerning is that more than 67% of respondent aircrew members did not take the medication as prescribed or did not take it at all; of those, over half of respondents stated too many pills/too many days and medication side effects as the main reasons for nonadherence. Furthermore, almost 70% of adherent members endorsed negative medication side effects, including upset stomach/nausea, vomiting, diarrhea, fever, heightened dreams, hallucinations, and headaches (**Fig. 2**).

Chi-Squared Analysis

The majority of both pilots (69.7%) and loadmasters (65.6%) were not compliant with malaria prophylaxis recommendations. No statistically significant association [$\chi^2(1) = 1.787$, $P = 0.409$] existed between crew position (pilots, loadmasters, and other) and malaria prophylaxis adherence. The strength of association between crew position and adherence was weak (0.133). The majority of all age groups (63.7%) were not compliant with malaria prophylaxis recommendations. No statistically significant association [$\chi^2(1) = 4.913$, $P = 0.296$] existed between age range and malaria prophylaxis adherence. The strength of association between age range and adherence was weak (0.221). There was also no statistically significant association [$\chi^2(1) = 0.001$, $P = 0.970$] between malaria prophylaxis side effects and adherence. The strength of association between the variables was very weak (0.004).

DISCUSSION

Although our study yielded no statistically significant results, we found that over 63% of aircrew members failed at adequate force protection when operating in areas with malaria. The findings were very revealing in terms of malaria prophylaxis adherence rates, attitudes among flyers, and factors contributing to nonadherence. This study also emphasized the need for continual policy evaluation,[5] reconsideration of current patient education processes, examination of current prophylaxis enforcement measures and involvement by line unit commanders, and conversations about perceived vs. actual risk. Prophylaxis nonadherence has the potential to detrimentally impact the global mission and it puts airmen at risk for contracting a very preventable condition.

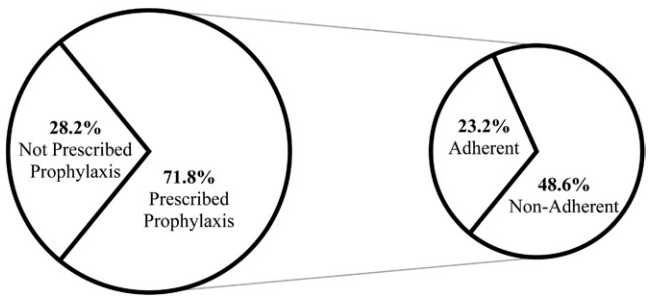

Fig. 1. Malaria prophylaxis prescription and adherence. Respondent ($N = 142$) prescription status was not validated by patient pharmacy records due to the de-identified nature of the data.

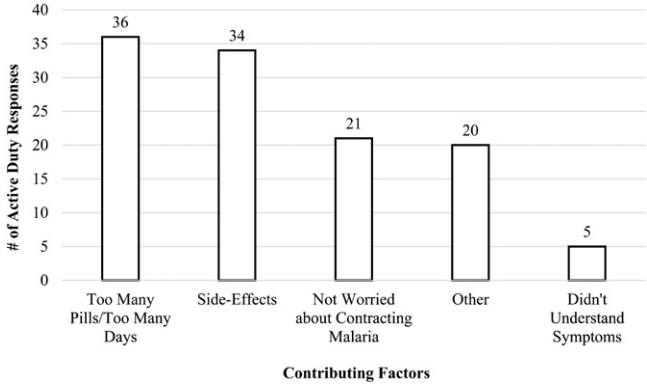

Fig. 2. Reasons for non-adherence. Nonadherent members ($N = 68$) who were prescribed malaria prophylaxis on a mission. Respondents were able to select multiple reasons for nonadherence.

More research needs to be done surrounding aircrew member attitudes toward prophylaxis. It is likely that a malaria prophylaxis prescription on previous missions would negatively influence future adherence. For instance, a member who is initially compliant and experiences negative side effects is less likely to adhere to medication regimens on future missions. Further, members who are compliant but have colleagues who are noncompliant without negative consequences are less likely to be compliant in the future. Although there was no statistical relationship between prophylaxis side effects and adherence, we still hypothesize that those who suffered from side effects would be either less compliant or not compliant on future missions—the more side effects experienced, the less likely a flyer is to be compliant. Our descriptive statistics affirmed this; about one-third of respondents noted at least two reasons for nonadherence, mainly too many pills/too many days and medication side effects. This data suggests the impact of the perceived risk of suffering from medication side effects (which could potentially preclude flying duties) is greater than the perceived risk of contracting malaria among aircrew members.

Other potential barriers to adherence that should be examined in future studies include malaria education scope and information fatigue, nature of missions (crossing time zones, operational tempo, stress levels), nature of prophylaxis regimen (quantity and duration), lack of enforcement or consequences for failure to follow policy, and perceived risk of contracting malaria. The impact of the unstructured duty day cannot be overstated. Aircrews frequently depart and land in different time zones, and due to the nature of this aircraft's capabilities, may execute extended missions over the course of several days. While times are standardized, following a regimen such as one

pill per day can prove to be more complicated than the concept might convey.

Our study had several limitations which would ideally be addressed in future efforts. First, this examination demonstrated trends, but did not reach statistical significance in any area, inhibiting the ability to draw any finite conclusions regarding the impact of individual factors. Given the magnitude of Air Force flying operations, attempts should be made to expand the scope of included patients, which could amplify the findings to reach significance. Second, due to its retrospective nature, information derived was wholly dependent on patient recollection of symptoms and adherence. This may explain the lack of correlation between experienced side effects and noncompliance.

In conclusion, malaria prophylaxis regimen compliance is very poor among aircrew members due to a myriad of line commander, medical, and social factors. While FOMC will continue to cultivate a trusting clinician-patient relationship and strive to keep aircrew educated on the appropriate use and compliance with medical therapies, the process itself must be examined. Line commanders must be educated and made aware of the risks to mission accomplishment of a malaria outbreak. The only way to ensure compliance is with direct line commander action, buy-in, and support. Further research must be done on the weighted risk of transmission based on exposure rate and time and true compliance across the relevant operational population. Prophylaxis guidelines should be optimized to avoid medication fatigue and unwarranted exposure to side effects, but maintain the continued health of our flying population. Effort should be made to facilitate compliance through process improvement; for example, adding the projected date and time to begin the prophylaxis regimen to mission planning documents in Zulu time would clarify the schedule in contrast to coordinating between the departure and arrival time zones. Finally, as the expeditionary risk environment evolves, Operational Medicine should continue to adjust, ensuring the provision of the most current, safe, and efficacious treatment to our warfighters.

REFERENCES

1. Arguin PM, Tan KR. Infectious diseases related to travel: Malaria. In: Brunette GW, Kozarsky PE, Brown CM, et al., editors. CDC yellow book 2018: health information for international travel. New York: Oxford University Press; 2017.
2. Centers for Disease Control and Prevention. 2018, July 12. Malaria parasites. [Accessed Sept. 2018]. Available from https://www.cdc.gov/malaria/about/biology/parasites.html.
3. Chambers JA. Military aviators, special operations forces, and causal malaria prophylaxis. Mil Med. 2003; 168(12):1001–1006.
4. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005; 353(5):487–497.
5. United States Department of Defense. DoDI 6490.03. Deployment health. Washington (DC): United States Department of Defense; 2006.
6. United States Department of Defense. DoDD 6200.04. Force health protection. Washington (DC): United States Department of Defense; 2007.
7. United States Department of Defense. DoDI 4150.07. DoD pest management program. Washington (DC): United States Department of Defense; 2008.
8. United States Department of the Army. AFJI 48-110. Immunizations and chemoprophylaxis. Washington (DC): United States Department of Defense; 2013.
9. United States Department of Defense. Assistant Secretary of Defense Health Affairs. HA-Policy 13-002. Guidance on medications for prophylaxis of malaria. Washington (DC): United States Department of Defense; 2013.