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An Assessment of the Tolerability and Compliance of Malaria Chemoprophylaxis in Australian Army Aviation Personnel [1]

by
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ABSTRACT

THE AUSTRALIAN DEFENCE FORCE (ADF) is currently maintaining large numbers of soldiers including aviators in malarious areas of East Timor for peacekeeping duties. The only approved malaria chemo suppressive agent for this group is doxycycline with primaquine post-exposure prophylaxis for vivax malaria. Aircrews are suspended from flying duties for the period of the post-exposure prophylaxis.

All Australian Army Aviation (AAAvn) personnel stationed in East Timor in July 2001 were interviewed on their opinions and experiences of the current chemoprophylaxis for malaria. Aircrew particularly reported erratic or poor compliance with doxycycline and dissatisfaction with primaquine post-exposure prophylaxis. Most air crew delayed post-exposure prophylaxis on return to Australia due to tasking requirements during which many also reported difficulties with doxycycline compliance. There is a pressing need for the investigation of a flexible antimalarial regime that is suited to the unique needs of AAAvn aircrew.

INTRODUCTION

THE AUSTRALIAN DEFENCE FORCE (ADF) is currently maintaining large numbers of soldiers including aviators in East Timor for peacekeeping duties. The area of operations is known to be malarious.[1] The first choice of malaria chemoprophylaxis is doxycycline (100mg once daily) beginning one day prior to malaria exposure and continued until 14 days after return to Australia. Primaquine (15mg twice daily) is given concurrently with the final 14 days of doxycycline administration for post-exposure prophylaxis.[2] Mefloquine and Malarone' are alternatives if doxycycline is poorly tolerated[3].

Currently; Australian Army Aviation (AAAvn) aircrew are only approved to use doxycycline as a chemoprophylaxis agent whilst performing flying duties, as neither mefloquine nor Malarone' are approved for use by aircrew. Recently, a study in aircrew of the Israeli Air Force found that mefloquine was safe and better accepted than doxycycline suggesting that further studies are needed to assess the safety of mefloquine in aircrew. Australian (AAAvn) aircrew who are intolerant of doxycycline are not currently authorised to use mefloquine and are classified as non-deployable into malaria endemic areas.

The use of primaquine for 14 days of post-exposure prophylaxis is known to cause side effects and be associated with compliance difficulties. Aircrew are suspended from flying duties for the period of the post-exposure prophylaxis due to inadequate information on the effects of primaquine on aviation high-level tasks. Additionally, aircrew are often required to delay primaquine post-exposure prophylaxis until recreation leave is taken in order to continue flying in the interim. In this case, daily suppressive doxycycline is continued until primaquine post-exposure chemoprophylaxis can be initiated.

Concerns of classification as non-deployable to a malarious area creates the potential for aircrew to avoid declaring adverse drug reactions to either doxycycline or primaquine. The potential also exists for non-compliance with primaquine post-exposure chemoprophylaxis if aircrew are delayed in initiating it due to continuing tasking requirements after return from the malarious area.

METHODS

All AAAvn unit personnel stationed in East Timor in July 2001 were interviewed on their opinions and experiences of the current chemoprophylaxis for malaria. Personnel were provided with a guarantee of anonymity in order to facilitate open and frank responses without consequences of disciplinary action.

Seventy-nine volunteers (30 aircrew and 49 non-aircrew) from two AAAvn units based in East Timor were interviewed. A standardised questionnaire was used and administered by a single interviewer. Four non-aircrew reported probable previous adverse drug reactions to doxycycline and were taking mefloquine as malaria chemoprophylaxis. They were included in the study. The East Timor postings for AAAvn units were four months in duration, with most aircrew interviewed undertaking their second tour of duty.

RESULTS

The results are summarised in the following tables:

Table 1:

Responses to: 'How long have you been taking doxycycline continuously?'	**Aircrew**	**Non-aircrew**
Mefloquine	0	4 (8%)
No chemoprophylaxis	1 (3%)	0
Less than one week	4 (13%)	0
One to six weeks	0	0
More than six, but less than 16 weeks	23 (77%)	44 (90%)
More than 16 weeks, but less than 12 months	0	0
12 months or more	2 (6%)	1 (2%)
Total	**30**	**49**

Table 2:

Responses to: Tell me about your experiences with doxycycline'	**Aircrew**	**Non-aircrew**
Difficult to remember to take it daily	6 (20%)	5 (10%)
Dislike taking it daily	2 (7%)	1 (2%)
Concerned about long term effects	2 (7%)	0
Concerned about drug interactions	1 (3%)	1 (2%)
Unsure of need, as few mosquitoes seen	1 (3%)	0
Suffer side effects, so don't take it	1 (3%)	0
Suffer side effects, so take mefloquine	0	4 (8%)
No concerns	17 (57%)	38 (78%)

Table 3:

Response to: 'It's quite difficult to remember to take medications daily – what has been your experience on this deployment?'	**Aircrew**	**Non-aircrew**
Missed about 10 days	6 (20%)	0
Missed about 7 days	0	1 (2%)
Missed about 5 days	3 (10%)	6 (12%)
Missed about 2 days	13 (43%)	12 (24%)
Never missed a day	7 (23%)	26 (53%)
Taking mefloquine	0	4 (8%)
No chemoprophylaxis	1 (3%)	0

Table 4:

Responses to: 'There are some side effects associated with doxycycline- do you think you've had any?'
with a request for elaboration as appropriate. (More than one response was received from some individuals.)

	Previous exposure, no symptoms now		1st fortnight		Ongoing		At night or without food	
	Aircrew	Non-aircrew	Aircrew	Non-aircrew	Aircrew	Non-aircrew	Aircrew	Non-aircrew
Nausea	2 (8%)	1 (3%)	1 (3%)	0	1 (3%)	3 (9%)	0	3 (9%)
Vomiting	0	1 (3%)	0	0	0	0	0	3 (9%)
'Burning throat' or 'indigestion'	2 (8%)	1 (3%)	0	0	4 (13%)	1 (3%)	5 (17%)	7 (21%)
Photosensitivity	3 (12%)	6 (17%)	3 (10%)	1 (3%)	4 (13%)	7 (21%)	0	0
Diarrheoa	0	0	2 (7%)	0	1 (3%)	0	0	0
Slow healing	0	0	0	0	2 (7%)	0	0	0

This was the first exposure to doxycycline for five aircrew and l3 non-aircrew. Of those, four non-air crew were taking mefloquine, two had suffered side effects with doxycycline previously and had deployed on this occasion using mefloquine, and two had commenced this deployment using doxycycline and been changed to mefloquine following intolerance. Some personnel had suffered side effects on previous exposure to doxycycline and now had no side effects. Others reported transient side effects that had since resolved, whilst some individuals reported ongoing side effects. Several respondents reported side effects from doxycycline when taken at night or without food.

Table 5:

Response to: 'Have you missed or shortened a post-exposure prophylaxis course?"	**Aircrew**	**Non-aircrew**
Completed all courses fully	9 (36%)	21 (61%)
Missed more than one post-exposure prophylaxis course	3 (12%) *	0
Missed one post-exposure prophylaxis course	6 (24%)	4 (12%)
Shortened to seven days or less	10 (40%) **	5 (15%)
Shortened to greater than seven days, but less than 14	1 (4%)	1 (3%) **
Erratic compliance	1 (4%)	1 (3%)
Intends to miss post-exposure prophylaxis course if symptom free after stopping doxycycline	2 (8%)	1 (3%)

(*One aircrew missed one course due to 'adverse events'; **One aircrew due to 'adverse events')

Five aircrew and 15 non-aircrew had not previously used post-exposure prophylaxis. Of the 15 non-aircrew, one was taking doxycycline long term (two years and 10 months) and intended to continue to do so on return to Australia in order to continue flying duties. Another had been evacuated from a previous deployment due to suffering an adverse drug reaction to doxycycline and post-exposure prophylaxis was not undertaken, and another individual was involved in a trial of tafenoquine post-exposure prophylaxis following a previous deployment.

36% of aircrew and 12% of non-aircrew had omitted post-exposure prophylaxis with primaquine, while 44% of aircrew and 18% of non-aircrew had shortened their post-exposure prophylaxis courses without medical direction.

Table 6:

Responses to discussion about 'eradication' (post-exposure prophylaxis) and the question 'Tell me about your experiences with the post-exposure prophylaxis course'

	Aircrew	Non-aircrew		Aircrew	Non-aircrew
Nausea	6 (24%)	4 (12%)	Post-exposure prophylaxis delayed until leave due to tasking requirements	16 (64%)	0
Vomiting	1 (4%)	1 (3%)	Doxycycline compliance erratic when post-exposure prophylaxis delayed	7 (28%)	0

Diarrhoea	2 (8%)	0	Nonflying component hampers the operations of the unit	2 (8%)	1 (3%)
Abdominal Pain	1 (4%)	2 (6%)	Alcohol abstinence is socially restrictive, especially on post-exposure prophylaxis on leave	7 (28%)	10 (29%)
Wind or bloating	0	2 (6%)	Delay post-exposure prophylaxis on leave by one week so can drink alcohol	3 (12%)	5 (15%)
Headaches	1 (4%)	2 (6%)	Drinks alcohol on post-exposure prophylaxis	9 (36%)	17 (SO%)
'Not right'*	4 (16%)	4 (12%)	Unaware of belief to abstain from alcohol	2 (8%)	0
No side effects	11 (44%)	21 (62%)	Will forego post-exposure prophylaxis	2 (8%)	1 (3%)

(*This group consistently found it very difficult to describe how they felt whilst using post-exposure prophylaxis. It was described variously as 'not feeling right', 'not feeling 100%', 'not myself ', 'difficulty in concentrating', and 'difficulty in planning things'.)

Table 7:
Responses to: 'Do you have any suggestions as to how the chemoprophylaxis and post-exposure prophylaxis courses could be improved?' Some personnel gave more than one response.

	Aircrew	**Non-aircrew**
Weekly chemoprophylaxis	14 (47%)	14 (29%)
Habituate personnel to malaria chemoprophylaxis by using vitamin C tablets when on exercise	0	2 (4%)
Chemoprophylaxis which does not requires post-exposure prophylaxis	5 (17%)	1 (2%)
A shorter post-exposure prophylaxis course	9 (30%)	6 (12%)
A post-exposure prophylaxis course compatible with flying duties	6 (20%)	1 (2%)
An alternative to primaquine due to the side effects	0	2 (4%)
Post-exposure prophylaxis that is compatible with alcohol consumption	1 (3%)	1 (2%)
Delay post-exposure prophylaxis so personnel can enjoy unrestricted social activities post deployment	0	1 (2%)
No suggestion for improvement	1 (3%)	10 (200)
Happy with the current system	2 (6%)	13 (27%)

DISCUSSION

A higher proportion of aircrew reported difficulty remembering to take doxycycline and displayed erratic or poor compliance when compared to the non-air crew. This difference may be due to variations in the daily routine of aircrew, including rotating between day and night crewing and spending time away from base on missions. Non-aircrew are generally not exposed to these variations, tending to have a set daily routine. Both AAAvn units approached made doxycycline freely available in a common area. In both, names were checked against a nominal roll to ensure daily compliance. Despite this system, a significant proportion of both aircrew and non-aircrew were still experiencing difficulties with compliance. Compliance would be likely to improve if a system of supervision was added to the self-registration of compliance.

With such a high rate of 'missed days' amongst the aircrew, the potential exists for sub-optimal doxycycline chemoprophylaxis. The risk of malaria infection is compounded by the mobility of the aircrew resulting in time spent in areas where collective vector control measures such as fogging and application of larvicide to groundwater are poor or non-existent.

Aircrew and non-aircrew reported adverse events whilst taking doxycycline at approximately the same rates -66% of aircrew compared to 59% of non-aircrew. Most adverse events reported were mild in nature, although for aircrew these may have the potential to impinge upon the safety of flight operations, particularly night vision goggle missions. Whilst non-aircrew may accept mild side effects, pilots and loadmasters may experience impaired concentration at critical points of flight, especially landing, formation flying and hoisting operations.

Four non-aircrew reported suffering significant adverse events from past exposure to doxycycline and were taking mefloquine as malarial chemoprophylaxis. One aircrew reported suffering from significant side effects from past exposure to doxycycline and elected to take no chemoprophylaxis. The individual had not sought medical evaluation for fear of being classified as non-deployable to malaria-endemic areas (effectively being restricted to flying operations in Australia only). This situation highlights the need for alternative malaria chemoprophylaxis to be available to aircrew who suffer adverse events whilst taking doxycycline.

Both aircrew and non-aircrew reported high rates of dissatisfaction with the post-exposure prophylaxis course, with the aircrew reporting at higher rates. Post exposure prophylaxis is generally used differently by aircrew than non-aircrew. About two-thirds of aircrew reported delaying post-exposure prophylaxis on their return to Australia due to AAAvn tasking requirements. Approximately half of this group also reported difficulties with doxycycline compliance during the period of delayed post-exposure prophylaxis. Many reported a pattern of not taking any suppressive chemoprophylaxis on their return to Australia, feeling healthy, and then not undertaking post-exposure prophylaxis in the absence of illness. Non-aircrew typically take post exposure prophylaxis on their return to Australia, with no restriction on duties during this time.

About one-third of aircrew and non-aircrew disliked the restrictions of alcohol abstinence whilst taking post-exposure prophylaxis. Alcohol abstinence is not a requirement of post-exposure prophylaxis; nonetheless, this was a commonly held perception. Despite this perception, about one-third of aircrew and non-aircrew consumed alcohol whilst taking post exposure prophylaxis. A small proportion delayed their post-exposure prophylaxis course by one week in order to take alcohol.

Approximately one-third of aircrew had missed post exposure prophylaxis courses completely. A further third of this group (36%) had missed more than one course, three times more frequently than with non-air crew. Higher rates of non-completion by aircrew are considered to be due to a combination of delay in initiating post-exposure prophylaxis, adverse events and social restrictions whilst on recreation leave resulting in diminished motivation to complete the post-exposure prophylaxis requirements. Individuals in this group specifically identified waning compliance on doxycycline when post-exposure prophylaxis was delayed. The perception was that they experienced "good health" and were malaria-free and that there was little or no benefit in continuing with long-term doxycycline or initiating the post-exposure prophylaxis with primaquine. Despite citing adverse events as an issue, the reason for the majority of 'short courses' of primaquine was a lack of motivation rather than adverse drug reactions (Table 5).

Adverse events were commonly reported on the post-exposure prophylaxis course (Table 6). Nausea was a common complaint along with subjective feeling of being 'not right'. Aircrew tended to have been exposed to post-exposure prophylaxis courses more than non-aircrew. This may explain the higher rate of adverse events compared to non-aircrew. As most aircrew tend to eradicate sometime after their return to Australia on their leave, it is unlikely that their adverse events are due to any change in environmental or social conditions associated with homecoming.

Of the non-aircrew, more than half were satisfied with, or had no suggestions for change to the current malaria chemoprophylaxis regime (Table 7).

In contrast, the majority of aircrew (27/30) suggested improvements. Weekly chemoprophylaxis would be preferred, particularly by aircrew (47%) in order to improve compliance. Chemoprophylaxis without the need for post-exposure prophylaxis, or at least a shorter post-exposure prophylaxis course was also identified (17% & 30% respectively). This would result in less impact on flying operations, as well as potentially removing the requirement for any delay in initiating post-exposure prophylaxis resulting in improved compliance. Aircrew specifically identified a preference for post-exposure prophylaxis compatible with flying duties (20%).

CONCLUSIONS

Current malaria chemoprophylaxis and post-exposure prophylaxis regimes currently in use in the ADF are not meeting the requirements of AAAvn aircrew. Aircrew delaying post-exposure prophylaxis for extended periods of time until taking their recreation leave is associated with significant problems with compliance. Whilst aircrew tolerance to doxycycline is no different to non-aircrew, aircrew compliance is poorer. The lack of any approved alternative to malaria chemoprophylaxis compatible with flying duties is precipitating non-disclosure of intolerance due to concerns about being classified as non-deployable for flying operations in malarious areas.

There is a pressing need for the investigation of a flexible anti-malarial regime that is suited to the unique needs of AAAvn aircrew. Preferences are for weekly chemoprophylaxis and a shorter post-exposure prophylaxis course compatible with flying duties. An alternative to doxycycline, compatible with flying duties, is also required. Further investigation into the effects of alternative malarial chemoprophylaxis agents on the performance of high-level tasking in AAAvn aircrew is required.

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