

Tolerability and Adherence to Mefloquine among Jordanian Troops Serving in Kinshasa

Ala'eddeen K. Abu-Rumman MSc, Tareq M. Aljbouri MSc*,
Mohammad G. Al-Sharayri MSc*, Sahar I. Al-Neimat MSc*,
Mohammed S. Alkhawaldeh MSc*, Salah S. Haddadin BSc**

ABSTRACT

Objectives: To assess adherence, investigate reasons for non-adherence and describe tolerability of Mefloquine among Jordanian military personnel, who served in level II military hospital in Kinshasa for a six months period.

Method: In 2011, 56 male military personnel agreed to complete an anonymous questionnaire which checked the degree of adherence, reasons for non-adherence, and both the frequency and severity of Mefloquine side effects. Participants were also asked if they received counselling about malaria and Mefloquine prior to departure. All participants were interviewed face-to-face to further investigate their experiences with Mefloquine. The Mefloquine weekly dosage was dispensed from the pharmacy to the public health inspector every Tuesday and then to the participants after lunch on that day.

Results: Thirty six participants (64.4%) took all doses. Fourteen participants (25%) skipped some doses, mostly due to forgetting (50%). Other reasons were travelling (14.2%), side effects (14.2%), acute disease (14.2%), and being careless (7.1%). Number of skipped doses varied between one and five from the 29 doses given. One participant (1.8%) took no Mefloquine at all due to previous side effects of the drug. Five participants (8.9%) permanently stopped using Mefloquine, four due to side effects and one due carelessness. Thirty two (57.1%) participants complained of side effects, the most common being: nightmares (16.7%), insomnia (15%), headache (13.3%), anxiety (11.7%), and diarrhoea (9.2%). Most of participants (93.8%) classified their side effects as being mild to moderate. Only 14 participants (25%) reported that they received counselling about malaria and Mefloquine.

Conclusion: The high adherence rate in this study reflects the method of dispensing Mefloquine which was used. Reasons for non-adherence should always be investigated in order to find solutions that will further enhance adherence. Although more than half of participants reported at least one side effect, Mefloquine was tolerated by the majority of participants over the study period. Education about malaria and Mefloquine is essential for both health care professionals and users.

Key words: Mefloquine, tolerability, adherence, military personnel.

JRMS September 2014; 21(3): 33-37 /DOI: 10.12816/0005525

Introduction

Malaria is one of the most common infectious diseases known to mankind. The number of malaria cases estimated by the World Health

Organization (WHO) in 2010 was about 219 million cases, among which about 660.000 died. Despite these high figures, in the period 2000-2010, the mortality rate of malaria decreased by

* From the Directorate of Medical Supply, Directorate of Royal Medical Services (RMS). Amman-Jordan
Correspondence should be addressed to Dr. A E Abu-Rumman, (RMS), E-mail: ala_rumman@hotmail.com
Manuscript received January 28, 2014. Accepted June 5, 2014

26% around the world. Furthermore, the number of malaria deaths that were prevented during this period was estimated to be about 1.1 million. Such progress in malaria prophylaxis was a result of two major interventions; mosquito avoidance measures and chemoprophylaxis.⁽¹⁾

The most commonly used drugs for malaria chemoprophylaxis are Mefloquine, Doxycycline, Chloroquine, Primaquine, Proguanil, and Atovaquone plus Proguanil. The selection between these drugs depends on many factors which include: efficacy and incidence of resistance in the country selected, cost, tolerability, drug interactions and contraindications. There are many guidelines for malaria prophylaxis in which all these factors are considered to help selecting the appropriate chemoprophylactic drug. Although these guidelines vary, there is a clear consensus that Mefloquine is considered a key chemoprophylaxis choice.⁽²⁾

Mefloquine was first used by the Jordanian Armed Forces (JAF) for malaria chemoprophylaxis in 1998. It is currently prescribed to military troops participating in peacekeeping and humanitarian missions who are deployed in malaria endemic areas such as Afghanistan, Haiti, the Ivory Coast, Liberia and the Democratic Republic of the Congo (DRC).

The safety of Mefloquine use for malaria chemoprophylaxis among military troops has been considered by a previous study.⁽³⁾ To our knowledge, only one short term study (3 months) has been carried out among Jordanian military troops who served in Afghanistan. It focused mainly on the prevalence of side effects and to a lesser extent on adherence to Mefloquine.⁽⁴⁾

This study assesses the adherence and the reasons for non-adherence and also describes the tolerability of Mefloquine among Jordanian military personnel over the longer time period of six months.

Methods

This study was carried out among Jordanian troops who served in a level II military hospital in Kinshasa as a part of the United Nations Organization Stabilization Mission in the DRC. The mission period was approximately six months from the 1st of March until the 10th of September 2011.

The total number of military personnel was 68 (4 females and 64 males). Females were excluded from the study as their number is not sufficient to provide enough data for analysis, besides it has previously been shown that females have higher incidence of Mefloquine side effects as they, generally, have a lower body weight.⁽⁵⁾ In addition, the majority of the Jordanian military personnel who serve in humanitarian and peacekeeping missions are males.

All members of the troop were military personnel but can be classified into medical and non-medical staff. The number of medical staff was 33; these include physicians, nurses, pharmacists, dentist, public health inspector and different technicians, while the rest were non-medical staff such as the commander, liaison officer, interpreters, drivers and others.

All military personnel were given one Mefloquine 250 mg tablet per week as malaria chemoprophylaxis. The first dose of Mefloquine was dispensed on the 22nd of February which was a week before the departure day. The second dose was dispensed on the departure day, on Tuesday, 1st March. Thereafter, the weekly supply of Mefloquine was dispensed from the pharmacy to the public health inspector every Tuesday. He then, dispensed one Mefloquine tablet to each member to be taken after lunch. The total number of doses that was dispensed to each individual was 29 doses. Mefloquine was voluntarily used by military personnel, as there were no military disciplinary actions taken against those who were not taking it.

In the last three days of the mission, the pharmacist asked all male military personnel to fill an anonymous questionnaire about adherence and tolerability of Mefloquine. This study was approved by the Human Research Ethics Committee at the Royal Medical Services (RMS).

All participants signed a consent form before filling in the questionnaire. The consent form clearly indicated that taking part in this study was voluntary. After filling in the questionnaire participants were interviewed face-to-face by the pharmacist to further investigate participants experience about Mefloquine adherence and tolerability.

The questionnaire determined the following data: age, present or past illnesses and previous usage of Mefloquine. Moreover, adherence to

Mefloquine was determined by checking if participants took all the doses, skipped any or did not take it at all. Reasons for non-adherence were also investigated. Furthermore, tolerability of Mefloquine was investigated by asking the participants about the frequency of side effects during the mission. Participants were asked to classify the severity of side effects into the following: mild (not affecting daily life), moderate (affecting daily life) and severe (medical care was provided). Finally, participants were asked if they received counselling about malaria and the importance of using Mefloquine and its possible side effects prior to departure.

Results

The number of participants who filled the questionnaire and were interviewed was 56. Eight male military personnel showed no interest in participating in the study and refused to fill in the questionnaire. The age range of participants was from 23 to 43 years with a mean of 31 years. The number of participants who had previous 'experience' with Mefloquine usage was 12 (21%).

The degree of adherence of participants to Mefloquine and reasons for non-adherence are shown in Table I. Out of 56 participants 36 (64.4%) stated that they adhered strictly to Mefloquine, *i.e.* they took all the doses throughout the mission period. The number of participants who skipped some doses was 14 (25%). The doses that were skipped ranged from one to five doses. The most common cause for skipping doses was simply forgetting to take the medication (50%). Five out of seven participants who forgot to take Mefloquine reported that they were on duty at the time of dispensing and distributing the weekly dosage. Two participants' skipped doses due to travelling to Uganda and two other participants skipped doses as they suffered some acute disease and preferred not to take Mefloquine as they were prescribed other drugs. In one case he noticed an increase in the frequency of side effects especially nightmares as he was prescribed omeprazole, clarithromycin and amoxicillin for treatment of *H. pylori* infection. Side effects forced two participants to skip some doses. One participant stated that he was careless and showed no interest

in taking the Mefloquine dose and thus he skipped some doses.

Five participants, (8.9%), stopped taking Mefloquine; four of them confirmed that the reason was due to side effects, while one stated that he did not care about taking Mefloquine. Furthermore, one participant (1.8%), did not take Mefloquine at all as he had taken it before and suffered from side effects and did not want to repeat the experience.

All side effects that are possibly caused by Mefloquine and reported by participants are shown in Table II. The number of participants who complained of at least one side effect was 32 (57.1%). The most common side effects were nightmares, 16.7%, and insomnia 15%. In addition, headache was reported in 13.3% of participants. Moreover; the incidence of anxiety and diarrhoea was 11.7% and 9.2% respectively. In spite of the fact that other side effects that are shown in the table are less common, participants classified some of these to be severe.

Twenty two participants (68.8%) classified their side effects to be mild. On the other hand, two participants (6.2%) classified their side effects as severe and thus they stopped taking Mefloquine. Although eight participants (25%) classified their side effects to be moderate, two of them stopped taking Mefloquine.

The number of participants who reported that they received counselling about malaria and the importance of using Mefloquine and its possible side effects was only 14 (25%). They stated that they attended a psychological counselling lecture, prior to going overseas, in which these topics were mentioned briefly.

Discussion

This study is the first to evaluate the tolerability and adherence to Mefloquine among Jordanian military troops serving in malaria endemic areas for a six month tour of duty.

It is ethically not acceptable to assign a control group in this study since malaria chemoprophylaxis must be given during such missions. Although environmental factors such as climate, stress and infection may affect the reporting of side effects, this was clearly explained to participants during the interview which was carried out by the pharmacist in order

Table I: Degree of adherence of participants to Mefloquine and reasons for non-adherence:

Degree of adherence	No. (%)	Reasons	N.
Took all doses	36 (64.3)		
Skipped doses	14 (25.0)	Forgot	7
		Travelling	2
		Side effects	2
		Acute disease	2
		Did not care	1
Stopped	5 (8.9)	Side effects	4
		Did not care	1
Did not use at all	1 (1.8)	Previous usage and suffered from side effects	1

Table II: Frequency of Mefloquine side effects among participants

Side effect	No. of cases	%
Nightmares	20	16.7
Insomnia	18	15.0
Headache	16	13.3
Anxiety	14	11.7
Diarrhea	11	9.2
Nausea	8	6.7
Itching	7	5.8
Paresthesia	6	5.0
Anorexia	5	4.2
Hallucinations	4	3.3
Bradycardia	4	3.3
Tachycardia	3	2.5
Dizziness	2	1.7
Hair loss	1	0.8
Myoclonus	1	0.8

to minimize the effect of such factors on the study results.

The presence of medical staff among the troop could contribute to the high adherence rate, as medical staff are supposed to be more aware of the risks of malaria and the importance of using Mefloquine. Surprisingly, it was found that three out of five participants who stopped or did not use Mefloquine at all were medical staff; this was due to serious side effects and previous bad experience.

The total percentage of those who skipped some or took all Mefloquine doses over the study period was high (89.3%). This was perhaps due the method of dispensing and distributing Mefloquine to participants during the mission and the appropriate times. This method reminded the participants about Mefloquine weekly dosage. In addition, participants encouraged each other to take Mefloquine as all members of the troops received it on the same day. A sufficient number of public health inspectors are perhaps needed in larger missions in order to be able to apply this method.

Despite the fact that 25% of participants skipped some Mefloquine doses, the actual number of skipped doses was low. Reasons for skipping doses of Mefloquine varied as was shown in Table I. The reasons such as being on duty and travelling showed that staff relied entirely on the method of dispensing for distributing Mefloquine. Therefore, the adherence can be further enhanced if the public health inspector reports any surplus of Mefloquine tablets and the

names of staff who did not receive the doses. Consideration should also be given to either remind those who were on duty to take their dose after finishing duty or dispensing Mefloquine to them before going on duty. Those who are travelling should be advised by their superiors to visit the pharmacy to take Mefloquine stock before travelling.

Table I show that side effects were not a common cause for skipping doses. On the other hand, a major cause for stop taking Mefloquine was due to an individual's intolerance to the drug and so they simply stopped taking it. Thus all participants should be informed and encouraged to report such events so that they can be provided with another chemoprophylactic drug.

In this study, many military personnel have previous experience with Mefloquine (21%). One of them did not take Mefloquine as he used it before and found that he could not tolerate it. Therefore, military personnel who have previous experience with Mefloquine should be screened prior travelling to determine those who could not tolerate it in order to prescribe them an alternative. Being careless about dosing had caused one participant to skip doses and another one to stop taking Mefloquine. Such behaviour could be avoided by educating the troops about the risks of malaria and the importance of taking Mefloquine.

Drug-drug interactions are a common cause for increasing the risk of side effects. One participant was prescribed omeprazole, clarithromycin and amoxicillin for the treatment of H.

pylori infection. He noticed an increase in the frequency of side effects even after skipping some doses of Mefloquine. This can be theoretically explained by the pharmacokinetic properties of both drugs. Mefloquine has a long half life (2-4 weeks) and metabolized by CYP3A4,⁽²⁾ therefore it needs several months to be eliminated from the body. Clarithromycin is considered a strong CYP3A4 inhibitor; thus it will decrease the metabolism and excretion of Mefloquine. This will lead to increase its plasma concentration which may increase the incidence of side effects. On the other hand, other drugs may decrease the blood concentration of Mefloquine thus jeopardize the success of malaria chemoprophylaxis. Therefore, pharmacists and other health professionals should be educated about Mefloquine drug-drug interactions as this drug is not commonly used in Jordan.

Although more than half of the participants (57.1%) reported at least one side effect 93.8% they classified their side effects as being mild to moderate. Furthermore, the frequency of each side effect among participants that are shown in Table II did not exceed those found in other studies.^(4,6,7) Moreover, the number of participants who stopped taking or never took Mefloquine due to side effects was five (8.9%). All of these findings indicate that Mefloquine was well tolerated among the majority of Jordanian troops over the study period.

The percentage of participants who were counselled about malaria and the importance of using Mefloquine and its possible side effects was only 25%. This poor knowledge may affect the participant's awareness of the risks of malaria and may decrease their adherence to Mefloquine as shown in those being careless. In addition, participants have the right to be informed about possible side effects of Mefloquine. Such findings highlight the importance of having a mandatory educational program that covers these topics which must be given to participants prior to travelling to malaria endemic areas.

Further studies are needed in the future about Jordanian Military personnel mission in endemic areas where Mefloquine compliance rate can be compared with, especially after health education programme.

Conclusion

The high adherence in this study reflects the method of dispensing Mefloquine which was used. Reasons for non-adherence should always be investigated in order to find solutions that will further enhance adherence to Mefloquine. Although more than half of participants reported at least one side effect, it was tolerable by the majority of the Jordanian military personnel over a six months period. All Mefloquine users should be monitored since some people cannot tolerate it and those so affected should be encouraged to report such events, in order to prescribe them an alternative. There is a need for a mandatory program to educate military personnel about malaria, the importance of using Mefloquine and its possible side effects. There is also a need for educating health care professionals about the complete drug information of Mefloquine as this drug is not commonly used in Jordan.

References

1. **World Health Organization**, World Malaria Report FACT SHEET.2012. Available on line from:http://www.who.int/malaria/publications/world_malaria_report_2012/wmr2012_factsheet.pdf. 2 February 2013.
2. **Schlagenhauf P, Adamcova M, Regep L, et al.** The position of Mefloquine as a 21st century malaria chemoprophylaxis. *Malaria Journal* 2010; 9:357.
3. **Kitchener SJ, Nasveld PE, Gregory RM, Edstein MD.** Mefloquine and doxycycline malaria prophylaxis in Australian soldiers in East Timor. *Medical Journal of Australia* 2005; 182(4):168-172.
4. **Muhareb H, Khalil O, Jumai'an A, et al.** Mefloquine side effects profile among a sample of Jordanian military personnel served in Afghanistan. *Journal of the Royal Medical Services* 2007; 14(2):68-67.
5. **Schlagenhauf P, Johnson R, Schwartz E, et al.** Evaluation of mood profiles during malaria chemoprophylaxis. *J Travel Med* 2009; 16:42-45.
6. **Matsumura T, Fujii T, Miura T, et al.** Questionnaire-based analysis of Mefloquine chemoprophylaxis for malaria in a Japanese population. *Japanese Society of Chemotherapy and the Japanese Association for Infectious Diseases* 2005; 11:196-198.
7. **Fujii T, Kaku K, Jelinek T, Kimura M.** Malaria and Mefloquine Prophylaxis Use Among Japan Ground Self-Defense Force Personnel Deployed in East Timor. *Journal of Travel Medicine* 2007; 14 (4): 226-232.