

Malaria: current prophylaxis options

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Abstract

Most South African travellers visiting sub-Saharan countries to the north will require protection against malaria. This should include personal protection measures (PPM) and chemoprophylaxis. PPM include: DEET based insect repellent, clothing (preferably impregnated with permethrin) that minimises skin exposure, bed nets, screening and use of knock down and residual application insecticides in rooms. Reliance on PPM alone will be insufficient for most malarious destinations. Currently available chemoprophylactic drugs in general use in South Africa are mefloquine, doxycycline, and atovaquone-proguanil. All three are highly efficacious, but attention must be given to drug contraindications when prescribing for an individual traveller. No prophylactic regimen is 100% effective, and all travellers who develop a fever or an influenza-like illness within six months of return should seek urgent medical attention and be tested for malaria. **(SA Fam Pract 2004;46(9): 43-45)**

Introduction

Malaria is a disease that is often underrated in non-endemic areas: *Plasmodium falciparum*, the causative parasite of principal concern, causes as many as two hundred and seventy million new infections every year.¹ The importance of the disease lies in its propensity to progress to complicated disease in non-immune individuals, and the fact that it is largely preventable. A recent study from the United States Centers for Disease Control showed that most malaria deaths in travellers were associated with either failure to use chemoprophylaxis, non-compliance, or the use of inappropriate chemoprophylaxis.² For these reasons it is imperative that travellers to malarious destinations receive the correct advice regarding malaria prevention. Malaria prevention rests upon three pillars: the provision of accurate malaria risk information, the adoption of effective personal protection measures (PPM), and the use of appropriate and effective chemoprophylaxis. No prophylactic regimen offers complete protection against malaria however, and trav-

ellers should be counselled to seek urgent medical attention should they develop influenza or gastroenteritis like symptoms with fever within six months of return from a malarious area.

Malaria risk information

It is not an uncommon experience to encounter travellers from the northern hemisphere taking chemoprophylaxis for itineraries that are non-malarious e.g. the Garden Route. Such individuals are needlessly exposed to the risk of adverse drug reactions. The first step in advising the traveller is to determine exactly what the malaria risk is at the destination to be visited. Not all parts of countries regarded as malarious necessarily harbour the malaria parasite. A good example is Zimbabwe: while most of the country is malarious, Harare is not. Travellers visiting Harare alone do not as a consequence require chemoprophylaxis.

For travellers to certain parts of South East Asia, e.g. popular tourist destinations in Thailand, the actual risk of contracting malaria is less than the risk of experiencing a seri-

ous adverse reaction to chemoprophylaxis. Current thinking is that such travellers would benefit more from the provision of emergency stand by medication (ESBM) than the prescription of chemoprophylaxis. ESBM is dealt with below. For the average South African practitioner though, counselling the average South Africa traveller bound for sub-Saharan Africa north of our borders, there will be a requirement for chemoprophylaxis.

Personal protection measures

Personal protection measures constitute the first line of defence against malaria. If a traveller is not bitten, he cannot contract malaria. The adoption of PPM has the added benefit of protecting the traveller against a range of other diseases transmitted by mosquitoes (dengue, Rift Valley fever), other biting insects (Leishmaniasis, sleeping sickness), and ticks (tick bite fever).

PPM shown to be effective include the following: the use of insect repellents containing DEET; the impregnation of clothing with a suitable insecticide; the covering of exposed

Table 1: Choices between clinic and traditional healers

Mefloquine	Doxycycline	Atovaquone-Proguanil
<i>Mefliam, Lariam</i> Well established	<i>Doximal, Doxitab, other brands</i> Familiar to most prescribers	<i>Malanil</i> Combination of two older drugs: atovaquone and proguanil, but less experience as an antimalarial
Avoid with neuropsychiatric or epilepsy history Has been used safely in children ≥ 5 Kg	Avoid in porphyria Avoid in children of 8 or younger	Not specifically contraindicated with neuropsychiatric disorders Has been used in children ≥ 11 kg, but paediatric dose tablets not generally available in RSA
May be used in pregnancy with caution	Avoid in pregnancy	Inadequate data on safety in pregnancy
Vivid dreams and nightmares and insomnia	Gastro- oesophageal irritation possible, especially if precautions not followed. Enteric coated tablets preferable	Diarrhoea
Mood alterations in susceptible individuals	Occasional photosensitivity to sunlight (uncommon)	Drug rash (uncommon)
Dizziness and nausea	Vaginal thrush	Nausea and vomiting
Once weekly dosage	Once daily dosage	Once daily dosage
Should start at least one week before departure	Should start two days before departure	Should start two days before departure
Should be taken for four weeks after return	Should be taken for four weeks after return	Should be taken for seven days after return
Inexpensive	Least expensive	Most expensive

skin; the use of mosquito (bed) nets; the screening of sleeping quarters; the use of indoor insecticides. PPM is particularly important between the hours of dusk and dawn, when female anopheles mosquitoes are most likely to bite and take a human blood meal.

There are a number of products available in South Africa which claim efficacy in repelling mosquitoes. Field testing has demonstrated however that it is only DEET based products that provide effective and dependable repellancy.³ DEET is available in a number of different formulations and strengths, expressed as percentage concentrations. The important point to remember when selecting a formulation is that strength indicates the duration of mosquito repellent effect, and not the strength of the repellent effect. DEET is known to be safe in the second and third trimesters of pregnancy, but should be applied sparingly in children.⁴ It dissolves certain plastics.

A supplementary strategy to DEET use is the impregnation of clothing with permethrin. This is safe for humans but kills mosquitoes. It is important that only permethrin specially formulated for this purpose is used: other insecticides are not

suitable. Bed nets may also be impregnated with permethrin.

Travellers should be advised to sleep in screened quarters, and rooms should be sprayed with a pyrethroid containing insecticide at night (vapour coils and mats may be used to the same effect). Where possible, accommodation should be sited at least 1,6km from known and possible mosquito breeding sites. The wearing of long sleeved tops and long trousers should be encouraged.

Chemoprophylaxis

Studies in tropical Africa have shown infection rates in non-immune travellers who do not take chemoprophylaxis that average 2% per month of stay. One study showed infection rates of 20% in travellers who had spent at least two weeks in Kenya.⁵

There are currently three readily available chemoprophylactic agents available on the South African market. These are mefloquine (Mefliam®, Lariam®), doxycycline (Doxitab®, Doximal®, and other brands), and atovaquone-proguanil (Malanil®). Each of these has its own advantages and disadvantages. The poor efficacy of chloroquine (Daramal®, Nivaquine®, other brands), either

alone or in combination with proguanil (Paludrine®), makes it unsuitable for chemoprophylaxis in Africa.

Mefloquine

This molecule showed a prophylactic efficacy of 95% in one observational study of travellers to Kenya.⁶

If attention is paid to the contraindications it is well tolerated, and it is a valuable member of the antimalarial armamentarium. Its reputation for causing serious adverse effects is a reflection more of poor prescribing habits than of any inherent lack of safety. The compound is potentially neurotoxic, and should be avoided in individuals with any history of mental illness or epilepsy. Mefloquine has cardiac effects: it may cause prolongation of the QT_c interval, and should be avoided in individuals taking drugs with similar potential, and in those with a history of cardiac rhythm disturbance. It is taken in an adult dose of 250mg weekly, which is helpful with compliance, and is best commenced two weeks prior to departure. It should be taken for four weeks after return from a malarious area.

Mefloquine may be used during the second and third trimesters of pregnancy, and with caution in the first trimester.⁷ It may be used in children with masses of 5 kg and above.⁸ Mefloquine is a relatively cheap antimalarial option.

Doxycycline

This is a familiar molecule, with which most practitioners will feel comfortable. It has efficacy similar to that of mefloquine when used for malaria chemoprophylaxis.⁹ Doxycycline is generally well tolerated, with principal adverse effects encountered being vaginal candidiasis, gastro-oesophageal irritation, and occasional photosensitivity. Gastro-oesophageal irritation can be minimised by prescribing enteric coated formulations. Travellers should be advised to wash down

their doxycycline with ample fluid, and to remain upright for at least thirty minutes after taking their dose. Doxycycline should be avoided in porphyria, pregnancy and children aged eight years or less. Doxycycline may be commenced two days before entering the malarious area, and should be continued for four weeks after return. The adult dose is 100mg daily. It currently is the cheapest antimalarial chemoprophylactic option.

Atovaquone-proguanil

This is fixed a combination of 250 mg of atovaquone (Wellvone) and 100mg of proguanil (Paludrine). Both are well established drugs, and act synergistically against both the blood and the liver phases of the parasite. Atovaquone-proguanil showed prophylactic efficacy of approximately 98% in international multi-centre studies in travellers, and is very well tolerated.¹⁰⁻¹² Principal adverse effects seen in practice are diarrhoea and drug rashes, although these are rare.¹⁰⁻¹² Atovaquone-proguanil may be commenced one to two days before entering the malarious area; the usual adult dose is one tablet daily. The fact that atovaquone-proguanil is active against the incubating hepatic stages of the parasite means that it needs only to be taken for seven days after return from a malarious area. This latter fact reduces the cost of atovaquone-proguanil prescriptions, but it nevertheless remains the most expensive chemoprophylaxis option.

Emergency stand by medication (ESBM)

For very low risk destinations, ESBM may be considered. In such instances the traveller must be counselled on the symptoms of malaria, and informed that ESBM is not a substitute for expert medical care, but merely an emergency measure that may buy time in situations where

care is not immediately available.¹³ Options include quinine and Malaril.

Conclusion

Travellers to malarious destinations require counselling on the risk the disease poses to them, and how it may be avoided. PPM should be encouraged, but not at the expense of chemoprophylaxis, which will be required for the majority of African destinations. Mefloquine, doxycycline, and atovaquone-proguanil are all highly efficacious, and generally well tolerated, although attention must be paid to contraindications.

See CPD Questionnaire p.47

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