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REVIEW

Malaria prevention in the pregnant traveller: A review

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Summary Malaria is still a major threat to health in tropical regions. Particular attention should be directed to malaria prevention in infants and pregnant women as they are at high risk for plasmodial infection and complicated malaria. In this review, we summarize and discuss current evidence on malaria prevention in pregnant travellers.

As neither anti-mosquito measures nor anti-malarial drugs have been proven to be unequivocally safe or toxic in pregnant women, the individual risk assessment should take into account the risk of transmission at the destination, the benefit of travelling despite being pregnant as well as the individual risk perception. All three factors may differ in various groups of travellers like tourist travellers, expatriate travellers as well as those visiting friends and relatives.

For pregnant women, mefloquine appears to be the drug of choice for prophylaxis and stand by-therapy if no contraindications exist – despite recent renewed warnings related to prolonged side effects. In areas with high resistance against mefloquine or in women with contraindications to mefloquine, atovaquone–proguanil or artemether–lumefantrine should be considered as an option for stand-by emergency therapy. Nevertheless, evidence on the safety of anti-malarials especially during the first trimester is still insufficient.

1. Introduction

In 2011 more than 100 million tourists travelled to malaria-endemic countries [1]. Pregnant women travelling to malaria-endemic areas usually fall into one of the following categories: Women seeking pre-travel advise for tourist travel, sometimes explicitly planning to get pregnant at the tropical destination (tourist traveller), women with their entire family destined to stay in malarious areas on longer term contracts/for professional purposes, already pregnant or planning pregnancy during a long-term stay (expatriate traveller) as well as migrant women needing to visit friends and relatives in their country of origin in order to attend

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important reunions/festivities with their family despite being pregnant (visiting friends and relatives, VFR traveller). Thus, health experts involved in travel medicine are frequently confronted with questions around malaria prevention during pregnancy.

2. Malaria and pregnancy

Malaria infection during pregnancy poses a serious risk for the mother and the unborn child [2,3]. The interaction of malaria and pregnancy is complex and not yet fully understood [4,5]. Malaria parasites adhere in the vascular system of the placenta which leads to impairment of the (micro) circulation and eventually placental insufficiency [4]. A relationship between concurrent malaria infection and abnormal uterine blood flow has been demonstrated [4].

Semi-immunity to malaria is of limited duration after leaving endemic regions [6]. Furthermore, in malaria endemic regions, pregnant women lose their acquired semi-immunity, especially during their first pregnancy [5].

Studies involving non immune women who live outside Africa have demonstrated that malaria infections during pregnancy considerably increase the risk of severe malaria and anaemia for the mother [2,7] and of stillbirth, preterm delivery, decreased birth weight and anaemia of the newborn [2,7]. As little data are available, long term consequences of placental malaria infection for the child development cannot be excluded [2].

3. Anti-mosquito measures

In Sub-Saharan Africa and in particular during the rainy season, the average transmission risk exceeds one infectious mosquito bite per person per day. Anti-mosquito measures aim to reduce infectious mosquito bites. Interestingly, it has been shown in rural Gambia that pregnant women attract twice as many Anopheles gambiae complex mosquitoes as their non-pregnant counterparts, probably due to physiological and behavioural changes [8]. This finding underlines the importance of protective measures for this vulnerable group against vector bites [8]. Anti-mosquito measures include mechanical as well as chemical barriers summarised in Table 1. A recent review on the efficacy of repellents underlined that the two synthetic repellents DEET and icaridin provide the best efficacy against mosquito bites lasting up to 10 h although differences were observed regarding the different mosquito species *Aedes*, *Anopheles* and *Culex* [9].

Table 1 Overview on anti-mosquito measures.

- Appropriate use of insecticide-treated bednets (pyrethroids like permethrin)
- Intact window-screens
- Air-conditioning
- Minimizing skin exposure by wearing long-sleeved shirts and long pants
- Avoiding outdoor stays during peak activity periods of anopheline mosquitoes (dusk to dawn)
- Consequent application of repellents (containing DEET 20—50% or icaridin 20%)
- Impregnation of clothes (pyrethroids like permethrin)

3.1. DEET

N, N-Diethyl-3-methyl-benzamide or N, N-diethyl-m-toluamide (DEET) is the main active ingredient of most commercial synthetic repellents. The anti-mosquito effect of DEET is proportional to its concentration within the respective repellent but reaches a plateau at about 50% [10]. DEET affects plastic material and especially long term usage of this repellent can cause skin irritations. DEET is partly absorbed by the skin and can be detected in blood after a few hours. Fast increase and high concentrations of blood levels have been seen after ingestion of the substance [10]. Side effects such as hypotension, seizures or coma where mostly reported after accidental oral intake of DEET.

A randomized, double blind study included 897 pregnant women in Thailand in their second or third trimester of pregnancy who used DEET on a regular basis as an repellent [11]. The authors demonstrated that DEET crossed the placental barrier. Yet, no negative effect on intrauterine survival, child development at birth or one year later could be shown [11]. No data are available on the safety of DEET in women during the first trimester of pregnancy. Data from some animal studies demonstrated an increase in embryo mortality, decreased birth weight, delayed development and high postnatal death rate after high dose application of DEET. Other animal studies, however, did not confirm embryo-toxic findings [11].

3.2. Icaridin

Until today, only few data on icaridin (formerly picaridin) are available from clinical trials. Nevertheless, a good tolerability — even in children — has been described [12]. Furthermore, systemic uptake of icaridin after topic application seems to be less compared to DEET [13]. The only data on the use of icaridin during pregnancy was obtained from animal studies. No teratogenity was observed [14].

3.3. Mosquito nets

Insecticide-treated nets (ITN) have been shown to increase mean birth weight and to reduce miscarriage/stillbirth as well as placental parasitaemia in Africa [15,16]. Pyrethroids are about 2250 times more toxic to insects than mammals. In addition to differences related to the mode of action, mammals are protected by poor dermal absorption as well as more rapid metabolism to non-toxic metabolites. Few reports on human pyrethroid poisoning in the literature have mostly been linked to occupational exposure via skin or inhalation [17]. No data exist on the risk and benefit of ITNs in pregnant travellers but the risk related to impregnated bed nets, used appropriately, seems to be negligible. Care should be provided when re-impregnating bednets and textiles.