Intermittent Preventive Treatment: A New Approach to Reduce the Burden of Malaria

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Abstract

Intermittent preventive treatment (IPT), the administration of curative courses of antimalarial drugs to a population at risk at specified time points without screening for parasitaemia is now an accepted approach to the reduction of burden of malaria in pregnancy and is being explored for the control of malaria in infants and in children. Trials of IPT in pregnancy (IPTp) in stable transmission areas in Africa showed that IPTp can reduce the incidence of maternal anaemia and low birth weight during the first and second pregnancy. IPT in infants (IPTi) has been shown to reduce the incidence of malaria (protective efficacy varies from 23 to 62%) and anaemia (protective efficacy varied from 13 to 50%). Seasonal IPT in <5 year-old children (sIPTc) has been shown to reduce the incidence of malaria by 86% (95% CI 80-90%). Currently a consortium of researchers (IPTi-consortium) is addressing several questions that need to be addressed before IPTi and/or IPTc can be adopted as a policy to control malaria in children.

Introduction

The use of antimalarial drugs to prevent malaria in non-immune visitors to malaria endemic areas has been a well accepted practice. However the use of drugs to prevent malaria in long term residents in endemic areas is controversial. Mass drug administration (MDA) of therapeutic doses of antimalarial drug to the whole population at risk has been used in several settings primarily to reduce the transmission of malaria.(Seidlein and Greenwood, 2003) However, difficulties in the delivery of MDA, emergence of drug resistance and the lack of a safe and effective gametocyte drug has limited the use of MDA. Greenwood et.al (1988) and Menendez et.al (1997) observed that malaria chemoprophylaxis has been shown to be effective to reduce the incidence of malaria and anaemia in infants and young children. However, chemoprophylaxis in children was never implemented at a larger scale because of the potentials for increased malaria episodes when chemoprophylaxis is discontinued and also the problems of delivery systems and drug resistance. (Menendez et al, 1997) Until recently, WHO recommended choloroquine chemoprophylaxis during pregnancy based on results of studies conducted in Africa (Greenwood et al, 1988) but this intervention has rarely been implemented at a larger scale. Administration of therapeutic courses of an antimalarial to at risk populations at predefined times regardless of whether they are infected or not, known as intermittent preventive treatment (IPT) has been shown to be efficacious to reduce the burden of malaria in pregnant women (Shulman et al, 1999) and children (Schellenberg et al, 2001, Chandramohan et al, 2005, Macete et al, 2005) in Africa. In this paper the effects of IPT in different target groups observed in studies conducted in Africa are summarised and the situation of IPT in India is discussed.

Intermittent Preventive Treatment in Pregnancy (IPTp)

In 1999, Shulman and colleagues reported that administration of therapeutic doses of sulphadoxine-pyrimethamine (SP) during second and third trimester of pregnancy can

reduce the incidence of severe anaemia by 35% [95% confidence limit (CI) 22-53] in primigarvid women in a stable malaria transmission area in Kenya. Further studies in Malawi and Kenya showed that IPTp using SP can reduce the incidence of low birth weight – IPT reduced the low birth weight by 50% (95% CI 6-73) in Kenya as reported by Van Ejik et al (2004) and 38% (95% CI 21-51) in Malawi by Rogerson et al (2000) . The WHO now recommends the "administration of full, curative-treatment doses of an effective antimalarial at predefined intervals during pregnancy" (WHO, 2000). Most countries in sub-Saharan Africa has adopted SP IPT as policy to reduce the burden of malaria in pregnancy.

Intermittent Preventive Treatment in Infants

The concept of IPT in infants (IPTi) has been tested in Tanzania, (Schellenberg et al, 2001) Ghana (Chandramohan et al, 2005) and Mozambique (Macete et al, 2005) and further studies are underway in many settings in Africa. All these three studies administered SP as IPT three times during infancy – the first dose was given at the time of DPT2 vaccination, the second dose at DPT3 vaccination and the third dose at measles vaccination. In the study in Ghana, an extra dose of SP was given at 12 months of age. The protective efficacy against clinical malaria in these three studies ranged from 59% (95% CI 41-72) in Tanzania to 22% (95% CI 4-37) in Mozambique and the pooled protective efficacy across the three sites was 25% (Fig. 1).

Fig. 1: Protective Efficacy of IPTi against clinical malaria in infants



The IPTi also reduced the incidence of anaemia in infant in Tanzania by 50% (95% CI 8 -73) and in Ghana by 35% (95% CI 11 – 53). A consortium of research institutes (IPTi consortium) is currently addressing the following issues: (1) efficacy in IPTi in different epidemiological settings; (2) Safety of IPTi; (3) effect of IPTi on in infant in Tanzania by 50% (95% CI 8-73) and in Ghana by 35% (95% CI 11-53). A consortium of research institutes (IPTi The IPTi also reduced the inimmune response of EPI vaccines; (4) drug

resistance and choice of drug for IPTi; (5) malaria immunology; (6) acceptability and cost of IPTi (Egan et al, 2005). The results of the IPTi consortium study will produce a sound evidence base to make an informed policy on IPTi for Africa.

Seasonal Intermittent Preventive Treatment in Children

In the Sahel and sub-Sahelian regions of Africa malaria transmission is highly seasonal and the incidence of severe malaria is high in children more than one year old. In such situations giving IPTi may not be adequate to reduce the burden of malaria in children. Furthermore since the malaria transmission season is restricted to 3 to 4 months it is probably more appropriate to give IPT only during the transmission season. A study in Senegal Conducted by Badara et al (2006) showed that administration of three treatment courses of artesunate + amodiaquine to 2-59 month old children during the rainy season can reduce the incidence of malaria by 86% (95% CI 80-90). However the feasibility of delivering seasonal IPT to under five year old children in a sustainable system is debatable.

Situation of IPT programmes and the Way Forward

Of the 45 malaria endemic countries in Africa, 24 have adopted IPTp as a policy. However the coverage of IPTp remain low in many countries.(WHO, 2005) For instance Kenya adopted IPTp as a policy in 1998, but the proportion of pregnant women receiving two or more doses of SP-IPT was only 4% in 2003. (Hill & Kazembe, 2006) The operational challenges such as inequitable access to antenatal services, cost of IPT, health workers skills and beliefs, shortage of human and material resources, lack of demand for antenatal services, late attendance at antenatal clinics, perceptions of safety of IPT drugs are hard to overcome in many countries. Chloroquine chemoprophylaxis during pregnancy has been the policy for prevention of malaria in pregnancy in India. However this policy is not implemented widely. Furthermore the chloroquine resistance is widespread in India and the adherence to choloroquine chemoprophylaxis regimen is low. Thus moving from choloroquine chemoprophylaxis to SP-IPTp in India may look attractive based on the experience in Africa. However, SP-IPTp may or may not be appropriate in India because the epidemiology and health care delivery system in India is very different from Africa. In India both falciparum and vivax cause malaria in pregnancy and almost all malaria infections will have serious consequences because the acquired immunity against malaria is extremely low. Thus the primary objective of IPTp needs to be preventing all infection not just reducing maternal anaemia or low birth weight the primary objectives of the IPT programmes in Africa. This means very long acting antimalarial drugs are needed to be used as IPT to prevent malaria in pregnancy in India. Mefloquine and Piperaquine+Artesunate have relatively long plasma half life and they may be appropriate drugs for IPTp in India. However, tolerability, safety and efficacy of these drugs in pregnancy have to be studied before they could be considered for IPT in India. The role of IPT in infants and children in India is unknown. Randomised controlled trials of IPT in pregnant women and children are needed to assess the applicability of this approach in India.

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