

Letter to the Editor

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Anti-malarial stewardship for India: an evidence-based approach

Sir,

Plasmodium falciparum (*Pf*) is a public health problem in both rural as well as urban areas due to changing environmental condition and extensive movement of people. Artemisinin combination therapy (ACT) is the cornerstone of treatment for *Pf* malaria. However, parasite susceptibility to either artemisinin or the partner drug is getting changed globally. Malaria endemic countries are doing robust surveillance on anti-malarial resistance throughout the year. The recommended ACT regimen differs from country to country and also in different states of the same country.

India is a malaria endemic country with eastern India having the major burden of disease. The National vector borne disease control programme (NVBDCP) guideline of India recommends artesunate (AS) plus sulfadoxine-pyrimethamine (SDP) for uncomplicated falciparum malaria. Severe complicated malaria will also require ACT following initial intravenous artesunate.¹

Artemisinin resistant *Pf* malaria was first reported from western Cambodia and surrounding greater Mekong area in 2009.² Resistance has reached an alarming level and has forced the health authority to change the treatment policy. Currently one of the effective treatment policies is a 6 days course of ACT. Initial 3 days of AS followed by an oral ACT for another 3 days. The oral ACTs used in this randomized controlled trial were dihydroartemisinin-piperaquine, artemether-lumefantrine (AL), AS-SDP, or artesunate-mefloquine.³ Prolonged artemisinin course has increased the healthcare expenses for these countries.

India being a sub-continent has also differential sensitivity of *Pf* to artemisinin companion drugs. *Pf* parasites have shown diminished sensitivity towards SDP in North-Eastern states of India. Using AS-SDP in these areas will facilitate development of artemisinin resistance. Treatment success in artemisinin resistant strains largely depends upon the partner drug efficacy. As North eastern states have already started to develop SDP resistance, using AS-SDP for sporadically found artemisinin resistant *Pf* may render the entire regimen to fail.

Since 2013 NVBDCP has changed its recommendation from AS-SDP to AL as the preferred ACT for these areas based on trends shown in various studies.^{4,5} Hence India has a dual antimalarial drug policy for *Pf* malaria. AL for North-eastern states and AS plus SDP for the rest of the country. Though the current recommendation is AS-SDP

from government dispensaries for the entire country except for those North-eastern hotspots, private hospitals and clinics have limited access to this combination. Most cases are being treated with AL in private clinics and hospitals throughout the country as SDP is unavailable there. *Pf* malaria cases in India except those NE states are being treated with two separate regimens though the guideline still favours AS-SDP as the preferred combination.

Using lumefantrine rampantly as partner drug may be of great concern in near future. As SDP is still highly effective for most of the Indian states. Lumefantrine exposure may stimulate developing resistance against it in near future.

In Africa, AL is being used for uncomplicated *Pf* malaria. Repeated infections during subtherapeutic lumefantrine blood concentration is making the parasites less sensitive by selecting *Pfmdr1* and *Pfcrt* mutations.⁶⁻⁹ Consequently in Africa, there is an urgent need to change partner drug from lumefantrine to amodiaquine.¹⁰

Lumefantrine stewardship will maintain its efficacy in India. National malaria experts and policy makers may think on making AS-SDP available from private hospitals as well. Thus, a uniform recommendation can be followed throughout the country and lumefantrine can be salvaged for future use.

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