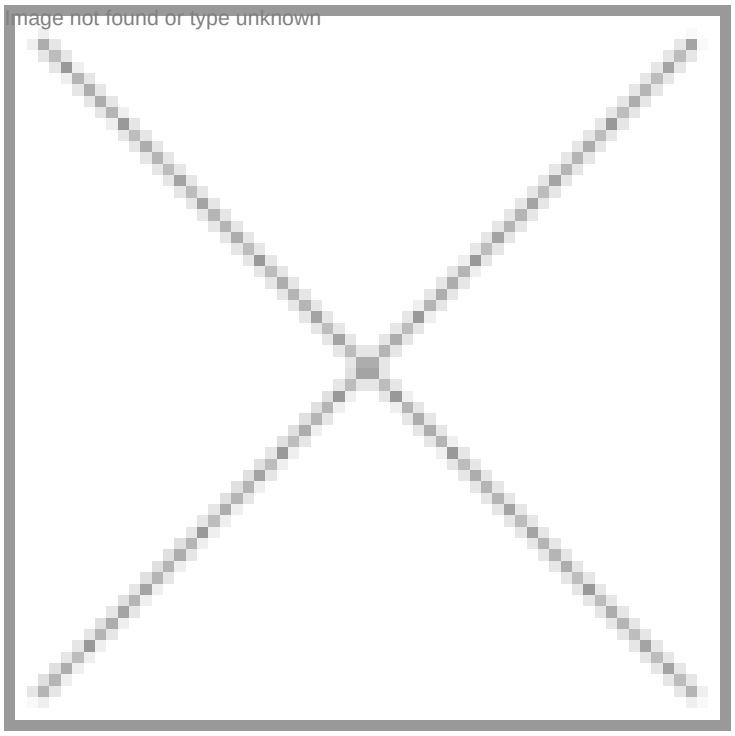
BioSpectrum the business of Bio & Health Sciences

Drug resistance keeps Malaria threat alive

11 May 2012 | News



With nearly 70 percent of the population at risk and increasing resistance to anti-malaria drugs, India can no longer ignore the threat from malaria

The current anti-malaria market is close to 450 crore with an annual growth rate of 17 percent, says the ORG IMS November 2011 report. According to statistics available with the directorate of National Vector Borne Disease Control Programme, close to 12 lakh cases of malaria were reported in India till December 2011 of which 436 were cases of deaths.

Increasing drug resistance is a possible cause for the continued rise in cases of Plasmodium falciparum in recent years, gradually increasing from 39 percent in 1995 to above 50 percent in 2008. Around 50 percent (6.4 lakh cases) were caused by the single-cell parasite Plasmodium falciparum. With P. falciparum, which causes the most dangerous forpotentially spreadms of the disease, becoming resistant to the drug chloroquine, artemisinin-based treatments have become popular. Globally, the number of courses of artemisinin-based therapies (ACT) procured by the public sector jumped nearly sevenfold between 2005 and 2006, and then more than doubled, reaching 181 million in 2010, according to the World Malaria Report 2011. The demand for these drugs was around 287 million treatments in 2011 and is expected to touch 295 million courses in 2012.

Resistance causes worry

â€œA looming threat to malaria control is the emergence of parasites that are resistant to anti-malarial medicines,â€? stated the World Health Organization (WHO) in its â€œGlobal Plan for Artemisinin Resistance Containmentâ€? published in 2011.

The strains that are resistant to even artemisinin have emerged in parts of South East Asia and could potentially spread.

Some facts about malaria

- Malaria largely affects people in the lower strata of society; thus cost of therapy influences the choice of treatment
- Seasonal trends peak during monsoon (August-September)
- Empirical therapy with chloroquine, pyrimethamine and sulfadoxine delivered without RDTs or Microscopy.
- Artemether and Lumefantrine formulation gaining momentum as first-line treatment in endemic areas

For instance, child mortality in Africa increased as P. falciparum strains that were resistant to chloroquine spread in the continent in the 1970s and the 1980s. Raising the important issue, Virander S Chauhan, director, International Centre for Genetic Engineering and Biotechnology (ICGEB), says, â€œThere have been reports of resistance in Cambodia and Thailand, and if it reaches Myanmar and y messy.â€?

Delivering artemisinin and its derivatives as monotherapies, instead of as a cocktail with another drug, can cause resistant forms of the parasite to arise and spread. Although oral artemisinin-based monotherapies are effective when taken as a full seven-day course, patient often stops taking them after a few days when the symptoms subside. Parasites that are sensitive to the drug get eliminated, allowing drug-resistant strains to proliferate and get transmitted to other people. WHO, in 2006, called for a halt on use of oral artemisinin monotherapies for treating uncomplicated malaria. A year later, a resolution was adopted by the World Health Assembly, WHO's apex decision-making body, that urged its member states to â€œcease progressivelyâ€? the provision, in both public and private sectors, of such monotherapies and promote the use of ACTs.

However, according to the latest World Malaria Report 2011, 25 countries are still allowing the marketing of these products and 28 pharmaceutical companies, as against 39 a year ago, are making these drugs. The report has also warned that there are Indian pharmaceutical companies among those manufacturing and marketing drugs that are likely to foster resistance to artemisinin in the malaria parasite. The Drug Controller General of India (DCGI) initiated action earlier this year to stop the production and export of these drugs. It wrote to all state drugs controllers requesting them to cancel licenses for manufacturing oral artemisinin-based monotherapies with immediate effect.

Challenges galore

- Correct diagnosis through microscopy
- Rising P. falciparum burden
- Fatty foods is a requirement for adequate bioavailability of Artemether and Lumefantrine and other anti-malarials; hence treatment failure is common
- Choloroquine resistance is widespread in India
- Emerging resistance to artemisinin, notified particularly in South East Asia

According to WHO, India is of greatest concern as there is widespread DDT-resistance (dichlorodiphenyltrichloroethane) and patches of resistance to pyrethroid and organophosphate (malathion). The WHO has recommended that an ACT should be first-line treatment for uncomplicated malaria caused by P. falciparum. The two-drug combination reduces chances of the parasite developing resistance. Moreover, a three-day course of a recommended ACT generally clears

Guidelines of National Institute of Malarial Research (NIMR) too recommends combination therapy for P. falciparum. Arterolane maleate, a rapidly acting drug in combination with long-acting piperaquine phosphate is an anti-malarial product in line with WHO-recommended combination therapy for the treatment of uncomplicated P. falciparum malaria. Though insecticide and spraying materials and insecticide-treated nets are other possible solutions to control malaria, they have not been very successful in India so far.

Trends of Malaria in India

Year	Total malaria cases (million)	*P. falciparum cases* (million)	Cases of *P. falciparum* (%)
2008	1.53	0.77	50.81
2009	1.56	0.84	53.72
2010	1.49	0.77	52.12

PL Joshi, faculty, National Institute for Health and Family Welfare (NIHFW), New Delhi, points out that apart from having the support of external agencies, developing nations must have its own redressal mechanism in place. Appreciating the funding from the World Bank and technical guidance from WHO, he says unless a proper preventive mechanism is enforced, it would be difficult to tackle the menace.

â€œThe Government of India has stepped up its efforts. This is clearly visible from the change in the drug policy. There are various programmes educating people about the preventive measures. In place of small projects a decade ago, there are currently projects worth 500-600 crore focusing on malarial research,â€? he adds.

Fresh hopes

The success of phase III trials of GlaxoSmithKline vaccine, which the company has been developing with Path malaria vaccine initiative, has raised hopes for an anti-malarial vaccine. GSK has already invested 1,500 crore ($300 million) in the project and will invest further 250 crore ($50 million) to 500 crore ($100 million) in it.

In India, Ranbaxy has developed Arterolane maleate, a rapidly acting drug in combination with long-acting piperaquine phosphate. It has also developed a new chemical entity, Arterolane, in combination with piperaquine, which is expected to have superior benefits over the currently available anti-malarial therapies. The new drug is a once-a-day therapy for three days.

Research done by Virander Chauhan and Chetan Chitnis at the ICGEB has led to the development of a first generation vaccine, MJAIVAC1, which is based on combination of two merozoite antigens (MSP-119 and EBA-175). The vaccine is presently being tested for safety and immunogenicity in a phase I clinical trial, the first for a malaria vaccine developed in India. The ICGEB has also developed a portfolio of novel antigens that is currently at different stages of preclinical development. Also, the center has developed a vaccine, PvDBPII, for Plasmodium vivax which is being produced by a biotechnology company for a phase I clinical trial.

Under a government-funded project, Mumbai-based IPCA Labs, along with Jamia Hamdard University, New Delhi, has developed a genetically modified variety of Artemisinin Annua that can generate high yield of artemisinin. Once approved, the variety will be put to confined-field trials for evaluation and then patented and commercialized for cultivation by farmers. The group expects that this variety will fetch more than one percent artemisinin in field trials.

Rahul Koul in New Delhi