Plasmodium falciparum Containment Strategy

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Abstract

World Health Organization (WHO) estimates 1.7-2.5 million deaths and 300-500 million cases of malaria each year globally. As an initiative WHO has announced Roll Back Malaria (RBM) programme aimed at 50% reduction in deaths due to malaria by 2010. The RBM strategy recommends combination approach with prevention, care, creating sustainable demand for insecticide treated nets (ITNs) and efficacious antimalarials in order to achieve sustainable malaria control. Malaria control in India has travelled a long way from National Malaria Control Programme launched in 1953 to National Vector Borne Diseases Control Programme in 2003. In India, the malaria eradication concept was based on indoor residual spraying to interrupt transmission and mop up cases by vigilance. This programme was successful in reducing the malaria cases from 75 million in 1953 to 2 million but subsequently resulted in vector and parasite resistance as well as increase in *P falciparum* from 30-48%. In view of rapidly growing resistance of *Plasmodium falciparum* to conventional monotherapies and its spread in newer areas, the programme was modified with inclusion of RBM interventions and revision of treatment guidelines for malaria. Early case detection and prompt treatment, selective vector control, promotion of personal protective measures including ITNs and information, education, communication to achieve wider community participation will be the key interventions in the revised programme.

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Key Words: Roll Back Malaria; Malaria in India; *Plasmodium falciparum* containment

Introduction

Malaria accounts for more than one million deaths every year, thus becoming a priority for the international health community and is now under focus of several new initiatives [1]. World Health Organization (WHO) has announced Roll Back Malaria (RBM) initiative aimed at 50% reduction in deaths due to malaria by 2010. The approach would be global with spearhead in Africa [2]. WHO estimates 1.7–2.5 million deaths and 300–500 million cases every year. Nine out of 10 deaths due to malaria take place in Africa [3]. WHO Southeast Asia office estimates 15 million cases and 20,000 deaths annually in India [4]. *Plasmodium falciparum* contributes to 48-52 % malaria cases in India [5].

Success in malaria control is impeded by the drug resistant parasites particularly *Plasmodium falciparum*, which have disseminated and enhanced mortality [6]. The RBM strategy recommends strengthening case management with prompt and efficacious treatment through existing health delivery systems. The strategy is based on a combination approach with prevention, care, creating sustainable demand for insecticide treated nets (ITNs) and efficacious antimalarials in order to contribute sustainable malaria control. Key interventions in RBM are vector control by insecticide-treated nets

(ITNs) and indoor residual spraying (IRS), intermittent preventive treatment during pregnancy (IPT), prompt and effective case management with artemisinin-based combination therapy (ACT). This paper reviews key RBM interventions, National Malaria Control Programme and its modification in India.

Vector Control

Insecticide-treated nets (ITNs)

ITNs can reduce the number of under-five deaths from all causes by about 20% and clinical episodes of malaria by about half [7]. In a study in Kenya [8] there were substantial health gains in children and pregnant women where protection was extended from homes with ITNs to adjacent homes without nets [9]. Regular treatment of nets with insecticide has proved difficult to sustain on a large scale. This problem should be overcome by the development of long lasting insecticidal nets. Different prototypes are being produced, two of which have been approved by WHO and are undergoing large-scale production. Inevitably, resistance to pyrethroids is emerging [10], but progress is being made in the identification of alternative insecticides that could be used to treat nets and other materials [11]. One approach to prevent insecticide resistance is the use of mixtures of insecticides on nets. Despite the proven

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benefits and cost-effectiveness of ITNs, achievement of widespread use has proved difficult. In most sub-Saharan countries, only a small percentage of individuals who should be protected by nets actually use them [12]. Free provision of ITNs, sometimes linked to other initiatives such as vaccination or attendance to antenatal clinics, has strong advocates and is gaining support, but this approach needs a major and sustained commitment from international donors [13].

Indoor residual spraying (IRS)

Use of DDT as IRS in malaria control provided spectacular success in all parts of world along with collateral benefits in the form of control of kala-azar, plague, other nuisance pest and overall economic development. However DDT lost its effectiveness in malaria control subsequently. This is partly due to six decades of spraying resulting in physiological resistance to DDT and/or pronounced exophilic vector behaviour encouraging extra-domiciliary transmission [14]. Despite attempts to ban DDT completely, the compound continues to be used for vector control although arguments about issues such as the effect on preterm births and the duration of lactation continue [15]. In some south African countries indoor house-spraying with DDT, carbamates, or pyrethroids, used alone or with ACTs has substantially improved malaria control [16]. As per Stockholm Convention each party that produces and/or uses DDT shall restrict such production and/or use for disease vector control in accordance with the WHO recommendations and guidelines on the use of DDT and when locally safe, effective and affordable alternatives are not available [17] and the necessary safety precautions are taken in its use and disposal [18].

Intermittent preventive treatment during pregnancy

Intermittent preventive treatment (IPT) involves the administration of full curative treatment doses of an effective antimalarial, sulfadoxine pyrimethamine (SP) combination, preferably single dose, at predefined intervals during pregnancy, beginning in the second trimester after quickening (when the movements of the foetus are first felt). In areas with stable malaria endemicity, IPT has been shown to be highly effective in reducing the malaria parasite load, thus reducing severe anaemia in the mother as well as the proportion of babies who are born with low birth weight, which contributes to higher infant mortality and impaired child development [19,20]. At present, there is no consensus on which antimalarial medicine should be used in IPT in situations of high resistance to SP for clinical case management.

Prompt and effective case management

Clinical and symptom-based diagnosis for malaria will be common in most areas of high transmission. However accurate microscopy can be helpful in diagnosis, but maintenance of the microscopes and the quality of microscopy in peripheral clinics is difficult [21]. Alternatively, several rapid diagnostic tests based on antigen-capture techniques have been developed that have high sensitivity and specificity for falciparum malaria and that could contribute greatly to improving malaria diagnosis [22]. However, these tests have limitations. In highly malaria-endemic areas, many healthy individuals have parasitaemia, therefore a negative test rules out malaria but a positive test does not prove that malaria is the cause of illness.

Antimalarial therapy

Global malaria control is being threatened on an unprecedented scale by rapidly growing resistance of *Plasmodium falciparum* to conventional monotherapies such as chloroquine, sulfadoxine-pyrimethamine (SP) and amodiaquine. Medicines used in combination are highly effective and make the development of resistance to antimalarials much less likely [23-25]. In revising their malaria treatment policies, countries should opt for a combination treatment, preferably an ACT. The WHO recommended combination therapies with potential for deployment on the basis of the available safety and efficacy data, in prioritised order, are artemether/lumefantrine, artesunate + amodiaquine, artesunate + sulfadoxine-pyrimethamine (in areas where SP efficacy remains high) and amodiaquine + SP (in West Africa where efficacy of both drugs remains high).

National Malaria Control Programme

The National Malaria Control Programme (NMCP) in India was based on indoor residual spraying with DDT twice a year in endemic areas. The programme was highly successful initially. Encouraged by the results, and the fact that insecticide resistance in vector species may evolve the control programme was converted to the National Malaria Eradication Programme (NMEP) in 1958. By 1964, malaria was eradicated from 88% of the area [26].

Early set backs in malaria eradication coincided with DDT shortages. Later in the 1970's malaria resurgence was the result of technical, financial and operational problems. As a result in 1976, 6.45 million cases were recorded by the NMEP. The implementation of urban malaria scheme (UMS) in 1971-72 and the modified plan of operation (MPO) in 1977 improved the malaria situation for few years. The Plasmodium falciparum Containment Programme (PfCP) launched in 1977 had

reduced the incidence of falciparum malaria. Malaria diversified under the pressure of developments into various ecotypes. These ecotypes have been identified as forest malaria, urban malaria, rural malaria, industrial malaria, border malaria and migration malaria. The malaria in the 1990's has returned with new features. These are the vector resistance to insecticides, pronounced exophilic vector behaviour, extensive vector breeding grounds created principally by the water resource development projects, industrialization, change in parasite formula in favour of *P falciparum*, resistance in *P falciparum* to chloroquine and other anti-malarial drugs [27].

To contain the spread of malaria, enhanced malaria control project (EMCP) was launched in 1997 with the assistance of the World Bank to cover areas where API is more than two for the last three years, *Pf* cases are more than 30% of the total malaria cases, 25% of the population of the area is tribal and the area has been reporting deaths due to malaria. Strategies adopted were early case detection and prompt treatment, vector control by indoor residual insecticidal spray in areas with API of 2/1000, free distribution of ITNs, health education and community participation. EMCP is operational in 1045 malaria hardcore tribal primary health care centres (PHCs) of 100 districts covering 62 million population in eight states [28]. NMEP was renamed National antimalaria programme (NAMP) in 1999. Key interventions adopted in NAMP are early case detection and prompt treatment, selective vector control and promotion of personal protective measures [29]. The treatment policy for malaria was revised by NAMP in 2001 with inclusion of primaquine in presumptive treatment in high risk area [30].

Low risk areas

Presumptive treatment with single dose of chloroquine base @ 10 mg/kg body weight. Radical treatment on confirmation of *P vivax* includes chloroquine 10 mg/kg body weight and primaquine 0.25 mg/kg body weight on day one, followed by primaquine 0.25 mg/kg body weight daily for next four days. Radical treatment for *P falciparum* includes chloroquine base 10 mg/kg body weight and primaquine 0.75 mg/kg body weight.

High risk areas

Presumptive treatment includes chloroquine base 10 mg/kg body weight with primaquine* 0.75 mg/kg body weight on first day, chloroquine base 10 mg/kg body weight on second day and chloroquine base 5 mg/kg body weight on third day.

Radical treatment in chloroquine sensitive areas for *P vivax* includes primaquine* 0.25 mg/kg for five days, while *P falciparum* requires no further treatment. In

chloroquine resistant *P falciparum* areas, sulfadoxine 25 mg/kg body weight plus pyrimethamine 1.25 mg/kg body weight on first day, followed by primaquine 0.75 mg/kg body weight on the second day is required. The use of primaquine is contraindicated in pregnancy, infants and G6PD deficiency.

The criteria for high-risk areas as per NAMP include one or more of the following; recorded deaths due to malaria with *P falciparum* infection; doubling of SPR during the last three years provided the SPR in second or third year reaches 4% or more. Where SPR does not show doubling trend as above but the average SPR of the last three years is 5% or more; *P falciparum* proportion is 30% or more provided the SPR is 3% or more; an area having a focus of chloroquine resistant *P falciparum* or tropical aggregation of labour in project areas. The reported nationwide incidence of laboratory confirmed cases has declined from 3.0 million in 1996 to 1.78 million in 2003, of which around 48% are caused by *P falciparum*.

National malaria control program was renamed National Vector Borne Diseases Control Program (NVBDCP) in 2003 to control malaria, and four other vector borne diseases; lymphatic filariasis, dengue, kala-azar, and Japanese encephalitis. The NVBDCP has been build upon successes and lessons learnt from the EMCP. It is likely to address the following challenges:

Drug Resistance : Chloroquine resistance is high in Northeast states of India. India has deployed monitoring teams to study antimalarial drug sensitivity and out of nine areas covered by the study, chloroquine treatment failure was observed in five. In these areas treatment with artesunate and sulfadoxine + pyrimethamine (SP) combination has been adopted.

Controlling malaria in urban settings : Incidence of malaria, as well as other vector borne diseases, is increasing in urban areas. Intersectoral collaboration and partnership with the private sector would be critical to bring about impact in the urban settings.

State variations in performance and disease burden : EMCP demonstrated wide variation in implementation capacity and resources between the states. Some states, such as Maharashtra, Gujarat, and Andhra Pradesh, have a better established health infrastructure with significant financing resulting in dramatic impact. Malaria burden dropped more than 70 % during the project period. While infrastructure and financing in states like Orissa, Jharkhand, and Chhattisgarh was not so well established.

Conclusion

Inclusion of primaquine in presumptive treatment in high risk area is a courageous step to contain falciparum

malaria. There are no new technologies on the horizon that are likely to change malaria situation in the near future. Strategy based on combination approach with prevention and creating sustainable demand for ITNs with efficacious use of antimalarials can achieve *Plasmodium falciparum* control.

Conflicts of Interest

None identified

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