ISSN 0377-4910

ICMR BULLETIN

Vol.32, No.10 October, 2002

CHEMICAL INSECTICIDES IN MALARIA VECTOR CONTROL IN INDIA

As early as in 18th century A.D. pyrethrum (Persian insect powder) and during 19th century A.D. many compounds were discovered as conventional pesticides *viz.*,mercuric chloride (1860) paris green (1865), phenol and cresols (1867), naphthalene (1882), Bordeaux mixture (1883), rosin-fish oil soap (1886), calcium arsenate (1907) and nicotine sulphate (1909). The remarkable discovery of the utility of DDT as insecticide in 1942 by Paul Mueller revolutionized the field of pest control and the control of insect vectors of medical importance like mosquito. In mosquito control, insecticides are used against both larvae (larvicides) and adults (adulticides). The present review gives a brief account of various aspects related to the use of chemical insecticides against malaria vectors.

Vectors of Malaria

In India malaria is transmitted by nine vector species. Of these, six are of primary importance. These are *Anopheles culicifacies* (transmits malaria in rural and peri-urban areas), *An. stephensi* (in urban areas), *An. fluviatilis* (in hills and foot-hills), *An. minimus* and *An. dirus* (in north-eastern states) and *An. sundaicus* (in Andaman and Nicobar islands)[1] (Fig.1). Of these, *An. culicifacies* is responsible for the transmission of 60-70% and *An. fluviatilis*, 15% of new cases of malaria in India[2]. Control of malaria in India is actually control of *An. culicifacies* as each year 60-70% of the allotted budget for malaria is spent for control of this species[3]. The understanding of the transmission of malaria is further complicated by the existence of species complexes of cryptic species or sibling species or isomorphic species in this taxon and also in other malaria vectors. Except for *An.stephensi* all other malaria vectors exist as species

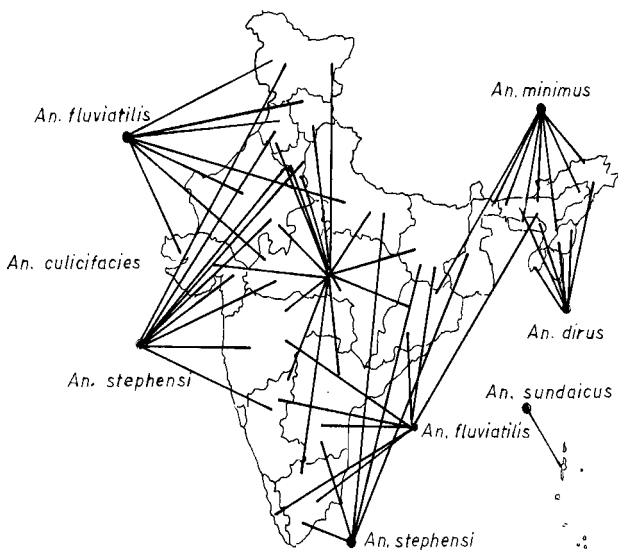

Fig.1. Distribution of primary malaria vectors in India

complexes comprising several cryptic species[4]. Studies have clearly indicated differences among sibling species that result in considerable impact on the transmission of malaria including susceptibility to commonly used insecticides in public health programmes[5-7].

Vector Control

Intervention measures to restrict the transmission of malaria by controlling the vector population forms the main part of the vector control. Effective vector control strategies are based on four facets *viz*. incrimination of vector species, knowledge and understanding of vector biology and ecology, surveillance, public education and implementation of effective control measures[8].

Vector control programme in India, as is the case with many anti-malaria programmes elsewhere in the world mostly rely on usage of natural and synthetic chemical molecules, which have potential to kill the target insects. During the years 1901-1903, a concept had emerged known as naturalistic control which was implemented in Malaya based on the knowledge of breeding habitats of anopheline species[9]. The other concept that was prevalent during the early thirties in South Africa was to attack the adult mosquitoes with pyrethrum extract space spray within the houses[10,11].

Presently different formulations of synthetic chemical insecticides are in use for vector control. Wettable powder (WP) formulation of different insecticides are used for adult vector control for indoor residual sprays (IRS) while emulsion concentrate (EC) formulations are used for larval control. For IRS insecticides in use are DDT 50% WP, malathion 25% WP as well as synthetic pyrethroids (SP). SP insecticides include deltamethrin 2.5% WP, cyfluthrin 10% WP, lambda cyhalothrin 10% WP and alpha cypermethrin 5% WP. Synthetic pyrethroid insecticides are also used for impregnation of bednets. For larvicidal control temephos EC 50% and fenthion EC 82.5% are in use, in addition to the application of a distillate of crude oil, and malaria larvicidal oil (MLO). For space sprays technical malathion and pyrethrum extract (2% WP) are used.

Pre-DDT era

The history of vector control in India can be divided broadly into two eras *viz* pre- and post-DDT era. In India, various control methods employed prior to 1936 were in close conjunction with the global efforts in the control of malaria. Most of the work was confined to the use of larvivorous fishes, oils and Paris green in breeding sites and provision of proper drainage system[12]. Stuides reveal that the application of thse methods coupled with legislative measures helped in significant reduction of vector population in Bombay city where *An. stephensi* was breeding in cisterns, fountains, water tanks, wells, *etc.*[13]. Following the success in South Africa using pyrethrum extract against adult mosquitoes, mosquito control trials were undertaken in human dwellings and cattle sheds in Delhi[14], Puttukottai[15] and Assam[16].

DDT era

Paul Mueller (Switzerland) discovered the high insecticidal action of DDT in 1939[17]. In 1942, for the first time DDT was used as an anti-mosquito spray in army camps in the United States and United Kingdom and in 1944 at Volturno in Italy in civilian areas[18]. The first trials with DDT, as a residual spray against adult mosquitoes in field, was a remarkable success.

In 1944, DDT was introduced in the mosquito control programme as a residual insecticide on experimental basis in the Assam-Burma front in the allied army camps of the second world war with excellent results[19]. Thus, DDT as an indoor spray was accepted as a possible control measure in the anti-malaria campaign. Later a few experiments were initiated in civilian areas in Orissa and Karnataka states[20, 21]. With the excellent results obtained in the above experiments in civilian areas, successful trials were carried out in Bombay state[22] and later in 1946 as a largest malaria control operation in rural areas in the districts of North Kanara and Dharwar in Karnataka[23]. Few more projects commissioned in Delhi[24], and Puttur, in Karnataka[25] gave good results. In 1950, DDT water dispersible powder containing 50% or 75% technical DDT was made available and the remarkable convenience in application prompted it to be an ultimate choice in the anti-malaria campaign. During the same period, another insecticide–BHC/HCH (Benzene hexachloride/Hexachlorocyclohexane) was used in Assam[26].

Prompted by the results so achieved in the aforesaid-localized studies and projects, 30 million population was brought under the ambit of anti-malaria programme by the year 1952. In 1953, National Malaria Control Programme (NMCP) was launched covering

a population of 45 million residing in the malarious areas in India. The programme was planned for a five-year period and by the end of 1958, 165 million population was brought under this programme. This programme had tremendous impact on the malaria situation in the country and all malariometric indices showed a dramatic reduction[27-30]. Equipped with spectacular success achieved during NMCP operations, and in accordance with the malaria eradication policy recommended by the Eighth World Health Assembly in 1955, India decided to change the Natioinal Malaria Control Programme to National Malaria Eradication Programme (NMEP) from the year 1958[29]. The objectives of the eradication programme were (i) to interrupt malaria transmission so that when this is accomplished there should not be any fresh (indigenous) case of malaria; and (ii) eliminate residual infection in the community[31]. Eradication programme had 4 distinct phases *viz.*, preparatory, attack, consolidation and maintenance. Different activities to be undertaken in each phase were also well defined and on reaching the target laid down for each phase, the programme moved into the next phase[32]. The major intervention method for the interruption of transmission during the eradication programme, apart from chemotherapy was indoor sprays with residual chemical insecticides. The standard spray methods included spraying of 5% suspension of DDT @ 100 mg/ft^2. DDT was found to have biological efficacy of 10 weeks and was sprayed @ 2 rounds per year and in areas with perennial transmission an additional round was suggested. In areas where local vectors had developed resistance to DDT, alternately HCH containing 6.5% gamma-isomer was used for spraying @ 20 mg/ft^2. The HCH has a biological efficacy of about 6 weeks and was sprayed @ 3 rounds per year[31]. Setbacks to the ongoing eradication programme started in the year 1966 mainly due to the short supply of DDT[29,33] coupled with recurrent focal outbreaks[34]. Later, to control *An. culicifacies* which was reportedly resistant to DDT[35,36] and HCH[37], malathion – an organophosphate insecticide was introduced into the programme in Gujarat and Maharashtra in 1969. And within 4 years *ie*. by 1973 the species was reported to be malathion-resistant[38,39]. Continued efforts to eradicate malaria by different intervention methods were not completely fruitful for various administrative and technical reasons[30]. One of the technical reasons identified for the resurgence of malaria in 1970s was resistance in malaria vectors to insecticides used in public health programmes[30,33] especially in those areas that were responsible for the transmission of the bulk of the cases annually[2].

During 1980s insecticides belonging to synthetic pyrethroid group were introduced in the public health programme. The first trial of deltamethrin spray was carried out in Ghaziabad district (UP) at three doses *viz.*,12.5 mg/m^2 (3 rounds), 20 and 25 mg/m^2 (2 rounds)[40] and was found effective for vector control as residual insecticide specially for controlling DDT-HCH resistant *An. culicifacies*[41]. During the last decade of the 20th century synthetic pyrethroids *viz.* deltamethrin, cyfluthrin and lambda cyhalothrin were introduced into public health programme and currently these are in use both as indoor residual insecticide and as impregnant on mosquito nets. Intervention by insecticide treated mosquito nets is carried out selectively at community level in some parts of the country as personal protection measure by following certain criteria[42].

Insecticide Resistance in Malaria Vectors

Presently insecticides belonging to different groups *viz.*, organochlorine, organophosphate and synthetic pyrethroid are used for public health sprays. Insecticides belonging to the carbamate group have yet not been introduced for public health sprays in India. Strategy for the change of insecticides has always been reactive. Successive changes in insecticide were made after the failure of the control by the ongoing insecticide intervention. A subsequent change in the insecticides has led to sequential selection pressure of insecticides resulting in multiple insecticide resistant malaria vectors. Malaria vectors in India are resistant to DDT alone or double resistant to DDT and HCH or triple-resistant to DDT, HCH, malathion and quadruple resistant to DDT, HCH, malathion and deltamethrin (synthetic pyrethroid). HCH has been phased out of the programme in 1997. Of the six principal vector species, two *viz. An. culicifacies* and *An. stephensi* (table I) have shown wide spread resistance. Other vector species are mostly susceptible to these insecticides.

An. *culicifacies* has developed resistance to all groups of insecticides used so far in the public health programme. This species is reported to be resistant to organochlorine insecticides–DDT and HCH, organophosphate insecticide – malathion and recently to synthetic pyrethroid

Table I. Status of insecticide-resistance in two important vectors of malaria and its geographical distribution in India.

Vector	Type of resistance	No. of states	No. of territories	Total districts
An.	DDT	18	2	286
Culicifacies	Double	16	2	233
	Triple	8	1	71
	Quadruple	2	-	2
An.	DDT	7	1	84
stephensi	Double	6	1	27
	Triple	3	1	8

also. Development of resistance to synthetic pyrethroid[43,44] warrants a caution of the impending possibility of wide-spread resistance to other compounds of this group that are introduced in public health programme for indoor residual spray as well as insecticide treated mosquito nets.

Studies on Insecticide Resistance

Studies carried out on the levels of insecticide resistance in *An. culicifacies* complex have indicated differential levels of resistance to commonly used insecticides in public health sprays[5-7]. The development of resistance in malaria vectors has been reported to be due to the selection by indoor sprays in the public health programmes and also by the use of pesticides in agriculture[45]. It may be mentioned that malathion-resistant *An. culicifacies* from Andhra Pradesh developed resistance owing to the selection pressure of pesticides used in agriculture[6]. Biochemical studies to determine the resistance mechanisms for organophosphate and carbamate insecticides indicated non-involvement of insensitive acetyl cholinesterase conferring broad spectrum of resistance. Biochemical and synergistic studies on malathion-resistant *An. culicifacies* from different states namely Haryana and Gujarat[46] and Madhya Pradesh (MRC: Unpublished observation) indicated involvement of carboxyl esterase mediated mechanism thereby indicating development of narrow spectrum of resistance. Biochemical assays on the field collected malathion resistant *An. stephensi* have also indicated involvement of carboxyl esterase for conferring malathion resistance (MRC: Unpublished observaiton). Information thus generated by insecticide bioassays, biochemical and cytotaxanomical studies, *etc*. will be of immense use for suggesting suitable situation specific methods for management of insecticide resistance especially in view of limitation of new insecticide molecules for vector control.

Management of Insecticide Resistance

In the present situation of insecticide resistance status in malaria vectors, especially *An. culicifacies*, the future of vector control mainly relies on the strategies for the management of insecticide resistance in malaria vector. So far the approach has been the replacement of insecticide by an effective and preferably by a new group of insecticides. Subsequent replacement of insecticides has led to the development of multiple-resistant malaria vectors. It may be mentioned that subsequent change of insecticides has burdened the programme with increased costs. The estimated per capita per annum cost of spraying is Rs. 21.06 with DDT, Rs. 54.10 with malathion and with Rs. 52.40 with synthetic pyrethroid. Thus, the cost of spraying with malathion and deltamethrin is ~ 2.5 folds than the cost of spraying of DDT. Not many new insecticide molecules are availalble for vector control in the immediate future. What is needed for the present day vector control programme is an approach for the management of existing resistance in malaria vectors and to limit its further spread. The strategy for this approach is to use the available insecticides rationally. The silver lining for the present day vector control programme in India is that the major vector species are still susceptible to synthetic pyrethroids and carbamates. Carbamates are not yet used in the programme. These compounds can be used rationally and in rotation with the available insecticides to manage the resistance. It is worth mentioning that the biochemical resistance mechanism against malathion in *An. culicifacies* and *An. stephensi* is specific and does not exhibit cross resistance to other organophosphate (except compounds with ester linkage) and carbamate insecticides.

Strategies to Delay/Avoid the Onset of Resistance

The most important aspect of the management of resistance is to either avoid or delay the onset of resistance by effectively manipulating or influencing the factors responsible for the development of resistance (Table.II). Various methods emphasize on the strategic use of available insecticides to delay the onset of resistance. The methods include avoidance of use of insecticides, that induce broad-spectrum resistance mechanisms and

confer cross-resistance to chemically related and unrelated insecticides and sequential use of insecticides in rotation is preferred.

Table II. Possible ways of avoiding development of insecticide resistance in field.

- Avoid indiscriminate use of insecticides.
- Avoid use of insecticides that simultaneously select resistance to other chemically related insecticides.
- Avoid use of insecticides that induce development of more than one type of resistance mechanisms of broad spectrum of resistance.
- Avoid use of the same insecticide both against adults and larvae.
- Using non-chemical control method *eg.* biopesticides, larvivorous fishes.
- Rotation of insecticides.
- Use of synergist with insecticides to reduce physiological resistance.

Startegies for Management of Resistance

Several strategies and recommendations have been proposed for the management of insecticide resistance in field populations[47-49]. Three major factors are taken into consideration while deciding these strategies and these relate to biological, operational and economic aspects. The strategies mostly suggest the use of insecticides in mixtures, in rotation or in mosaics. Rotation of insecticides is contemplated to be more effective than the use of insecticide mixtures[49] or in mosaic as for mixture or in mosaics a multiplicity of insecticides is needed which is not operationally feasible[49]. Field studies on management of resistance by rotation of insecticides as well as by using other srategies are scarce. One such successful experiment was the structured Onchocerciasis Control Project in Africa for the management of temephos resistance in Simulium complex[50]. In India so far no such studies have been carried out to manage resistance in malaria vectors.

Conclusions

It may be emphasized that the use of insecticides in vector control is limited due to non-availability of new insecticide molecules in near future. The strategy of replacement of insecticides being followed till now also has limitations due to the non-availability of new insecticides. It is not even cost effective and results in cost escalation for the vector control. The need of the hour is intensive research on management tactics and integration of such tested strategies in the ongoing vector control programmes.

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This article has been contributed by Dr. K. Raghavendra, Senior Research Officer and Dr. S.K. Subbarao, Director, Malaria Research Centre, Delhi.

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Printed and Published by Shri J.N. Mathur for the Indian Council of Medical Research, New Delhi
at the ICMR Offset Press, New Delhi-110 029
R.N. 21813/71