Review Article

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Vector control in leishmaniasis

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Indoor residual spraying is a simple and cost effective method of controlling endophilic vectors and DDT remains the insecticide of choice for the control of leishmaniasis. However resistance to insecticide is likely to become more widespread in the population especially in those areas in which insecticide has been used for years. In this context use of slow release emulsified suspension (SRES) may be the best substitute. In this review spraying frequencies of DDT and new schedule of spray have been discussed. Role of biological control and environment management in the control of leishmaniasis has been emphasized. Allethrin (coil) 0.1 and 1.6 per cent prallethrin (liquid) have been found to be effective repellents against *Phlebotomus argentipes*, the vector of Indian kala-azar. Insecticide impregnated bednets is another area which requires further research on priority basis for the control of leishmaniasis. Role of satellite remote sensing for early prediction of disease by identifying the sandflygenic conditions cannot be undermined. In future synthetic pheromons can be exploited in the control of leishmaniasis.

Key words Biological control - insecticides - leishmaniasis - *Phlebotomus argentipes*

Leishmaniasis is the vector borne disease transmitted by the Phlebotomine flies in the Old World and *Lutzomyia* in the New World[1]. The vector of various leishmaniases worldover belong to order Diptera of class Insecta (Phylum Arthopoda). Fauna of Indian sub-zone is represented by 46 species, of these 11, belong to Phlebotomine species and 35 to sergentomyia species[2]. *Phlebotomus argentipes* is the proved vector of kala-azar (visceral leishmaniasis, VL) in India[3].

Control of VL mainly depends on its epidemiological features. In the zoonotic foci where carriers are involved and dogs are the main vertebrate host, the effective methods include destruction of dogs and elimination of sandflies by environmental and chemical control. In India, Bangladesh and Nepal where visceral leishmaniasis is anthroponotic the only choice is chemical and environmental control. Best method to interrupt any vector borne disease is to reduce man-vector contact. Many methods exist at present for leishmaniasis control which can be used individually or in combination. The selection of the method or combination of methods depends on the type of the leishmaniasis to be controlled and also the method should be situation specific. In this article attempts have been made to discuss the conventional and some latest technologies of vectors control measures being used worldwide.

Present status of kala-azar and chemical control in India

Visceral leishmaniasis is a serious public health problem in the country since 1970s, in the State of Bihar and latter spread to West Bengal and eastern Uttar Pradesh. In 1977 a sample survey estimated the number of cases to be about one lakh with 4500 deaths in Bihar[4]. The disease is prevalent in more than 30 districts in the State of Bihar (old Bihar). In India, there is no definite control programme for kala-azar but control was only as a byproduct of anti-malaria activities. Under National Malaria Control Programme in 1953 and later National Malaria Eradication Programme (NMEP) now National Vector Borne Disease Control Programmes, DDT was extensively used. The DDT spray operation reduced the sandfly population to the very low levels resulting in interruption of kala-azar transmission and virtual elimination of the disease. Spraying of residual insecticide was withdrawn under NMEPin phased manner from different areas from 1962. In 1970s, kala-azar cases started being reported from Muzaffarpur, Sitamahari and Samastipur in Bihar signaling a simmering outbreak[5]. Kala-azar incidence recorded an increasing trend after resurgence till 1992.

Until 1989-1990 kala-azar control activities were undertaken by the States on focal basis diverting NMEP resources. However, during 1990-1991 planning commission approved a centrally sponsored Kala-azar Control Scheme which was implemented in both the endemic States namely Bihar and West Bengal. After the implementation of this scheme kala-azar cases showed a sharp decline from 1993 and continued till 1999. However, in 2000 number of cases significantly increased to 12964 cases with 202 deaths (Data obtained from Bihar Directorate of Health Services). A mandate committee of Government of India decided to evaluate the efficacy of DDT and malathion in malaria and kala-azar control programme. In 2000, a multicentric study was initiated by the Indian Council of Medical Research (ICMR) and Rajendra Memorial Research Institute of Medical Sciences (RMRIMS), Patna conducted the evaluation of DDT as indoor residual spraying (IRS) in the control of kala-azar with the objectives to assess the susceptibility status of *P. argentipes* to DDT and other commonly used insecticides.

Insecticide of choice: Indoor residual spraying is a simple and cost-effective method of controlling vector. DDT still remains the insecticide of choice because of its low cost, high efficacy, long residual action and relative safety when used for indoor residual spray. Dosage schedule of 1 or 2 g/m^2 or 100-200 mg/ft^2 has been found to be quite effective; 5 per cent emulsified suspension of DDT is the choice[6]. Mukhopadhya *et al*[7] in a study in an endemic focus in Bihar reported two rounds of spray, one in March-April and other in June-July. The study was based on two ascending phases in *P. argentipes* population. They further advocated two rounds of DDT spray for three successive years keeping in mind the long incubation period of kala-azar[8]. If the probability of a female *P. argentipes* being infected with *Leishmania donovani* does not vary with season, peak transmission of this parasite to humans probably occurs between February and May at mid night[9]. This also substantiates the proper schedule of DDT spray.

Under the anti-vector control strategies as introduced by NMEP since 1992[10], the schedule adopted in Bihar was two rounds of spray, first round in February-March and second round in May-June. Whereas in West Bangal first round of spray was done in May-July and second in August-October. In a separate observation Palit *et al*[11] suggested April-May and September-October with a spacing of 4 months for 1st and 2nd rounds of spray, respectively. Kumar *et al*[12] have suggested June-July and October-November, for 1st and 2nd rounds of spray.

Spraying procedure: Spraying of DDT in the indoor human dwellings including the roof structure should be done. It should also cover animal shelters (especially cow-sheds) and other structures in peridomestic situations as sandflies have been recovered both from human as well as animal dwellings. People living in mixed dwelling are at the greatest risk of contracting the disease. Special care should be taken to spray into cracks/crevices in which sandflies seek shelter. Before spraying, evaluation of technical know-how among spraying personnel, *viz.*, spraying technique, stroke of spraying machines, handling of pumps, total area of coverage by a given amount of insecticide, *etc.*, should be undertaken. DDT should be mixed in the proportion of 3.3 pounds/3gallons (*i.e.*, 1.1 kg/ 15 l) resulting in a 5 per cent suspension at the flow rate of 750 ml/ minute and 45 mm distance from the target, using single nozzle. According to WHO recommendation[13], 2 liter of 5 per cent water dispersible powder (3.3 pounds) DDT suspension sprayed at the rate of 100 mg/sq.ft. should cover 1000 ft^2.

Susceptibility status: DDT still being the choice insecticide, is going to be used extensively in the kala-azar control programme. However, some workers have reported development of tolerance in *P. argentipes* against DDT therefore its sensitivity level needs to be taken into consideration while formulating any control strategies. Development of tolerance against DDT in *P. argentipes* has been reported from Samstipur[5], Bakhtiyarpur[9], Darbhanga, Samastipur and Vaishali districts[14]. Development of tolerance to DDT in *P. argentipes* of Vaishali[15] and Muzaffarpur (unpublished) districts has also been reported. Thus, the magnitude of the problem is well recognized, warranting new approaches by developing more effective and feasible control measures. Use of slow release formulation of polyvinyl acetate based malathion SRES may be feasible proposition since this formulation is expected to give desired effect for a longer time. Further, *P. argentipes* is still susceptible to most of the insecticides[16]. Malathion SRES, paint formulation has been tried against triatomid bugs which proved to be very effective in control of Chagas disease in Brazil[17].

A pilot study was conducted by RMRIMS in Patna district with 5 per cent malathion, SRES suspension was used in the dose of 2 mg/m^2 with manually operated stirrup pressure pump. The study was conducted in an endemic village of Bihar, Gulmahiabagh. On the basis of house index and man hour density (MHD) of the vector species the study revealed the effectiveness of malathion, SRES, for 25-26 months[18]. In a study on evaluation of cholinesterase levels in endemic population exposed to malathion suspension, plasma cholinesterase level remained within the normal range[19]. Oleveira-Filho *et al*[20,21] reported the polyvinyl acetate based suspension of malathion quite effective against *Lutzomyia longipalpis* though DDT was cheapest, and gave estimated cost ratio of 0.9 becoming cheaper than DDT due to its long residual effect. The effectiveness of spraying is not the only issue of concern, other problems are the side effects on human health and environment and their sustainability. Several factors such as cost of the insecticides, the logistic constraints low acceptance by the community and low community participation and the emergence of resistance affect the long term effectiveness and sustainability of these interventions.

Use of insecticide impregnated bed nets in the control of leishmaniasis: Insecticide impregnated bed nets (ITN) were shown as one of the most effective methods of reducing man-vector contact and intra- and peridomicilliary transmission of vector-borne diseases. In most studies the insecticides used were synthetic pyrethroids (permethrin, deltamethrin, Lambda-cyhalothrin), which combine the properties of low to moderate mammalian toxicity[22], low volatility and high insecticidal activity. ITNs act as 'baited traps' but have also important deterent and repellent effect. Compared with house spraying ITNs have theoretically the following advantages: (*i*) their effectiveness is independent of the endophilic and exophilic behaviour of the vectors; (*ii*) less insecticide is used; and (*iii*) the household exerts control over its application and thus depends less on the performance of a knock-down planned disease control programme.

In the laboratory bioassays, wild *P. perniciosus* and *P. papatasi* confined in a cage were stimulated, using a bait, to cross-treated curtains (cotton 0.5 cm mesh size) to test the effect of treatment on repellence, feeding rate and mortality[23]. The results showed that permethrin (1000 mg/m^2) had a low repellent effect on both sandfly species, but reduced the feeding rates by 67 per cent for *P. perniciosus* and 80 per cent for *P. papatasi* and caused high 24 h mortality (>90% for each species).

Environmental control

Sandflies breed in dark corners in the crevices of the walls having rich humus and moisture. The principle behind the environmental control is to manage the environment to make it unsuitable for breeding. In 1980, Vyokov[24] in USSR successfully controlled leishmaniasis by destroying rodent burrows. In a study on technological control of sandflies, the walls of the resting sites were plastered filling all the cracks and crevices by mud and lime, and the breeding of sandflies could be stopped successfully[25]. Lime has a powerful water absorbing capacity which makes it unsuitable for the sandfly breeding. In another experiment Dhiman[26] successfully controlled 70 per cent population of *P. papatasi* by constructing cement skirting of 9" vertically on the wall and 9" horizontally on the floor.

Biological control

Very scanty information is available on the biological control of sandfly. As the application of biolarvicides in the field condition is difficult due to diverse breeding habitat of sandfly, their practical application appears to be of limited use in the control of visceral leishmaniasis. In the laboratory experiment De Barjac *et al*[27] first time demonstrated the role of *Bacillus thuringiensis* var. israelensis in the control of larvae of *P. papatasi* and *Lutzomyia longipalpis*. Robert *et al*[28] successfully used *Bacillus sphaericus* in the control of *P. martini* in Kenya based on the work of Schlein[29] and Yuval and Warburg[30]. This approach requires further evaluation. They also observed inhibitory effect of *B. sphaericus* on hatching of eggs of *P. dubosqui*[31].

Prophylactic methods

These include self protection by use of mosquito nets and of repellents. Use of nets for sandflies of approximately 36-42 mesh would definitely prevent from its biting. DEET (diethyl tolumide) was found to be quite effective against *L. longipalpis*[32]. Essential lemon oil also gave good results with 70 per cent protection[33]. Soap solution containing 20 per cent DEET and 0.5 per cent permethrin was effective against *L. longipalpis*, its effect lasted for 4 h[34]. Sharma & Dhiman[35] found that concentration of 2 per cent neem oil mixed in coconut or mustard oil provided 100 per cent protection against *P. argentipes* throughout the night in the field conditions. Application of mustard oil alone exposed to the uncovered areas acts as repellent against *P. argentipes* (unpublished observation). Recently it was found that 0.1 per cent allethrin (in coil) and 1.6 per cent prallethrin in liquid form can give maximum protection against the bite of *P. argentipes* (unpublished data).

Role of community participation in sandfly control

Health education for control of leishmaniasis is of great importance. Simple eradication of all possible resting sites of vector within a locality by the population itselt can result in a significant reduction of disease incidence. Like other communicable diseases of public health importance, general and broad basic knowledge about leishmaniasis should be widely disseminated.

Recent development in the control of leishmaniasis

Remote sensing: Satellite remote sensing has been successfully used in the identification of high risk areas for malaria. Recently a pilot study has been concluded at RMRIMS, Patna, for identifying and mapping of *P. argentipes* distribution for early prediction of disease with the help of satellite remote sensing in integration with geographical information system (GIS)[36]. Kala-azar or visceral leishmaniasis has been continuing unabated in India for over a century and now considered one of the major health problems in the eastern states mainly Bihar, West Bengal and Uttar Pradesh. In absences of any suitable 'epidemic prediction tool', it is very difficult to forewarn or predict epidemic outbreak of the disease. With increasing accessibility to new technologies *viz.*, remote sensing and GIS, it has become possible to monitor land-use features on earth's surface over various time intervals to develop methods for rapid stratification of high susceptive areas and for the design of remedial measures.

As such, two study sites representing different types of ecosystem were selected in Bihar. Eighteen villages in Patepur block in Vaishali district, one of the high endemic areas of Kala-azar in north Bihar (as endemic foci) and 12 villages in Lohardagga block in Lohardagga district, (as non endemic foci), were selected for addressing and evaluating the use of satellite data for monitoring the macro-ecosystem *i.e.*, specific vegetation cover and human settlement, and relating them with the changing conditions favourable for sandflies for assessing its role as potential epidemic predictor.

Season-wise data on temperature, humidity, vector density, incidence of VL cases and soil samples were collected through ground surveys carried out in the selected sites during November 1999 to March 2000. Satellite data of Indian Remote Sensing Multispectral IRS-1D LISS3 data for both the blocks were analysed in Silicon Graphic Image Processing System using ERDAS software. The preliminary analysis of both ground and satellite data sources included the construction of digital maps, which were overlaid on the digital environmental data and the relevant data for the collection sites using GIS software[37].

Statistical analysis showed significant correlation of vector density with variables like temperature, humidity, settlement, crop areas, moist fallow, dry fallow, minimum normalized digitized vegetation index (NDVI) and standard deviation of NDVI. Multivariate regression analysis performed using significantly correlated variables, generated six models and the best model gave detailed mapping of sandfly density in both endemic and non endemic sites. This model derived from the environmental variables and land cover features can produce a map of distribution of *P. argentipes*. Although, this model was based on data pertaining to two blocks of the State, it can be used for the prediction of vector density in other endemic areas of Bihar.

Cross *et al*[37] on the basis of NDVI values have advocated the low and high probability of *P. papatasi* zone. In another study Miranda *et al*[38] in Brazil demonstrated strong co-rrelation between cutaneous leishmaniasis (CL) infection and creeks and relevant vegetation.

Future prospects

Role of pheromons: Pheromons are chemical substances which help in attracting the insects at a particular site for mating. This property of pheromons is yet to be exploited in the control of vector of leishmaniasis. A pilot project is being initiated at RMRIMS, Patna in collaboration with Keele university, UK, to explore the role of synthetic pheromons in control strategies.

Concluding remarks

Vigorous research efforts need to be done to develop the larvicide for successful elimination of the vector. Application of satellite remote sensing, insecticide impregnated bed nets and synthetic pheromons traps are other exciting areas which require attention. Health education about the habitat and breeding of vector species may go a long way in the vector control.

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