

Impact of etofenprox (Vectron[®] 20 WP) indoor residual spray on malaria transmission

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Background & objectives: A longitudinal study was carried out to assess the impact of indoor residual spray with Vectron[®] 20 WP (etofenprox) against *Anopheles culicifacies* and on malaria transmission in a selected village of Dadri primary health centre (PHC), District Gautam Budh Nagar, Uttar Pradesh, India.

Methods: Two villages, namely Patadi and Anandpur in District Gautam Budh Nagar, Uttar Pradesh, with similar malaria incidence and vector prevalence were selected for the present evaluation. In one village two rounds of indoor spraying of etofenprox (0.1 g/m²) were done at an interval of 12 wk and the other village was kept as control where no intervention except intensive active surveillance for early detection and prompt treatment (EDPT) was undertaken during the study period. Entomological and epidemiological data were collected using standard procedures.

Results: Persistence of the effectiveness of etofenprox against *An. culicifacies* was observed up to 12 wk. Spraying of etofenprox significantly reduced the density ($P<0.001$) and proportion of parous *An. culicifacies* mosquitoes ($P<0.05$) in the experimental village. There was a significant reduction in malaria cases in the experimental village during the post-spray period when compared to the control village ($P<0.05$). No adverse effect was reported by the sprayers and inhabitants during and after the spray.

Interpretation & conclusion: Indoor residual spray of etofenprox (0.1 g/m²) with an interval of three months in between two rounds of spray produced the desired impact in reducing the indoor resting density of vector mosquitoes and also in curtailing malaria transmission in the sprayed village when compared with the control village without spray.

Key words *Anopheles culicifacies* - etofenprox - indoor residual spray - malaria transmission - vector control

National Vector Borne Disease Control Programme (NVBDCP), India, recommends use of indoor residual spray (IRS) with insecticides recommended under the programme; and use of chemical larvicides like abate in potable water; aerosol space spray during day time and malathion fogging during outbreaks as chemical control methods; and use of larvivorous fish

in ornamental tanks, fountains, *etc.*, and biocides as biological control methods for malaria vector control in India¹. As per national insecticide policy, DDT, malathion and synthetic pyrethroids like deltamethrin, cyfluthrin, lambda-cyhalothrin, alpha-cypermethrin, *etc.*, are selectively being used for vector control^{2,3}. However, persistent use of insecticides since

introduction of DDT in 1955 resulted in precipitation of resistance against DDT and also against other alternative insecticides such as hexachlorocyclohexane (HCH) and malathion used in public health spray^{4,6}. Continued use of insecticides of a given group results in development of resistance. Thus, there is a need for alternative insecticides for indoor residual spraying in order to sustain the efficacy of existing insecticides in use in the Programme and also to avoid development of resistance in vectors. As an alternative to these insecticides, efficacy of Vectron® 20WP (etofenprox) was evaluated as an indoor residual spray against *Anopheles culicifacies* (Diptera: *Culicidae*) and its impact on malaria transmission. Etofenprox, a non-ester pyrethroid has very low mammalian toxicity and the highest safety factor⁷. A few laboratory and field trials have been carried out with this insecticide in different countries⁷⁻¹⁰ and it is recommended for indoor residual spraying by World Health Organization Pesticide Evaluation Scheme (WHOPES) at 0.1-0.3 g/m² with an effective duration for 3-6 months^{7,11}. We carried out a village-scale trial with etofenprox sprayed at 0.1 g/m² against *An. culicifacies* in Dadri, Uttar Pradesh, India.

Material & Methods

Study site: Based on the malaria incidence data collected from the District Malaria Office, District Gautam Budh Nagar and Chief Medical Officer, National Thermal Power Corporation (NTPC), Dadri, Uttar Pradesh, India, a few villages under Dadri primary health centre (PHC) were surveyed and baseline data on malaria incidence and vector density were collected from March to June 2004. A mass blood survey (blood smears only from children aged 1-14 yr irrespective of fever) was conducted in two villages, namely Patadi and Anandpur. The results of mass blood surveys revealed that 3 out of 75 blood smears were positive in the Patadi village and 4 out of 100 were positive for malaria in the Anandpur village and there was no significant difference between the two villages. Patadi village (population 1800, 2001 Census) near to NTPC, Dadri, was selected for spraying of etofenprox. Anandpur village (population 2000, 2001 Census) located in the same PHC was selected as a control village. No intervention was undertaken in the control village during the study period and active surveillance was strengthened for early detection and prompt treatment. The distance between experimental and control villages was about 8 km. Census on number of houses, temporary structures and cattle sheds were

collected in both the villages. Both experimental and control villages had more or less the same composition of mosquito fauna, man to cattle ratio, vector species and malaria prevalence. Main profession of inhabitants was farming through irrigation channel. The study was conducted from March 2004 to May 2005.

Insecticide dose and spraying: Vectron® 20 WP [2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether] supplied by M/s. Sumitomo Chemicals India Pvt. Ltd., Mumbai, India, was used. Insecticide spray was carried out at 0.1 g/m² with the help of stirrup pumps (Aspee Bucket sprayer, M/s. American Spring & Pressing Works Pvt. Ltd., Mumbai) after calibration of nozzle as per standard procedure^{2,3}. Two rounds of spray were carried out in the experimental village (first round from July 2-4, 2004 and the second round from September 30 - October 1, 2004).

Insecticide susceptibility tests and persistence studies: *An. culicifacies* mosquitoes were collected from the experimental and control villages. Blood-fed female mosquitoes were exposed to WHO diagnostic dose of insecticide impregnated papers of DDT (4%), malathion (5%), dieldrin (0.4%) and deltamethrin (0.05%) using the WHO tube method¹². After exposure, mosquitoes were held in holding tubes for 24 h. During holding, mosquitoes were provided 10 per cent glucose soaked cotton wool swab. Per cent mortality was calculated after 24 h holding and corrected using Abbott's formula¹³ when the control mortality was >5 and <20 per cent. Persistence of insecticide on different surfaces was assessed by cone bioassay tests on different sprayed surfaces selected randomly. Bioassay tests were performed as per WHO standard procedures^{12,14}.

Collection of mosquitoes: Hand collections of indoor resting mosquitoes were done fortnightly in the study villages using suction tube and flashlight in the early morning hours. Four houses were selected randomly in different directions for sampling indoor resting mosquitoes. Collections were done for 15 min in each selected room and number of mosquitoes collected per man hour (MHD) was calculated. Mean number of mosquitoes caught per man hour in a month was calculated. Field collected mosquitoes were brought to the laboratory for species identification and further processing. *An. culicifacies* mosquitoes collected were dissected and their parity or nulliparity was assessed from the tracheolar skeins¹⁵. Gut and gland infections with *Plasmodium* were recorded by dissection method¹⁵.

Parasitological survey: Three mass blood surveys were conducted in the study villages, one in May 2004 before spray and the other two after spray in October 2004 and May 2005. Blood smears were collected from inhabitants in the age group of 1-14 yr irrespective of presence of fever, randomly. In addition, door-to-door active surveillance was carried out fortnightly in the study villages. All fever cases were identified and blood smears were collected, stained with Jaswant Singh Bhattacharjee (JSB) stain and examined under microscope (KF2 microscope, M/s. Zeiss, West Germany) for malaria parasites. Presumptive treatment was given to all fever cases, while radical treatment was given to only positive cases as per NVBDCP drug schedule in study villages. Slide positivity rate (SPR), slide falciparum rate (SFR) were calculated using standard formulae¹⁶.

Social acceptability and safety to inhabitants: Data on social acceptability and their response based on pre-structured questionnaire (prescribed in Protocols for Uniform Evaluation of Insecticides for Use in Vector Control¹⁶) were collected and analyzed. Every third house was surveyed and the perceptions of the head of the family or adult member were obtained on the indoor residual spray.

Statistical analysis: Fisher's exact test was used for *Plasmodium* positive or negative smears and parity status of *An. culicifacies* mosquitoes to test the differences in control and experimental villages.

Differences in number of mosquitoes caught per man hour between control and experimental village were tested using Student's *t* test.

Results

The first round of etofenprox spray was carried out in July 2004 (0.1 g/m²) in Patadi village. A total of 212 human dwellings, 6 temporary structures and 21 cattle sheds were sprayed in the first round with 96.7 per cent house coverage. In the second round, 202 houses were sprayed of 221 targeted with 91.4 per cent house coverage. Coverage was low in the second round due to festival season and non availability of households during the spray. Mopping of spray was done a day after spray. Due to non availability of desired quantity of insecticide, cattle sheds and temporary structures were not sprayed in the second round.

Susceptibility tests using WHO specified diagnostic doses of insecticide impregnated papers on *An. culicifacies* mosquitoes revealed variable susceptibility. *An. culicifacies* was 30 per cent susceptible to DDT, 44 per cent to dieldrin, 100 per cent to malathion and deltamethrin. Cone bioassay tests carried out against *An. culicifacies* on different surfaces sprayed with etofenprox revealed 100 per cent mortality up to 8 wk on both cement and brick wall surfaces followed by gradual decline in successive weeks. The mortality reduced to <80 per cent after 10 wk of second round spray.

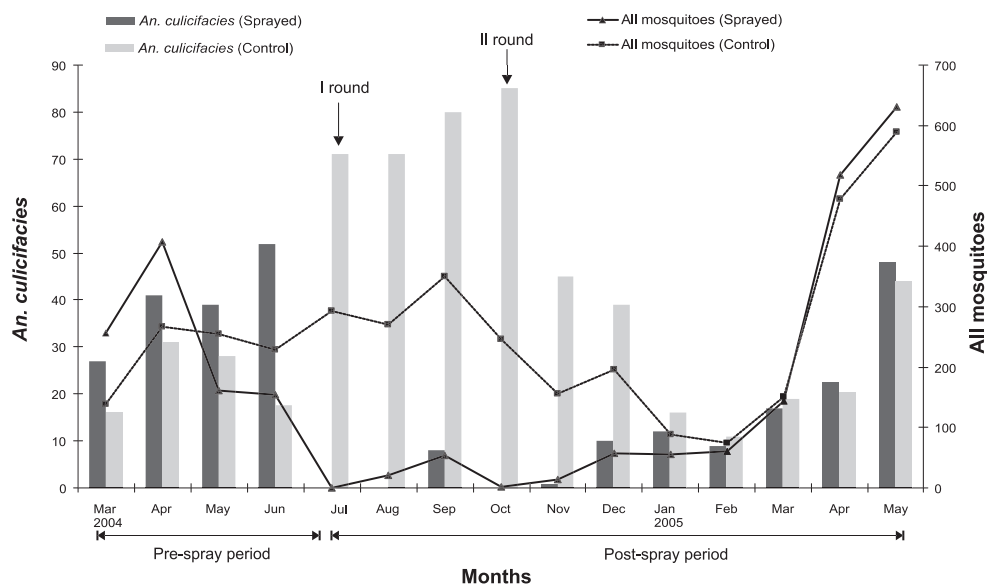


Fig. 1. Mean number of mosquitoes caught per man hour of *An. culicifacies* and all other mosquitoes in sprayed and control villages. All mosquitoes included *Anopheles culicifacies*, *An. subpictus*, *An. annualis*, *Culex quinquefasciatus*, *Cx. vishnui*, etc.

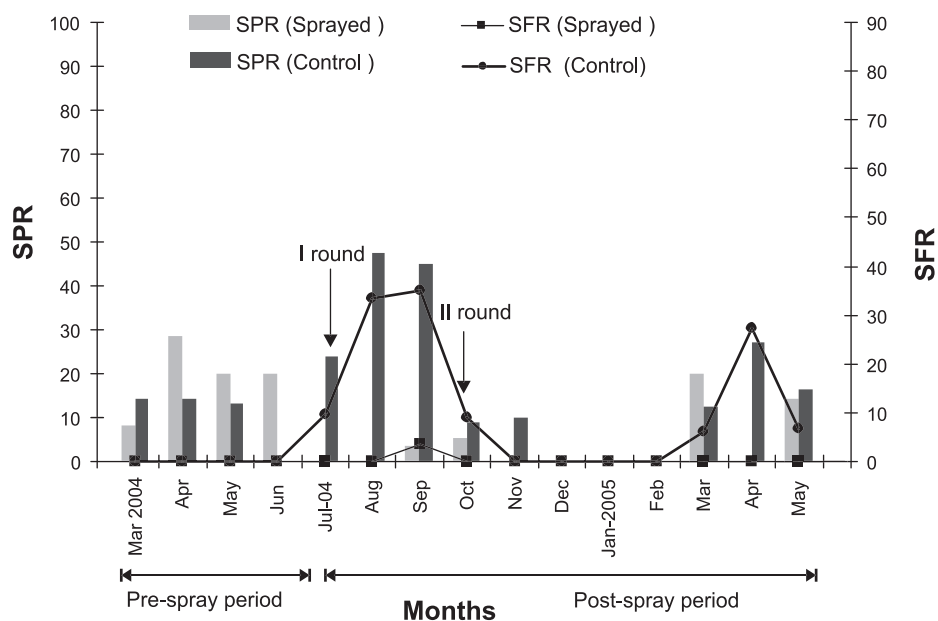


Fig. 2. Slide positivity rate (SPR) and slide falciparum rate (SFR) in etofenprox-sprayed and control villages.

The mean number of *An. culicifacies* mosquitoes caught per man hour during pre-spray period (March to June 2004) in Patadi village was 40.5 ± 10.04 which was significantly higher ($P < 0.001$) than that in Anandpur village (23.5 ± 7.3) (Fig. 1). The mean number of all other mosquitoes caught during pre-spray in Patadi village was 247.5 ± 108.7 as against 242.8 ± 74.1 in Anandpur village. After the intervention (July 2004 to May 2005), the mean number of *An. culicifacies* caught per man hour in the experimental village was 11.8 ± 14.2 and that of in the control village was 46.8 ± 26.1 , and both the villages differed significantly ($P < 0.001$). Similarly, the mean number of all mosquitoes caught per man hour in the etofenprox sprayed village was 141.3 ± 212.9 and that of in the control village was 270.6 ± 157.3 , and both the villages differed significantly ($P < 0.05$). The residual effect of etofenprox (>80% mortality in cone bioassays) lasted up to 10 wk only after the second round spray and also there was an increase in the density of mosquitoes gradually from December 2004 onwards in the experimental village.

Female *An. culicifacies* mosquitoes were dissected for determining longevity and infectivity. The results revealed that 75 of 125 *An. culicifacies* were found parous in the etofenprox sprayed village and 318 of 469 were parous in the control village after spray (July 2004 to May 2005), and the difference was significant ($P < 0.05$). Observations among those that were caught inside the rooms sprayed with etofenprox

for sporozoites revealed zero from the experimental village and 1/353 from the control village.

Before intervention the incidence of fever associated with parasitaemia for either parasite (*Plasmodium falciparum* or *P. vivax*) was slightly higher in Patadi village which was later sprayed than the control village (Fig. 2). However, soon after the spray, such cases ceased to be found in the study village which was sprayed with etofenprox but cases (including *P. falciparum*) continued in the control village. SPR and SFR were reduced significantly in the experimental village as compared to the control village ($P < 0.05$). Only one case of *P. falciparum* was reported from Patadi village whereas malaria cases were continued in the control village. Results of mass blood surveys (irrespective of presence of fever in <14 yr age group) are shown in the Table. The results showed no significant difference in control and experimental villages prior to spray, whereas after the spray in the first mass blood survey conducted in October 2004 only one case of *Plasmodium vivax* was reported. In contrast, in the control village 15 cases were reported in this age group (9 *P. vivax* + 6 *P. falciparum*). In the second mass blood survey conducted in May 2005, malaria cases were reported in the control village only (3 *P. vivax*).

Altogether, 77 households were surveyed randomly covering every third house and information was collected from the head of the family or adult member who was available during the survey. The information

Table. Results of mass blood surveys irrespective of fever in control and experimental villages carried out before and after spray in 1-14 yr age group

Month	Experimental		Control	
	TBS	Total positive (Pv+ Pf)	TBS	Total positive (Pv+ Pf)
<i>Pre-spray</i>				
May 2004	75	3 (3+0)	100	4 (4+0)
<i>Post-spray</i>				
Oct 2004	95	1 (1+0)	100	15 (9+6)*
May 2005	80	0 (0+0)	96	3 (3+0)*

TBS, Total blood slides collected; Pv, *Plasmodium vivax*; Pf, *P. falciparum*; Statistical analysis was done by Fisher's exact tests; (* $P < 0.001$ compared to experimental village)

collected on the acceptability and perceived side effects of spray indicated that 90.9 per cent of inhabitants were using protection measures like bed nets, mosquito coils, repellent creams, smoke of leaves and cow dung, *etc.* Regarding smell of the insecticide, 93.5 per cent conveyed that there was no smell, and 96 per cent of interviewees expressed that the insecticide does not leave stains on walls. About 93 per cent inhabitants expressed satisfaction on the reduced mosquito density and reduced nuisance of houseflies, cockroaches, ticks, spiders, lizards, *etc.*

Discussion

Results of the present study showed that etofenprox indoor residual spraying reduced the density of *An. culicifacies*, the principal malaria vector, and also curtailed malaria transmission in the experimental village. Bioassay tests carried out on different surfaces showed 100 per cent mortality up to 8 wk and > 80 per cent mortality up to 12 wk on both cement and brick wall surfaces against *An. culicifacies*. The results of the present study are in conformity with other efficacy studies carried out in laboratory and field with this insecticide in different countries⁸⁻¹⁰. In an operational trial of Vectron (Etofenprox, OMS 3002) conducted in East Flores, Timur Province in Indonesia¹⁰, etofenprox 10EW was applied at 0.2 g/m² as an indoor residual spray and as an impregnant for bednets in two separate areas. Bioassay tests on bamboo surfaces gave 100 per cent mortality for 150-160 days post-spray against malaria vectors, while wooden surfaces and treated bednets both gave complete mortality for at least 120 days. Malaria cases monitored by successive malariometric surveys showed steady decline in positivity rates, particularly in children¹⁰.

In the present study also malaria cases were not seen in the experimental village after spray. All these studies including the present one clearly showed the effectiveness of etofenprox against malaria vectors and on disease transmission.

Due to festival season and refusal from the inhabitants, house coverage in the second round was lower than the first round, hence, the impact on mosquito density was reduced and lasted only for couple of months after the second round. Further, due to non availability of desired quantity of insecticide, cattle sheds and temporary structures could not be sprayed in the second round, which might have contributed for reduced impact on mosquitoes. However, malaria cases were not reported even after second round spray in the experimental village.

Since etofenprox has very low mammalian toxicity and has the highest safety factor⁷, it can be used as a safer alternative for indoor residual spray against pyrethroid susceptible strains of malaria vectors. Two rounds of spray at an interval of three months during the transmission season may be appropriate to curtail the active malaria transmission.

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