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Evaluation of Possible Health Effects of Pyrethroid Insecticides, Bifenthrin 10% WP, and Deltamethrin 25% WG, on Spraymen Exposed in a Field Trial in India

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Indoor residual spraying of insecticides is the mainstay of malaria control in rural areas in South-East Asia (SEA). In India, which contributes to over three-fourths of the total burden of malaria in SEA countries, pyrethroid insecticides are being used for malaria control in endemic rural areas with local mosquito vectors resistant to the conventional insecticides. The pyrethroids have been found to be valuable insecticides with differing stability to light, low volatility, low mammalian toxicity and high insecticidal potency under normal conditions of use (WHO 1985). It is reported that most water-based pyrethroids are not absorbed by skin and present a negligible risk to users (WHO 1989). For example, deltamethrin is not mobile in the environment and its dermal absorption is reported to be very low. Bifenthrin is a third-generation synthetic pyrethroid insecticide, which is characterized by a strong environmental persistence and high insecticidal activity. It is virtually stable to aqueous hydrolysis and photolysis producing only one minor by-product, 4'-hydroxy Bifenthrin. The mammals remain unaffected on exposure to bifenthrin, except at very high dose levels (Fecko 1999). In the studies with laboratory animals, bifenthrin and deltamethrin have been shown to have moderate toxicity if swallowed, and these cause low dermal toxicity if overexposed (Barlow et al. 2001).

During 1999 to 2002, two new formulations of pyrethroids, bifenthrin 10% WP and deltamethrin 25% WG were field evaluated for malaria vector control in India. Both insecticides caused a significant decline in densities, longevity and human landing rate of the local malaria vector, *Anopheles culicifacies*, when sprayed indoors at 25 mg/m^2 and 20 mg/m^2 doses, respectively (WHO 2002; Yadav et al. 2003). As part of the field evaluation, we also considered it pertinent to evaluate the possible effects of the two insecticide formulations on the health of the spray men. The results of the possible effects of on short-term occupational exposures are presented in this paper.

MATERIALS AND METHODS

Thirteen healthy, trained male spray men aged between 20 and 40 years who had no previous exposures to pyrethroids were employed for spraying in the study. Earlier, an institutional ethical committee had cleared the study and written

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consent of each volunteer spray man was obtained before hand. Clinical and biochemical examination, chest X-ray, pulmonary function, nerve conduction study and electromyogram were performed on the enrolled spray men to exclude presence of any disease, as well as to establish pre-exposure baseline data.

Plasma urea and creatinine were estimated to assess the renal status. Serum bilirubin, serum glutamate pyruvate (alanine amino) transferase (SGPT), serum glutamate oxalate transferase (SGOT), total proteins and albumin were estimated to assess hepatic functions. All biochemical tests were done on a Ciba-Corning Express plus autoanalyzer using Sigma and Sandoz test kits.

The nerve conduction tests and electromyogram were taken at the Shree Krishna Hospital on Recorded and Medicare System, Electromyogram Evoked Potential system with sterile technique and appropriate safety. Needle electromyography was performed on Biceps brachii, Brachioradialis and Abductor digiti minimi. Motor nerve conduction tests included measurement of the amplitude, latency and conduction velocity were performed on Median and Ulnar nerves of the upper limb and lateral popliteal nerve of lower limb. Sensory nerve conduction was done on the Median and Ulnar nerves of the upper limb and Sural nerve (antidromic sensory) of the lower limb. Facial nerve conduction was also tested for amplitude and latency at Frontalis, Nasalis and Orbicularis oris muscles. Blink reflex was checked on Supra orbital stimulation.

Ten volunteers (a group of five volunteers for each insecticide), who had successfully passed medical tests, were engaged for spraying of the insecticides in separate villages. All the volunteers wore protective gears. The insecticides (deltamethrin at 20 mg/m^2; bifenthrin at 25 mg/m^2) were sprayed indoors on local walls six hours daily for three consecutive days and thereafter two days. Spray men used stirrup pumps with flat fan nozzle that are used by the National Vector Borne Disease Control Program. They bathed using bath soap after spraying each day. All above mentioned medical tests were repeated on days 4 and 7 post-exposure.

The lung function tests were done by COSMED, Polygraphic-3.5, Spirometer before and 6 hours after spraying to see any immediate effect of the insecticides. Forced vital capacity (FVC), forced expiratory volume (FEV1) and peak expiratory flow rate (PEFR) were measured for all the spray men.

The data were analyzed statistically and the Student's *t* test was applied to determine statistical differences in the pre- and post-exposures health parameters.

RESULTS AND DISCUSSION

Clinical examination of spray men on days 4 and 7 showed no significant changes from normal values of the vital signs such as the blood pressure, body temperature, and gastro-intestinal, neuro-muscular, cardio-respiratory, eye functions and on the skin. Deltamethrin sprayers reported a mild burning

sensation on the face and exposed body parts. These were transient and vanished after bathing.

Biochemical, hematological and chest X-ray screening tests showed that liver, renal and hematological functions of the spray men remained well within the reference ranges after 4 and 7 days of exposure to deltamethrin and bifenthrin (Table 1). The differences in the serum protein levels on days 0 and 4 were statistically significant on exposure to bifenthrin ($p < 0.001$) or deltamethrin ($p < 0.04$). There was a significant ($p < 0.04$) but small increase in the creatinine level

Table 1. Clinical chemistry of volunteer spray men exposed to bifenthrin or deltamethrin[1].

Parameters	Reference value	Bifenthrin			Deltamethrin		
		Day-0	Day-4	Day-7	Day-0	Day-4	Day-7
Urea	10-50 mg/dl	20.80 ±4.6	21.60 ±4.7	20.60 ±6.1	21.80 ±7.0	17.20 ±1.6	16.40 ±3.2
Creatinine	0.5-1.5 mg/dl	0.78 ±0.1	0.74[a] ±0.1	0.86[a] ±0.2	0.80 ±0.1	0.74 ±0.1	0.68 ±0.1
Serum proteins	6-8 g/dl	7.28[b] ±0.3	6.84[b] ±0.2	7.12 ±0.8	7.60[c] ±0.4	7.18[c] ±0.3	7.52 ±0.5
Albumin	3.5-5.5 gm/dl	4.30 ±0.1	3.66 ±0.8	4.12 ±0.2	4.50 ±1.5	4.14 ±0.1	4.00 ±0.1
Globulin	1.5-3 gm/dl	2.98 ±0.2	2.78 ±0.1	3.00 ±0.6	3.66 ±0.5	3.04 ±0.3	3.52 ±0.4
Bilirubin	0.25-1 mg/dl	0.54 ±0.1	0.54 ±0.1	0.56 ±0.1	0.56 ±0.1	0.60 ±0.0	0.54 ±0.1
Alkaline phosphatase	15-112 Iμ/L	80.20 ±42.2	64.80 ±18.9	65.00 ±15.7	63.40 ±17.1	78.20 ±12.7	79.20 ±13.5
SGOT	5-36 Iμ/L	20.00 ±1.9	22.40 ±4.5	35.20 ±7.7	17.00 ±4.6	12.40 ±3.6	14.60 ±3.6
SGPT	5-38 Iμ/L	14.40 ±4.0	14.00 ±3.7	24.00 ±17	11.00 ±2.3	10.40 ±3.6	8.40 ±2.3
Urine protein		A	A	A	A	A	A
Urine sugar		A	A	A	A	A	A
Urine WBC/RBC/ epithelial cells		5/O/O	5/O/O	5/O/O	O/A/O	O/A/O	O/A/O
X- Ray chest screening		NAD	NAD	NAD	NAD	NAD	NAD

[1]Results are expressed as arithmetic means of five samples ± SD.
Values followed by the same letter in superscript (a,b,c) within a row are significantly different from each other ($p < 0.05$).
A = Absent;
O = Occasionally seen;
NAD = No abnormality detected.

of three bifenthrin sprayers on day 7, though the values remained well within the reference range. Increase in creatinine might be due to exhaustion and environmental conditions. The normal values of the total proteins and bilirubin, and enzymes SGOT, SGPT and alkaline phosphatase show that the liver function of the exposed subjects remained normal. The values of urea and creatinine remained normal post-exposure to either of the two pyrethroids. Similar results were reported for cyfluthrin sprayers in India (Satpathy et al.1997).

Results of the nerve conduction test on bifenthrin sprayers are summarized in Table 2. There was no significant change in the latency and velocity of the motor and sensory nerves when compared to the pre-exposure values. On day 7 post-exposure, although the latency of the Oris muscle supplied by facial nerve

Table 2. Nerve conduction tests on volunteer spray men exposed to bifenthrin[1].

Nerve	Latency (m/sec) mean ± SD			Velocity (m/sec) mean ± SD		
	Day-0	Day-4	Day-7	Day-0	Day-4	Day-7
1. Motor nerves						
Median	3.02±0.2	2.82±0.4	2.70±0.3	61.18±3.9	60.70±3.5	60.00±5.1
p		0.14	0.31		0.82	0.72
Ulnar	2.16±0.2	1.88±0.4	1.98±0.4	58.28±4.3	59.02±6.2	59.68±3.9
p		0.35	0.19		0.56	0.63
Peronel	3.20±0.2	3.14±0.3	3.00±0.2	49.42±2.4	50.40±3.9	50.02±3.3
		0.62	0.36		0.45	0.62
2. Sensory nerves						
Median	2.64±0.1	2.56±0.1	2.54±0.2	50.06±3.0	52.00±1.4	51.22±2.3
p		0.48	0.37		0.50	0.49
Sural	2.90±0.7	2.56±0.3	2.54±0.7	51.46±8.3	53.44±5.9	57.06±10.6
p		0.25	0.94		0.32	0.29
Ulnar	2.28±0.1	2.36±0.4	2.22±0.1	51.80±3.1	52.00±3.2	50.56±2.7
		0.60	0.40		0.87	0.51
	Latency (m/sec) mean±SD			Amplitude (mv/μv) mean±SD		
3. Facial nerves						
Oris	2.66±0.5	2.46±0.4[a]	3.12±0.3[a]	2.18±1.1	1.92±1.3	1.52±1.1
p		0.41	0.02		0.78	0.53
Frontalis	3.38±1.0	3.76±0.3	3.30±0.8	1.16±0.9	1.08±0.5	0.88±0.6
p		0.29	0.23		0.78	0.42
Occuli	2.38±0.8	2.62±0.9	2.84±1.1	1.64±0.8	1.26±0.7	1.06±0.4
p		0.56	0.65		0.24	1.00

[1]Results are expressed as arithmetic mean of five samples ± SD.
Values followed by the same letter in superscript within a row are significantly different from each other ($p < 0.05$).
m/sec = metre per second;
mv/μv = milli volt or micro volt

increased significantly ($p < 0.02$) and the amplitude dropped by about 30 % ($p = 0.53$), the values remained within the normal ranges.

Except for a significant reduction in the latency of Ulnar motor nerve on day 4 ($p < 0.01$) and Frontalis muscle supplied by facial nerve on day 7 ($p < 0.01$), exposure to deltamethrin caused no significant changes in nerve function (Table 3). Although these value were also within the normal ranges for the Indian population (Mishra and Kalita 1999).

Table 3. Nerve conduction test on volunteer spray men exposed to deltamethrin[1]

Nerve	Latency (m/sec) mean ± SD			Velocity (m/sec) mean ± SD		
	Day-0	Day-4	Day-7	Day-0	Day-4	Day-7
1. Motor nerves						
Median	2.76±0.2	2.66±0.3	2.74±0.3	64.14±5.4	58.72±3.0	60.82±3.1
p		0.52	0.57		0.70	0.18
Ulnar	2.14±0.2[a]	1.88±0.2[a]	1.96±0.1	63.42±3.9	61.72±3.6	62.24±3.1
p		0.01	0.55		0.22	0.82
Peronel	2.62±0.2	3.40±0.3	3.30±0.5	42.50±22.4	52.74±2.7	51.84±2.8
p		1.00	0.63		0.60	0.40
2. Sensory nerves						
Median	2.50±0.2	2.48±0.1	2.54±0.2	52.02±2.5	53.62±3.0	50.84±2.3
p		0.37	0.30		0.41	0.06
Sural	2.42±0.2	2.70±0.2	2.54±0.2	56.82±8.0	53.10±3.7	53.64±2.3
p		0.13	0.21		0.41	0.71
Ulnar	2.22±0.1	2.22±0.1	2.24±0.1	52.30±2.9	52.64±1.0	51.32±2.0
p		1.00	0.62		0.81	0.07
	Latency (m/sec) mean±SD			Amplitude (mv/μv) mean±SD		
3. Facial nerves						
Oris	2.92±0.8	2.30±0.5	2.06±0.5	1.14±0.3	1.22±0.5	1.06±0.4
p		0.21	0.57		0.77	0.64
Frontalis	2.98±0.9	3.32±0.4[b]	2.40±0.5[b]	0.92±0.2	0.80±0.3	0.72±0.2
p		0.49	0.01		0.18	0.46
Occuli	2.30±0.5	2.64±0.6	2.10±0.7	1.28±0.6	1.12±1.2	1.64±1.0
p		0.49	0.09		0.40	0.52

[1]Results are expressed as arithmetic mean of five samples ± SD.
Values followed by the same letter in superscript within a row are significantly different from each other ($p < 0.05$).
m/sec = metre per second; mv/μv = milli volt or micro volt

Abnormal spontaneous activities in the form of fibrillation, fasciculation and myotonic discharges were absent and insertional activity and interference pattern

were normal when electromyography was performed on Biceps brachii, Brachioradialis and Abductor digiti minimi muscles on all the occasions.

Blink reflex test showed non-significant differences in the latency and in the early and late responses indicating no effect of both the pyrethroids on facial and trigeminal nerves (Table 4).

Table 4. Blink reflection tests on volunteer spray men[1]

Test day	Latency (m/sec)	Early response (m/sec)	Late response (m/sec)	Difference (m/sec)
Bifenthrin				
0	11.24 ± 1.0^{a}	33.38±4.9	34.80±4.5	1.62 ± 0.6^{b}
4	11.10 ± 1.5^{a} ($p = 0.45$)	40.24±7.5	41.52±8.0	1.28 ± 4.1^{b} ($p = 0.38$)
7	11.16 ± 1.3^{a} ($p = 0.38$)	33.60±4.9	36.20±5.5	2.56 ± 1.1^{b} ($p = 0.39$)
Deltamethrin				
0	10.90 ± 0.5^{c}	33.46±2.9	35.92±2.3	2.46 ± 0.7^{d}
4	10.62 ± 0.7^{c} ($p = 0.26$)	35.58±4.8	37.18±4.7	1.60 ± 0.7^{d} ($p = 0.19$)
7	10.22 ± 0.8^{c} ($p = 0.93$)	33.26±4.5	34.90±4.9	1.64 ± 0.8^{d} ($p = 0.15$)

[1]Results are expressed as arithmetic mean of five samples ± SD.
Values followed by the same letter in superscript within a column are not significantly different from each other ($p < 0.05$).

The lung function tests showed that there was no statistically significant difference in pre- and post-exposure values of FVC, FEV1 and PEFR (Table 5). The mean PEFR at 0 and 6 hours were > 80% of the predicted value. The FEV1 showed >65% of the predicted value for all the subjects on all occasions, except for one each of the sprayers of two insecticides. The difference in PEFR values of all subjects after 6 hours of exposure was non-significant since the predicted value was ≥60%. The PEFR is believed to be less effort dependent and merely determined the anatomy and physiology of the flow through small airways. The FVC and FEV1 of some volunteers were less after 6 hours of exposure than those on day 0 but the PEFR values were preserved to ≥60%. This may be because the FEV1 is thought primarily to reflect the adequacy of patient's forced expiratory effort whereas PEFR is less effort dependent. However, these non-significant differences between pre- and post-exposure values indicate no adverse affect on the lung functions.

The clinical assessment together with biochemical and nerve conduction tests indicate that bifenthrin and deltamethrin should pose no major occupational health hazard to spray men during relevant exposures provided the spraying is done by trained spray men taking all protective measures. Although the dosage of pyrethroids that are recommended for application in vector control have been shown to present negligible risk to human beings at the relevant dosages, it has

been reported that long-term exposure can cause neurotoxic symptoms and skin irritation (He et al. 1989). Karen et al. (2001) reported that dopaminergic neurotransmission is affected by exposure to pyrethroids and may contribute to the

Table 5. Results of the lung function test on volunteer spray men

Subjects	FVC (L)		FEV1 (L)		PEFR (L/second)	
	0 h	6 h	0 h	6 h	0 h	6 h
Bifenthrin						
1. GSZ	2.51	2.24	2.17	2.14	6.96	5.7
2. IRB	2.35	2.5	2.35	2.5	6.03	7.11
3. KSP	2.14	2.06	2.14	2.06	4.75	5.21
4. AVB	3.03	3.04	2.61	2.66	4.84	5.87
5. KMB	2.86	3.17	2.79	3.04	4.19	6.05
Mean ±SD	2.58 ±0.36[a]	2.60 ±0.49[a]	2.41 ±0.28[b]	2.48 ± 0.4[b]	5.35 ±1.10[c]	5.99 ±0.70[c]
p		0.82		0.32		0.29
Deltamethrin						
1. KBP	2.53	2.84	2.53	2.79	8.39	7.67
2. KLP	2.43	1.29	2.43	1.29	4.61	3.49
3. DBP	2.01	2.61	2.01	2.61	7.85	7.67
4. RMP	2.84	3.3	2.84	3.07	5.82	6.43
5. PRP	2.04	2.09	2.00	2.04	4.27	4.33
Mean ±SD	2.37 ±0.35[d]	2.43 ±0.77[d]	2.36 ±0.36[e]	2.36 ±0.71[e]	6.19 ±1.87[f]	5.92 ±1.92[f]
p		0.87		0.99		0.42

Values followed by the same letter in superscript within a row are not significantly different from each other ($p < 0.05$).
FVC: Forced vital capacity
FEV1: Forced expiratory volume in one second
PEFR: Peak expiratory flow rate

overall spectrum of neurotoxicity caused by these compounds. In view of the past experiences, operational supervisor of public health programs should remain alert to such possibilities. It would be relevant to further evaluate possible effects of pyrethroids on long-term exposure.

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