DISCUSSION
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Pesticides have been heavily promoted as a means to increase agricultural productivity and eradicate many vectors-borne diseases. Pesticides are dispersed in water and then sprayed manually on mango trees using mechanized sprayers.

Farmers pesticide formulators and sprayers are the biggest users of Organophosphorous pesticides and therefore they consist of high risk groups pesticide exposure among the farmers and farm workers was raised by the high prevalence of neurotoxicity induced by pesticide poisoning in India and else where in the world. The Natural Resources Defense Council (NRDC) considers pesticides to be one of the top five environmental threats to rural Indians health. In this dissertation a cross-sectional study was conducted on 150 OP pesticide sprayers in the age group of 18 to 45 years having at least one year’s exposure to the pesticides in the rural areas of Mylavaram, Krishna district in Andhra Pradesh. A reference group consisting of 50 male workers unexposed to pesticides in their work place was taken as a control groups. The pesticide sprayers are frequently sprayed insecticides to control the pests of mangoes. The commonly sprayed OP pesticides were Malathion, endosulfan, monocrotophos, methyl parathion etc and their mixtures in different combinations. Pesticides exposure was associated with a number of clinical symptoms including the muscarinic as well as the nicotinic effects pointing towards acute and chronic neurotoxicity.

The overall prevalence of neurotoxicity observed in the pesticide sprayers was 16%. The maximum neurotoxicity was caused in areas where chloropyrifos and dimethoate OP pesticides were sprayed. The most prominent symptoms recorded in the exposed group were the burning sensation in the eyes (15.3%), watering of eyes (14%), headache (12.6%) and dizziness (12%). The clinical manifestations of OP poisoning included, salivation, miosis which were the cardinal features (muscarinic effects) and tremors, tachycardia, mydriasis and sweating (nicotinic effects) in pesticide sprayers. Similar studies on the prevalence of symptoms in OP exposed workers have been reported earlier in the United states and India.
The prevalence of headache, blurred vision and nausea were 2.7, 3.5 and 3.3 times more in US OP applicators than in the non-exposed group. The prevalence of these symptoms were 3.6, 2 and 1.5 times higher in Indian OP formulators. Our finding seem to agree with the results of studies by Ou et al among OP manufacturor employee which identified an increase in the prevalence of mild to moderate cholinergic symptoms in increasing with length of exposure and accompanied by a reduction in blood cholinesterase activity. There have been suggestions for this kind of poisoning to be called as sub acute poisoning distinct from chronic poisoning (chronic neurotoxic syndrome).

The symptoms of OPIDN were also observed in the present study. Parathesia of extremities and weakness of facial and proximal limb muscles were some of the symptoms reported by the pesticide sprayers. Babiniski sign was found to be positive in 11.33% cases there by indicating involvement of lower limb superficial and deep reflexes.

The study also revealed that besides occupational exposure the sprayers also had potential exposure to pesticides indirectly by take home contamination as 92.7% sprayers stored OP pesticides in homes. Curwin et al also reported that the majority of farmers had domestic exposure to OP pesticides in their study.

The reduction in ventilatory capacity confirms earlier study conducted by Rastogi et al recorded their observations on 489 pesticide workers engaged in spraying operations on mango plantations. Their findings of respiratory impairment (36.5%) among the sprayers was found to be significantly higher than reported in this study suggesting that occupational exposure to pesticides had a direct bearing on the respiratory impairment identified in the exposed workers. Similar findings have also been reported by Weimer and worth (1969) Newton and Breslaw (1983) observed asthmatic reactions to a commonly used insecticides. On the contrary same previous reports by Charkravorty (1969), Gupta et al (1980, 1984) and Saiyed et al (1984) did not show any impairment of respiratory health problems associated with abnormal lung function values among the pesticide sprayers.

Organophosphate insecticides showed inhibitory effect on acetyl-cholinesterase (AChE) as the level of AChE was found to be significantly lower than that estimated in the control group, and that is why OP pesticides are also called as anticholinesterase agents. Our finding of decreased levels of AChE in the exposed pesticide sprayers confirm the inhibitory role of organophosphates on AChE reported in earlier studies.
Our study further reported that organophosphate insecticides also induced changes characteristic of oxidative stress. Malondialdehyde (MDA) and Glutathione (GSH) are proved to be the effective bio-markers to study oxygen free radical effects on lipids due to toxicity of pesticides\textsuperscript{13,14} leading to impairment of lung function by both free radical and oxidant exposure and the increased lipid peroxidation was associated with pulmonary airway narrowing or bronchial obstruction in the exposed population there by supporting previous work of 1997\textsuperscript{15}. The decreased AchE levels observed in the exposed workers reflected the inhibition of cholinesterase activity due to pesticide exposure in the body. Similar observations were reported earlier on acetyl cholinesterase activity during O.P pesticide toxicity\textsuperscript{12,16}.

The pesticide toxicity in sprayers leads to a decrease in glutathione and elevated levels MDA among the sprayers. Another study \textsuperscript{17} on chronic exposure to organophosphate insecticides formulators showed increased activities of catalase, superoxide dismutase and glutathione peroxidase in erythrocytes. The available data on experimental animals and in vitro studies showed that the enzymes associated with antioxidant defense mechanisms are altered under the influence of pesticides \textsuperscript{18,19,20}. The results of the present study indicate that glutathione linked enzymes involved in cellular antioxidant defence system in human erythrocytes were affected following exposure to organophosphate pesticides. The decreased GSH levels in blood samples accompanied by an increase in MDA level probably indicates an adaptive measure to tackle any insecticide accumulation in the body tissues. Erythrocytes GSH efficiently scavenges toxic free radicals and are partly responsible for production against lipid peroxidation due to acute /chronic pesticide exposure \textsuperscript{21,22}.

The inhibition of AChE observed in the pesticide sprayers resulted in the accumulation of Ach which may cause stimulation of lymphocytes and elevated concentration of cellular cGMP, increased lymphocytes motility and cytotoxicity \textsuperscript{23}. Since AChE is a membrane bound enzyme, GGT contd interact with amino acid neurotransmitter (Ach) which may be removed from the binding with AChE and may result in decreased activity of AChE \textsuperscript{24} while the decreased levels of GSH may be due to its participation in the activation, initiation and progression of lymphocytes \textsuperscript{25}, mortality of lymphocytes due to increased accumulation of AChE may cause the depletion of lymphocytes GSH in human poisoning \textsuperscript{26}.

The OP pesticide exposure increased cholinergic stimulation as well as alteration of biochemical parameters (reduced GSH, decreased AchE and increased MDA) in the exposed pesticide sprayers may serve as sign posts for pesticide toxicity in humans. The reduction of GSH in blood may have resulted from the activity of GPx in reducing lipid hydroperoxides to stable non-radical lipid alcohols utilizing GSH as the source of reducing equivalents. Alternatively, the observed GSH reduction may be the direct utilization of GSH as an antioxidant in terminating free radical reactions initiated by organophosphorous pesticides. The biochemical changes observed in the
The higher levels of MDA and decreased activity of AChE indicated that organophosphate pesticides induces changes characteristic of oxidative stress and the reactive oxygen species (ROS) have been implicated in the toxicities of the pesticides.

The determination of urinary dialkyl phosphates (DAP) in the exposed group showed that DMTP was the commonest metabolite found in 99% of the urinary samples collected. The high levels of DAP in the urine samples are indicative of occupational and environmental exposure to OP pesticides. The wide spread use of phosphoric esters estimation in urinary samples is reported to be more sensitive and accurate and reliable than the estimation of the blood cholinesterase activity (AchE) due to its poor sensitivity and its activity does not significantly vary at exposure levels commonly encountered in occupationally exposed subjects. Previous studies have also recommended the determination of OP pesticides metabolites in urinary samples of exposed workers due to occupational risks.

The urinary alkyl phosphates are metabolites derived from a fragment common to many members of this class of compounds by the action of esterases. However in his study found that the most common metabolites seen was DMTP. In the present study excretion of DMTP as well as DMP was associated with reported potential exposure to methylated OPs so it is reasonable to assume that in the population at the time of study urinary DMTP was organophosphate metabolites.

The nerve conduction studies were carried out in both motor and sensor nerves of upper and lower limbs –median, ulnar and sural nerves were used for sensory nerve conduction tests while median, peroneal motor nerves were tested for motor conduction. The nerve conduction velocity was also correlated with type of pesticide being sprayed were exposed. Chlorpyrifos exposure resulted in worse peroneal motor nerve conduction velocity and ulnar sensory amplitude followed by methyl parathion moderately affecting both motor and sensory ulnar nerve conduction. The other OP pesticides used by the sprayers such as Diazinon, Mevinphos and Dimethoate showed no significant effect on nerve conduction in the present study. The finding of impairment in nerve conduction on exposure to OP pesticide in the pesticide sprayers indicate early peripheral neurotoxicity resulting from excess accumulation of acetylcholine at the nerve endings due to inhibition of AChE. Acetylcholine is a cholinergic neurotransmitter and possess excitatory function and is released at the preganglionic and post ganglionic sympathetic and parasympathetic nerve endings thereby impairing the nerve conduction velocity among insecticide exposed workers.
Our study showed that both orthodromic and motor conduction were equally affected as a result of exposure to OP pesticide indicating an acute sign of neurotoxicity. Loss of Ach (Enzyme) function allowed accumulation of AChE peripherally at cholinergic neuroeffector junctions (muscarinic effects) and autonomic ganglion (nicotinic effects) as well as centrally. In view of this the effect organs become over stimulated by the excess Ach (Ach is the impulse transmitting substance) and therefore affects nerve impulse transmission from nerve fibers to smooth and skeletal muscle cells.

The hematological profile was done in the study population and the findings were compared with those obtained in the reference group. The study showed no significant differences in the mean values of hematological parameters thereby indicating that OP pesticides do not cause hematotoxicity. However, reported adverse effects of OP pesticides on hematological parameters.


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