EVALUATION OF SUSPECTED CHRONIC PESTICIDE POISONING AMONG RESIDENTS NEAR AGRICULTURE FIELDS

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The present study was performed to evaluate the incidence of organophosphorus toxicity among agrarian and non agrarian subjects residing near agriculture fields. The location of this study was Nawakot village, Multan. From the cotton producing area of Multan, 225 volunteers (farmers) including 103 females and 122 males were selected. Children <12 years of age constitute 15% of the population. A total of 100 volunteers (non agrarians) from Multan city were taken as control. Blood (4 ml) was drawn from the volunteers to test the level of acetylcholine esterase (Ach E) in plasma. The blood samples were then analysed at the laboratory of National Poison Control Center (NPCC). Organo-phosphate (OP) & carbamates (CM) both act to block Ach E hydrolysis, necessary for synaptic response in the CNS. Acute illnesses were seen in 6 (2.67%), children (group 1). They had fever and signs of pulmonary infections. Generalised weakness was found in 9 males and 13 females. Paraesthesia was found in 11 volunteers of group IV. Blood sampling test revealed that 6 volunteers (2.67%) had plasma Ach E below 5300 IU/ml (< 50% reduction), whereas 4 volunteers had Ach E level between 5300 - 5500 IU/ml (< 45% reduction), 81 volunteers fall in group “c”, and 126 individuals had an Ach E reduction of at least 25% and 8 volunteers had the serum cholinesterase level above 10000 IU/ml. None of volunteers had the value above 11000 IU whereas plasma Ach E level of control population was between 11500 - 13500 IU/ml. Medical tests of the level of Ach E in plasma suggest that the overall incidence of poisoning from exposure to OP & CM is quite high, and appears to be consistent with the results from other studies in other developing countries.

Indiscriminate use and improper handling of synthetic pesticides in agriculture have resulted into serious problems for human health in many developing countries. However, the true extent of the problem is hard to determine for a variety of reasons. First, farmers with mild pesticide poisoning often do not report because treatment services are costly, inaccessible, or fear that drawing attention to themselves may result in the loss of employment opportunities. Second, health-care professionals in rural areas often fail to correctly diagnose poisoning, as many of the related symptoms are quite general in nature or mimic other common health problems e.g. headaches, dizziness, vomiting (FAO, 2001) etc. At least 20,000 workers die from exposure every year, the majority in developing countries. World Health Organization.

Although the health hazards of pesticides are serious, support from policy makers for remedial measures has been lukewarm in developing countries. There is a widespread concern about diverting resources to alternative pest control methods when poverty, illiteracy and infant mortality are still major problems. In part, the resistance of policy makers is due to uncertainty about the severity of the problem, its sources, and suitable interventions. Their uncertainty is understandable, since systematic studies of the health effects of pesticides are scarce. Most existing studies rely on farmers’ self-reported symptoms, as appropriate pathological tests are costly and relatively difficult for many developing country institutions to administer.

To assess the potential health hazards of pesticides, the NPCC with the technical collaboration of WHO studied the pesticide poisoning among the families of agriculture workers. The study included clinical examination by doctors from the NPCC, along with blood tests for cholinesterase inhibition due to contamination by organophosphates and carbamate. Epidemiological studies have linked carbamates (CM) and organophosphates (OP) with foetal death, hormonal changes, DNA damage, birth defects, and abnormal sperm and ova. In addition, OP, as a class of insecticides,
has been linked with Non-Hodgkin’s lymphoma, leukaemia, and lung cancer. In children OP have been linked to aplastic anaemia, the failure of the bone marrow to produce blood cells, and leukaemia. Children with asthma may have severe reactions to OP in particular.

Human beings have three types of cholinesterases: red blood cell (RBC) cholinesterase, called “true cholinesterase”; plasma cholinesterase, called “pseudocholinesterase”; and brain cholinesterase. RBC cholinesterase is the same enzyme that is found in the nervous system, while plasma cholinesterase is made in the liver. When a cholinesterase blood test is taken, two types of cholinesterases can be detected. Physicians find plasma cholinesterase readings helpful for detecting the early, acute effects of organophosphate poisoning, while RBC readings are useful in evaluating long-term, or chronic, exposure. In this study we only performed the plasma AchE level due to limited resources.

Human exposure to cholinesterase-inhibiting pesticides can result from inhalation, ingestion, or eye or skin contact during the manufacture, mixing, or applications of these chemicals. Signs and symptoms of cholinesterase inhibition from exposure to CM or OP include the following:

1. Mild cases: tiredness, weakness, dizziness, nausea and blurred vision.
2. Moderate cases: headache, sweating, tearing, drooling, vomiting, tunnel vision, and twitching.
3. Severe cases: abdominal cramps, diarrhea, muscular tremors, staggering gait, pinpoint pupils, hypotension, slow heartbeat, breathing difficulty, and possibly death, if not promptly treated by a physician.

SUBJECTS AND METHODS

To investigate the health impacts of pesticide use, structured questionnaires designed by NPCC team were used to collect information on farming systems, pesticide use and practices, applicator precautions, and protective measures. The study was carried out to determine the incidence of organophosphate toxicity in the families of agriculture workers who were not involved directly in agriculture. Outskirts of Multan city, Nawakot village, was selected, that is basically, a cotton producing area. The families of farmers, include children, young and elderly of both genders. A total of 225 volunteers were evaluated in three days among which 103 (46%) were females and 122 (54%) were males. Children, < than 12 years of age constitutes 15% of the population. All participants were examined by doctors from NPCC. 100 volunteers from Multan city and its outskirts were taken as control population (non-agrarians). They all were healthy individuals, who underwent the same protocol of clinical examination and blood test (Fig. 1 and 2).

Using clinical examination results, the team collected the blood samples for cholinesterase inhibition test. In each case, a 4 ml blood sample drawn from the volunteer was used to test the level of AchE in plasma (Serum Butyryl Cholinesterase Kit, Randox Laboratories Ltd. UK). The normal value for serum AchE ranges between 5300 – 13300 IU/ml according to the kit used. The blood samples were then analysed at the laboratory of NPCC. OP and CM act so as to inhibit acetylcholine hydrolysis, a necessary task for synaptic response in the central nervous system. The presence of cholinesterase inhibiting chemicals prevent the breakdown of acetylcholine. Acetylcholine can then build up, causing a “jam” in the nervous system. The normal value for serum cholinesterase according to the kit used in this study ranges between 5300-13300 IU/ml. Groups have been constituted showing age and cholinesterase levels (Fig. 3).

RESULTS

Total 225 volunteers were included in the study out of which 122 were males and 103 were females. Various age groups has been constituted, the largest population size was between 20-45 years (45%), and the smallest was found in group I (< 12 years) that constitutes 15% of the total (Fig. 1 & 2).
History taking and physical examination revealed that 64 volunteers were symptom free that includes 39 males and 25 females. A total of 133 volunteers (55 males and 78 females) had complaints of decrease appetite (59.1%), abdominal pain in 103 (45.78%), and diarrhoea in 94 volunteers (41.78%). Acute illnesses were seen in 6 (2.67%) children (group I), who had fever and signs of pulmonary infections. Generalised weakness and easy fatigability were found in 9 males and 13 females. Peripher al numbness and tingling were present in 11 volunteers of group IV (Fig. 3).

Building upon the initial clinical examination, the medical team carried out blood tests for 225 volunteers to check for cholinesterase enzyme inhibition from exposure to organophosphate and carbamate pesticides. The results displayed in graph IV indicate that (2.67%) 6 volunteers had plasma AchE below 5300 IU/ml (≤ 50% reduction), whereas 4 volunteers had AchE level between 5300 and 5500 IU/ml (≤ 45% reduction), 81 volunteers fall in group “C”, 126 individuals had an AchE reduction of at least 25%, and 8 volunteers had the serum cholinesterase level just above 10000 IU/ml. No single individual had the value above 11000 IU where as plasma AchE level of control population ranged between 11500 – 13500 IU/ml with an average of 12500 IU/ml.

We calculated the correlation of the blood test results against an index of equally weighted symptoms that are commonly associa-

**Table 1: Age groups of volunteers and control population**

<table>
<thead>
<tr>
<th>Group</th>
<th>Group I &lt; 12 Years</th>
<th>Group II 12 – 20 Years</th>
<th>Group III 21 – 45 Years</th>
<th>Group IV &gt; 45 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volunteers</td>
<td>34</td>
<td>47</td>
<td>101</td>
<td>43</td>
</tr>
<tr>
<td>Control</td>
<td>0</td>
<td>25</td>
<td>35</td>
<td>40</td>
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EVALUATION OF SUSPECTED CHRONIC PESTICIDE POISONING

DISECUSSION
Unintentional poisonings kill an estimated 355,000 people each year.41,42 Two-thirds of these deaths occur in developing countries, where such poisoning is strongly associated with excessive exposure to, and inappropriate use of, toxic chemicals. In many such settings, the toxic chemicals may be emitted directly into soil, air and water.43

There are many pesticides with thousands of trade names. Two-thirds of their total use is in agriculture.42 Chronic pesticide exposure is often a problem in occupational settings, particularly among poor rural populations, where men, women and children all work and live in close proximity to fields on which chemicals are applied and stored.

There is paucity of data on the possible deleterious effects of chronic exposure to OPCs in occupational and/or environmental settings. In general, the literature brings out three types of non-acute OPC poisoning: occupational exposure with reductions in AchE levels; occupational exposure with no reduction in AchE levels; and environmental exposure. However, the relationships between chronic exposure, AchE inhibition and symptoms do not, as yet, seem to be well established.

Available evidence suggests that there is a possibility of adverse effects occurring below OPC concentrations that are generally considered to be safe based on measurements of AchE inhibition; i.e. these effects are not clearly related to the inhibition of cholinesterases. Studies on health hazards to agricultural workers who handle, store and use OPC pesticides have documented a range of non-specific self-reported symptoms that have been attributed to chronic exposure. These include: burning or prickling of the skin; tingling or numbness of hands and face; muscular twitching or cramps in the face, neck, arms and legs; respiratory symptoms, including chest pain, cough, running nose, wheezing, shortness of breath, irritation of the throat; excessive sweating; nausea, vomiting, diarrhoea; excessive salivation; abdominal pain; lacrimation and irritation of the eyes; difficulty in seeing; restlessness; difficulty in falling asleep; trembling of hands; and irritability.1,24 In this study acute toxicity was observed in 13.5% cases below 12 years of age.22, 31 Volunteers showed 59.1% gastrointestinal symptoms referred as loss of appetite, off and on abdominal pain and diarrhoea.38 64 individuals had no symptoms and their serum cholinesterase levels ranged from 7500 – 1100 IU/ml. No individual in the study was directly involved in the farming or spray even then they are suffering from sub clinical and delayed effects of pesticide toxicity. The expected source of exposure observed was the use of empty cans of pesticide as drinking water reservoir, storage of pesticides in houses and bad hygiene. If we look into serum cholinesterase level it was observed that 6 individuals had the value below 5300 IU/ml that means acute exposure whereas rest of them had their cholinesterase level within range, although none of them reached the upper limit. This shows that the individuals even with cholinesterase levels within range were also suffering from sub clinical long-term exposure to organophosphates.

After literature search and evaluation of our findings we came to the conclusion that sub clinical damage does occur, however longer follow up studies are needed. It is suggested that the government in collaboration with pesticide industry should encourage awareness programs for the farmers that may help in the reduction of pesticide mortality and morbidity.

Detailed, long-term studies of occupational or environmental exposures to OPC are needed to distinguish the effects of the active OPC. Subtle abnormalities on neurological examination, such as impaired two-point discrimination and vibration sensation, have also been reported in workers chronically exposed to OPCs.4,39 Some report evidence of nerve abnormalities during occupational exposure9,38 while others do not.11,22 A recent study from Sri Lanka has shown inhibition of AchE enzyme activity and impairment of sensory and motor nerve conduction due to long-term, low-level exposure to OPC.25 Evidence of toxicity was found not only among the farmers who directly handled (sprayed) OPCs, but also among those employed in inland fisheries living within a 25 km radius of the cultivated land, who were not directly exposed.

Chronic organophosphate-induced neuropsychiatric disorders (COPIND) occur without cholinergic symptoms, and although the underlying mechanisms are not established, they do not seem dependent on AchE inhibition.6,28,29,34 Clinical features reported include: anxiety disorder; depression; psychotic symptoms; dysthyemic disorder.
(DSM-III-R); problems with short-term memory, learning, attention, information processing, eye-hand coordination and reaction time; autonomic dysfunction; and extra pyramidal symptoms. Similar clinical features have also been reported by soldiers suffering from the much-publicised Gulf-war Syndrome, which led to the, so far unproven, hypothesis that the illness was caused by chronic exposure to chemical agents with similar effects to OPCs. Some organophosphates (such as methamidophos, leptoephos, fenthion, merphos) inhibit a second enzyme, neuropathy target esterase (NTE). Severe inhibition of this enzyme may be accompanied by a peripheral neuropathy 10-14 days after exposure. This delayed neuropathy typically affects the motor and sensory nerves of the legs and is caused by a “dying back” of the distal axons. Symptoms include tingling sensations with weakness and ataxia that develop into paralysis in severe cases. Effects are often reversible but may persist. In our study 22 individuals have the complaints of weakness and easy fatigability among which 11 had the symptoms of peripheral neuropathy indicating low level long term exposure.

Chronic toxicity to OPCs may be related to the rate of regeneration of AchE and the speed at which pesticide metabolites are hydrolysed and eliminated from the body. This ‘fast’ or ‘slow’ enzymatic hydrolysis status seems to be determined by gene polymorphisms of hydrolyases such as paraoxonase. However, in some situations where there is chronic exposure to OPC, there seems to be poor correlation between evidence of toxicity and the degree of AchE inhibition. It may well be that toxicity in these situations is mediated more by other mechanisms, such as oxidative stress through OPC-induced generation of free oxygen radicals leading to lipid peroxidation, rather than inhibition of AchE.

In this study, we have assessed the incidence and determinants of pesticide poisoning among the family members of farmers in Pakistan. We believe that our results are of particular interest because they rely on explicit medical parameters for poisoning, rather than conventional self-reporting of symptoms by farmers. Medical tests of the level of AchE in plasma suggest that the overall incidence of poisoning from exposure to OP and CM is quite high, and appears to be consistent with the results from other studies in other developing countries.

Using the laboratory test results as bench-marks, we find that self-reported symptoms have very weak associations with actual poisoning. Both the incidence of poisoning and their own apparent inability to distinguish its symptoms from other health problems suggest that regular checkups and blood tests should be conducted for those who were directly or indirectly exposed to toxic organophosphate and carbamate pesticides although there is no definite relationship established yet between the signs and symptoms of poisoning and AchE activity.

REFERENCES
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