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ABSTRACT	A prospective study of changes in some selected biochemical markers in the acute phase of OPI poisoning was undertaken with the aims of determining their usefulness as a predictor or diagnostic tool for IMS and with the aims of ascertaining the possible involvement of specific organs/tissues such as skeletal and cardiac muscles, liver, pancreas and kidneys. The biochemical markers selected for the study were red blood cell cholinesterase (RBC ChE), serum cholinesterase (SE ChE), total serum creatine kinase (CK-Total), serum creatine kinase myocardial fraction (CK MB), serum aspartate aminotransferase (AST), serum gammaglutamyl transferase (GGT) , serum amylase, serum creatinine and serum electrolytes (Na+ and K+). These biochemical markers were measured in the first week of organophosphorous insecticide poisoning (OPI) in 60 patients, who were admitted to the Peradeniya Teaching Hospital and the General Hospital Kandy in the period 1st April, 1995 to 31 st March, 1996. Among them, 24 cases had features of intermediate syndrome (IMS). Sixty healthy individuals matched for age and sex served as a control group. The hypotheses entertained were that, following OPI intoxication, the biochemical markers specified above will serve as predictors or diagnostic tools for IMS and also serve as indicators of involvement or damage of different organs/ tissues. The methods of study included clinical procedures to obtain clinical data and laboratory procedures to measure biochemical parameters mentioned above. The mean RBC ChE activity of Day 1 OPI poisoning in the IMS group and in the other group without IMS was 88.6percent and 82 percent of the control mean value, respectively. Similarly, the mean SE ChE activity of Day 1 OPI poisoning in the IMS group and the other group without it, was 41 percent and 50 percent of the control mean value respectively. The difference in the activities of both of these enzymes, between IMS group and others without IMS, became clearer when a series of measurements from Day 1 to Day 7 of poisoning were made. The lowest mean activity of RBC ChE in the IMS group was 1 8 percent of the control mean value on Day 7 of poisoning, while that in the other group without IMS was 49 percent of the control mean value on Day S. Similarly, the lowest mean activity of SE ChE in the IMS group was 1 3 percent of the control mean value on Day 3 of poisoning, while that in the other group without IMS was 39 percent of the control mean value on'Day S. Compared to without IMS group, there was severe degree of inhibition of both

of theses enzymes in the IMS group. It appeared that, the measurement of these enzymes at least for first three consecutive days of OPI poisoning, can predict the development of IMS. It is also important to note that the severe degree of inhibition of these two cholinesterase activities may be responsible for the accumulation of excess amount of acetylcholine in the cholinergic nerve endings over a longer duration of time than the normal. It has been proven by animal experiments that, prolonged receptortransmitter interaction at the cholinergic nerve endings can initiate cellular injury and produce skeletal and cardiac muscle myopathies and pancreatitis. The highest activity of total serum CK of 1040 percent of the control mean value (1 0 fold increase) in the IMS group was found on Day 3 of OPI poisoning, while that of the without IMS group was 472 percent of control on Day 2. In the IMS group, the elevated activity of total serum CK was sustained over a period of first week of OPI poisoning, while that in the other group without IMS, it came towards normal on Day 5 of poisoning. This higher and more sustained elevated activity of total serum CK found in the IMS group of OPI poisoning, lend support to the hypothesis that, necrosis of skeletal muscle seen in experimental animals after OPI poisoning is equally likely to occur in humans too. The 'intermediate syndrome' seen in humans following OPI poisoning, although not investigated histologically, behaves biochemically in a similar manner seen in animals with muscle necrosis . The Day 3 tenfold increase with sustained elevation above normal over a period of first week of OPI poisoning of the total serum CK activity showed that, it is useful as a diagnostic tool for IMS. The serum concentration of cTnl reached relatively at lower level (mean +/SO of 0.03 +/- 0.014 ng/ml) compared to other muscle related biochemical indicators on Day 2 of poisoning. This indicates that the myocardium is less damaged in OPI poisoning than the skeletal muscle, which in some cases may be severely necrosed. However, its increase in the serum level above 0.1 ng/ml following OPI intoxication can be used as a marker of cardiac muscle involvement. The serum creatine kinase myocardial fraction (CK MB) isoenzyme also had its highest activity of 392 percent of the control mean value in the IMS group on the same Day 3 of poisoning, while that in the group without IMS was 187 percent of control on Day 2. The CK MB is also distributed in a significant proportion in the skeletal muscle. The relatively lower level of cardiac troponin I and relatively higher level of total serum CK activity supported that, the major contribution of this elevated activity of the serum CK MB in the IMS group of OPI poisoning was from the skeletal muscle with possible little contributions from the cardiac muscle. Therefore, the measurement of serum CK MB in OPI poisoning cases is not a reliable marker to rule out cardiac muscle involvement. The measurement of serum cardiac troponin I seems to be the best alternative to fulfill this purpose. Although the elevation of mean serum AST activity in the IMS group was marginal, yet it was

statistically significant on Day 1 (153 percent control), Day 2 (157 percent), Day 3 (193 percent) and Day 5 (146 percent). But the elevation in the activity of this enzyme in the other group without IMS was never statistically significant from the control. The source of this mild increase in the serum AST activity in the IMS group appeared to be either from the liver, the cardiac or the skeletal muscles or all of them. But the highly elevated activity of the total serum CK and relatively low levels of serum cTnl and GGT found in the same first week of OPI poisoning supported that, the major contribution of this mildly elevated activity of serum AST was from the skeletal muscle itself and not from the cardiac muscle or the hepatic tissue. It seemed that, compared to other biomarkers, the measurement of serum AST activity in OPI poisoning was not so organ specific. Unlike other biochemical measurements, which had their respective abnormal values during first week of poisoning, serum GGT had its maximum activity of 354 percent of the control mean value on Day 11 of poisoning. Its elevated activity started to rise steeply first on Day 7 and continued up to Day 15 of poisoning. This rise in activity is compatible with repair of injured tissues. Serum GGT may therefore be used as a marker of the active reparative process going on in the necrosed part of skeletal muscles and other tissues following OPI poisoning. The highest activity of serum amylase in the IMS group was on Day 2 of poisoning and was 482 percent of the control value, while in the other group, it was 246 percent of the control mean value on Day 1. This may be due to the cholinergic stimulation of the exocrine function of the pancreas. The source of raised levels of serum creatinine on Day 1 (107.5 Ilmol/L), Day 2 (106.6 Ilmol/L) and on Day 3 (100.9 Ilmol/L) in the whole study group of OPI poisoning and the highest mean serum creatinine level of 109.6 Ilmol /L in the IMS group on Day 2 of poisoning, seems to be due to alteration in the levels of high energy phosphate compounds in the skeletal muscle. This view is supported in other studies. Except for individual variations in the levels of PCV, Hb, and serum electrolyte (Na + and K+) levels, the levels of these biochemical parameters in both study groups remained unchanged on an average basis.