Summary

Pesticide self-poisoning is a major health problem in India mostly affecting the agricultural population. OP poisoning is responsible for most suicidal deaths in Southern part of India. Majority of them were males belonging to the age group of 21-30 years. Majority of the people consumed WHO Ia category of pesticide with intentional harm. Majority of them received GI decontamination followed by atropine and few patients received glycopyrrolate with atropine in combination. Based on the severity of poisoning, different patients received different regimens of pralidoxime. Outcome analysis of OP poisoning with different treatment regimen showed that gastric lavage and activated charcoal did not show any significant benefit in the patient’s outcome. Addition of glycopyrrolate with atropine improves the quality of treatment with reduction in number of adverse drug reactions of atropine. Use of oximes in OP poisoning is controversial. WHO recommends the use of 500mg/hour pralidoxime infusion till the patients are asymptomatic, but other randomized clinical trials and meta-analysis suggest controversial opinion regarding the effectiveness of pralidoxime therapy in OP poisoning. Different opinions exists regarding the dose, duration of administration and dosage regimen of oxime. There are very limited numbers of studies available in the literature which recommend the most suitable regimen of pralidoxime in OP poisoning patients. Hence a study was carried out to assess the safety and effectiveness of different dosage regimen of pralidoxime by comparing the different dosage regimen of pralidoxime with clinical outcomes. OP poisoned patients were categorized into four different groups based on the type of pralidoxime dosage regimen received in the hospital. Patients with higher severity scores received continuous infusion of PAM either as 500mg/hour or 1g/hour. Primary outcome of the different dosage regimen of pralidoxime were assessed in terms of percentage of recovery, percentage of sequel and percentage of fatality. On comparing the different dosage regimens of pralidoxime it was observed that in the continuous infusion groups there was a significant increase in recovery rate, lower incidence of sequel and fatality when compared to control and intermittent dose. Among the continuous infusion group 1g/hour infusion showed better recovery and lower mortality rate when compared to 500 mg/hour infusion group. Sub-group analysis of primary outcome in moderate to severe poisoning cases showed better outcome in terms of recovery in continuous infusion group. The secondary outcomes of the different dosage regimens of pralidoxime were assessed in terms of mean hospitalization days, mean ventilatory days, mean atropine requirement and percentage of
intermediate syndrome. Comparing the secondary outcomes with the different dosage regimen of pralidoxime, the mean hospitalization period was less in 500mg/hour infusion group when compared to other groups. However the mean ventilator period was comparatively less in the both infusion groups when compared to control and intermittent group. The incidence of intermediate syndrome was comparatively less in 500mg/hour infusion group when compared to other groups. The mean atropine requirement was comparatively less in the both infusion groups when compared to control and intermittent groups. Intergroup efficacy analysis of mean hospitalization and mean ventilatory period among the 4 groups by Dunn’s multiple comparison showed a significant difference only in the ventilatory period between control group and 500 mg/hour infusion group. Sub group analysis of secondary outcomes in patients who recovered from moderate to severe poisoning showed better outcome in continuous infusion group. Overall, continuous infusion of pralidoxime showed significantly better clinical efficacy than other regimen in terms of primary and secondary outcomes. Among the continuous infusion, 1g/hour showed better efficacy than 500mg/hour regimen in terms of percentage of recovery or percentage of mortality. The inter group analysis showed that 500 mg/hour infusion group had significant difference in the ventilatory period when compared to control group. Use of oximes in OP poisoning is controversial. WHO recommends the use of 500mg/hour pralidoxime infusion till the patients are asymptomatic, but other randomized clinical trials and meta-analysis suggest controversial opinion regarding the effectiveness of pralidoxime therapy in OP poisoning. Different opinions exists regarding the dose, duration of administration and dosage regimen of oxime. There are very limited numbers of studies available in the literature which recommend the most suitable regimen of pralidoxime in OP poisoning patients. Hence a study was carried out to assess the safety and effectiveness of different dosage regimen of pralidoxime by comparing the different dosage regimen of pralidoxime with clinical outcomes. OP poisoned patients were categorized into four different groups based on the type of pralidoxime dosage regimen received in the hospital. Patients with higher severity scores received continuous infusion of PAM either as 500mg/hour or 1g/hour. Primary outcome of the different dosage regimen of pralidoxime were assessed in terms of percentage of recovery, percentage of sequel and percentage of fatality. On comparing the different dosage regimens of pralidoxime it was observed that in the continuous infusion groups there was a significant increase in recovery rate, lower incidence of sequel and fatality when compared to control and intermittent dose. Among
the continuous infusion group 1g/hour infusion showed better recovery and lower mortality rate when compared to 500 mg/hour infusion group. Sub-group analysis of primary outcome in moderate to severe poisoning cases showed better outcome in terms of recovery in continuous infusion group. The secondary outcomes of the different dosage regimens of pralidoxime were assessed in terms of mean hospitalization days, mean ventilatory days, mean atropine requirement and percentage of intermediate syndrome. Comparing the secondary outcomes with the different dosage regimen of pralidoxime, the mean hospitalization period was less in 500mg/hour infusion group when compared to other groups. However the mean ventilator period was comparatively less in the both infusion groups when compared to control and intermittent group. The incidence of intermediate syndrome was comparatively less in 500mg/hour infusion group when compared to other groups. The mean atropine requirement was comparatively less in the both infusion groups when compared to control and intermittent groups. Intergroup efficacy analysis of mean hospitalization and mean ventilatory period among the 4 groups by Dunn’s multiple comparison showed a significant difference only in the ventilatory period between control group and 500 mg /hour infusion group. Sub group analysis of secondary outcomes in patients who recovered from moderate to severe poisoning showed better outcome in continuous infusion group. Overall, continuous infusion of pralidoxime showed significantly better clinical efficacy than other regimen in terms of primary and secondary outcomes. Among the continuous infusion, 1g/hour showed better efficacy than 500mg/hour regimen in terms of percentage of recovery or percentage of mortality. The inter group analysis showed that 500 mg /hour infusion group had significant difference in the ventilatory period when compared to control group. Very limited studies are available regarding the kinetics of pralidoxime and its clinical outcome. Even though RCTs were conducted with higher doses of pralidoxime, there were no sufficient kinetic studies available for the blood level of pralidoxime with its doses in the clinical setup. So this study was planned based on the kinetics of pralidoxime with its different dosage regimen to study the outcome in OP poisoning patients. Blood level of pralidoxime was estimated from serum by using HPLC method. Continuous infusion of pralidoxime maintained an uniform higher blood concentration when compared to intermittent dosing which showed large fluctuation in the blood concentration levels and as the serum concentration was higher, better was the recovery rate. Higher the serum levels of pralidoxime greater the reactivation of AchE. The reactivation rate was higher in continuous infusion groups when compared to intermittent
dosing. A significant negative correlation was observed with serum pralidoxime concentration and creatinine clearance. Hypotension was the most common adverse effect observed with higher blood levels of pralidoxime which reversed on reduction of the dose.

Acute methyl parathion poisoning is the most common cause of poisoning among all the OP compounds. It falls under the category of WHO Ia which constitutes extremely hazardous compounds and is the most common cause of death among OP poisoning because of its diversity in kinetics in humans. Outcome analysis of different dosage regimen of PAM showed that the 1g/hour infusion group had a better outcome in terms of recovery when compared to the other groups. Blood level of methyl parathion is negatively correlated to AChE levels and GCS indicating that it directly correlated with severity of poisoning. The higher blood level of pralidoxime greatly influences the methyl parathion level after treatment. Blood level of PAM had a significant effect in the outcome of these patients. There are very few studies available to understand the clinical outcome and kinetics of methyl parathion in humans. The oxime dosage plays an important role in clinical outcome of methyl parathion poisoning.