

Role of Intravenous Magnesium Sulphate in Predicting Outcomes of ICU in Acute Organophosphate Poisoning

Sri Harsha J.¹, Srinivas Prabhu N.C.², Ronak M. Raheja³, O.R. Ranjan¹

Author's Affiliation:

¹Post Graduate ²Professor and HOD ³Under Graduate, Department of Emergency Medicine, Kempegowda Institute of Medical Sciences, Bengaluru, Karnataka 560004, India.

Corresponding Author:

Sri Harsha J., Post Graduate, Department of Emergency Medicine, Kempegowda Institute of Medical Sciences, Bengaluru, Karnataka 560004, India.
E-mail: drnakraheja@gmail.com

Received on 10.06.2017,

Accepted on 28.06.2017

Abstract

Organophosphorus chemicals (OPs) are the pesticides most often involved in serious human poisoning in developing countries like India. Treatment of intoxication with OPs conventionally involves atropine for reduction of muscarinic signs and oximes that increase the rate of hydrolysis of the phosphorylated enzyme acetylcholinesterase (AChE). Although oximes (pralidoxime or obidoxime) are traditionally considered specific antidotes and used in the management of such poisoning, their efficacy remains a major issue of debate. Thus, the goal of this clinical study was to elaborate the value of magnesium sulfate (MgSO₄) in the management and outcome of acute OP insecticide poisoning. This unicenter, randomized trial study was conducted on patients who were acutely poisoned with OPs and admitted to Kempegowda Institute of Medical Sciences & Hospital. In this study patients were randomly divided into 2 groups (25 patients each). Control group and test group. Control group received conventional management with injection atropine and injection PAM while the test group in addition to above received intravenous Magnesium sulphate. Magnesium sulphate was administered at dose of 4 g/day intravenous infusion over 4 hours within first 24 hours after ingestion. There was a significant decrease in number of days of ventilation ($z=-2.1$, $p=0.04$) and days of ICU stay ($z=-4.1$, $p<0.001$) on independent Mann Whitney Tests in patients who received MgSO₄ than those who had not received MgSO₄. The mortality rate, total atropine required and hospitalization days of patients who received MgSO₄ treatment were significantly lower than those who had not received MgSO₄ ($P<0.05$). It is concluded that administration of MgSO₄, in a dose of 4 g/day concurrent to conventional therapy, in OP acute human poisoning is beneficial by reducing the hospitalization days and rate of mortality.

Keywords: Human; Magnesium Sulphate; MgSO₄; Organophosphate Poisoning; OP; Treatment; Mg²⁺.

Introduction

Organophosphorus poisoning (OP) is the most common poisoning in India because of its easy availability. Organophosphorus pesticides are used widely for agriculture, vector control, and domestic purposes. Despite the apparent benefits of these uses acute organophosphorus pesticide poisoning is an increasing worldwide problem, particularly in rural

areas. Organophosphorus pesticides are the most important cause of severe toxicity and death from acute poisoning worldwide, with more than 2,00,000 deaths each year in developing countries. Unintentional and intentional OP poisonings continue to be a significant cause of morbidity and mortality in India [1]. The farmers are the most hard working and underpaid socioeconomic group in India. They work for hours in the fields without sufficient equipment and machines and despite their

vigorous efforts, they fail to meet their financial requirements. Many of the people consuming organophosphorus poison, that were appearing in the emergency department were suffering from financial insufficiency, and were usually un-insured. Thereby this study was taken up to decrease the cost involved in the treatment of these kind of poisonings. This study was performed in Kempegowda Institute of Medical Sciences a reputed tertiary care hospital, owned by the Vokkaliga Sangha (which means association of Vokkaliga group). The majority of the native farmers endogenous to Karnataka belong to the Vokkaliga (Gowda) group, which personally looks at Kempegowda Institute as its primary health access site, in case of any medical emergency, which explains the appropriateness of the Location chosen to do this study. Intravenous magnesium sulphate has been used in few smaller studies that has shown promising results which motivated us to start this study [4,5,6].

Aims and Objectives of the Study

- To assess the usefulness of MgSO₄ in acute OP poisoning in terms of decreasing duration of hospitalization, days of stay required in intensive care unit to return to a stable condition, and directly decreasing the cost and severity of symptoms of organophosphorus poisoning, without compromising the quality and efficiency of care.
- To assess and compare the use of MgSO₄ along with conventional standard therapy versus conventional standard therapy alone.

Materials and Methods

All patients with history of organophosphorous poisoning only were included in the study.

- All patients were decontaminated, treated with gastric lavage and the standard treatment based on severity of symptoms in accordance to standard treatment dose of iv atropine. Also iv pralidoxime was included in both treatment and control arms of the study.
- Patients who fulfil the inclusion criteria were divided into 2 groups.
- Two groups (25 each) - one group received intravenous magnesium sulphate 4gms along with iv atropine and iv pralidoxime (TEST). While second group received only iv atropine and iv pralidoxime (Control).

- Usually when a patient comes to the emergency department a bolus of 5 mg of atropine is given, and then the required dose of atropine is titrated in accordance to severity of presenting cholinergic symptoms.

Source of Data

Data was collected from all In-patients who fulfilled the inclusion and exclusion criteria. Patients with a history of OP poisoning in the time period from November 2013 to September 2015 were received in the emergency department of Kempegowda institute of medical sciences Hospital, decontaminated, given a gastric lavage and given bolus 5mg atropine dose and then admitted in the Intensive care unit for further management.

Inclusion Criteria

Patients admitted with history of OP compound poisoning within 24 hours of consumption.

Patients/ attenders who were willing to give written informed consent.

Ingestion of poison by oral route only.

Patient survived the episode of poisoning and did not die.

Exclusion Criteria

Patients with Renal dysfunction.

Organophosphorous compound mixed with other compounds.

Any medical Contraindications for MgSO₄ therapy.

Death of the patient irrespective.

Type of Study

Comparative Interventional study.

Analysis of Outcome Measures

Data were analyzed using SPSS version 17 for windows. Frequency distribution of category variables were compared between intervention (MgSO₄) and control groups using Chi-square test for proportions. The means were compared between the groups at baseline using ANOVA. The dose of atropine, PAM, ICU stay and ventilation were compared between groups using non parametric Independent Mann Whitney tests as they differed from a normal distribution. P value of less than 0.05 was

considered significant. Extreme care and appropriate steps like matching were taken under the guidance of statistical experts to prevent confounding and other statistical errors.

Discussion

The present study was undertaken in the department of emergency medicine of KIMS Hospital to assess the efficacy of intravenous magnesium sulphate in the management of acute organophosphorous poisoning. Traditional treatment of this form of poisoning includes injection atropine to manage the muscarinic symptoms and injection PAM as specific antidote to salvage the enzyme acetyl cholinesterase with or without mechanical ventilator support on a need basis.

In recent times the use of PAM in acute OP compound poisoning has become a subject of debate, as mentioned previously the requirement for alternative drug/therapeutic modality which could decrease the mortality and hospital stay with better outcomes was needed. A couple of small studies have appeared in medicine literature regarding the benefits of intravenous magnesium sulphate in acute OP poisoning [4,5,6]. After reviewing sufficient literature the study was started.

50 patients who met the eligibility criteria were included in the study and they were divided in two groups. The first group referred to as control group received conventional standard management of OP compound poisoning in the form of GI decontamination, injection atropine for muscarinic symptoms control and injection pralidoxime chloride as specific antidote.

The other group referred to as test in addition to the above treatment received a one time only intravenous magnesium sulphate 4 gram dose as an infusion over 4 hours. A total number of 1200 poisoning cases were admitted and managed during the study period between December 2013 and August 2015 in Kempegowda Institute of Medical Sciences. Out of which 200 Patients were organophosphorus compound poisoning.

A total number of 8 organophosphorus poisoning cases died during the study period that was not included in the study because they failed to meet the inclusion criteria. Poisoning cases admitted and managed by the Department of Emergency Medicine of which, 50 subjects full filling the inclusion/exclusion criteria were included the study.

Sex

The present study there were 33 males and 17 females ratio of 2:1, this male domination has also been noticed in similar studies by other authors. This sex difference could probably be attributed to the male subjects going out to purchase the easily accessible insecticide and consuming outdoors.

Age

In the present study majority of the subjects were in the age group of 21-30 years this is collaborated by similar study done by various other authors in the country. The younger age group seem to be much more vulnerable to emotion upheavals and impulsive decision making. Since all cases included in the study were oral consumption with suicidal intention. There were no cases of accidental exposure we encountered.

Occupation

Among the study subjects enrolled majority were students (42%) compared to other occupational groups. This explains the younger age group vulnerability. Followed by farmer (14%) and house wives (14%). Other studies done in the country shows the farmers among the occupation group being more vulnerable to organophosphorus poisoning. Since OP insecticides are used in their profession. Many of the students who consumed this organophosphorus poison, had their families in the agricultural background.

Place of Consumption

The present study was done in a tertiary care teaching hospital located in city. Hence majority of cases were from urban area (76%). While other similar studies were done at suburban or rural population which were catering to rural population. This also explains the majority of population being from rural background with agricultural workers dominance in their studies.

Clinical Observations

The common clinical features and presenting symptoms in the present study among the subjects were of gastrointestinal manifestation in form of vomiting and diarrhea. Oral ingestion was the only route of poisoning. Patients presented to the emergency room with parasympathetic, muscarinic symptoms in form of excessive secretions i.e. sweating, lacrimation etc. the similar presentations were noticed by other authors in their studies.

Ingestion to Admission Interval

A majority of the study population presented to the emergency department quite early after ingestion. This being an urban setup with easy access to transportation from place of ingestion to medical facility. Hence time interval between ingestion to admission was shorter and of milder severity. Similar reporting has been done by other studies. They were 12 cases of severe poisoning as determined by modified driesbach score included in the study requiring ventilator support for respiratory failure. Out of which 9 were in control group and 3 were in test group.

Regarding the Type of OP Compound

Dichlorvos (22%) was the most commonly encountered OP compound followed by dimethionate (14%). Methyl parathion (12%) and propenfos (12%). Majority of the OP compounds were methoxy organophosphates (20%). And other (20%). Hence early aging of acetyl cholinesterase is to be expected in our study.

Since methylated OP compounds age much faster and earlier than ethylated group. Propenfos and phorate cause aging very rapidly as compared to methylated OP compounds. Other studies shown similar grouping of OP compound poisoning depending on the geographical area which determines the type of OP compound. Since these insecticides are need based on the agricultural produce of that area. All patients were treated initial atropine bolus to overcome the muscarinic symptoms of OP compound poisoning and later titrated through slow atropine infusion to alleviate these symptoms based on severity.

Injection pralidoxime chloride was used as the specific antidote in both the groups. But at doses which could be considered sub optimal compared to WHO guidelines (30mg/kg bolus followed by 8-10mg/kg/hour). In this study only 20% of poisoning were due to ethoxy OP compound which age slowly hence treatment with oximes would be useful. The other 20% were due to phorate, propenfos which age rapidly the use of oximes is of less proven efficacy. Other 60% were methoxy OP compound which age relatively early compared to ethoxy OP hence efficacy of oximes as antidote in this group is debatable.

Mortality

There was no mortality in the present study however other studies home reported mortality of

13.3-18% This nil mortality in present study could be due the selection. Wherein patients who had consumed OP compound poisoning < 24 hours were included in the study. A vast majority of them presented earlier and received medical attention within 4 hours of consumptions. Urban population constituted 3/4th of study population (76%) who had probably consumed less concentrated OP compounds used for domestic purposes as compared to more toxic and lethal field poisons used in rural area. Prompt mechanical ventilator support was given to cases with severe poisoning is another factor reducing mortality. In present study, The study population was divided into 2 arms with one group receiving conventional therapy as described earlier. The other group in addition receiving intravenous magnesium sulphate.

In present study there was significantly decrease in the total number of days patients needed to be on ventilator (0.8days) and the total duration of ICU stay (5 days) in TEST group as compared to Total number of days needed to be on ventilation (4.28 days) and ICU stay (10.68 days) in the control group. In study done by pajamound et al [4] mean ICU stay in the test group (2.90±0.60 days) was significantly less as compared to the number of days as needed in the control group (5±0.82days). In study done by Basher et al [68]. Mean atropine required in control group was 127 mg and in test was 159mg.

Since there was a near significant difference in distribution of severity across control and test groups, We performed an analysis of co-variance (ANCOVA) for outcome measures in ICU stay and days of ventilation required between the groups using severity, age and other statistical significant matching processes. There was a significant effect of severity on ICU stay $F(1,47) = 20.9, P < 0.001$. Nevertheless intervention also reduced the ICU stay irrespective of the severity $F(1,47) = 6.8, P = 0.01$. There was a significant effect of severity on number of days of ventilation $F(1,47) = 30.8, P < 0.001$, but interventional effects were non-significant for days of ventilation.

Conclusion

- Male sex and younger age were predominant in the study population which is reflected in other similar studies done across the country.
- Ingestion with suicidal intention was the only route of poisoning there were no accidental or homicidal incidents.
- Methylated OP compounds with other class like propenfos dominated as the type of compound

ingested which age faster and the efficacy of using injection PAM in these cases remains questionable.

- In spite of the above there was no mortality in the study population.
- Majority of the subjects in both the groups presented with mild degree of severity as per Driesbach's severity score.
- All subjects presented with GI manifestations predominantly since oral route of ingestion was the only modality of poisoning.
- Intravenous magnesium sulphate 4 grams administered in the test group did not have any form of adverse events like hypotension, hyporeflexia.
- The test group which received intravenous magnesium sulphate had better outcomes in terms of lesser number of days in ICU, lesser number days on ventilator and lesser amount of total atropine required.
- The study is small with differences in distribution of severity between the two groups, further studies including larger number of cases and inclusion of more severe cases in test group would be adding more credence to the future of intravenous magnesium therapy in acute OP poisoning.

Summary

Organophosphorus compounds are commonly used agents for suicidal purpose because of their easy availability. Male sex and younger age were predominant in the study population Among these compounds the most common compound present in our study is dichlorvos (22%). Intravenous magnesium sulphate 4 grams administered in the test group did not have any form of adverse events like hypotension, hyporeflexia or respiratory depression. The test group which received intravenous magnesium sulphate had better outcomes in terms of lesser number of days in ICU, lesser number days on ventilator and lesser amount of total atropine required. The study is small with differences in distribution of severity between the two groups, further studies including larger number of cases and inclusion of more severe cases in test group would be adding more credence to the future of intravenous magnesium therapy in acute OP poisoning.

List of Abbreviations

Ach - Acetylcholine

CVS - Cardiovascular system
 ECG -Electrocardiography
 GIT - Gastrointestinal system
 IMV - Intermittent Mandatory Ventilation
 IMS - Intermediate Syndrome
 IPPV - Intermittent positive-pressure ventilation
 MS - Musculoskeletal system
 NMJ -Neuromuscular Junction
 OPP - Organophosphate poisoning
 PEEP - Positive end expiratory pressure
 RS - Respiratory system
 RBC -Red blood cells
 SIMV - Synchronous intermittent mandatory ventilation
 AchE - Acetylcholinesterase
 CNS - Central Nervous System
 DPN - Delayed Polyneuropathy.
 OP - Organophosphorus
 OPC - Organophosphorus compound
 PAM - Pralidoxime chloride
 Mg²⁺ - Magnesium
 MgSO₄ - Magnesium sulphate
 mg- milligrams

References

1. Roberts Darren M, Aaron Cynthia K. Management of acute organophosphorus pesticide poisoning. *BMJ* 2007;334:629-634.
2. Brunton Laurence L. Principles of toxicology and treatment of poisoning. In: Klaassen Curtis D, editor. Goodman and Gilman's the pharmacological basis of therapeutics. New York (NY): McGraw-Hill; 2006. 1156-1159.
3. Peter G Blain ,Organophosphorus poisoning (acute). clinical evidence, Search date April 2010.
4. Pajoumand A, Shadnia S, Rezaie A, Abdi M, Abdollahi M. Benefits of magnesium sulphate in the management of acute human poisoning by organophosphorus insecticides. *Hum Exp Toxicol.* 2004 Dec.23(12):5659.
5. A.Basher, S. H. Rahman, A. Ghose, S. M. Arif, M. A. Faiz, and A. H. Dawson. a pilot trail in Dhaka medical college, Bangladesh. Accessed google.com 2013-11-26.
6. Basher A, Rahman SH, Ghose A, Arif SM, Faiz MA, Dawson AH. Phase II study of magnesium sulphate in acute organophosphate pesticide poisoning. *Clin Toxicol (Phila).* 2013 Jan;51(1):3540.