

EFFICACY OF HIGH DOSE OF MAGNESIUM SULPHATE FOR CARDIAC ARRHYTHMIAS IN PATIENTS OF WHEAT PILL POISONING

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ABSTRACT

Objective: To study the prophylactic effects of High Dose Magnesium Sulphate on Cardiac Arrhythmias, Cardiogenic shock and associated mortality in Cases of Aluminum Phosphide Poisoning.

Methodology: Seventy One patients of wheat pill poisoning were randomly selected. Thirty seven were given high dose of Magnesium Sulphate (study group) and 34 were given low dose of magnesium sulphate (control group) through intravenous route along with other supportive measures. Patients were observed for cardiac arrhythmias and mortality in both groups. Study end point was safe discharge from the hospital or death.

Results: The mean age of the sample was 25.27 ± 7.48 years. Frequency of cardiac arrhythmias was 40.54% ($n=15$) in study group versus 55.88% ($n=19$) in the control group. Average length of stay and frequency of cardiogenic shock was slightly lower in the study group, i.e., 1.42 ± 0.65 days while it was 1.78 ± 1.38 days for the control group. Overall, mortality in both the groups was 66.20% ($n=47$), which remained almost equal in both groups or slightly favored study group with 64.86 % ($n=24$) in the study and 67.65% ($n=23$) in the control group.

Conclusion: High dose magnesium sulphate administration was found to be helpful for cardiac arrhythmia and shock but mortality remained unchanged.

Key Words: Magnesium sulphate, Wheat pill, Aluminum phosphide, Phosphine, Cardiotoxin.

This article may be cited as: Hassan AW, Meo MH, Saqib N, Saleem NM. Efficacy of high dose of magnesium sulphate for cardiac arrhythmias in patients of wheat pill poisoning. J Postgrad Med Inst 2013; 27(3):257-61.

INTRODUCTION

Wheat pill is a commonly used pesticide and fumigant, and is banned for sale due to high toxicity and mortality even at lower doses. Yet it is commonly available, and routinely used for storage of wheat grains. Its accidental ingestion is very rare due to obnoxious, pungent smell and bad taste, but it is common method of suicide^{1,2}. Its active ingredient is Aluminum phosphide. The ingestion of half tablet

containing 50 grams of the active Aluminum Phosphide is considered fatal according to studies done in India and Hong kong^{1,4}. Phosphene gas is immediately produced once it enters the acidic medium of the stomach. The effects of aluminum phosphide after ingestion are diverse ranging from local gastritis to acute Respiratory Distress Syndrome (chemical pneumonitis) and myocarditis^{3,5}. These effects are mainly because of membrane disruption and destabilization secondary to ATP depletion associated mitochondrial damage.

Cardiac arrhythmias are one of the prognostic indicators besides renal and hepatic dysfunction⁵. Mortality rates are extremely high in untreated patients⁶. Arrhythmias are a frequent finding, difficult to treat and leading to hemodynamic instability and mortality. Severity of disease is dependent on age, number of pills ingested, time lapse between ingestion to presentation; vomiting and prompt treatment⁷⁻¹¹. Magnesium Sulphate is a known cardio-protective agent with membrane stabilizing properties and also a known anti-arrhythmic¹²⁻¹⁴. Several studies

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Date Received: October 30, 2012

Date Revised: April 22, 2013

Date Accepted: April 29, 2013

conducted in many parts of the world have shown its ability to reduce mortality in wheat pill poisoning provided it is given within 4 hours of ingestion¹⁵. Phosphine gas and phosphoric acid produced as a result of aluminum phosphide ingestion are both hypoxic agents and cause cellular damage by production of free radicals in abundance, as it binds with cytochrome oxidase and inhibiting catalase. Magnesium is known for its property of scavenging free radicals. An intravenous dose of magnesium sulphate eliminates free radicals from the blood, and it also will act as an agent which will prevent development of deadly arrhythmias.^{14, 16}

Previously, it was studied that survival was better in patients who presented within 4 hours of ingestion, and it was recommended to start the magnesium sulphate therapy as early as possible.¹⁴ as it was a known membrane stabilizer and a cardio-protective agent and was a known therapy for cardiac arrhythmias and Torsade De Pointes. The purpose of this study was to observe the difference in incidence of cardiac arrhythmias in patient treated with higher doses of Magnesium Sulphate Versus the standard dose.

METHODOLOGY

The study was conducted at Lahore General Hospital over a period of 8 months starting from 01.12.2010 till 31.07.2011. A total of 71 patients were randomly selected in the study with confirmed diagnosis of wheat pill poisoning. Inclusion criteria was a positive history of ingestion by either gender aged 15-45 years. Exclusion criteria included prior history of Cardiac Disease. Each patient with confirmed diagnosis was given initial resuscitation at the ER. First set of Vital signs were taken manually, and then the patients were connected to cardiac monitors. Oxygen was given by nasal cannula at the rate of 4 liters/minutes. All the patients were catheterized under aseptic conditions and baseline investigations including Arterial blood gases, CBC, Renal Profile, SGPT, SGOT, Cardiac Enzymes and portable chest X-Rays were done for all the patients. Gastric lavage was done with 3 liters of KMnO₄ (1:10,000) which oxidized the unabsorbed aluminum phosphide. This was followed by Naso-gastric feeding of activated charcoal at dose of 1g/kg, and 350 ml of coconut oil which was used as a buffer, to prevent gastritis and to discourage absorption of undigested ingredients.

Base deficit was calculated using formula; Base deficit = $0.4 \times \text{body wt.} \times \text{desired HCO}_3^- - \text{measured HCO}_3^-$ (mEq/Lt). Sodium bicarbonate was replaced according to base deficit and arterial blood gases. Half of it was given stat, and was repeated at an interval of every 3 hours. A standard dose of 100

mg of hydrocortisone was given to all the patients at presentation as a prophylactic measure against pulmonary edema and for cortisone replacement, as its deficiency is a usual finding in these patients. All patients received symptomatic therapy for associated symptoms like vomiting, gastritis, and hypotension. Hypotension was found in more than 86% patients.

Hypotension and shock in all cases were treated with volume replacement, dopamine and dobutamine. Hepatic injury is one of the prognostic indicators after 24 hours in these patients, so patients were given Hepamerz (L-ornithine L-aspartate) and silymarin prophylactically at admission and standard doses were given for next day. Patients were randomly divided into two groups, one group was given high dose (2gm followed by 2gms of Mg Sulphate given every 4 hourly to keep levels of magnesium above 4.0 but not more than 5.1 mEq/Lt and the second group was given standard dose (2gm IV stat, followed by 1gm given every 4-6 hourly to keep magnesium in safe range of 3-3.6 mEq).

End point of the study was either discharge from the hospital or death. Patients who developed cardiac arrhythmias were treated with other antiarrhythmic agents including amiodarone. Patient data was collected in specially designed forms. Number of patients with arrhythmias, and cardiogenic shock was noted in both groups. Time elapsed between ingestion and presentation was of prime importance as previous studies showed a strong correlation between the two.

Patient data was analyzed after recording all the variables. Frequency of cardiac arrhythmias in all the admitted patients was noted and also categorized according to the dose of Magnesium Sulphate and ultimate endpoint was discharge from the hospital or death.

RESULTS

A total number of 71 patients were enrolled in the study during the study period. The mean age was 25.27 ± 7.48 years. Average time lapse between ingestion and presentation was 2.49 ± 1.13 hours. Majority of the patients took 1-2 pills the detail is in table 1. One case of accidental ingestion of half pill was also reported, who was enrolled in control group.

Sinus Tachycardia was observed in 51.35% (n=19) in the study group as compared to the 61.76% (n=21) in control group. Cardiac arrhythmias were noted in 40.54% patients at some point of time in the study group as compared to 55.88% in control group. Detail of arrhythmias is tabulated in table 2.

Most of the patients who developed arrhythmia had more than one type of it, and were treated accordingly. Frequency of Cardiogenic shock in study group was 40.54% (n=15) as compared to 47.05% (n=16) of the control group. Hypotension was found in 85.92% of the patients (n=61) in both the groups combined. Hypoxia as evident by pulse oximeter and arterial blood gases was present in 78.87% of all the patients (n=56). 77.46% of all, had metabolic acidosis (n=55). Nine patients had vomiting within 30 minutes of ingestion, while overall incidence of

vomiting was 81.69% (n=58). Only 2 patients presented in a state of coma and shock and both were enrolled in the study group.

Mortality among the two groups was not much different. Overall mortality was 66.20% (n=47), while 64.86 % (n=24) in the study and 67.65% (n=23) in the control group. Average length of stay at the hospital for expired patients in the study group was 1.42 ± 0.65 days while it was 1.78 ± 1.38 days for the control group. Overall, average length of

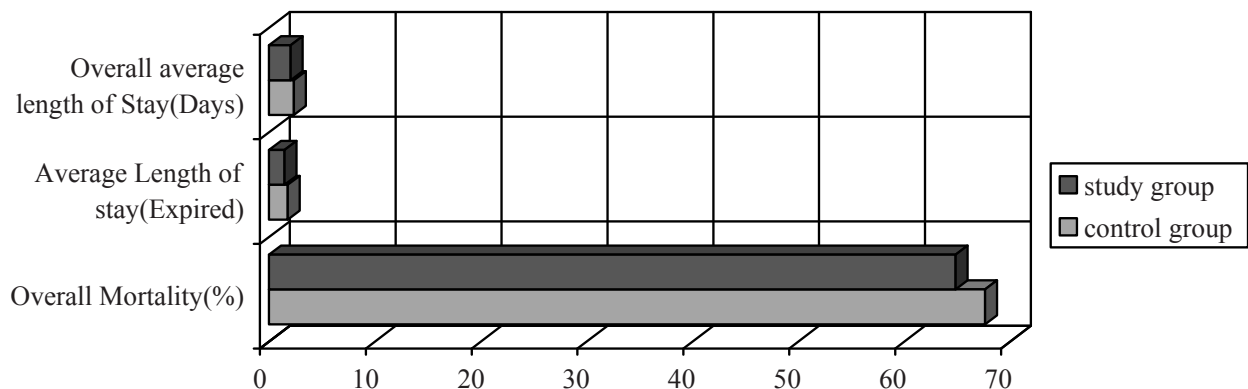
Table 1: Number of wheat pills ingested by patients in both the groups combined

No of pills Ingested (estimated)	Number of patients	% of total
Less than 1	2	2.82
1	37	52.11
1.5	14	19.72
2	8	11.27
More than 2	10	14.08

Table 2: Incidence of each arrhythmia in both the groups

Type of Arrhythmia	Study group		Control group	
Sinus tachycardia	19	51.35%	21	61.76%
Cardiac arrhythmias	15	40.54%	19	55.88%
SVT	3	8.11%	3	8.82%
A. Fibrillation	3	8.11%	2	5.88%
V. Tachycardia	11	29.73%	15	44.12%
Torsade de pointes	1	2.7%	1	2.94%
V. Fibrillation	5	13.51%	8	23.53%

Figure 1: Average length of stay at the hospital



stay for all the patients of study group was 2.06 ± 1.15 days compared to 2.36 ± 1.52 days (Figure 1). None of the patients was discharged before completing minimum of 96 mandatory hours at the hospital except one who left against medical advice on the second day. Mortality was calculated according to number of pills ingested for both groups. One patient of control group, who was admitted with ingestion of one tablet, developed acute pancreatitis on the third day of admission, followed by renal and hepatic failures. She developed pulmonary edema, and underwent two sessions of hemodialysis 48 hours apart, but ultimately died on 7th day of admission from multi-organ failure.

DISCUSSION

Our study was designed to see dose related response of magnesium sulphate on incidence of sinus tachycardia, cardiac arrhythmias, cardiogenic shock, and mortality in cases of wheat pill poisoning. It was noted that patients who received higher dose of magnesium sulphate had tachycardia, cardiac arrhythmias and Cardiogenic shock at a lesser rate as compared to the control group who received standard doses of magnesium sulphate. We found that mortality and average hospital stay remained almost equal for the groups who expired but the hospital stay was bit lower for the patients treated with higher dose of magnesium sulphate who survived and discharged home. Previously, some studies showed positive dose related response of magnesium sulphate on ECG and shock when the serum level was raised to 5.2 mEq/Lt^{14} , but other studies done for the effects of higher doses of magnesium sulphate on mortality in aluminum phosphide poisoning showed no effect on mortality regardless of the doses of magnesium sulphate^{17,18}. Statistically our study shows the same results for mortality, but good intensive care, dialysis and treatment of other derangements may improve the survival.

This is evident that although, not much difference on the overall mortality is observed in the two groups, yet a lower incidence of cardiac events was noted in the study groups. This shows that besides cardiac events, pulmonary, hepatic and metabolic disturbances are important causes of high mortality. So, the patients should receive hepato protective agents like hepamerz (L-ornithine, L-aspartate), silymarin and low protein diet.

The study had limitations of a small sample size. Need was felt for another study that should observe the effects of various other interventions including those for prevention of other causes of its increased mortality i.e. pulmonary and metabolic disturbances.

CONCLUSION

Lack of specific antidote for aluminium phosphide makes its treatment very challenging. High dose of Magnesium sulphate along with early supportive measures including gastric lavage with Potassium permanganate, activated charcoal, coconut oil and oxygen inhalation along with close cardiac monitoring showed better outcomes in terms cardiac arrhythmias and Cardiogenic shock but no significant effect on overall mortality. So, research should be carried out to find an antidote.

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CONTRIBUTORS

AWH conceived the idea, planned and wrote the manuscript of the study. MHM, NS & NMS did the data collection and helped in the write-up of the manuscript. All the authors contributed significantly to the research that resulted in the submitted manuscript.