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Original Article

Comparison of the prognosis of the new and old therapeutic protocols in poisoning by phosphide compounds

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Abstract

Introduction: Rice tablets (aluminum phosphide) are used to fight insects and pests in the grain storage spaces. This tablet produces phosphine gas which is a toxic substance for mitochondria. New measures have merely been recommended to save the lives of poisoned patients at referral clinical toxicology centers. The purpose of this study is to compare the prognosis of the new and old protocols in rice tablet poisoning.

Methods: This clinical trial recruited 126 eligible patients poisoned with rice tablets presenting to the Imam Khomeini Hospital in Kermanshah in 2013, who were assigned into two groups of the new (magnesium sulfate) and old protocols. Data were analyzed using statistical tests in SPSS software version 21.

Results: The age of the patients was between 12 and 76 years, with a mean of 30.78 years and a standard deviation of 12.88 years. Among the patients, 77 (58.3%) were male and 55 (41.7%) were female. 43.9%/59.1%, 16.7%/31.8%, 9.1%/25.8%, and 40.9%/42.4% subjects suffered from cardiac, renal, hepatic and pulmonary complications, in new and old treatment groups respectively. Renal (P=0.046) and hepatic (P=0.12%) complications were significantly lower in patients under the new treatment. Furthermore, the mortality rate in the new protocol was significantly lower (P=0.036).

Conclusion: In this study, the new protocol was better able than the old one to reduce morbidity and mortality rates. Therefore, the use of this new treatment protocol can be beneficial in the treatment of patients poisoned with rice tablets.

Introduction

The use of pesticides for agricultural use improves the quality and quantity of products through the destroying pests and plays an important role in supplying the food needed for today's human population. However, the incorrect use of these pesticides causes a variety of acute and chronic poisoning, which is important as a medical, health and social problem. The metal phosphides are a group of pesticide agents that have been used as rodenticide and fumigants for a long time. Due to low prices, high detoxification potential, and availability, these agents can cause general and accidental acute poisoning and eventually death (1). After oral consumption, phosphorus gas is released and is rapidly absorbed and causes systemic poisoning and cell hypoxemia. Severe sweating, severely reduced blood pressure, arrhythmia, tachypnea, and severe metabolic acidosis are common manifestations of poisoning (2).

Unfortunately, there is no specific antidote for phosphate compounds, and most clinical toxicology centers try to improve the prognosis of poisoning with phosphite compounds as symptomatic treatment (3). The treatment method used in the our center can be optimized in line with the methods that have improved the prognosis of poisoning with phosphide compounds according to the latest achievements of the clinical toxicology centers in the world.

The methods currently used in this center include lavage with water, charcoal and sorbitol. Other treatments are administered according to the symptoms of the patient, which usually do not have a specific time for start. In the proposed method, after lavage with permanganate solution (1/10000), gavage begins with charcoal, sorbitol and a mixture of coconut oil and bicarbonate (4). Furthermore, bicarbonate is administered for acidosis in patients with a specific time and dose, and calcium gluconate (5) and magnesium for electrolyte disturbances as indicated (6). Meanwhile, some supportive measures are taken, such as the administration of crystalloids and colloid and the improvement of electrolyte balance (7). Some new measures are now proposed to save the lives of poisoned patients at clinical toxicology centers. We collected several new methods that have been reported to be more effective than other methods and implemented them on patients presenting to our center and tried to propose a new protocol for the treatment of poisoning with aluminum phosphide (rice tablets) and phosphide

compounds, and to compare the prognosis of the new method with that of the conventional methods.

Materials and Methods

This clinical trial study enrolled all patients presenting to the clinical toxicology center of Imam Khomeini Hospital in Kermanshah in 2013 who had a positive diagnosis of consuming phosphate compounds. Furthermore, in the absence of a history and uncertainty of the consumed compounds, the new protocol was applied in the presence of clinical symptoms and signs of poisoning in accordance with poisoning with phosphate compounds (1). First, the gastric acid was diluted with 3%-5% baking soda. Then, lavage was performed with potassium permanganate ($\frac{1}{10000}$ solution), followed by gavage of 1 g/kg of charcoal (30% solution) and 1 mg/kg of sorbitol (70% solution). Then, 0.5 g/kg of charcoal was repeated every 3 hours. Coconut oil (200 cc) along with 50 cc of sodium bicarbonate was gavaged every 2 hours. This compound absorbs the released phosphine gas in the stomach. Charcoal and sorbitol continued for up to 24 hours and coconut oil and sodium bicarbonate continued for up to 6 days (1). If the patients had acute lung injury (ALI) or reduced level of consciousness, they were intubated (GCS≤7) (2). The magnesium sulfate solution 50% (2 cc) was injected every 12 hours providing that the serum magnesium was less than 2 mg/dL (3). The calcium gluconate solution 10% was injected (10 cc) if any changes occurred in ECG and repeated in half an hour if there were no responses. Ranitidine (50 mg) was injected every 8 hours (4). In the event of a decrease in blood pressure and a heart attack (systolic pressure less than 90 mm Hg), dopamine (10 mg/kg/min) and digoxin (0.5 mg) were injected. If blood pressure did not increase after 24 hours, the dose of dopamine was increased in the following days and digoxin (0.25 mg) was injected daily (4). Blood ABG was taken from the patients at the arrival and carefully corrected in case of metabolic acidosis (Full Correction) (5). The required bicarbonate content was calculated using the following formula.

Required $NaHCO_3$ (mg) = 0.6 × BE × body weight

This amount of bicarbonate was rapidly injected and ABG was re-taken after 1 hour. If metabolic acidosis was not corrected, this procedure was repeated every 1 hour until there was no metabolic acidosis in 2 consecutive ABGs. ABG was then repeated every 2 hours, then every 4 hours, and then every 6 hours and bicarbonate was prescribed in case of disorder (6). All patients initially received 200 mg of intravenous hydrocortisone, and 150 mg of intravenous hydrocortisone was repeated every 8 hours (7). The electrolytes (Mg/Ca/Na/K) were checked every 6 hours on the first day, every 12 hours on the second day, and daily from the third day on. The (D,T) Bill, Alk/p, AST Alt, CPK, LDH, Alb, cr, and BUN were checked daily (8). In the event of elevated liver enzymes and billirubin, patients were given lactulose every 6 hours. NAC (N-Acetylcysteine) was administered with a 21-hour intravenous regimen: an amount of 150 mg/kg (up to 15 g in 1 hour) was infused in the loading dose, 50 mg/kg (up to 5 grams in 4 hours) in the second dose, and 100 mg/kg (up to 10 grams in 16 hours) in the third dose (9). Food gavage started on the third day through NGT (10). The SPSS software v. 21 was used for data processing and analysis. The chi-square test was used to compare nominal variables, and the independent t-test and nonparametric Mann-Whitney U-test were used for quantitative variables. The two groups matched in terms of age and sex.

Results

In this study, 140 patients poisoned with rice tablets were enrolled, of which 8 patients were excluded from the study due to lack of cooperation and the study was conducted on 132 patients. In this study, 66 patients (50%) were treated with the new protocol and 66 (50%) with the old protocol. Patients' mean age was 30.78±12.88 years ranging from 12 to 76 years. Among the patients, 77 (58.3%) were male and 55 (41.7%) were female. Descriptive features, frequency, and comparison of cardiac, renal, hepatic and pulmonary complications between the new and old protocols in patients poisoned with rice tablets were determined (Table 1). The new and old protocols did not have a significant difference in terms of cardiac (P=0.082) and pulmonary (P=0.086) complications. The new and old protocols had a significant difference in terms of renal (P=0.046) and hepatic (P=0.012) complications. Frequency and comparison of the rate of heart attack and mortality between the new and old protocols in patients poisoned with rice tablets were determined (Table 1). There was no significant difference in terms of the heart attack rate between the new and old protocols (P=0.71). There was no significant difference in terms of the mortality rate between the new and old protocols (P=0.36).

Table 1. Comparison of the frequency of cardiac, renal, hepatic, and pulmonary complications and the consequences of a health attack and mortality between the new and old protocols.

Feature	Treatment protocol group		Pvalue
	New	Old	
Heart attack	29(43.9%)	39(59.1%)	0.082
Renal complications	11(16.7%)	21(31.8%)	0.046
Hepatic complications	6(9.1%)	17(25.8%)	0.012
Pulmonary complications	27(40.9%)	28(42.4%)	0.082
Shock	21(31.8%)	23(34.8%)	0.71
Mortality	24(36.4%)	36(54.5%)	0.036

Discussion

In 2009, Juiswal et al. investigated the effect of correction of severe metabolic acidosis with intravenous bicarbonate on the prognosis of patients who were poisoned with aluminum phosphide and noted that the prognosis improved (11). Gurjar et al. (2011) suggested that the onset of early treatment of the patient, reduced contact with poison with potassium permanganate, coconut oil lavage, supportive treatments, and severe monitoring improved prognosis of patients (12). Mehrpour et al. (2011) reported a successful treatment of aluminum phosphide poisoning with digoxin, where the patient had a heart attack and was treated with

digoxin (13). In a review article, Moghadamnia (2012) considered supportive therapies such as magnesium sulfate, NAC, glutathione, vitamin C and β-carotenes, coconut oil and melatonin effective and important in reducing the toxic effects of oxidative phosphine (14). Furthermore, Tehrani et al. (2012) examined the protective effects of NAC on aluminum phosphide-induced oxidative stress and concluded that NAC can have therapeutic effects and reduce mortality (9). Chaudhry et al. (2014) investigated the effects of NAC in poisoning with aluminum phosphide and found it beneficial (15). Agrawal et al. investigated the role of supportive measures in poisoning with aluminum phosphide in the absence of a specific antidote and considered treatment with diluted potassium permanganate lavage, coconut oil, sodium bicarbonate, intravenous magnesium sulfate, and vasopressors effective (16). Sanaei-Zadeh et al. (2016), described the use of water-based solutions (such as potassium permanganate, sodium bicarbonate, and sharkol) dangerous for lavage and gastric decontamination of poison, and in contrast considered vegetable oil or castor oil lavage effective (17). Taghaddosinejad et al. (2016) investigated the effect of NAC on aluminum phosphide poisoning (inducing cardiovascular toxicity) and concluded that the use of NAC can have a positive role in patients with increased cardiac markers (18). Hashemi-Domeneh et al. (2016) provided a treatment flowchart where sodium bicarbonate and potassium permanganate lavage are performed, and metabolic acidosis is corrected by sodium bicarbonate injection and used by the injection of magnesium sulfate and NAC and oral vitamin E as an antioxidant (19).

The proper care of patients in the early hours after taking rice tablets is the most important factor in this way. Acidosis weakens cardiovascular activity, making it difficult and sometimes impossible for to recover a patient. A different cardiac arrhythmia that is due to the direct effect of the medicine on heart, as well as acidosis and low blood pressure, are the main causes of death in the early hours. Vital signs, blood gas monitoring, pH, cardiac monitoring and continuous attendance of physicians and nurses on the patients' bedside are required to save them. Thus, transfering the patients to ICU is the main pillar of poisoning treatment. Recent reports have emphasized the use of calcium and magnesium. Due to the high prevalence of hypomagnesemia during poisoning with rice tablets and its association with fatal arrhythmias and death, magnesium sulfate treatment is recommended. In many studies, this treatment has had a major impact on reducing mortality rate in patients. The mechanism of magnesium effect is probably neutralizing the effect of phosphine oxidase (20-23). Moreover, frequent gavage of sorbitol charcoal and mineral oils is useful for preventing the release of phosphide and accelerating excretion (24-26). According to the results, the mean age of people with rice tablets poisoning was about 31 years, which is consistent with the results of other studies, but it is a little higher (27-29). This slight difference in the age of poisoning with rice tablets between this study and other studies can be due to differences in samples and, consequently, differences in cultural, social and geographical factors. In this study, men were poisoned with rice tablets more than women (58.3%). Jaiswal et al. reported similar results (70%) (11). They indicated that 29 (43.9%) patients in the new protocol group and 39 (59.1%) in the old protocol group suffered from cardiac complications, but the difference was not significant. Furthermore, 11 (16.7%) patients in the new protocol group and 21 (31.8%) in the old protocol group suffered from renal complications, and the difference was significant. Additionally, 6 (9.1%) patients in the new protocol group and 17 (25.8%) in the old protocol group suffered from hepatic complications, and the difference was significant. Moreover, 27 (40.9%) patients in the new protocol group and 28 (42.4%) in the old protocol group suffered from pulmonary complications, but the difference was not significant. In this study, 21 patients (31.8%) in the new protocol group and 23 (34.8%) in the old protocol group needed electro shock (had cardiac arrhythmia, which required the use of the ECT device to stabilize them), but this difference was not significan between the protocols. Finally, 24 (36.4%) patients in the new protocol group and 36 (54.5%) in the old protocol group died, and the difference was significant. Patients who presented with shock and ultimately died were not treated with magnesium sulfate.

Conclusion

According to the above, the new protocol appears to reduce some of the complications of taking rice tablets, especially the renal and hepatic complications. It is worth noting that the new protocol reduced the mortality rate of patients poisoned with rice tablets.

It appears that the new protocol was better able to reduce morbidity and mortality rates than the old one. Therefore, the use of this new treatment protocol can be beneficial in the treatment of patients poisoned with rice tablets. Regarding the high value of the new protocol for the treatment of patients poisoned with rice tablets, it is recommended to the physician along with other methods. It is also recommended that a similar study be conducted with a larger sample size and long-term follow ups.

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