

# The relationship between rice tablet consumption and pathological signs leading to death: a study in Tehran

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## ABSTRACT

**Purpose:** To investigate the effects of phosphide on some human biological systems in order to find a way to control it and facilitate the prevention and treatment of its poisoning.

**Materials and Methods:** In this study, 67 files of autopsy description, forensic pathology results and forensic toxicology were studied as nominal qualitative variables in terms of each type of histological changes in the liver, heart, lungs, brain, cerebellum and other organs. Also, forensic toxicology results in terms of positive (positive phosphine) or negative silver nitrate test were studied. The achieved data were analyzed by Statistical Package for Social Sciences (SPSS) version 17 software.

**Results:** Using rice tablet leads to macroscopic and microscopic pathological changes in the liver. No significant relationship was found between the different effects created in the course of treatment with pathological changes in the liver, but there was a significant relationship between the average numbers of tablets used with pulmonary changes. No significant relationship was found between the different effects with pathological changes in brain and cerebellum. Among the deceased, 71.42% negative phosphine was reported whose different biological samples were tested by silver nitrate.

**Conclusion:** Aluminum phosphide poisoning is a major problem which can result in severe damages to the internal organs and possibly death.

**Keywords:** Aluminum phosphide; autopsy; toxicity; pathology; hospital.

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## INTRODUCTION

Rice tablet is a dangerous combination of phosphide for preventing stored rice pests. Phosphide is also used to remove pests of stored cereal grains and prevent mold, rodenticide and so on.<sup>1,2</sup> When it contacts moisture and acid, dangerous phosphine gas is released which is the main reason for its toxicity. If this tablet is fresher, more gas will be released, becoming more dangerous.

Human contact with rice tablet can have severe and fatal consequences. Aluminum phosphide can cause severe irritation of gastrointestinal tract, cardiovascular disorders, hypotension, shock, arrhythmias, heart failure, pulmonary edema, metabolic acidosis, liver and kidney

damage, thrombocytopenia, convulsion and finally coma and death within 72 hours after consumption. Gastrointestinal side effects occur 5 to 10 minutes after consumption and then other symptoms appear. Hastening the cure, even in apparently asymptomatic patients, has a significant importance in improving patients' condition.<sup>3-5</sup> Symptoms of retrosternal burning, abdominal pain, nausea and vomiting occur almost in all patients immediately after taking the pill. Other symptoms include watery diarrhea, gastrointestinal bleeding, jaundice, stomach ulcer,<sup>6,7</sup> acute hepatic failure, hepatomegaly and ascites.<sup>8-10</sup> Its cardiovascular symptoms are hypotension, bradycardia, tachycardia, cardiogenic shock, myocarditis, pericarditis,

heart palpitations and so on. Also, some of its pulmonary signs are tachypnea, cyanosis, bilateral pulmonary rales sounds, and pulmonary edema. This toxin also affects the kidney with signs such as oliguria, anuria, acute renal failure, metabolic acidosis,<sup>11-14</sup> proteinuria<sup>15</sup> and edema.<sup>11</sup>

Since this substance is toxic and dangerous for human health and unfortunately, it can be seen in many suicides with it, this study aimed to investigate its effects on some human biological systems in order to find a way to control and avoid its easy availability at the community level by being aware of its dangerous effects.

## MATERIALS AND METHODS

At the beginning of this study, the poisoning of all poisoned patients admitted to the emergency department of our center during the years 2008-2009 was investigated and all cases poisoned with rice tablet were studied. Afterwards, the clinical and emergency files of those who had stayed in the emergency room and then in intensive care unit (ICU) were examined according to the names and numbers of recorded files. Variables were assessed separately; the required data were collected by a questionnaire. Lastly, if any of these poisoned patients died because of rice tablet, their files at Kahrizak forensic center were reviewed based on the name and date of death. Pathological and necropsy findings were observed in the autopsy of the deceased patient.

In our center, 87 patients were diagnosed with poisoning, among whom 85 patients had been poisoned with rice tablet. 18 patients had used herbal pills or been discharged at different stages of diagnosis and treatment with personal satisfaction. Thus, they were excluded from our study. So, diagnosis of poisoning with aluminum phosphide tablet was investigated in the remaining 67 patients according to the history of using the tablet, its clinical and paraclinical manifestations of poisoning and also the smell of garlic from patient's expiration or patient's vomitus or lavage contents. The patients had undergone diagnostic and therapeutic measures and if they had died, the body was sent to the Kahrizak Forensic Center for a full autopsy.

The second part of study was conducted in Kahrizak Forensic Center during 2008 to 2010. The extension of the research in Kahrizak Research Center was due to prolonged fixation time of autopsy specimens, H&E staining of samples and microscopic examinations, as well as, silver nitrate and other toxicological tests. Chi-square, analysis of variance (ANOVA), student *t*-test, and correlation tests were used to analyze the data. Also, the achieved data were analyzed by Statistical Package for

Social Sciences (SPSS) version 17 software.

In this study, the required variables and data were obtained by checking patients' records and obtaining information from the moment of using the pills until full recovery or death. Preparation of necropsy results, and names and personal information were not published at any step of the investigation.

## RESULTS

All necropsies were performed during 12 to 48 hours after death and none of the bodies had undergone decomposition in the time of autopsy.

### Pathological changes in the liver

Liver changes were observed in 19 deceased patients (67.85%), including hyperemia (43% of deceased), microvesicular steatosis (14.3%), tubular necrosis (14.3%), hydropic degeneration and hepatocyte vacuoles (10.7%) and micro- and macro-vesicular steatosis (released) (3.5%). Hepatic changes were observed in patients who had referred at least 45 minutes after taking the pill and died at least 2.5 hours after consumption. There was no significant relationship between the different side effects created in the course of treatment, patients' age, the number of tablets used, the time between taking the pill and starting the treatment, the time between taking the pill and the onset of symptoms, the time between taking the pills and death, the level of prothrombin time, alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase with pathological changes in the liver ( $P > .051$ ).

### Heart changes

Heart changes were observed in one deceased patient (3.6%) who was 66 years old and included hyperemia focus in the free wall of the heart and inter-ventricular septum. The patient had no history of heart disease and had referred four hours after taking the two tablets. He died because of myocardial infarction and cardiac arrest, four hours after the initial treatment.

### Pathological changes in the lung

Pulmonary pathological changes were observed in 25 deceased patients (89.3%), including pulmonary edema (7.5%), hyperemia (68%) and bleeding in the alveolar space or alveoli wall (46.5%). These changes were seen in 83.3% of patients who had consumed one tablet and all of those who had consumed more than one. There was no significant relationship between the different side effects created in the course of treatment, patients'

age, the time between taking the pill and the onset of symptoms and the time between taking the pills and death ( $P > .053$ ). The average numbers of pills taken by the deceased with and without pulmonary changes were  $1.47 \pm 0.71$  and  $1 \pm 0$ , respectively and there was a significant correlation between the number of taken pills and pulmonary changes ( $P = .003$ ).

### Pathological changes in the brain and cerebellum

Pathological changes were observed in the brain and cerebellum of two deceased patients (7.1%), including edema (7.1%), small foci of hemorrhage in cerebellar cortex (3.5%) and degenerative morphological changes induced by hypoxia (7.1%). These changes were only seen in patients complaining of weakness, lethargy, nausea and vomiting. There was no significant relationship between different types of side effects, patients' age, the number of tablets used, the time between taking the pill and starting the treatment, the time between taking the pill and the onset of symptoms, the time between taking the pills and death with pathological changes in the brain and cerebellum ( $P > .051$ ).

### Toxicology Findings at Autopsy

From a total of 28 patients died during necropsy, toxicology samples were prepared for 21 patients. Silver nitrate test was performed on these samples. 15 cases were phosphine-positive (71.5%) and six cases were phosphine-negative (28.5%). Among the deceased on which silver nitrate test was conducted on their different biological samples, 71.42% of the samples were phosphine-negative. All phosphine-negative cases were observed in patients who had taken a tablet. In case of using more than one tablet, the result was positive (phosphine-positive). Phosphine-positive and phosphine-negative cases were referred to a medical center with the interval of at least 30 and 45 minutes, respectively. Death in the phosphine-negative cases had occurred at least after four hours later.

There are multiple organ failures in autopsy and microscopic examination of patients poisoned with aluminum phosphide.<sup>16</sup> Thus, this study found that it is less likely to see pathological changes in macroscopic examination of various organs of the body.

## DISCUSSION

Acute aluminum phosphide poisoning is a large, though under-reported, problem in countries such as Iran. The toxicity of aluminum phosphide is attributed to the

liberation of phosphine gas, a cytotoxic compound that causes free radical mediated injury, inhibits vital cellular enzymes and is directly corrosive to tissues.

In this study, hepatic pathological changes were seen in 67.85% of the deceased studied patients. It was impossible to check the statistically significant relationship between the types of findings and symptoms before death with pathological changes. Thus, no significant association was found. Pathological changes were observed in all microscopic examinations of liver samples, but the liver was normal in all cases examined macroscopically, except hyperemia in some autopsies.

In our study, the level of hepatic hyperemia in autopsies was 43%. This number has been 28%,<sup>18</sup> 88-100%,<sup>19</sup> 97.4%,<sup>17</sup> 68.9%,<sup>20</sup> and 100%<sup>21</sup> in other similar studies.

According to our findings and Sutay and Tripude's study on hepatic changes of poisonings, it was found that the level of hepatic hyperemia in poisoning with rice tablet is more toxic than other poisonings. In our study, hepatic microvesicular steatosis was observed in 14% of the deceased patients. This number was 28.5%<sup>18</sup> and 48.9%<sup>20</sup> in other studies. Also, tubular necrosis was obtained in 14.3% of autopsies in this study. This number was 17-100%,<sup>19</sup> 43.4%,<sup>21</sup> 7.9%,<sup>17</sup> and 17.8% in other studies.<sup>20</sup> Tubular necrosis due to poisoning with rice tablet is higher than other poisonings.<sup>22</sup> Hydropic degeneration and hepatocyte vacuoles were seen in 10.7% of autopsies in this study. This number has been 48.9%<sup>20</sup> and 73.58%<sup>21</sup> in other studies. There were micro- and macro-vesicular diffuse steatoses in 13.2%<sup>17</sup> and 31.1%<sup>20</sup> of necropsies. In our study, the percentage and the type of pathological findings in liver was lower than other studies which might be because of the lack of microscopic examination in the majority of patients poisoned with rice tablet in Kahrizak Forensic Center.

In our study, pathological changes in heart were observed only in one autopsy sample, which were compatible with pre-death symptoms, such as myocardial infarction. Hyperemia, necrosis, myocytolysis, degeneration and infiltration of inflammatory cells in heart muscle tissue have also been mentioned in various studies<sup>18,19,23-25</sup> which is induced by cellular hypoxia.<sup>26</sup>

In our study, 89.3% of the deceased had pathological changes in their lung during the autopsy. There was a significant correlation between the number of pills and pulmonary pathological changes observed at autopsy that might be because of a significant relationship between the consumed dosage and a number of complications, clinical signs, and laboratory findings during the course of the disease and also because of the increased toxicity and

cell death after increased dosage. In our study, pulmonary edema was seen in 75% of autopsy cases. This number has been 48-100%,<sup>19</sup> 68.9%<sup>20</sup> and 92.45%<sup>21</sup> in other studies. Thus our finding is consistent with these studies and pulmonary edema seems to be due to direct cytotoxic effects on lung cells.<sup>11</sup>

Pulmonary hyperemia was seen in 68% of autopsies in our study. This number has been 34-100%,<sup>19</sup> 73.3%<sup>21</sup> and 100%<sup>21</sup> in other studies. The reason for pulmonary hyperemia and edema is the direct effects of phosphine and cellular hypoxia. Pulmonary hemorrhage was reported to be 58.46%<sup>21</sup> and 68.9%<sup>20</sup> in other studies. The alveolar hemorrhage was 46.5% during autopsy in our study. Given that all of the alveolar hemorrhage cases were observed microscopically during examinations, low blood levels observed in our study was acceptable compared to other studies and were caused by less microscopic examinations. All these studies showed autotoxic effects of aluminum phosphide on different lung cells.

In our study, microscopic pathology of the brain and cerebellum was performed only in two cases. Pathological changes were seen in both cases. There were edema and degenerative morphological changes induced by hypoxia in both cases and small focus of hemorrhage in the cerebellar cortex was observed in one case. In the study of Mehrpour and colleagues, cerebral edema was observed in 60%, cerebral edema in 53.3%, degenerative morphological changes induced by hypoxia in about 60% and intraparenchymal hemorrhage in 67% of the cases.<sup>20</sup> In autopsies performed in our study, peripheral area fluid was observed in 64.3% and peritoneal fluid in 35.7%, which can be caused by physiological changes in small peripheral blood vessels and capillary leak.<sup>11,12,14</sup>

Various factors cause changes in substance concentration in the time of death to autopsy. In this study, silver nitrate test was negative in 28.5% of samples sent for toxicological examination, that possibly can be due to a variety of reasons such as how to save and send the sample, the time between the consumption and sampling, the time between tests, consumed dosage, and the stability of phosphine gas and aluminum phosphide in tissues. In this study, there was a significant relationship between dosage and the response of silver nitrate test and patients died following the use of more than one pill. All had a positive silver nitrate test in terms of phosphine and the findings of our study suggest that negative silver nitrate in patients with aluminum phosphide poisoning cannot reject the poisoning, especially in cases in which the test is conducted after the death. If the performed biography, clinical and laboratory signs, examinations and autopsy

are consistent with poisoning by aluminum phosphide, even if the result of silver nitrate test is negative, rice tablet poisoning can be considered as the reason of patient's death.

## CONCLUSION

Rice tablet poisoning can lead to severe damage to organs such as the heart, lungs and liver. Public education is essential to know the side effects of rice tablet. The results of this study can also be used to develop an appropriate protocol for the treatment of aluminum phosphide poisoning.

## CONFLICT OF INTEREST

None declared.

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