Changes of QT Dispersion in Patients Suffering from Aluminium Phosphide Poisoning (Rice Pill)

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Abstract

BACKGROUND: Aluminium phosphide (ALP) or rice pill is a substance used in developing countries due to its low cost as pesticides. The availability of this substance has been lead to an increased rate of the use of this toxic inorganic compound for suicide. Complications are considered to be dose-related toxicity and hospitalisation time, varying from hemodynamic disorder, hypoglycemia, hyperglycemia, shock, cardiotoxicity, pulmonary and renal failures. The consumption of this substance is one of the major causes of mortality due to heart arrhythmia. QT dispersion represents a regional difference in ventricular repolarisation and electrical instability of the heart.

AIM: The purpose of this study was to investigate the effect of ALP poisoning on QT dispersion.

METHODS: In this study, 70 patients with ALP poisoning were enrolled, and 10 patients were excluded due to the exclusion criteria. QT dispersion rate was calculated in 60 patients using the standard electrocardiography at the time of referral. The above data were compared with the control group, which included 40 subjects with normal coronary angiography, and without cardiovascular risk factors.

RESULTS: The findings presented herein indicated a significant correlation between QT dispersion and control group (P < 0.0.5). There was a significant relationship between the severity of acidosis and the patient's tablets – taking a number (P < 0.05). However, there was no relationship between QT dispersion with the severity of acidosis and mortality in patients.

CONCLUSION: Because there is no CAD risk factor in the population, it can be concluded that increase in QT dispersion in these individuals can be due to ALP poisoning; nevertheless, this is not considered to be a factor in increasing the morbidity of these patients.

Introduction

Aluminium phosphide (ALP) or rice tablet is a substance that is used in developing countries because of its cheapness as pesticides [1]. The availability of this substance has been led to an increased rate of the use of this toxic inorganic compound for suicide [2]. ALP poisoning is considered to be one of the major causes of suicidal deaths, and is sometimes accidental and rarely due to homicide [2], [3]. ALP poisoning has a high degree of mortality (30-100%), and the survival of patients is unlikely when swallowing more than 1.5 g of ALP [4].

Toxicity with this substance is observed in both children and adults. ALP releases phosphine in the gastrointestinal tract, which is cytotoxic and releases free radicals and thus exerts its high toxicity [1]. These effects are not unique to a particular organ and are multisystemic [5], [6]. The effects of phosphine toxicity occur in a minute to 60 minutes after taking it. Phosphine causes cell hypoxia and small vessel damage, which ultimately leads to cardiotoxicity following anoxic myocardial damage and shock [7]. The cardiovascular effects of rice tablet include increased jugular venous pressure, S3, hypotension, shock, arrhythmia, myocarditis, and pericarditis [7]. As a matter of fact, the greatest toxic effect of ALP is myocardial suppression and severe cardiovascular collapse [8]. In various studies, myocardial damage and its effects on the electrocardiogram have been proven to be responsible for the mortality caused by ALP poisoning

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[8]. Various studies have reported that 38-91% of patients have electrocardiogram changes as cardiac conduction defects, including RBBB, LBBB, atrioventricular block, and rarely sinus block.

On the other hand, there is arrhythmia, including junctional rhythm, extra supraventricular systole and ventricular fibrillation (V-fib or VF). Eventually, reparative disorders such as ST-segment depression, ST-segment elevation, and T wave inversion occur following ALP poisoning [8]. Therefore, the patient should be monitored for cardiac arrhythmias immediately.

QT dispersion was defined to be the difference between the maximum and minimum QT interval of the 12-standard lead of electrocardiography (ECG), which indicates ventricular repolarisation and electrical instability of the heart. If this difference is at a high level, the risk of arrhythmias can be increased (9). QT dispersion is a phenomenon described by Campell et al. They showed that there are small but consistent differences between the QT intervals of different leads. Evidence suggests that the degree of QT variability in a variety of leads can provide valuable clinical information demonstrating the underlying abnormalities, including ventricular repolarisation [9]. Previous studies have shown that QT dispersion changes during myocardial ischemic episodes. Recent studies indicate that QT dispersion reaches its highest level during the early hours of ischemia and decreases over time as a result of receiving thrombolysis treatments. It also increases in patients who develop ventricular fibrillation (VF). Ischemia at the microvascular level or autonomic changes at the heart rate may be the cause of this phenomenon.

Changes in QT dispersion during myocardial infarction have been interesting but have not yet been clinically proven. Although they were already used in the area of the efficacy and safety of antiarrhythmic drugs [9]. The difference between the QT intervals of different leads and its measurement as a 'QT dispersion' can make challenging our current approach more likely to assess the risk of arrhythmias. QT dispersion provides a simple, inexpensive and non-invasive potential method of measuring the underlying dispersion of improved ventricular irritability. Continued development of QT dispersion can be linked to important clinical benefits, especially the benefits and risks of treatment with antiarrhythmic drugs [9].

Accordingly, this study was conducted to determine the effect of ALP on QT dispersion as a possible risk factor for sudden cardiac death, arrhythmias and a fatal change in ECG. Since this substance is one of the most important causes of mortality and morbidity of heart arrhythmia [10], the aim of this study was to investigate the cardiotoxicity effects of ALP on the cardiovascular system and particularly the QT dispersion in ALP poisoning.

Material and Methods

The medical records of 70 patients diagnosed with ALP poisoning were investigated in Emam Reza Hospital, Mashhad, Iran. ECG was evaluated at the time of admission, and their QT dispersion was calculated. Also, prognostic factors such as the number of hospital days, the need for a ventilator, the severity of acidosis, and the use of drugs such as magnesium sulfate and calcium gluconate were used.

The control group consisted of 40 patients without a cardiovascular risk factor that had normal coronary angiography,

Inclusion criteria: Patients with a definite diagnosis of ALP poisoning that did not have a history of heart disease.

Exclusion criteria: Patients who have a branch block in the ECG and patients with a history of heart disease.

Data analysis

Data are presented using descriptive statistics like frequency and mean ± standard deviation. T-test and Mann-Whitney-U tests were applied to assess the relationship between qualitative and quantitative variables. Also, the Kruskal-Wallis test was used as a non-parametric method for testing groups, and the relationship between qualitative variables was determined using chi-square test. Statistical analysis was performed using SPSS version 22. A p-value of less than 5% was considered statistically significant.

Ethical considerations

A) The patient's secrets were completely preserved until the end of the study. B) In the case of intervention or diagnosis, common diagnostic and therapeutic methods along with success rate, complications and benefits of common and interventional methods were determined.

Results

In this study, out of 70 patients, 10 patients were excluded according to the exclusion criteria. Then, patients were compared with the control group. The average age of the patients was 25.55 ± 7.53 in the population. The lowest and highest age was determined as 12 and 45 years, respectively. Of the 60 patients, 27 (45%) were female, and 33 (55%) were male. The distribution of smokers and non-smokers showed that 30% of patients were smokers. In the present study, blood pressure, hyperlipidemia

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and diabetes were also investigated. Among all 60 patients enrolled in the study, only one person was found to suffer from hypertension, and no diabetic or hyperlipidemic patients were diagnosed (Table 1).

Table 1: Basic characteristics of patients with aluminium phosphide poisoning

	Number of patients with poisoning with aluminium phosphide: 60 patients		
	Number	Per cent	Mean ± SD
Age			25.55 ± 7.53
Female	27	45%	
Male	33	55%	
Cigarette	18	30%	
Blood pressure	1	1.7%	
Diabetes	–	–	
Hyperlipidemia	–	–	

Table 2 shows the frequency of QT dispersion changes in the population under study, with an average QT dispersion of 60.66 ± 22.08.

Table 2: Frequency QT dispersion changes in patients with ALP poisoning

QT dispersion (ms)	Number	Percent
40	30	50%
60	2	3.33%
80	25	41%
100	2	3.33%
120	1	1.6%

Based on T-test, there is a significant relationship between patient group and control group, with QT dispersion was increased in the patients' group (P = 0.027), (Table 3).

Table 3: Comparison of QT dispersion values between the control group and the patient's group

QT dispersion values	Number	Mean	Standard deviation
Group case	60	60.66	22.08
Group control	40	39.25	19.26

Comparison of two variables such as age, number of hospital days, number of pills, duration of hospitalisation, acidosis severity and QT dispersion was performed. The results demonstrated a significant relationship between the number of taking the pills and the severity of acidosis. The increase in the number of pills consumed was highly linked to increased acidosis (P = 0.020), and no significant relationship was found between other variables such as acidosis and QT scattering. There was also a correlation between age and QT dispersion, where QT dispersion increased with age (P = 0.040; Table 4).

Table 4: Correlation test for age variables, hospital admission time, acidosis severity, number of pills, duration of hospital visits in comparison with QT dispersion

	Comparison of QT dispersion value with hospital admission time	Comparison of QT dispersion value with the number of pills	Comparison of QT dispersion value with a duration of a hospital visit	Comparison of QT dispersion value with acidosis severity	Comparison of QT dispersion value with patient age
P value	0.293	0.236	0.692	0.902	0.040

Figure 1 shows the frequency distribution of hospital admission time in patients with ALP

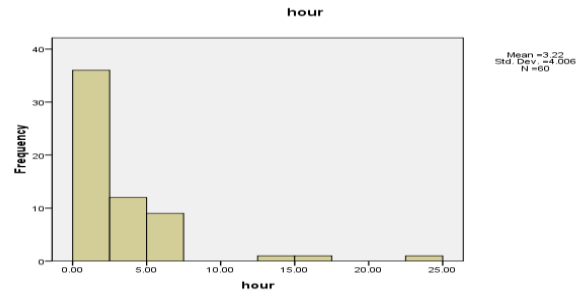poisoning, demonstrating an average referral time of 4.006 ± 3.22.

Figure 1: Frequency distribution of hospital visit time in patients with ALP poisoning

The frequency distribution of patients based on the number of pills consumed is shown in Figure 2 that patients consumed an average of 1.09 ± 1.70 pills.
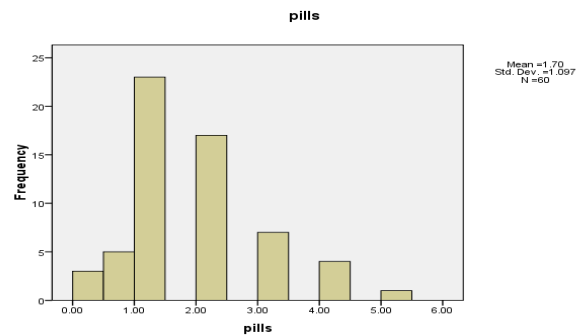

Figure 2: Distribution of patients in terms of the number of pills used

In the current study, the patients' medical records were reviewed, and the type of treatment was recorded, were 4 treatment groups was found (Table 5).

Table 5: Frequency of patients with ALP poisoning based on the type of treatment received

type of treatment received	Number of patients	per cent
HCO3+MgSO4+CaGluconate (First therapeutic group)	24	40%
HCO3+MgSO4 (Second Therapeutic Group)	12	20%
HCO3 (Third Therapeutic Group)	20	33.33%
Conservative Tx (Fourth Therapeutic Group)	4	6.66%

The frequency of patients with ALP poisoning is indicated in Figure 4, based on the number of hospital admissions days, and the average number of admission days was determined as 5.343 ± 3.08.

Frequency of mortality in patients with ALP poisoning by sex revealed that 8 of the patients who died were female and 10 were male, as well as 19 of the surviving patients were female, and 23 were male. Based on the Chi-Square test, mortality of patients with ALP poisoning was not related to their sex (P = 0.955). The findings revealed that 33.3% (20 patients) of the patients needed intubation, and the remaining

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did not require intubation. Of the 18 dead patients, 5 were smokers. Among 42 survivors, 13 patients were found to be smokers. Chi-Square test indicated no significant relationship between the mortality rate of the patients and their smoking (P = 0.806).
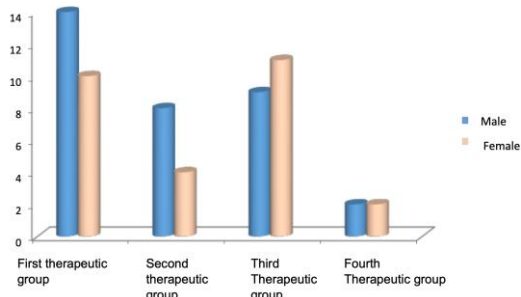

Figure 3: Frequency of patients with ALP poisoning by type of treatment and sex

The Mann-Whitney test revealed that there was no significant correlation between QT dispersion and mortality in patients with ALP (P-value = 0.471).
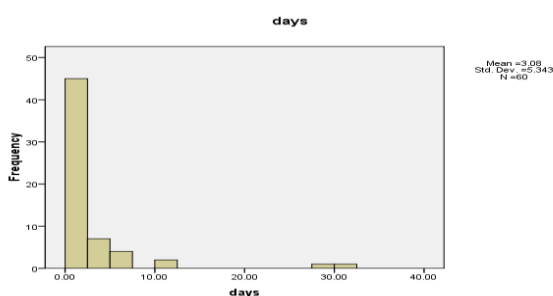

Figure 4: Frequency of patients with ALP poisoning based on the number of hospital admissions days

According to the T-test, a significant correlation was found between the mortality of the patients and the severity of acidosis (P = 0.000).

Based on the Chi-Square and Cross tab tests, out of the 20 cases underwent intubation, 18 of them finally died. In other words, all died patients were under intubation. Also, a direct linear correlation was found between the patients who died and the patients with intubation (P = 0.000). Additionally, no significant correlation was determined between the mortality rate and the type of treatment (P-value: 0.232).
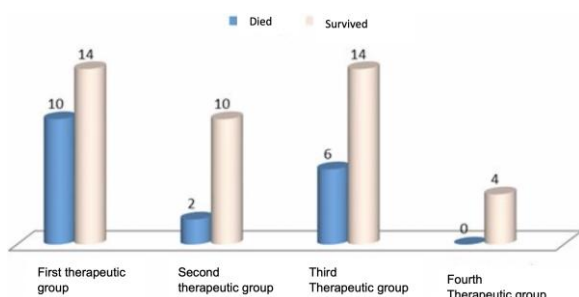

Figure 5: Frequency of mortality in patients with ALP poisoning based on the type of treatment

Mann-Whitney test exhibited that there is a significant relationship between mortality rate and several pills used (P = 0.018), as well as between mortality rate and several hospital days (P = 0.004). Based on the findings presented herein, no relationship was observed between mortality and the age of the patients and the duration of the visit.

Discussion

ALP poisoning has a high toxic effect, where its complications are dose-dependent and hospital-based, and vary from hemodynamic disorder, hypoglycemia, hyperglycemia, shock, cardiotoxicity, pulmonary and renal failures [10], [11], [12], [13].

Direct toxic damage of ALP on the myocardium causes cardiac arrhythmias [14]. Hypotension and shock occur 3 to 6 hours after taking ALP. In patients who survive, cardiotoxicity and hypoxia can be disappeared after 5 to 7 days following phosphorus excretion and the return of normal cell metabolism. This toxic injury causes a variety of lethal changes in the ECG 6 to 24 hours after taking ALP in patients who have died, and non-lethal changes appear in patients who survive, within the first 12 to 24 hours of use, and also disappear 56 to 80 hours later. Death following the use of a rice pill in the first 24 hours is cardiogenic due to ECG abnormalities and shock [7]. In a study by Lall et al., (1997), it was reported that ECG changes were found at all dose in rats, including initial tachycardia and ST-segment elevation progressing to QRS broadening. The cause of cardiotoxicity of ALP, in addition to reducing cellular metabolism of the myocardium, is due to necrosis of the cardiac tissue following the release of reactive oxygen intermediates [15].

In a study by Katira et al., (2005), 90 patients with ALP poisoning were studied over 3 years. According to this study, death was due to poison-induced toxic chemical myocarditis, which was accompanied by electrocardiographic changes [16]. In the study of Chugh and colleagues, arrhythmias, it has been revealed that conduction disturbances and ischaemic pattern were observed in the same frequency. ECG abnormalities, including varied sino-atrial blocks, early repolarisation syndrome bradycardia-tachycardia syndrome that has not been reported before, were seen in this study. Clinical profile of patients was the same regardless of the existence or absence of ECG changes. According to the aforementioned study, ECG abnormalities do not affect motility. Hypoxemia and shock, as well as severity of poisoning, dose of poison consumed, were not known to cause these abnormalities [17].

According to these studies, several ECG changes have been discussed, but QT dispersion

changes have not yet been evaluated. Therefore, the current study was aimed to determine the effect of aluminium phosphide on QT dispersion as a possible risk factor for sudden cardiac death and arrhythmias and a deadly change in ECG. In the study, 70 patients with aluminium phosphide poisoning were enrolled, and the QT dispersion rate was calculated in 60 patients using a standard electrography that was taken at the time of referral. Furthermore, the data were compared with the control group in which 40 subjects included without cardiovascular risk factors, with normal coronary angiogram.

Regarding the findings, the prevalence of ALP poisoning in the young population of Iran was higher. Also, the prevalence of ALP poisoning in the study population was higher in males than females. The mean QT dispersion in the studied population and the control group was calculated as 60.66 ± 22.08 and 39.25 ± 19.26, respectively. There was a significant correlation between QT dispersion as a comparison of both group (P = 0.027), and the QT dispersion rate was found to be higher in the patient's group when compared with the control group. The findings revealed no significant correlation between mortality rate of patients with QT dispersion rate. Also, no significant relationship was found between the mortality rate of patients with the type of treatment received. QT dispersion did not correlate with the severity of acidosis in patients. However, there was a significant correlation between QT dispersion rate and ageing (P = 0.040).

On the other hand, a significant relationship was observed between the severity of acidosis and patient's tablets –taking the number (P = 0.02). Moreover, there was a significant relationship between the mortality of the patients and the severity of acidosis (P = 0.000), but there was no relationship between the severity of acidosis and the hospitalisation time. A significant correlation was also found between the mortality rate of patients and the taking numbers of pills and the number of hospital admissions days (P = 0.004), were taking larger numbers of pills was associated with the more mortality rate in patients (P = 0.018). Also, there was a significant relationship between patients in need of intubation and those who eventually died, as a matter of fact, most intubated patients died (P = 0.000). According to the patient records, the cause of mortality was the appearance of multiple organ failure symptoms, as well as cardiogenic shock, and arrhythmia.

In conclusion, given that there is no risk factor for CAD in the population studied, it can be concluded that increased QT dispersion in these individuals was due to ALP poisoning. But this is not a factor in increasing the morbidity of these patients. However, further studies are recommended in this area to assess the risk of arrhythmias following increased QT dispersion in these patients.

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