Ain Shams Journal of Forensic Medicine and Clinical Toxicology
January 2023, 40: 1-14

Comparison between Gastric Lavage with Paraffin Oil versus Coconut Oil in Acute Aluminum Phosphide Poisoning: A Randomized Controlled Clinical Trial

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Abstract

Background: The high mortality incidence of acute aluminum phosphide poisoning (ALP) poses serious problems for healthcare workers, especially in developing countries. There is no precise antidote, and the treatment is mainly supportive. As a result, novel therapeutic approaches must be evaluated to reduce the morbidity and mortality. **Aim of the Study:** Evaluation of the safety and efficacy of gastric lavage with paraffin oil versus coconut oil as adjuvants to sodium bicarbonate 8.4% solution for ALP poisoned patients. **Methods:** This double-blinded, parallel-group, randomized trial (Trial ID: NCT04724655) enrolled 60 symptomatic patients of both gender who presented within two hours of ALP exposure. The patients were randomly allocated into three equal groups (20 patients each). All groups received the conventional treatment. In paraffin group, patients were subjected to gastric lavage with a mixture of paraffin oil in addition to sodium bicarbonate 8.4%. In coconut group, patients were subjected to gastric lavage with a mixture of coconut oil and sodium bicarbonate 8.4%. In the saline group, patients were subjected to gastric lavage with a mixture isotonic saline added to sodium bicarbonate. Outcomes were recorded in all groups. **Results:** The percentage of deaths among patients who received paraffin and coconut oily substances for gastric lavage were non-significantly lower than patients in the saline group. In addition, there was a significant prolongation of hospital stays with higher survival time in both paraffin and coconut treated groups than in the saline group ($p < 0.001$). Meanwhile, there was no significant difference between the paraffin and coconut groups. Furthermore, there were no reported significant adverse events of paraffin or coconut oil use. **Conclusion:** Paraffin oil and coconut oil might give hope to ALP poisoned patients; lowering the need for mechanical ventilation and significantly improve the survival time in patients who received oily gastric lavage solution than the saline-based solution with no adverse events.

Received in original form: 18 June 2022 Accepted in a final form: 1 September 2022

Key words Aluminum Phosphide, Coconut Oil, Paraffin Oil, Gastric Lavage

Introduction

Aluminum phosphide (ALP) is used as a fumigant to keep insects, rats, and other pests away from stored grains. It's a solid inorganic phosphide that's frequently used as a grain preservative in Egypt, Iran, and India. Because of its inexpensive cost, great potency, and widespread availability, its tablets are widely utilized (Yan et al., 2017; Bagherian et al., 2021).

Aluminum phosphide tablets emit phosphine gas when they encounter water or hydrochloric acid in the stomach. The generated phosphine gas is absorbed by the gastrointestinal tract through simple diffusion. Phosphine gas prevents mitochondrial cytochrome oxidase from oxidizing oxygen in the cell. This prevents oxidative respiration, resulting in a significant drop in mitochondrial membrane potential (Singh et al., 2014).

Phosphides and phosphine have a direct corrosive effect added to their systemic toxic effect on body systems, especially the cardiovascular system. A profound circulatory collapse occurred due to direct toxicity on cardiac myocytes, fluid loss, and adrenal gland (Ataei et al., 2021).

Rapidly upon phosphine exposure, metabolic acidosis, cardiogenic shock, pulmonary edema together with acute renal failure are the most evident manifestations. Disseminated intravascular coagulation and liver failure may occur several hours later (Montazer et al., 2016).

Diagnosis depends on a history of exposure, garlic odor of the breath, severe thirst sensation, resistant metabolic acidosis, in addition to the revealing of phosphine gas in gastric aspirate or breath (Gupta & Ahlawat, 1995).

Treatment is mostly supportive because the exact mechanism of toxicity is still not well understood; there is no antidote for acute ALP toxicity. Hence, several studies are conducted in order to develop a specific therapy for this lethal poison (Bogale et al., 2021). Gastric lavage is an essential step during ALP management. The efficiency of gut decontamination is mostly determined by the length of toxic exposure and should be performed as soon as possible (Bhalla, 2017). Different gastric lavage

approaches include potassium permanganate, sorbitol, activated charcoal (Chyka et al., 2005), liquid paraffin (Helal et al., 2022), coconut oil (Dayananda et al., 2018), vegetable oil (Goswami et al., 1994), and sweet almond oil (Saidi & Shojaie, 2012) were used for ALP decontamination. However, few randomized controlled trials have been registered. Sodium-bicarbonate mainly neutralizes the stomach hydrochloric acid (HCl) decreasing the catalytic reaction of phosphide with HCl, inhibiting the release of phosphine (Devi et al., 2016). Water-based gastric lavage could worsen the clinical condition as it help ALP tablets release more phosphine gas (Sanaei-Zadeh & Marashi, 2016).

In vitro research, vegetable oils and liquid paraffin were effective at suppressing phosphine release from ALP. Paraffin oil is composed of saturated hydrocarbons extracted from petroleum (Farahani et al., 2016). However, it is used in different modalities such as treatment of pediatric constipation (Torabi et al., 2017). In addition, coconut oil is plant derived oil that possess antioxidant capacity, and safely used as food additive, cosmetics, and weight reduction (Ghani et al., 2018; Khan et al., 2020).The present study aimed to evaluate the safety and efficacy of gastric lavage with paraffin oil versus coconut oil versus isotonic saline as adjuvants to sodium bicarbonate 8.4% solutions in aluminum phosphide poisoned patients.

Patients and Methods

Ethical considerations:

Following approval by the Ethics Committee of Tanta Faculty of Medicine, Tanta University, the study was carried out (approval ID:34347/12/20). The procedures used in this study adhere to the tenets of the Declaration of Helsinki. This trial was registered at clinical trials.gov registry (Trial ID: NCT04724655). Written informed consents were obtained from the patients or his/her guardians (if the patient was unable to participate in the consent process) after an explanation of the purpose and technique of the study. All data were kept confident.

Study design, setting, and date:

This randomized controlled clinical trial, double-blind and parallel- groups was carried out at Tanta poison control center, Emergency Hospital, Tanta University, Egypt between January, and June 2021.

Eligibility criteria:

The present study included 60 patients aged more than 12 years of both genders who were symptomatic and presented within 2 hours' post-exposure to ALP. Sample size was calculated using G power 3.1.9.4 software program depending on primary outcome. The level of power 80%, margin of error 5%, allocation 1:1:1, p1=0.38, p2=0.40, p3=0.78.

The diagnosis based mainly on the history of ALP tablet consumption, the container presented by the patient's relatives, symptoms, and signs that consistent with ALP ingestion. Vomiting is the most common symptom, with smelling like decomposing fish or garlic odor. In addition, signs of abnormalities in heart rate or rhythm, severe profound hypotension, and metabolic acidosis were the most characteristics. The triad of hypotension, acute metabolic acidosis, and a garlic odor raise suspicion of ALP poisoning (Bhalla, 2017). Silver nitrate test was done for confirmation of ALP poisoning. It could detect phosphine in stomach aspirate (Chugh et al., 1989).

We excluded patients aged less than 12 years, pregnant and lactating women, who were unconscious and post-cardiac arrest patients. Patients who had a co-exposure to other toxic substances, presented late (more than 2 hours) after ALP ingestion, or who received any medical treatment before admission were excluded. Patients with a history of major medical diseases such as cardiovascular, renal or hepatic disorders were also excluded.

Randomization, allocation concealment, and blinding

Sixty patients were randomly allocated into three equal groups (20 patients each). Randomization and allocation concealment were done independently by a researcher who was not associated with the care or assessment of the patients. Allocation of patients was performed using the sequentially numbered, opaque, sealed envelopes method (Doig et al., 2005). Used envelopes were impermeable to light. The allocation sequence was hidden from the physician assessing and enrolling participants. To avoid subversion of the allocation order, name and patient hospital admission number were written on the envelope. Carbon paper was put inside the envelope to copy patient's information to the allocation card. Envelopes were opened after enrolling participants has been completed. The patients and the outcome evaluators were kept blinded to group allocation.

Interventions

All patients were subjected to full medical history and a thorough physical examination. Arterial blood gases, hemoglobin level, platelet count, prothrombin time, liver function tests, serum creatinine, and random blood sugar were performed as part of the usual investigations. Upon arrival to the toxicology unit, heart rate, blood pressure, temperature, respiratory rate, and oxygen saturation were measured. The severity of poisoning was assessed on admission by poison severity score (PSS) where (0) none, (1) minor, (2) moderate, (3) severe, and (4) fatal poisoning (Persson et al., 1998).

All patients received the conventional treatment including resuscitation, intubation, mechanical ventilation, inotropes, fluids, and antiarrhythmic agents were administered if needed. Oxygenation, endotracheal intubation, and mechanical ventilation were considered for compromised airway and breathing. Intravenous (IV) fluids and IV infusions of vasopressors (norepinephrine) were used to treat hypotension and refractory shock indicated by central venous pressure monitoring. Intravenous sodium bicarbonate (Na HCO3 8.4%) was used for metabolic acidosis correction. In addition, IV infusions of one gram magnesium sulphate were given to hypomagnesemia cases every 1 hour for the first 3 hours, then 1–1.5 g every 6 hours for the next 24 hours.

Gastric lavage technique:

Gastric lavage was performed for all patients by inserting nasogastric tube through nose to the stomach. The gastric tubes were a polyvinylchloride (PVC) Ryle's Tube, structured from Ultra Med Company, Egypt. To reduce the risk of aspiration of gastric contents, patients' position was in the left lateral decubitus. The hands of an uncooperative patient were restrained to prevent removal of the gastric tube. To confirm the intra-gastric tube placement, auscultating the stomach while introducing air with a 60-mL syringe. Before starting gastric lavage, the gastric contents were carefully aspirated for medicolegal preservation and silver nitrate test. Within the first 2 hours from ALP oral intake, gastric lavage was performed for nearly 10–15 minutes.

Paraffin oil group

Twenty patients received the previously described conventional treatment. Nevertheless, the lavage solution in this group was 50 ml of paraffin oil added to 50 ml of Na HCO3 8.4%. This mix was given through the nasogastric tube with frequent aspiration after 3 to 5 min. repeated gastric lavage with paraffin solution was done. Once the aspirate became clear, 50 ml of paraffin oil was administered and left in the stomach.

Coconut oil group

Twenty patients received the previously described conventional treatment. Nevertheless, the lavage solution in this group was 50 ml of coconut oil mixed with 50 ml of Na HCO3 8.4%. To generate a miscible solution containing sodium bicarbonate, coconut oil was simply heated to a moderate temperature tolerated by gastric mucosa. This mixture was introduced through the nasogastric tube with subsequent aspiration after 3 to 5 min. Repeated gastric lavage with coconut solution was done till clear aspirate.

Saline group (control group)

Twenty patients received the previously described conventional treatment. Nevertheless, the lavage solution in this group was 0.9 % normal saline mixed with 8.4 % Na HCO3 solution (50 ml Na HCO3 was added to each 500 ml saline). After 3 to 5 minutes, the lavage solution was aspirated through the tube. The gastric lavage was continual till the aspirate returned clear.

All sixty patients were followed up for complications such as aspiration, vomiting and any adverse events were documented in detail.

Outcomes:

The primary outcomes included the mortality incidence. The second outcomes were the amount of vasopressor needed, the need and duration of mechanical ventilation, the duration of hospital stays, and any adverse effects.

Statistical analysis

Sorting and analysis of data were performed using Statistical Package for Social Sciences (SPSS) version 26 for Windows (IBM© Corp., Armonk, N.Y., USA). Qualitative data were described using number and percent. Chi-square and Monte Carlo exact tests were used for analysis as appropriate. Distributions of quantitative data were tested for normality by Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed data were presented as mean and standard deviation (SD), and analysis was performed using analysis of variance (ANOVA) and paired sample t-test. Non-normally distributed data were presented as median and interquartile range (IQ), and analysis was performed using Kruskal-Wallis H test. The Kaplan-Meier survival analysis was performed to assess the impact of the intervention on the patients' survival and was compared to the control group using the Log-rank test. The mean survival time and the hazard ratio (HR) of death were calculated along with their 95% confidence intervals (CI). $P < 0.05$ was adopted as the level of significance.

Results

In the present study, 90 patients were reported during study period with toxic ALP ingestion and were assessed for eligibility. Thirty patients were excluded: 13 with late presentation after ingestion, 15 received previous medical intervention prior to admission, one patient reported co-ingestion of ALP with other poisons, and one was pregnant. Next, 60 patients with acute ALP poisoning fulfilling inclusion criteria were randomly allocated into three groups Figure (1).

Sociodemographic and toxicological data are shown in Table (1). The median age of the studied patients was 19.5 years. Females, single (not married), and from rural areas were the most common cases. The median delay time was 1.5 hours. Remarkably, all patients (100%) alleged suicidal ingestion of ALP tablets. There were no statistically significant differences between the paraffin, coconut and saline groups regarding the pre-mentioned parameters.

Tables (2) and (3) show that there were no statistically significant differences between the studied groups regarding the clinical characteristics, except the pulse where there was a significant difference between the paraffin and saline groups. The severity of poisoning showed no significant difference. Furthermore, ECG findings plus the results of laboratory investigations on admission were not statistically significant.

After treatment, table (4) revealed non statistically significant differences among the studied groups regarding arterial blood pH, PCO2, HCO3, and PO2.

Table (5), illustrates the difference in outcomes among the three studied groups, the fatalities in the paraffin and coconut groups were relatively lower in both the oily groups than the saline group (65%, 75% versus 80% respectively; $p= 0.551$) but statistically not significant. In additions, the need for intubation and mechanical ventilation was higher in the saline group than both the oily groups ($p= 0.138$). The total amount of vasopressors (norepinephrine) was similarly higher in the paraffin group and the coconut group (48 mg) than the saline group (32mg). Remarkably, the median of hospital stay duration in both paraffin and coconut groups was significantly longer than those in the saline group (12.5 hour, 12 hours versus 7 hours, respectively; $p<0.001$). However, there was a non-

significant difference (p= 0.389) among the studied groups as regards the median duration of ventilation.

The Kaplan- Meier survival analysis was done in order to assess the effect of the intervention on the survival of the patients compared to the standard treatment (Table (6), Figures (2a and 2b). The paraffin group had a significantly higher mean survival time than the saline group (18.9 hour versus 8.2 hour, respectively). The death hazard was 2.96 times greater in the saline group compared to the paraffin group. The coconut group had a significantly higher mean survival time than the saline group (16.3 hour versus 8.2 hour, respectively). The death hazard was 2.11 times greater in the saline group compared to the coconut group.

Regarding the amount of used oil, nearly 240 ml paraffin was needed compared with 100 ml coconut oil with a significant difference (p= 0.013). Most (80%) of patients in the paraffin and coconuts groups showed no adverse effect from the oily lavage solutions with no significant difference. Diarrhea occurred in 15% of the paraffin group meanwhile, nausea occurred in 20% of the coconut group.

Table (1) Comparison of baseline characteristics of the studied groups (n=60)

	Paraffin (n=20)	Coconut(n=20)	Control(n=20)	Name of test	p
Gender					
Male	7	8	6	χ^2 **0.440**	0.803
	35.0%	40.0%	30.0%		
Female	13	12	14		
	65.0%	60.0%	70.0%		
Age group				**Kruskal Wallis test 0.036**	0.982
Median (IQR)	19.5 (18-24)	19.5 (18-24.75)	19.5 (18-26)		
Marital status					
Single	12	14	11	**MC 3.078**	0.576
	60.0%	70.0%	55.0%		
Married	8	5	7		
	40.0%	25.0%	35.0%		
Divorced	0	1	2		
	0.0%	5.0%	10.0%		
Residence					
Urban	9	5	8	χ^2 **1.866**	0.393
	45.0%	25.0%	40.0%		
Rural	11	15	12		
	55.0%	75.0%	60.0%		
Education					
Low	1	4	3	**MC 2.268**	0.717
	5.0%	20.0%	15.0%		
Moderate	13	10	12		
	65.0%	50.0%	60.0%		
High	6	6	5		
	30.0%	30.0%	25.0%		
Occupation					
House wife	8	0	3	**MC 11.709**	0.167
	40.0%	0.0%	15.0%		
Farmer	3	3	3		
	15.0%	15.0%	15.0%		
Worker	3	7	5		
	15.0%	35.0%	25.0%		
Employee	2	4	4		
	10.0%	20.0%	20.0%		
Student	4	6	5		
	20.0%	30.0%	25.0%		
Delay time (hr.)				**Kruskal Wallis test 1.993**	0.369
Median (IQR)	1.5 (1 – 2)	2 (1 – 2)	1.5 (1 – 2)		
The toxic amount had been ingested				**Kruskal Wallis test 2.247**	0.325
Median (IQR)	1 (1 – 1)	1 (0.5 – 1)	1 (0.5 – 1)		

χ^2: Chi square test, MC: Monte Carlo Exact test, IQR: Interquartile range, hr: Hour

Table (2) Comparison of clinical characteristics, ECG and PSS at admission among studied groups (n=60)

	Paraffin (n=20)	**Coconut (n=20)**	**Control (n=20)**	**Name of test**	**p**
GCS				**Kruskal Wallis test 3.281**	0.194
Median (IQR)	15 (15 – 15)	15 (15 – 15)	15 (15 – 15)		
Pulse				**F 4.113**	0.021*
Mean ± SD	98.7 ± 17.41	97.4 ± 20.49	82.4 ± 21.60		
Range	52 - 122	60 - 130	54 - 124		
P (Paraffin & Coconut) = 1.000 P (Paraffin & Control) = 0.037* P (Control & Coconut) = 0.063					
Systolic Blood Pressure				**F 2.325**	0.107
Mean ± SD	95.0 ± 22.12	89.5 ± 25.64	76.5 ± 34.38		
Range	50 - 140	30 - 130	30 - 160		
Diastolic Blood Pressure				**Kruskal Wallis test 5.790**	0.055
Median (IQR)	60 (50 – 70)	50 (40 – 70)	45 (22.5 – 60)		
Respiratory Rate				**Kruskal Wallis test 5.923**	0.052
Median (IQR)	22 (20 – 24)	23 (19.25 – 28)	28 (24 – 32)		
Temperature				**Kruskal Wallis test 1.090**	0.580
Median (IQR)	37 (36.8 – 37)	37 (36.7 – 37.15)	37 (36.9 – 37.2)		
Oxygen saturation				**Kruskal Wallis test 3.336**	0.189
Median (IQR)	93.5 (88 – 97.75)	95.5 (92 – 98.75)	98 (92 – 99)		
ECG				**MC 9.215**	0.782
Normal sinus rhythm	9	9	12		
	45.0%	45.0%	60.0%		
Sinus tachycardia	3	5	5		
	15.0%	25.0%	25.0%		
Ventricular tachycardia and ventricular fibrillation	4	1	1		
	20.0%	5.0%	5.0%		
Inverted T wave	1	1	0		
	5.0%	5.0%	0.0%		
Atrial fibrillation	1	0	0		
	5.0%	0.0%	0.0%		
Asystole	1	3	2		
	5.0%	15.0%	10.0%		
ST segment	1	1	0		
	5.0%	5.0%	0.0%		
On admission (PSS)				**MC 2.997**	0.565
1	4	5	8		
	20.0%	25.0%	40.0%		
2	12	9	8		
	60.0%	45.0%	40.0%		
3	4	6	4		
	20.0%	30.0%	20.0%		

F: ANOVA, p≤ 0.05 (Statistically significant), MC: Monte Carlo Exact test, ECG: Electrocardiography, PSS: Poison severity score, n: number, GCS: Glasgow coma scale, IQR: Interquartile range, SD: Standard deviation.

Table (3) Comparison of on admission laboratory parameters among three studied groups (n=60)

	Paraffin (n=20)	Coconut (n=20)	Control(n=20)	Name of test	p
ABG				**MC 5.356**	0.294
Normal	10	7	7		
	50.0%	35.0%	35.0%		
Metabolic acidosis	7	11	13		
	35.0%	55.0%	65.0%		
Alkalosis	3	2	0		
	15.0%	10.0%	0.0%		
pH				**Kruskal Wallis test 2.409**	0.300
Median (IQR)	7.365 (7.33-7.44)	7.34 (7.3325-7.4225)	7.34 (7.33-7.37)		
HCO_3				**Kruskal Wallis test 2.245**	0.325
Median (IQR)	19.1 (16.075-21.975)	18 (16-20.45)	19.8 (17.85-23)		
PCO_2				**Kruskal Wallis test 2.235**	0.327
Median (IQR)	30.4 (22.925-32.75)	28.7 (26-32)	32 (28-38)		
PO_2				**Kruskal Wallis test 5.883**	0.053
Median (IQR)	98.8 (85.15 – 114.8)	106.35 (88.475 – 161)	189 (92-210)		
Na				**F 1.022**	0.366
Mean ± SD	139.9 ± 5.01	142.3 ± 4.70	141.6 ± 6.31		
Range	130 - 150	134 - 150	132 – 150		
K				**F 0.495**	0.612
Mean ± SD	3.5 ± 0.46	3.5 ± 0.42	3.6 ± 0.52		
Range	2.56 – 4.20	2.8 – 4.2	2.8 – 4.6		
Mg				**F 0.529**	0.592
Mean ± SD	2.0 ± 0.40	2.1 ± 0.31	2.0 ± 0.43		
Range	1.5 - 3	1.6 – 2.8	1.1 – 2.60		
RBS				**Kruskal Wallis test 5.446**	0.066
Median (IQR)	122.5 (107.5 – 197.5)	107.5 (85 – 127.5)	109 (99 – 122.25)		
SGPT				**Kruskal Wallis test 5.538**	0.063
Median (IQR)	19.5 (15.25 – 23.75)	24.5 (14.25 – 32)	27.5 (18.25 – 34)		
SGOT				**Kruskal Wallis test 3.083**	0.214
Median (IQR)	25 (19.25 – 29.75)	29.5 (20.5 – 33.75)	31.5 (20 – 44)		
Creatinine				**Kruskal Wallis test 0.179**	0.914
Median (IQR)	0.975 (0.8 – 1.115)	0.95 (0.8 – 1.1)	1 (0.825 – 1.1)		
Urea				**Kruskal Wallis test 4.827**	0.089
Median (IQR)	26 (21.25 – 31.575)	32 (27.25 – 34)	32 (22.5 – 340)		
WBCs				**Kruskal Wallis test 0.385**	0.825
Median (IQR)	8950 (5550 – 10200)	8200 (6025 – 9950)	8450 (5425-11200)		
INR				**Kruskal Wallis test 4.972**	0.083
Median (IQR)	1.18 (1.015 – 1.3)	1 (1 – 1.1875)	1 (1 – 1.2)		

MC: Monte Carlo exact test, n: number, F: ANOVA test, IQR: Interquartile range, SD: Standard deviation, HCO3: Bicarbonate, PCO2: partial pressure of carbon dioxide, PO2: partial pressure of oxygen, Na: Sodium, K: Potassium, Mg: Magnesium, RBS: Random blood glucose, SGPT: Serum glutamic pyruvic transaminase, SGOT: Serum glutamic-oxaloacetic transaminase, WBCs: White Blood cells, INR: International normalized ratio

Table (4) Results of arterial blood gas after treatment in the studied groups (n=60)

	Paraffin (n=20)	Coconut (n=20)	Control (n=20)	Name of test	p
ABG					
Normal	7	4	6	**MC 2.824**	0.618
	35.0%	20.0%	30.0%		
Metabolic acidosis	12	12	12		
	60.0%	60.0%	60.0%		
Alkalosis	1	4	2		
	5.0%	20.0%	10.0%		
pH				**Kruskal Wallis test 0.136**	0.934
Median (IQR)	7.34(7.31-7.4075)	7.335(7.3125-7.4450)	7.33(7.3125-7.4275)		
HCO_3				**F 1.512**	0.229
Mean ± SD	17.1 ± 4.54	17.7 ± 4.73	19.9 ± 6.45		
Range	8.8 - 25.7	8.8 - 25	8-32		
PCO_2				**Kruskal Wallis test 2.870**	0.238
Median (IQR)	29.35(19.75-34.15)	30(26-36.025)	34(28.5-38)		
PO_2				**Kruskal Wallis test 5.392**	0.067
Median (IQR)	106.7(91.575-127.525)	102(60.5-128.475)	143.5(100-196.25)		

MC: Monte Carlo exact test, F: ANOVA, n: number IQR: Interquartile range, SD: Standard deviation, HCO3: Bicarbonate, PCO2: partial pressure of carbon dioxide, PO2: partial pressure of oxygen

Table (5) Comparison of outcome among three studied group (n=60)

	Paraffin(n=20)	Coconut (n=20)	Control (n=20)	Name of test	p
Mortality					
Death	13	15	16	**χ^2 1.193**	0.551
	65.0%	75.0%	80.0%		
Survivor	7	5	4		
	35.0%	25.0%	20.0%		
Need of ventilation					
No	10	7	4	**χ^2 3.956**	0.138
	50.0%	35.0%	20.0%		
Yes	10	13	16		
	50.0%	65.0%	80.0%		
Oil side effects					
No	16	16	20	**MC 11.815**	0.012*
	80.0%	80.0%	100.0%		
Diarrhea	3	0	0		
	15.0%	0.0%	0.0%		
Nausea	1	4	0		
	5.0%	20.0%	0.0%		
P (Paraffin & Coconut) = 0.114 P (Paraffin & Control) = 0.106 P (Control & Coconut) = 0.035*					
Amount used oil (ml)				**Kruskal Wallis test 49.189**	<0.001*
Median (IQR)	240 (180 – 360)	100 (80 – 160)	0 (0 – 0)		
P (Paraffin & Coconut) = 0.013* P (Paraffin & Control) = <0.001* P (Control & Coconut) = <0.001*					
Vasopressor amount (mg)				**Kruskal Wallis test 2.800**	0.247
Median (IQR)	48 (32 – 64)	48 (32 – 64)	32 (32 – 32)		
Duration of ventilation (hr.)				**Kruskal Wallis test 1.886**	0.389
Median (IQR)	1 (0 – 5.75)	4 (0 – 6.75)	2.5 (1.25 – 4)		
Length of hospital stay				**Kruskal Wallis test 20.457**	<0.001*
Median (IQR)	12.5 (10.5 – 19)	13 (10 – 18)	7 (6 – 10)		
P (Paraffin & Coconut) = 1.000 P (Paraffin & Control) = <0.001* P (Control & Coconut) = <0.001*					

χ^2: Chi square test, MC: Monte Carlo Exact test, p≤ 0.05 statistically significant, <0.001 highly significant, n: number IQR: Interquartile range.

Table (6) Survival time and hazard ratio of mortality (The Kaplan- Meier survival analysis to assess the effect of the intervention on the survival of the patients compared to the standard treatment)

Variables		N	Progression free survival			
			Mean (95% CI)	SE	Log rank	P value
Group	Paraffin	20	18.9 (13.2-24.8)	2.96	16.432	<0.001*
	Coconut	20	16.3 (12.2-20.4)	2.11		
	Control	20	8.2 (6.7-9.7)	0.77		

N: number, CI: Confidence interval, SE: Standard error.

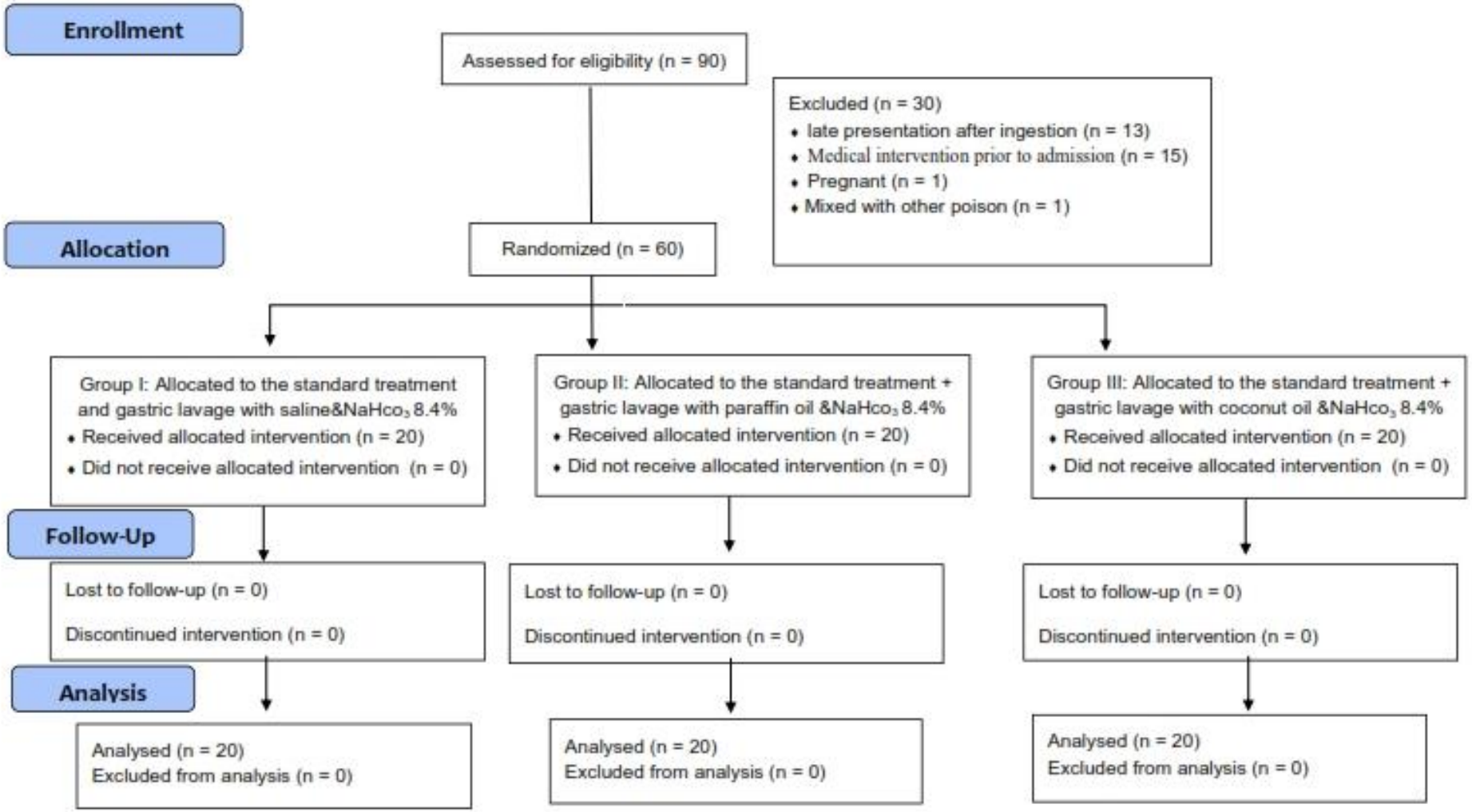
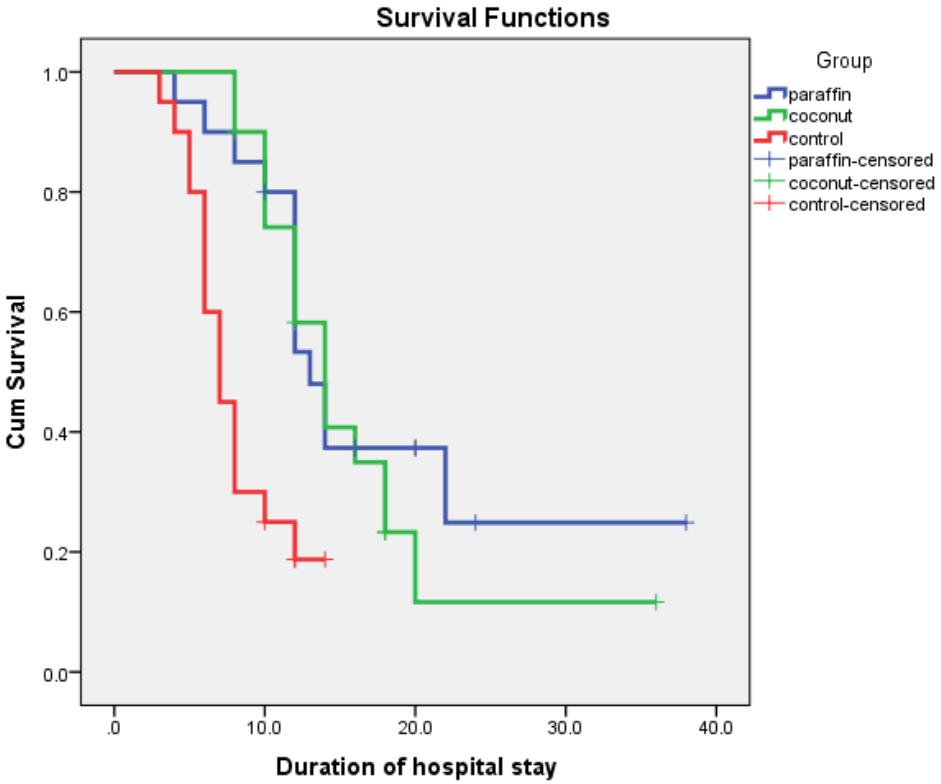
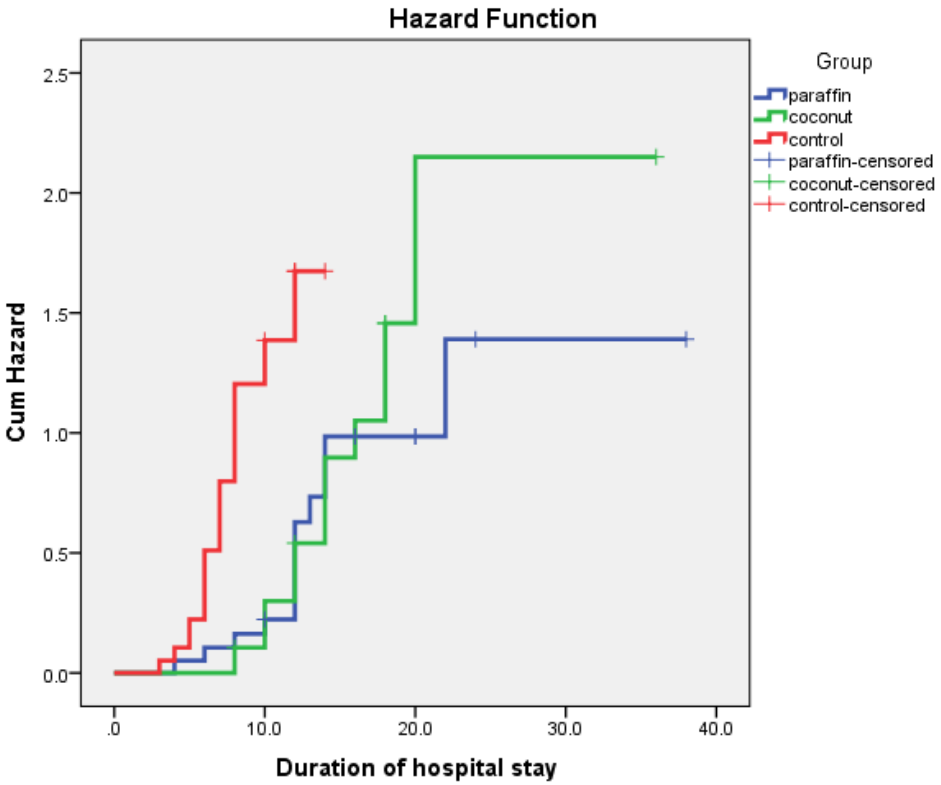


Figure (1): CONSORT 2010 Flow Diagram





Figures (2a and 2b): survival time and hazard ratio of mortality (The Kaplan- Meier survival analysis to assess the effect of the intervention on the survival of the patients compared to the standard treatment)

Discussion

In Egypt, a great ALP poisoning-related mortality have drawn a lot of attention, which was the primary motivation for conducting this study. The earliest signs of exposure are usually gastrointestinal manifestations (Bhalla, 2017). Managements of ALP poisoned patients aim to prevent phosphine gas release and to keep people alive by administering proper resuscitation techniques until the phosphine has been eliminated from the body. Hence, early gastric lavage is crucial (Amiri et al., 2016; H. Abdel-Hady et al., 2019). This study aimed to evaluate safety and efficacy of gastric decontamination by paraffin oil versus coconut oil as adjuvants to sodium bicarbonate 8.4% solution in acute ALP poisoned patients.

In terms of sociodemographic data, toxicological data, clinical characteristics, laboratory investigation results, and ECG findings, there were no significant changes between the saline and both the paraffin and coconut groups. These were comparable to previous research (Farahani et al., 2016; Elgazzar et al., 2019; Darwish et al., 2020; Emam et al., 2020; Helal et al., 2022). These findings suggest that the sequentially numbered opaque sealed envelopes (SNOSE) approach was used to achieve optimal randomization in this research. Pulse showed significant difference between the three groups, this could be explained by Elkins (Elkins, 2015) who noted that small trials are liable for baseline imbalance. However, pulse alone does not affect the outcome as it is not considered a prognostic factor for mortality (Abd Elghany et al., 2018).

After 12-hour from lavage, ABG showed non-significant values between the three studied groups. That disagreed with Darwish et al., (Darwish et al., 2020) who found that patients receiving paraffin oil lavage had non-significantly higher pH and PaCO2 values than the patients receiving potassium permanganate lavage solution (1:10000) at three-time intervals. Bicarbonate levels were significantly higher after 16 and 24 hours after admission. Dayananda et al., (2018) studied the effect of multiple doses of coconut oils through Ryle tube for 48 hours versus the potassium permanganate lavage solution and reported that the control group was more acidotic than the coconut oil group 24 hours after admission. Metabolic acidosis is the net result of phosphine-induced cytotoxicity. Furthermore, the acidotic state is aggravated by severe hypotension, which leads to inadequate tissue perfusion. Metabolic acidosis may exacerbate cardiac dysfunction, resulting in a vicious cycle that leads to patient death (Bhalla, 2017).

In the present study, the fatality rate was higher in the saline group compared to paraffin and coconut groups but without statistically significant differences Our results were in agreement with Dayananda et al., (2018), who reported significant lowering mortality rate in coconut group than the control group. Helal et al., (2022), studied the efficacy of paraffin oil lavage versus saline as adjuvants to sodium bicarbonate 8.4% solution and also reported non-significant lower mortality in paraffin group than control group. These non-statistically significant differences could be attributed to the smaller sample size in each group.

The requirements for intubation and mechanical ventilation was insignificantly lower in paraffin group and coconut group compared to the saline group. Results reflected some improvement on using oils in our study in accordance to findings reported in other clinical trials using vegetable oils in gastric decontamination of ALP poisoning (Dayananda et al., 2018). Meanwhile, a statistically significant differences were reported by Darwish et al., (2020) and Helal et al., (2022), who found lower need of mechanical ventilation in paraffin group in comparison with the control group. Intubation of patients and mechanical ventilation may be required depending on the severity of hypoxia, acute lung injury, and mental condition. Respiratory failure occurs as a result of myocardial depression combined with shock and acidosis, necessitating artificial ventilation (Louriz et al., 2009; Abd Elghany et al., 2018).

Additionally, the median amounts of vasopressors (norepinephrine) in the intervention group were relatively higher but non-significant in both paraffin and coconut groups than saline group. Our results were different from Darwish et al., (2020) and Helal et al., (2022) who reported lower vasopressor need in paraffin group than control group. In addition, Dayananda et al., (2018) also found lower need for vasoactive drugs in the coconut oil group than the control group. These contradictory results could be attributed to the rapid mortality of a considerable number of the saline group. Thus, there was no time for more vasopressor administration especially, with the small number of our studied patients.

Length of the hospital stay was significantly higher in the coconut group and paraffin group than the saline group. Meanwhile, there was no significant difference between the paraffin and coconut group. This is confirmed by the analysis of Kaplan-Meier survival curves. It showed that the mean survival time was significantly higher in the oil groups than in saline group. The death hazard was 2.96 times greater in the saline group compared to the paraffin group while it was 2.11 times greater in the saline group compared to the coconut group. This is in accordance with Helal et al., (2022), where the death hazard was 2.5 times greater in the control than the paraffin group. Darwish et al., (2020), found that the patients receiving potassium permanganate had a considerably shorter ICU admission and hospital stay in comparison to the patients receiving paraffin oil lavage and patients receiving CO Q 10 as an adjuvant to paraffin oil. This result could be explained by the rapid mortality of a considerable number of patients in the control group.

Another aim of this study was to evaluate safety of paraffin versus coconut versus isotonic saline for gastric lavage solutions. For the sake of safety, healthcare personnel were instructed to closely monitor any adverse effect. Diarrhea and nausea were seen in small number of patients. This can verify for the safety of using oil. Other research, too, have confirmed safety

of paraffin and coconut (Urganci et al., 2005; Farahmand et al., 2010, Torabi et al., 2017; Dayananda et al., 2018). The method by which coconut oil and paraffin oil diminish phosphide toxicity is unknown. Vegetable oils and liquid paraffin are probably effective in suppressing phosphine release from ALP. That is due to the physiochemical characteristics of ALP and its non-miscibility with fat (Goswami et al., 1994). Furthermore, medicated liquid paraffin could speed up ALP and phosphine excretion from the gastrointestinal tract (Agrawal et al., 2015). Coconut oil forms a protective coating cover the gastrointestinal mucosa, inhibiting phosphine gas absorption. Furthermore, coconut oil aid in the dilution of HCl, limiting the breakdown of phosphide from the pellet once more (Shadnia et al., 2005; Devi et al., 2016).

Limitations

This was a pilot single center study, with limited number of participants; a lot of patients didn't fit inclusion criteria and were excluded from the trial. However, its findings may pave the way for larger, multicenter trials.

Conclusion

Gastric lavage with paraffin oil or coconut oil when added to sodium bicarbonate was associated with a decline in ALP-related need for intubation and mechanical ventilation compared to saline added to sodium bicarbonate lavage solution. A significant reduction in hospital stays, and greater hazard ratio in the saline group in comparison with both paraffin group and coconut group.

Recommendations

Further multicenter studies on a larger scale of patients are required before making a conclusion regarding efficacy of paraffin or coconut oil gastric lavage in Aluminum phosphide toxicity. Restriction of Aluminum phosphide trade should be done due to higher mortality rate in spite of full medical supportive care.

Funding

The authors did not receive any specific funding.

Competing Interests

The authors declare that they have no conflict of interest.

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مقارنة بين غسيل المعدة بزيت البارافين مقابل زيت جوز الهند في حالات التسمم الحاد بفوسفيد الألومنيوم: تجربة سريرية إكلينيكية عشوائية

سماح ماهر البسطويسى و الشيماء محمود المنسى[١]

الملخص العربى

المقدمة: يشكل معدل الوفيات المرتفع للتسمم الحاد بفوسفيد الألومنيوم (والمعروفه فى مصر بحبة الغلة) تحديا كبيراللعاملين في مجال الرعاية الصحية، وخاصة في البلدان النامية. حيث أنه حتى الوقت الحاضر لا يوجد ترياق خاص به. نتيجة لذلك ، يجب تقييم الأساليب العلاجية الجديدة لتقليل معدلات الاعتلال والوفيات. الهدف من الدراسة هو تقييم سلامة وفعالية غسل المعدة بزيت البارافين مقابل زيت جوز الهند مقابل المحلول الملحي كمواد مساعدة لمحلول بيكربونات الصوديوم ٨,٤٪ للمرضى المصابين بالتسمم الحاد بفوسفيد الألمونيوم.

طريقة البحث: ضمت هذه التجربة الاكلينيكية العشوائية مزدوجة التعمية ، ٦٠ مريضًا يعانون من أعراض التسمم الحاد بفوسفيد الألمونيوم من كلا الجنسين الذين قدموا في غضون ساعتين من التعرض. تم تقسيم المرضى بشكل عشوائي إلى ثلاث مجموعات متساوية (٢٠ مريضًا لكل مجموعة). تلقت جميع المجموعات العلاج التقليدي. في مجموعة البارافين تم عمل غسيل معدة للمرضى بمزيج من زيت البارافين وبيكربونات الصوديوم ٨,٤٪. في مجموعة جوز الهند تم عمل غسيل المعدة بمزيج من زيت جوز الهند وبيكربونات الصوديوم ٨,٤٪. بينما فى مجموعة المحلول الملحي استخدمنا مزيج من المحلول الملحي متساوي التوتر وبيكربونات الصوديوم ٨,٤٪ لعمل غسيل المعدة.

النتائج: أظهرت النتائج بأن النسبة المئوية للوفيات بين المرضى الذين تم استخدام مواد زيتية لعمل غسيل معده لهم سواء بارافين أوجوز الهند أقل بكثير من المرضى في مجموعة المحلول الملحى. بالإضافة إلى ذلك، لاحظنا طول في فترات الإقامة في المستشفى مع البقاء أحياء لفترة أطول فى كلا مجموعتي البارافين وجوز الهند مقارنة بالمجموعة المالحة. وفي الوقت نفسه، لم يكن هناك فرق كبير بين مجموعتي البارافين وجوز الهند. علاوة على ذلك، لم يتم الإبلاغ عن أي أحداث عرضية جانبية خطيرة حال استخدام زيت البارافين أو زيت جوز الهند.

الاستنتاج: قد يعطي زيت البارافين وزيت جوز الهند الأمل للمرضى المصابين بالتسمم الحاد بفوسفيد الألمونيوم. بالإضافة الى تقليل الحاجة إلى أجهزة التنفس الصناعى وطول فترة البقاء أحياء بشكل ملحوظ في المرضى الذين تلقوا محلول غسيل معدى زيتي عن مجموعة المحلول الملحي بدون حدوث أية أعراض جانبية سلبية خطيرة عند استخدام تلك الزيوت.

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