ORIGINAL ARTICLE

Outcome of Patients with Cholinergic Insecticide Poisoning Treated with Gastric Lavage: A Prospective Observational Cohort Study

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Abstract

Background: Gastric lavage (GL) is one of the most commonly used decontamination method for cholinergic insecticide ingestion in developing countries despite lack of supporting evidence. This study was designed to evaluate the outcome of patients with cholinergic insecticide poisoning treated with GL in regards to timing and frequency of the procedure.
Methods: In this prospective observational cohort study, GL was planned to be administered to patients with cholinergic insecticide poisoning after initial stabilization irrespective of lavage given in peripheral hospitals. Therefore, some patients received one procedure (single GL) and some received more than one procedure (multiple GL). Early GL was defined as GL given within one hour of poison exposure and late GL was referred to performing the procedure after one hour.
Results: During the study period, 238 patients with cholinergic insecticide poisoning received GL comprising of 93 who received early, 145 who received late, 127 who received single and 111 who received multiple GL. Seventy-six GL treated patients (31.9%) died. Mortality, early RF and duration of assisted ventilation were not significantly different between patients receiving early and late, or single and multiple GL. Patients receiving multiple GL compared to those who received single GL developed late RF (9.0% vs. 20.5%, P = 0.01) and IMS (9.9% vs. 23.6%, P = 0.005) in significantly lesser extents. In multiple logistic regression analysis, effect of multiple GL on IMS and late RF remained significant (P = 0.04).
Conclusion: Number or timing of GL does not show any association with mortality while multiple GL had protective effect against development of late RF and IMS. Hence, GL might be beneficial in cholinergic insecticide poisoning.

Keywords: Gastric Lavage; Cholinesterase Inhibitors; Poisoning; Insecticides; Respiratory Insufficiency

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INTRODUCTION

Deliberate self-harm with cholinergic insecticides is common in developing countries and constitutes a major cause of suicide related deaths (1,2). Circulatory and ventilatory support, various decontamination measures, atropine, oximes (notably pralidoxime) are routine standard treatments. Nevertheless, mortality is observed to be relatively high in published literature (2-5).

Removal of the poison from stomach by gastric lavage (GL) seems to be a practical approach for decontamination. Although high quality evidence showing the benefit of GL in acute poisoning is lacking, it is one of the most commonly used decontamination method for cholinergic insecticide ingestion in developing countries (6). Data from western countries show that many clinicians are not using or remained unaware of the benefits of GL (7). Drug poisoning predominates in developed countries as the common method for deliberate self-harm, in which mortality is low (8). In contrast, insecticide poisoning with high mortality predominates in developing countries where various decontamination measures may be useful (9). Activated charcoal, forced emesis, ipecac, cathartics are the other methods of gut decontamination used in different parts of the world to varying extents (10).

Cholinergic insecticides are slowly absorbed across skin and removal of contaminated clothes and washing the poison off skin is an accepted decontamination method (11). Absorption of cholinergic insecticide can be rapid from the gut (12,13), but a Chinese clinical experience suggested that the poison may remain in stomach for hours to days (14). Moreover, absorption of poison depends on its chemical nature and may be affected by presence of other substances in stomach.

While removal of poison from gut appears to be reasonable to prevent further absorption of poison, especially during first hours of exposure, the benefit of GL is limited by its complications (15). Aspiration pneumonia

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can occur, especially in patients with depressed sensorium and unprotected airway. Worsening of hypoxia, laryngospasm, cardiac arrest, perforation of esophagus, electrolyte imbalance and sheer exhaustion are other possible complications (6). Moreover, the benefit of GL abates if the presentation to hospital is delayed and thus in poisoning with toxic agents, GL has not been advocated after 4 hours (10). However, there are Chinese studies showing beneficial impacts of multiple GL on the outcome of OP poisoning which led to being this treatment as a routine clinical practice for acute OP poisoning in China. Nevertheless, due to some methodological weaknesses, those studies were not considered as high-quality evidence in systematic reviews (6). Therefore, it is necessary to investigate the benefit of this relatively non-invasive method for treatment of insecticide poisoning.

In India, the procedure of GL has been advocated as an adjunct treatment for OP poisoning (16). Our institution policy is to give GL to all patients with insecticide poisoning within 24 hours of ingestion of poison on arrival at emergency room, once the general condition is stabilized. As several patients are referred from the primary and secondary healthcare facilities after receiving GL, some of them may receive the procedure twice. In this observational study, we aimed to evaluate the outcome of patients with cholinergic insecticide poisoning treated with GL in regards to the timing and frequency of the procedure. Autopsy findings were also analyzed for the cause of death and possible complications of GL.

METHODS

Study design and patients

In this prospective observational cohort study, patients with cholinergic insecticide poisoning admitted to Government Medical College (GMC) Thrissur Hospital, a 400-bed tertiary care hospital in Thrissur, India, between January 2011 and December 2012 were enrolled. Patients with clinical manifestations of cholinergic insecticide exposure who received routine emergency treatments were included in the study.

Data collection

Demographic features and clinical manifestations of the patients entered into a predesigned checklist. Details of the poison ingested were obtained from history, referral letter or bottle labels. Nature of poisons was additionally categorized into organophosphate, carbamate and unidentified cholinergic compounds. Lipid solubility of compounds was assessed with logP value which determines highly lipid soluble with higher logP (17). Probable cause of death was noted from autopsy findings.

Treatment protocol

Initial stabilization was performed for all patients and atropine was given until the chest was clear (18,19). GL was given to patients after stabilizing the vital signs regardless of whether it was given by a peripheral hospital or not. The procedure was performed in left lateral position for cooperative patients with a large bore Faucher orogastric tube (33-french). A nasogastic tube was used for patients who did not cooperate with insertion of orogastric tube, and in patients with depressed consciousness after securing the airway. Gastric contents were suctioned and then lavage was performed with 200 to 300 mL of plain water. Each aliquot was allowed to drain initially by gravity and remaining solution was suctioned out. The procedure was repeated with aliquots of 200 to 300 mL of water until the aspirate became clear. For all patients, single dose activated charcoal 1g/kg body weight was given after the lavage and oral magnesium sulfate were given until stool passed.

GL was given to patients even if they received it from elsewhere. In addition, patients with unclear lavage fluid remaining at the end of procedure received a second procedure later. As a result, some patients received single lavage and some others received more than one lavage (multiple). Early GL was defined as GL given within one hour of poison exposure (either from our centre or periphery) and late GL is referred to performing the procedure after one hour. All patients received standard care and were followed during admission until recovery or death.

Outcome measures

Primary outcome was in-hospital mortality. Secondary outcome measures included incidence of respiratory failure (RF), intermediate syndrome (IMS), duration of mechanical ventilation and the related complications. Some scientists proposed that RF following cholinergic insecticide poisoning occurs as a result of two distinct clinical syndromes; either by acute cholinergic syndrome or the IMS (18,20). RF was defined as presence of any of the following situations: (a) decrease in oxygen saturation to less than 90% shown by pulse oxymetry, (b) labored breathing with application of accessory muscles of respiration, (c) PaO2 less than 60 mmHg in arterial blood gas analysis. RF that developed within 24 hours of poison exposure was regarded as early RF and if developed after 24 hours post-exposure was defined as late RF. Onset of IMS was detected by the development of weakness of neck, proximal limbs, extra-ocular and/or respiratory muscles in a conscious patient after 24 to 96 hours of poison exposure in the absence of cholinergic signs (20,21).

Ethics

The patients were treated according to routine standard treatments and they received no additional intervention (16). The study was approved by the local ethics committee for medical research of GMC. Informed consent was obtained from the patients or their relatives (if they were unconscious).

Statistical analysis

Data were analyzed using SPSS 16 (SPSS Inc., Chicago, USA). Categorical variables are reported with frequency and percentage. Continuous variables with normal distribution are presented with mean and standard deviation (SD), and with non-normal distribution are presented with median and interquartile range (IQR). The mean difference of normally distributed variables in two groups was analyzed with independent samples t-test. The distributions of non-normal variables in two categories were compared with Mann-Whitney U-test. The difference of proportions in categorical variables was analyzed using chi squared test. P values of less than 0.05 were considered as statistically significant. To

establish the magnitude of effect, we calculated the relative risk with 95% confidence interval (RR; 95% CI). Multivariate logistic regression was used to reduce the effects of confounding factors on the outcome.

RESULTS

General findings

Over the period of two years, 254 patients (72% men) with mean age of 42.7 ± 15 years were admitted with cholinergic insecticide poisoning. Greater number of patients (134 patients) was primary attendees to our hospital and 120 were referred patients. One-hundred and thirteen patients (44.5%) were poisoned with carbamates, 94 patients (37.0%) with organophosphates and 47 patients (18.5%) with unidentified compounds. The most common compound identified was carbofuran (n = 111, 43.7%) followed by chlorpyrifos (n = 44, 17.3%), quinalphos (n = 37, 14.6%), phorate (n = 5, 2.0%), dimethoate (n = 4, 1.6%), methyl parathion (n = 4, 1.6%) and carbaryl (n = 2, 7.9%).

For 16 patients no GL was administered due to unstable clinical conditions. Ninety-three patients received early and 145 patients received late GL. One-hundred and twenty-seven patients received single and 111 patients received multiple GL.

Mortality

Eighty patients died during the study period (mortality rate = 31.5%). Four patients died soon after admission without receiving GL. Twenty-three patients died within 1 hour of admission with hypotension and RF probably due to direct effect of poison on cardiovascular system and central nervous system (CNS). Twenty-eight patients died secondary to early RF and 29 died secondary to late RF. Thirty patients had cardiac arrest which none of them were during GL.

Outcome analysis

Mean age of the non-survivors was significantly higher compared to survivors (49.3 ± 13.4 vs. 39.7 ± 14.7, P < 0.001). Median (IQR) time interval from poisoning to GL was 2 (0.5-2.5) hours in non-survivors and 2.5 (0.5-2.3) hours in survivors which were not significantly different from each other (P = 0.49). RF occurred in 93 patients (36.6%) and was strongly associated with mortality as RF was present in 95% of deceased patients compared to 9.8% of survivors (RR (95%CI): 32.89 (12.43-86.98); P < 0.001).

Analyses of patients' outcomes according to timing of the GL are presented in table 1. As can be seen, there was no significant difference in gender distribution and mean age between patients who received early and late GL. Regarding the outcomes, development of early RF, duration of assisted ventilation and mortality rate were not significantly different between patients receiving early and late GL. However, patients receiving early GL compared to those who received late GL developed late RF (9.7% vs. 18.6%, RR (95% CI): 0.52 (0.25-1.05), P = 0.06) and IMS (11.8% vs. 20.7%, RR (95% CI): 0.57 (0.30-1.08), P = 0.07) in lesser extent, although the differences for both outcomes were only close the level of statistical significance.

Table 2 shows the analyses of patients' outcomes according to frequency of the GL. As has been shown, no significant difference in gender distribution and mean age between patients who received single and late GL existed. In addition the two groups, did not differ significantly with regards to time elapsed from poisoning to admission to hospital. Considering the outcomes, development of early RF, duration of assisted ventilation and mortality rate were not significantly different between patients receiving single and multiple GL. However, patients receiving multiple GL compared to those who received single GL developed late RF (9.0% vs. 20.5%, RR (95% CI): 0.45 (0.26-0.88), P = 0.01) and IMS (9.9% vs. 23.6%, RR (95% CI): 0.43 (0.23-0.82), P = 0.005) in significantly lesser extents. Multiple logistic regression analysis was done to assess the effect of multiple GL on IMS and fully adjusted P remained significant (P = 0.04). The factors included in the adjustment was age of patients, timing of lavage, frequency of lavage, chemical nature of poison (organophosphate or carbamate), lipid solubility of compound suggested by logP value.

Table 1. Analysis of outcomes according to timing of gastric lavage

	Timing of gastric lavage*		RR** (95% CI)	P value
	Early gastric lavage (n = 93)	Late gastric lavage (n = 145)		
Male gender; n (%)	66 (71.0)	108 (74.5)	0.95 (0.81-1.12)	0.55
Age (years); mean ± SD	41.1 ± 14.2	44 ± 15.6	---	0.49
Time interval between poisoning and admission to hospital (hour); median (IQR)	1 (1-1.5)	3.25 (2.5-5.3)	---	<0.001
Early respiratory failure; n (%)	13 (14.0)	31 (21.4)	0.65 (0.36-1.18)	0.15
Late respiratory failure; n (%)	9 (9.7)	27 (18.6)	0.52 (0.25-1.05)	0.06
Duration of assisted ventilation (hours); median (IQR)	15 (9-26)	17 (12-28)	---	0.73
Intermediate syndrome; n (%)	11 (11.8)	30 (20.7)	0.57 (0.30-1.08)	0.07
Mortality; n (%)	29 (31.2)	47 (32.4)	0.93 (0.63-1.37)	0.71

* Early gastric lavage was given within one hour of poison ingestion and late gastric lavage was given after one hour post-ingestion.
** Relative risk for early gastric lavage

Table 2. Analysis of outcomes according to frequency of gastric lavage

	Frequency of gastric lavage		RR* (95% CI)	P value
	Multiple** (n = 111)	Single (n = 127)		
Male gender	81 (73.0)	94 (74.0)	1.01 (0.87-1.18)	0.85
Age (years); mean ± SD	42.6 ± 15.3	43.1 ± 15	---	0.81
Time interval between poisoning and admission to hospital (hour); median (IQR)	2 (1.1-3.1)	2 (1.1-4.0)	---	0.11
Early respiratory failure; n (%)	18 (16.2)	26 (20.5)	1.26 (0.73-2.18)	0.39
Late respiratory failure; n (%)	10 (9.0)	26 (20.5)	0.45 (0.26-0.88)	0.01
Duration of assisted ventilation (hours); median (IQR)	14 (9-26)	18 (11-30)	---	0.88
Intermediate syndrome; n (%)	11 (9.9)	30 (23.6)	0.43 (0.23-0.82)	0.005
Mortality; n (%)	36 (32.4)	40 (31.5)	0.99 (0.68-1.43)	0.95

* Relative risk for multiple gastric lavage
** Multiple gastric lavage: more than one procedure of lavage

Complications of the procedure

No patient at autopsy showed esophageal perforation or pneumothorax. Pneumonia occurred in 65 patients (25.6%), of which 33 patients recovered with standard treatments. Fifty cases of pneumonia occurred in patients under ventilator. Twenty-nine patients with pneumonia received single GL (29/127: 22.8%) and 36 received multiple GL (36/111: 32.4%) showing no significant difference (RR (95% CI: 0.70 (0.46-1.07), P = 0.097).

DISCUSSION

The benefit of GL in cholinergic insecticide poisoning lacks adequate evidence. A systematic review of 56 studies on GL found that 23 studies were randomized controlled trials (RCTs) with weak methodology (22). A large RCT by Li et al (23), aimed at finding the effectiveness of multiple vs. single GL in OP poisoning has not been materialized so far, probably due to technical reasons. Nevertheless, the importance of this minimally-invasive treatment should not be neglected, especially in resource-limited medical settings. In this study, we were able to show some benefits of GL in cholinergic insecticide poisoning. It was found that multiple GL has protective effect against development of late RF and IMS. Moreover, early GL was shown to reduce the risk for development of late RF and IMS compared to late GL though its impact was only close to level of significance. However, overall mortality and duration of assisted ventilation were not significantly different between patients receiving early and late, or single and multiple GL.

Early vs. late GL

In this study, mean time interval between poisoning and GL was similar in both survivors and non-survivors. We noted that early GL may not have any impact on the overall mortality or morbidities similar to previous observations (22,24) . Since the absorption of organophosphates is rapid, GL is claimed to be most effective within 30 minutes of ingestion, although GL done within four hours may also be beneficial (10). Our study also suggests that for the insecticide poisoned patients, other emergency measures should be given priority over gut decontamination in early hours post-exposure. In this regard, maintaining the airway, breathing and circulation along with treatment with atropine should be done before attempting GL in patients with decreased consciousness as it can cause more harm than benefit in such situations.

Multiple vs. single GL

Multiple GL had no impact on overall mortality and incidence of early RF. However, late-onset complications such as incidence of IMS and associated RF were significantly reduced by multiple GL, similar to a previous observation (21). The reason might be the reduction of continued absorption of poison from gut by extensive decontamination and consequently decrease in late-onset complications. Available data shows that early RF is mainly due to direct effect of poison on CNS and may be related to the type of compound and rapidness of absorption, whereas the cause of late RF is peripheral, attributed to persistent depolarization of neuromuscular junction by activity of acetylcholine (25,26). Prolonged absorption and potential deposition of the poison in fat with late release can also be the reason for persistent activity of acetylcholine (27). Therefore, removal of poison may not be fully effective with a rapidly absorbing poison that induces immediate central respiratory failure, but may be effective in cessation of further absorption-storage-slow release process and thereby decreasing late-onset complications.

We considered the possibility that in the present study, patients who received multiple GL were those who received early GL as well. Therefore, one might assume that the benefit of multiple GL we ascertained in this study originally emanated from early GLs done at peripheral healthcare settings. In this regard, we found that early GL can decrease the incidence of IMS and late RF though it only approached statistical significance. However, to clarify this hypothesis, we controlled the effect of timing of GL on frequency of GL in multivariate logistic regression analysis when the protective effect of multiple GL still remained statistically significant. Therefore, we believe that the early GLs performed in primary or secondary healthcare facilities prior to admission to our hospital may unlikely be the confounding factor in the benefit of multiple lavage.

Other outcomes

Mortality was significantly associated with RF in our series. RF has been recognized as the main cause of death in cholinergic insecticide poisoning (28-30). It should be noted that most of the deaths in the present study occurred from early RF whose incidence was not changed with multiple lavage and hence no effect of multiple GL on overall mortality could be observed.

Aspiration pneumonia is one of the common complications attributed to GL. In our series, 25.6% of patients developed pneumonia (both ventilator associated and aspiration related). However, over half of them recovered with antibiotics. Moreover, the frequency of lavage was not associated with likelihood of pneumonia. Chances of aspiration are minimal when smaller quantities of lavage fluid are used and airway is protected. Bhardwaj et al observed only minor complications in patients who received GL through nasogastric ryle's tube with close monitoring in the hospital and combined with prophylactic endotracheal intubation in those with Glasgow coma scale less than 10 (31). They also found higher rate of pneumonia in patients receiving GL in the peripheral healthcare settings prior to admission into their hospital which might have been due to aspiration during transport to hospital and also performing the procedure at poorly equipped peripheral settings (31). Moreover, pushing off poison to distal to stomach is another complication discussed in literature (32). However, we gave activated charcoal to all patients after GL and magnesium sulfate to ensure gut motility and passage of stool. Furthermore, serious complications of GL such as cardiac arrest, esophageal perforation and pneumothorax did not occur in our study group.

In the present study, autopsy was performed for all deceased patients. However, we could not evaluate the presence of poison in stomach by chemical analysis. In a study, kerosene smell of organophosphates was shown to be remained in stomach up to three days post-ingestion for which chemical analysis of poison was positive in 70% of cases (33). This suggests that lavage was ineffective in removing poison from stomach similar to a previous observation of Saetta and Quinton that showed multiple GL could not completely remove toxic agents and drugs from stomach (34).

LIMITATIONS

We could not quantify the ingested poison or retrieved poison in the lavage fluid. The chemical identity of the poisons could not be confirmed by toxicological analysis. The concentration of poison in blood before and after GL was not quantified. Also, details of GL performed at the peripheral hospitals were only based on information given in the referral letter. The overall risk or benefit of GL cannot be commented in our study as we did not compare GL with non-receiving GL group which has been considered unethical in India.

CONCLUSION

Mortality from cholinergic insecticide poisoning is strongly associated with the presence of RF. Although GL, single or multiple and early or late, did not create a meaningful difference in the overall mortality from this type of poisoning in this study, multiple GL appeared to decrease morbidity by reducing the incidence of late RF and IMS. Evidence of the presence of poison in stomach even after 24 hours of ingestion implies theoretical benefit of multiple GL, so that practice of a carefully done GL is not discouraged for this type of poisoning. Performing a randomized controlled trial with three arms including single GL, multiple GL and controls not receiving GL is recommended to confirm clinical benefit of GL for this type of poisoning.

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