Journal of the
Korean Society of
Clinical Toxicology

ORIGINAL ARTICLE

pISSN 1738-1320 | eISSN 2508-6332
J Korean Soc Clin Toxicol 2024;22(1):1-9
https://doi.org/10.22537/jksct.2024.00001

Enteral nutrition in mechanically ventilated patients after organophosphate poisoning

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Received: January 6, 2024
Revised: January 22, 2024
Accepted: February 8, 2024

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Purpose: Nutritional therapy is a crucial component of therapy for critically ill patients, but there is a lack of nutritional support guidelines for organophosphate (OP) poisoning, likely due to the gastrointestinal effects of atropine, the main antidote for OP. This study investigated whether enteral nutrition (EN) during atropinization is acceptable for mechanically ventilated patients after OP poisoning.

Methods: This retrospective study classified 82 patients with OP poisoning according to whether they were fed during atropinization while on mechanical ventilation (MV). Data on the baseline characteristics, nutritional support, and clinical outcomes were compared. Univariate and multivariate regression models were constructed to analyze the associations between atropine administration for OP poisoning and feeding intolerance-related EN after adjustment for risk factors.

Results: Eighty-two patients received EN after 72 hours on MV, and 40 of them simultaneously received 2 mg/hr atropine for the first 120 hours after EN initiation. The overall incidence of feeding intolerance was 57.3% during the first 12 days after EN initiation and did not differ according to atropine administration. Appropriate atropinization during EN in regression model 1 and the dosage of atropine administered during EN and the duration of EN during atropinization in model 2 were not associated with feeding intolerance in patients on MV after OP poisoning.

Conclusion: Appropriate atropinization is not associated with feeding intolerance after EN provision in patients on MV after OP poisoning. This study will help establish nutritional guidelines for OP poisoning patients. More research on nutritional support is needed to validate our results.

Keywords: Atropine, Enteral nutrition, Mechanical ventilation, Organophosphate, Poisoning

INTRODUCTION

The proportion of patients needing mechanical ventilation (MV) after organophosphate (OP) poisoning is as high as 20%–44%[1]. Furthermore, the mortality rate in patients requiring MV after OP poisoning remains at 10%–37% despite the widespread availability of an antidote[2]. This high mortality rate in mechanically ventilated patients after OP poisoning highlights the need for the medical community to review the current management strategy in detail.

Nutritional support has evolved as a central part of the critical care paradigm because malnutrition is associated with increased mortality and morbidity, including enhanced susceptibility to infectious and noninfectious complications[3]. However, guidelines for nutritional support for patients with OP poisoning have not yet been established. Because of the lack of guidelines, the time for EN initiation varies in OP poisoning. A recent prospective study investigated the effect of nursing based on early EN combined with the poisoning severity score (PSS) on 99 mechanically ventilated OP poisoning patients who received EN on the first day of OP poisoning[4]. Comparably, no nutritional support was provided to 28% of 45 patients

during atropinization[5], and EN was resumed at 41 days after weaning from MV[6]. The current guidelines for nutrition in critical care recommend the early initiation of EN within 24–48 hours of admission[7,8]. For OP poisoning patients, the key challenge to establishing a nutritional delivery strategy, in particular related to EN, may be atropine, which is the main antidote to OP poisoning but slows mouth-to-ileum transit and reduces gastric emptying in healthy subjects in a dose-dependent manner[9-11]. The mean atropine loading dose was 23.4 mg to achieve initial atropinization in patients following intentional OP ingestions requiring intubation[12]. Atropine was administered more than 10 days after OP poisoning in patients who required MV, while patients required MV as soon as 2 hours after OP poisoning[7,13]. It is highly likely that early EN in mechanically ventilated patients after OP poisoning should be provided during atropine administration. Moreover, feeding intolerance resulting from inappropriate EN attempts is associated with mortality and nosocomial infection[14]. Therefore, to standardize EN initiation times in patients with OP poisoning and ultimately establish nutritional support guidelines for OP poisoning patients, studies on the safety of EN during atropinization must be prioritized. No study concerning the safety of EN during atropinization has been performed.

Therefore, this study aimed to investigate whether atropine, which was administered as an antidote during OP poisoning to achieve appropriate atropinization, intervenes in the provision of EN in OP poisoning.

METHODS

1. Study design

This investigation was a single-institution, retrospective, observational case study performed by chart review. The study design was reviewed and approved by the Institutional Review Board of Chonnam National University Hospital (no., 00-2021-405). The requirement for informed consent from individual patients was omitted because of the retrospective design of this study.

2. Patients

We included 146 patients over 18 years of age who presented at our emergency department (ED) of chonnam national university within 24 hours after OP ingestion between January 2005 and January 2019, who needed MV within 24 hours of admission and who needed to remain on MV for more than 48 hours. The diagnosis of OP poisoning was made based on the following criteria: a history of OP ingestion provided by the patient or a witness, clinical manifestation consistent with OP poisoning, decreased butylcholinesterase (BuChE) activity, and improvements in the signs and symptoms after atropine and pralidoxime (PAM).

The exclusion criteria were no initiation of EN during MV (n = 51); transfer before determination of the outcome (n = 5); death on arrival (n = 2); gastroprokinetic administration within 24 hours prior to the start of EN (n = 1), discharge against medical advice (n = 1); and a history of underlying disease to which mortality could be attributed, such as malignancy (n = 1) (Fig. 1). We defined EN as the delivery of nutrition via a nasogastric tube into the stomach, duodenum or jejunum[15].

We found 85 patients; 82 patients were given EN and supplemental parenteral nutrition (PN) (delivery of nutrition via a venous catheter), and three patients were given only EN during MV. Because the provision of supplemental PN might confound the clinical outcomes, such as the duration of MV[16], we included only 82 patients who were provided combined EN and PN during MV after OP poisoning in this study.

The 82 patients were divided into two groups according to the administration of atropine during EN (atropine group versus no atropine group). Patients given EN during atropinization were assigned to the atropine group, and the remainder of the patients belonged to the no atropine group.

For all of the patients in the study, general supportive measures, which included decontamination and the administration of atropine and PAM, were available if required. Atropine is given to reduce muscarinic symptoms induced by OP such as bronchorrhoea, bronchospam, and diarrhea, not mydriasis. Also, it is used to reverse bradycardia and hypotension. Atropine was administered as a continuous infusion after targeting atropinization by bolus injection according to the severity of OP poisoning, and the dosage of infusion was titrated to achieve adequate atropinization, indicated by dry bronchial secretions, a systolic blood pressure of greater than 80 mm Hg, and a heart rate of greater than 80 beats/min.

EN through bolus feeding was provided by the intensive care unit (ICU) nurse 3–5 times per day using a 50 mL syringe through a nasogastric tube over the course of 10–15 minutes, which was confirmed daily to be intragastrically positioned on chest X ray. The head and shoulder of each patient was raised at 30° during feeding and for at least 45 minutes after feeding. The ICU nurse checked the gastric residual volume daily prior

 https://doi.org/10.22537/jksct.2024.00001

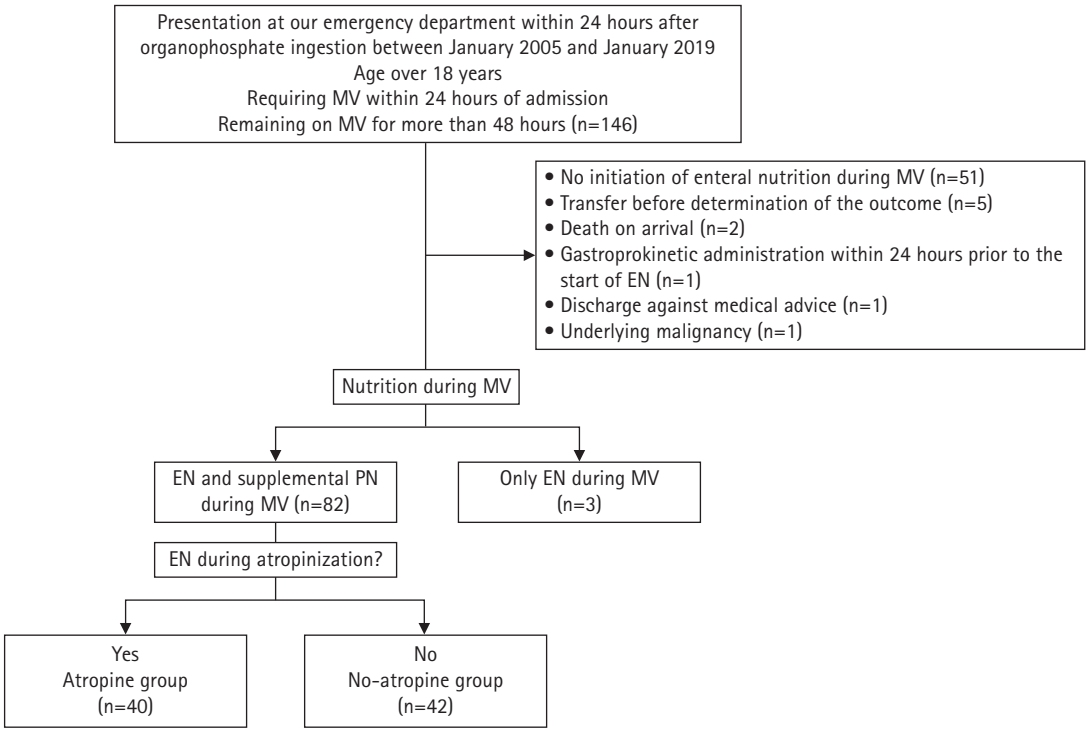

Fig. 1. Study flow. MV: mechanical ventilation, EN: enteral nutrition, PN: parenteral nutrition.

to each feeding episode and recorded gastrointestinal events such as diarrhea or vomiting. The nasogastric tube was flushed with at least 30 mL of water prior to feeding. Feeding was initiated at 50–100 mL boluses, which increased as gastric tolerance was established to a maximum of 400 mL/bolus. The Department of Nutrition in the hospital provided the volume of a standard liquid formula (1 kcal/mL) determined by the ICU physician referring to the opinion of the nutritional support team in our hospital. No prokinetics agents were routinely used.

3. Data collection

The following data were collected directly from the electronic medical records or from a review of the patient medical records by a trained physician who was blinded to patient prognosis: demographic data (age, sex, body mass index [BMI] calculated as body weight divided by height squared [kg/m^2], etc.), data related to the OP ingestion event (intentionality, amount of OP ingested, and time from ingestion to arrival at the ED), data obtained at presentation (Glasgow Coma Scale [GCS] score, acute physiology and chronic health evaluation [APACHE] II score, etc.), data related to treatment, and data related to the clinical course (duration of MV, duration of hospitalization, and in-hospital mortality). The following data related to nutritional support were also collected: data obtained at EN initiation (GCS, APACHE II, the level of serum albumin, the presence of acidosis (pH <7.35), hyperglycemia (serum glucose ≥ 198 mg/dL) and pancreatitis (an elevation of serum lipase at least 3 times greater than upper limits of normal and abdominal pain)[17], and the administration of sedatives or analgesics), time interval from arrival to PN, time interval from MV to initiation of EN, the highest dosage of atropine administered during EN on MV, the duration of EN during atropinization, the maximal volume of each bolus feeding during the first 12 days, the maximal volume of bolus feeding under the highest dosage of atropine administration, feeding intolerance during the first 12 days, and EN interruption after the development of feeding intolerance. In the no atropine group, data on the maximum volume of bolus feeding during the median duration of atropine administration in the atropine group were collected for comparison with the maximal volume of bolus feeding under the highest dosage of atropine in the atropine group. Feeding intolerance was defined as diarrhea (frequency >3 times/day with the loss of consistency), vomiting or regurgitation, large gastric residual volume (>200 mL), abdominal distension, and other gastrointestinal events[18,19]. Because feed-

ing intolerance develops between 1 and 12 days after initiation of EN in critically ill patients, we collected nutrition support data until 12 days after the initiation of EN in our study[18].

4. Outcomes

The development of any feeding intolerance related to EN was the primary outcome.

5. Statistical analysis

Descriptive statistics are presented as proportions and medians with interquartile ranges (IQRs). For continuous variables, Student *t*-test or the Mann-Whitney test was used for comparisons according to the normality of the distribution of the data, which was tested with the Shapiro-Wilk test. For categorical variables, the χ^2 test was used.

To examine the relationship between atropine and EN-related feeding intolerance in OP poisoning, univariate and multivariate regression analyses were performed. A multivariate logistic regression model using the entering technique was applied to factors that were obtained at presentation and that were significant in the univariate analyses, the time interval from MV to initiation of EN, the maximal volume of each bolus feeding during the administration of the highest dose of atropine, the maximal volume of each bolus feeding during the first 12 days, and variable related atropine. Variable-related atropine was entered in the form of a continuous variable (the highest dosage of atropine administered during EN on MV and the duration of EN during atropinization) or categorized variable (the presence/absence of atropine administration) in each separate regression model. In addition, general condition (age, sex, BMI), patient condition at EN initiation and the time interval from arrival to initiation of PN were entered into the multivariate regression model as confounders of feeding intolerance[20]. These confounders were included in the multivariate model regardless of the *p*-value associated with feeding intolerance in univariate analysis. Before modeling, if two or more variables retained in the multivariate analysis were highly correlated in the linear regression analysis, one variable was removed to avoid collinearity. Estimated odds ratios and 95% confidence intervals were calculated for all significant variables. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS ver. 21.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Table 1 shows the baseline characteristics of 82 patients in whom EN was delivered during MV after OP poisoning. The

Table 1. Baseline characteristics and data related to treatment including nutritional support according to the administration of atropine during enteral nutrition

Characteristic	No atropine (n=42)	Atropine (n=40)	Total (n=82)	*p*-value
Age (yr)	76.6 (64.5–82.1)	69.1 (52.6–80.6)	72.5 (60.0–82.0)	0.144
Male sex (%)	29 (69.0)	29 (72.5)	58 (70.7)	0.731
Body mass index (kg/m^2)	23.2 (21.5–24.8)	21.5 (19.9–24.6)	22.8 (20.8–24.6)	0.131
Diabetes mellitus (%)	6 (14.3)	5 (12.5)	11 (13.4)	0.813
Hypertension (%)	16 (38.1)	10 (25.0)	26 (31.7)	0.203
Intentional ingestion (%)	36 (85.7)	38 (95.0)	74 (90.2)	0.157
Time interval from ingestion to ED (hr)	2.5 (1.0–3.1)	3.5 (2.3–6.0)	3.0 (2.0–5.0)	0.003
Amount of ingested organophosphate (mL)	100.0 (50.0–200.0)	125.0 (63.7–300.0)	100.0 (50.0–250.0)	0.152
APACHE II score	14.5 (7.8–22.3)	16.0 (9.5–23.8)	15.5 (9.0–23.0)	0.311
Glasgow Coma Scale score	12.0 (5.3–15.0)	9.5 (3.0–15.0)	10.0 (3.0–15.0)	0.316
pH	7.37 (7.31–7.43)	7.36 (7.24–7.42)	7.36 (7.28–7.42)	0.346
White blood cell count (×103/μL)	14.1 (9.0–18.3)	14.9 (9.9–20.2)	14.7 (9.6–18.9)	0.464
Log butylcholinesterase activity (U/L)	7.23 (5.94–8.64)	6.54 (5.48–7.63)	6.8 (5.6–7.9)	0.035
Treatment and clinical course				
Time interval from arrival to MV (hr)	0.4 (0–4.5)	0 (0–5.1)	0.1 (0–4.5)	0.396
Time interval from ingestion to atropine administration (hr)	2.3 (0.5–5.5)	2.0 (1.0–5.8)	2.0 (1.0–5.1)	0.947
Time interval from ingestion to pralidoxime administration (hr)	2.0 (1.0–3.5)	2.5 (1.0–4.1)	2.3 (1.0–3.9)	0.529
The duration of MV support (day)	11.5 (6.8–24.3)	16.5 (8.3–22.8)	15.0 (7.0–23.0)	0.307
In hospital mortality	9 (21.4)	6 (15.0)	15 (18.3)	0.138

Values are presented as median (interquartile range) or number (%).
ED: emergency department, APACHE II: acute physiology and chronic health evaluation, MV: mechanical ventilation.

 https://doi.org/10.22537/jksct.2024.00001

patients were on the MV for 15 days (IQR, 7–23 days) after OP poisoning, and atropine was administered for 9.5 days (IQR, 2–19.3 days) after OP poisoning in 82 patients. Among these 82 patients, 40 (48.8%) were provided EN during atropine administration. At presentation, the atropine group arrived at our ED later after ingestion and had lower BuChE activity than the no atropine group. However, the delay from ingestion to the administration of antidotes did not differ.

Regarding nutritional support, patients in the atropine group were provided EN for 2 mg/hr as the median highest dosage of atropine administration for a median of the first 120 hours after EN initiation (Table 2). The time interval from arrival to the initiation of PN or from MV to the initiation of EN did not differ between the two groups. The patient's condition at EN initiation did not differ between the two groups. The maximum feeding volume during the first 12 days after EN initiation and the maximal volume of feeding under the highest atropine administration did not differ between the two groups. During the provision of EN, the overall incidence of feeding intolerance was 54.8% in the no atropine group and 60% in the atropine group (p-value = 0.632) (Table 3). The number and duration of EN interruption due to feeding intolerance also did not differ

Table 2. Nutritional support during mechanical ventilation support

Variable	No atropine (n=42)	Atropine (n=40)	Total (n=82)	p-value
Time interval from arrival to PN (hr)	20.0 (13.0–33.0)	26.0 (16.2–40.0)	23.0 (15.0–38.1)	0.184
Data related to EN				
Time interval from MV to initiation of EN (hr)	75.0 (37.4–198.5)	72.0 (43.4–160.5)	72.0 (40.5–168.0)	0.777
Patients condition at EN initiation				
GCS at EN initiation	10.0 (7.0–10.0)	7.0 (4.0–10.0)	9.0 (5.0–10.0)	0.090
APACHE II at EN initiation	14.5 (12.0–19.0)	14.0 (10.3–17.0)	14.0 (11.0–17.3)	0.849
Serum albumin at EN initiation	2.9 (2.7–3.1)	3.1 (2.7–3.5)	3.0 (2.7–3.3)	0.058
Acidosis at EN initiation	7 (16.7)	4 (10.0)	11 (13.4)	0.376
Hyperglycemia at EN initiation	4 (9.5)	2 (5.0)	6 (7.3)	0.432
Pancreatitis at EN initiation	3 (7.1)	2 (5.0)	5 (6.1)	0.685
Administration of sedative or analgesic agents at EN initiation	18 (42.9)	23 (57.5)	41 (50.0)	0.185
Maximum volume of each feeding during the first 12 days of EN	200.0 (100.0–350.0)	200.0 (100.0–300.0)	200.0 (150.0–300.0)	0.502
Maximum volume of each feeding under the highest dosage of atropine*	150.0 (100.0–237.0)	100.0 (75.0–200.0)	150.0 (100.0–212.0)	0.273
The highest dosage of atropine administered during EN on MV (mg/hr)	-	2 (1–4)	2 (1–4)	<0.001
The duration of EN during atropinization (hr)	-	120.0 (53.5–204.0)	120.0 (53.5–204.0)	<0.001

Values are presented as median (interquartile range) or number (%).
PN: parenteral nutrition, EN: enteral nutrition, GCS: Glasgow Coma Scale, APACHE: acute physiology and chronic health evaluation, MV: mechanical ventilation.
*In the no-atropine group, data on the maximum volume of bolus feeding during the median duration of atropine administration after EN initiation in the atropine group were collected to compare with the maximal volume of bolus feeding under the highest dosage of atropine in the atropine group.

Table 3. Feeding intolerance according to atropine administration during enteral nutrition

Variable	No atropine (n=42)	Atropine (n=40)	Total (n=82)	p-value
Overall feeding intolerance	23 (54.8)	24 (60.0)	47 (57.3)	0.632
Diarrhea	20 (47.6)	11(27.5)	31 (37.8)	0.060
Vomiting	1 (2.4)	4 (10.0)	5 (6.1)	0.150
High gastric residual volume	5 (11.9)	10 (25.0)	15 (18.3)	0.125
Others	1 (2.4)	3 (7.5)	4 (4.9)	0.282
Feeding interruption due to feeding intolerance				0.425
No interruption	34 (81.0)	28 (70.0)	62 (15.6)	
Interruption ≤24 hr	4 (9.5)	9 (22.5)	13 (15.9)	
24 hr< interruption ≤48 hr	2 (4.8)	1 (2.5)	3 (3.7)	
Interruption >48 hr	2 (4.8)	2 (5.0)	4 (4.9)	

Values are presented as number (%).

between the two groups.

Neither atropine administration in regression model 1 nor the dosage of atropine administered during EN on MV or the duration of EN during atropine administration in regression model 2 was associated with feeding intolerance (Tables 4, 5).

Table 4. Univariate analysis of the development of feeding intolerance in mechanically ventilated patients after organophosphate poisoning

Variable	OR (95% CI)
Age >70 yr	2.479 (0.993–6.191)
Male sex	0.943 (0.360–2.471)
Body mass index (kg/m^2)	0.925 (0.905–1.083)
Diabetes mellitus	0.575 (0.160–2.065)
Hypertension	1.637 (0.625–4.291)
Intentional ingestion	2.415 (0.457–12.759)
Time interval from ingestion to emergency department (hr)	0.979 (0.860–1.114)
Amount of ingested organophosphate (mL)	1.001(0.997–1.005)
Glasgow Coma Scale at presentation	1.028 (0.940–1.120)
Acute physiology and chronic health evaluation II at presentation	0.980 (0.929–1.035)
Acidosis (pH <7.35) at presentation	1.357 (0.558–3.298)
White blood cell count (×10^3/μL) at presentation	0.993 (0.937–1.053)
Log butylcholinesterase activity (U/L) at presentation	1.047 (0.747–1.467)

OR: odds ratio, CI: confidence interval.

DISCUSSION

Our study demonstrated that feeding intolerance developed in 57.3% of patients who were provided EN during atropinization in mechanically ventilated patients after OP poisoning; however, atropine administration, in particular the dosage of atropine and the duration of atropinization, did not contribute to the overall incidence of feeding intolerance in cases of appropriate atropinization.

When atropine is used in the absence of a cholinergic agonist, adverse effects such as dry mouth begin at 0.5 mg intravenously in adults. However, in the presence of muscarinics or anticholinesterases such as OPs, these effects do not typically occur until many milligrams of atropine are administered because atropine and acetylcholine competitively block each other at the muscarinic receptor[21]. Therefore, despite prolonged administration of a high dose of atropine in OP poisoning, gastrointestinal complications of atropine are rare[22,23]. Atropine infused at a rate of 20 mg/hr for the first 24 hours after OP poisoning did not result in any gastrointestinal anticholinergic effect, including ileus[22]. One Korean study reported that the incidence of ileus was 6.8% during the median dosage of 658.9 mg of atropine administration after OP poisoning[5]. Similar to ours, Moses et al.[24] demonstrated that atropine did not inter-

Table 5. Multivariate analysis of the development of feeding intolerance in mechanically ventilated patients after organophosphate poisoning

Variable	Adjusted OR (95% CI)	
	Model 1	Model 2
Age >70 yr*	2.384 (0.511–11.128)	2.215 (0.466–10.533)
Male sex*	1.305 (0.259–6.572)	1.330 (0.262–6.758)
Body mass index (kg/m^2)*	0.940 (0.712–1.242)	0.959 (0.726–1.267)
Glasgow Coma Scale score ≤8 at EN initiation*	1.420 (0.232–8.690)	1.542 (0.253–9.418)
APACHE II score (≥20) at EN initiation*	0.107 (0.009–1.259)	8.033 (0.650–99.295)
Acidosis (pH <7.35) at EN initiation*	0.399 (0.032–4.981)	0.450 (0.037–5.433)
Hypoproteinemia (albumin <3.5 mg/L) at EN initiation*	0.099 (0.009–1.041)	9.792 (0.905–105.912)
Hyperglycemia (serum glucose ≥198 mg/dL) at EN initiation*	2,670,965,157.1 (0.0-)	2,815,738,129 (0.0-)
Pancreatitis at EN initiation*	0.091 (0.005–1.703)	0.079 (0.004–1.616)
Sedative or analgesic agent at EN initiation*	1.619 (0.317–8.269)	1.807 (0.332–9.833)
Time interval from arrival to initiation of PN (hr)*	1.066 (1.007–1.128)	1.063 (1.005–1.125)
Time interval from MV to initiation of EN (hr)	1.002 (0.997–1.006)	1.001 (0.997–1.006)
The maximal volume of bolus feeding during the first 12 days (mL)	1.003 (0.994–1.013)	1.004 (0.994–1.015)
The maximal volume of bolus feeding during atropine administration (mL)	1.0 (0.991–1.010)	1.0 (0.991–1.010)
Atropine administration	0.752 (0.180–3.139)	
The highest dosage of atropine administered during EN on MV (mg/hr)		1.104 (0.728–1.674)
The duration of EN during atropinization (hr)		0.999 (0.991–1.008)

OR: odds ratio, CI: confidence interval, EN: enteral nutrition, APACHE: acute physiology and chronic health evaluation, PN: parenteral nutrition, MV: mechanical ventilation.
*General condition (age, sex, and body mass index), patient's condition at enteral nutrition initiation, and the time interval from arrival to initiation of PN were entered into multivariate regression as confounders regardless of the *p*-value in the univariate analysis.

https://doi.org/10.22537/jksct.2024.00001

fere with EN in patients poisoned with OP, although they did not provide dosage or duration of atropine administration during the provision of EN. Beards et al.[22] described paralytic ileus that developed after 3–20 mg/hr atropine infusion for 35 days due to OP poisoning. They concluded that ileus during atropinization appeared after the resolution of OP toxicity as a sign of recovery from OP poisoning. However, our study should be cautiously interpreted in that no association between atropine administration and feed intolerance is in case of appropriate atropinization, which aims to counteract excess cholinergic symptoms, not to lead to anticholinergic symptoms.

Similar to our result showing 57.3% incidence, feeding intolerance developed in one-third to one-half of all critically ill patients receiving EN and MV in another study[18]. Similar to our results showing a 27.5% incidence in the atropine group, diarrhea developed in 3 (33.3%) of nine patients who were mechanically ventilated and were fed during atropinization after OP poisoning[5]. In contrast to our findings, diarrhea related to EN developed in none of 29 patients who were fed within 48 hours of intubation after OP poisoning, and gastric stasis occurred in only two patients[24]. This discrepancy could be partially explained by the difference in feeding methods. In that study, the patients were continuously fed at a very restricted total volume of 500–1,000 mL over 24 hours, while we provided bolus feeding. EN is mainly performed with two methods: continuous feeding and bolus feeding[25]. Continuous EN seems to alleviate intolerance to EN; however, there is no evidence that any given feeding method is superior[25].

When we started this study, we noted that EN initiated after weaning from MV at a mean of 10 days after OP poisoning in 51 (34.9%) of the 146 mechanically ventilated patients who were excluded in this study. Furthermore, EN during MV support was initiated from 1 to 37 days after the initiation of MV in 82 patients. Thirty-six (61.1%) of 45 mechanically ventilated patients after OP poisoning received PN or no nutritional support without obvious reason for EN avoidance until weaning from MV[5]. These variations in EN initiation are likely due to concerns about the effect of atropine and a lack of nutritional support guidelines. This study may be a starting point for additional research on optimal nutritional support, in particular the benefit of EN, and the establishment of guidelines for nutritional support in patients poisoned with OP.

The time interval from arrival to supplemental PN was a risk factor for feeding intolerance in this study. Early supplemental PN may reduce malnutrition at EN initiation, which is a risk factor identified by the healthcare staff in the interview as affecting the occurrence of feeding intolerance[20]. Because the effect of supplemental PN on outcome is not the objective of this study, we did not further explore the association between PN and feeding intolerance.

This study has several limitations. First, our study is limited by the small number of patients. This is an inherent problem in the field of toxicology. Second, there may be a number of confounders, such as the dosage of administered sedatives and the use of catecholamine drugs, that could have influenced feeding intolerance but were not measured[26]. It is possible that residual confounding factors reflected the prevalence of feeding intolerance. Third, the effect of OP on the function of the gastrointestinal barrier and absorption was not considered in this study, which might confound the results of our study. However, intestinal permeability is normally maintained in patients with OP poisoning[27]. Fourth, this study suggested that atropine was not associated with feed intolerance in cases of appropriate atropinization. However, no objective marker to achieve appropriate atropinization has been described. However, the dosage of atropine is titrated only by the clinical response and not by any objective marker in the clinical field[28]. Fifth, there is no widely agreed upon definition of feeding intolerance[29]. The cutoff of defining large gastric residual volume in previous studies has varied over a wide range from 150 to 500 mL[29]. Some definition did not include any gastrointestinal symptoms, such as diarrhea. The different definition of feeding intolerance can lead to a variability in its prevalence.

CONCLUSION

This study showed the tolerance of EN during appropriate atropinization in mechanically ventilated patients after OP poisoning. Prospective research with larger numbers of patients is needed to validate our results. Nutritional support should be considered a crucial part of comprehensive therapy after OP poisoning. This result serves as a foundation for the establishment of structured nutritional guidelines for OP poisoning.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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