Official Journal of the Asian Pacific Society of Respirology
Respirology

ORIGINAL ARTICLE

# Early onset pneumonia in patients with cholinesterase inhibitor poisoning

CHEN-YU WANG,[1] CHIEH-LIANG WU,[1,2] YU-TSE TSAN,[3] JENG-YUAN HSU,[1] DONG-ZONG HUNG[4] AND CHIH-HUNG WANG[5]

*Departments of [1]Internal Medicine and [3]Emergency Medicine, Taichung Veterans General Hospital, [2]Department of Life Science, National Chung Hsing University, and [4]Toxicology Center, China Medical University Hospital, Taichung, and [5]Graduate Institute of Education, National Chang Hua University of Education, Chang Hua, Taiwan*

## ABSTRACT

*Background and objective:* **Organophosphates and carbamates are potent cholinesterase inhibitors that are widely used as insecticides in agriculture. Pneumonia is a frequent complication of cholinesterase inhibitor poisoning (CIP) and a risk factor for death. The aim of this retrospective study was to assess the risk factors for pneumonia in patients with CIP.**

*Methods:* **The medical records of 155 patients, who were treated for CIP in a 1300-bed medical centre in central Taiwan, from January 2002 to December 2004, were retrospectively analysed. Pneumonia was diagnosed by a new or persistent infiltrate on CXR, as well as clinical symptoms. Demographic data, comorbidities, acute respiratory failure and in-hospital mortality were also recorded.**

*Results:* **Of the 155 patients, 31 (20%) died and 92 (59.4%) developed acute respiratory failure. Thirty-four patients (21.9%) were diagnosed with early onset pneumonia during hospitalization. Acute respiratory failure (OR 12.10, 95% CI: 2.55–57.45), underlying cardiovascular disease (OR 3.02, 95% CI: 1.02–8.91), undergoing gastric lavage at peripheral hospitals (OR 6.23, 95% CI: 1.52–25.98) and development of respiratory failure at the study centre after gastric lavage (OR 3.43, 95% CI: 1.17–10.0) were predictive factors for early onset pneumonia. Cardiopulmonary resuscitation (OR 23.58, 95% CI: 6.03–92.29), early onset pneumonia (OR 7.45, 95% CI: 2.02–27.5) and lower Glasgow coma score (OR 1.26, 95% CI: 1.08–1.48) were predictive factors for mortality.**

*Conclusions:* **Pneumonia was a significant risk factor for death in patients with CIP. In addition to aggressive management of patients with CIP who develop respiratory failure, careful respiratory evaluation before and after gastric lavage would help to decrease the incidence of early onset pneumonia in patients with CIP.**

## SUMMARY AT A GLANCE

The relationship between pneumonia and cholinesterase inhibitor poisoning is rarely discussed in the literature. This is the first study reporting risk factors for early onset pneumonia in patients with cholinesterase inhibitor poisoning.

**Key words:** carbamate, cholinesterase inhibitor, organophosphate, pneumonia, poisoning.

## INTRODUCTION

Organophosphates and carbamates are potent acetylcholinesterase inhibitors. These agents are widely used as insecticides in agriculture. Due to their widespread use and high toxicity, these agents are a leading cause of self-poisoning in patients presenting to the emergency department.[1–3] The inhibition of acetylcholinesterase leads to overactivation of the autonomic nervous system at cholinergic synapses. Overstimulation of muscarinic receptors results in clinical features such as bradycardia, miosis, lacrimation, salivation, bronchospasm, urination, emesis and diarrhoea. Overstimulation of nicotinic receptors results in fasciculation, muscle weakness and paralysis. These toxic effects lead to compromise of the respiratory system.[4,5]

Pneumonia is a frequent complication of cholinesterase inhibitor poisoning (CIP) due to loss of consciousness and hypersecretion of mucosal fluids. Among patients with CIP, 26%–58% develop pneumonia and in about 80% of these patients this is associated with respiratory failure.[4,6] The mortality rate is as high as 50% in CIP patients with acute respiratory failure.[7] In addition to early decontamination, resuscitation and adequate therapy with atropine and

Correspondence: Dong-Zong Hung, No. 2. Yu-Der Road, Taichung City, Taiwan 404. Email: dzhung@mail.cmu.edu.tw

Received 30 April 2009; invited to revise 17 June 2009, 30 October 2009, 5 March 2010; revised 12 September 2009, 20 January 2010, 2 April 2010; accepted 22 April 2010 (Associate Editor: Jerry Brown).




doi: 10.1111/j.1440-1843.2010.01806.x

oximes, keeping the airways clear and early diagnosis of pneumonia may decrease morbidity and mortality.[4] This study examined the detrimental effects of pneumonia in patients with CIP.

## METHODS

This study was approved by the institutional review board of Taichung Veterans General Hospital. The medical records of patients with CIP, admitted to this 1300-bed medical centre in central Taiwan from January 2002 to December 2004, were reviewed.

Cholinesterase inhibitor poisoning was diagnosed if the patient had a history of ingestion or exposure to an organophosphate or carbamate, and presented with typical features of cholinergic hyperstimulation. The exclusion criteria were: (i) CIP in combination with exposure to other poisons; and (ii) death on arrival at hospital.

After decontamination, all patients with CIP were admitted to an adult respiratory intensive care unit (ICU). Skin, respiratory and gastric decontamination were performed. Skin decontamination included removal of all clothing, jewellery and shoes, if skin contact had occurred. This was followed by washing with water and mild liquid detergent. Respiratory decontamination included removal of possible airborne exposure by ensuring adequate ventilation and oxygenation. Endotracheal intubation was performed if necessary. Gastric decontamination was performed immediately in the emergency department if the patient had not received gastric lavage at a peripheral hospital. The steps for gastric decontamination included: (i) insertion of a nasogastric tube; and (ii) administration of activated charcoal (1 g/kg in 300–800 mL of normal saline) and lavage with the patient in the left decubitus position.

After decontamination, all patients received treatment for CIP according to a standard protocol. This included: (i) keeping the patient's airway patent by placement in the left decubitus position if the patient was not intubated; (ii) oxygen therapy or endotracheal intubation if necessary; and (iii) monitoring of bowel movements, pupil size, heart rate, bronchospasm, salivation and sweating, to titrate the atropine dose to 0.02–0.08 mg/kg/h with a 1–2 mg bolus injection if indicated. Pralidoxime chloride was administered as 2-g bolus doses for 5–10 min and then as a 500 mg/h continuous intravenous infusion for 3–7 days after the initial bolus. Demographic data, including age and gender, as well as type of poisoning, resuscitation and comorbidities were recorded. Clinical manifestations of acute respiratory failure, early onset pneumonia, appearance of tracheal secretions, charcoal contamination of sputum and Glasgow coma scale (GCS) scores were assessed. Red blood cell cholinesterase (normal range: 7500 ± 2200 U/L) and plasma pseudocholinesterase (normal range: 6600 ± 1000 U/L) activities, white blood cell counts and CXR were retrieved. Pseudo- and acetyl cholinesterase activities were determined by an automated kinetic method based on Ellman's colorimetric assay, using butyrylthiocholine and acetyl (β-methyl) thiocholine as the substrates.[8] The time from poisoning to arrival in the emergency department, and the time from poisoning to diagnosis of pneumonia in the study hospital were recorded. The numbers of patients who had undergone gastric lavage and intubation at peripheral hospitals, and who had developed respiratory failure in the study hospital after gastric lavage at peripheral hospitals or the study hospital were also determined. The outcomes of CIP and the durations of ICU and hospital stays were also recorded.

Pneumonia was diagnosed if the patient had a new or persistent infiltrate on CXR, and fever, respiratory symptoms and crackles on physical examination. The respiratory symptoms included cough, sputum production, pleurisy and dyspnoea.[9] Pneumonia was defined as: (i) definite: clinically present with abnormal CXR and isolation of a likely pulmonary pathogen, or the isolation of a likely or possible pulmonary pathogen in high concentration from a quantitative lower respiratory tract sample; (ii) probable pneumonia: clinically present with abnormal CXR but without microbiological confirmation; or (iii) possible pneumonia: abnormal CXR finding of uncertain cause, with low or moderate clinical suspicion of pneumonia, but consistent with the microbiological criteria for definite pneumonia.[10] Pneumonia that occurred less than 5 days after admission was considered to be related to CIP. Late onset pneumonia was assumed to be the result of infection acquired in hospital.

### Statistical analyses

Standard descriptive statistics were calculated (SPSS version 14.0) to evaluate the mean data for all patients. Multivariate analysis of variance was used to test differences in paired data (early onset pneumonia vs no pneumonia, survival vs death and respiratory failure vs no respiratory failure) among dependent variables at a significance level of 0.05. Multivariate logistic regression analysis was performed to identify predictors of early onset pneumonia, mortality and respiratory failure. Forward stepwise selection was used to estimate odds ratios.

## RESULTS

One hundred and fifty-five patients (100 men, 55 women) were included in this retrospective study. Only one patient visited the emergency department of the study hospital directly, all other patients were transferred from peripheral hospitals. The mean age was 51.3 (SD 16.8) years, 92 (59.4%) had acute respiratory failure. Overall mortality was 20% (31/155). Thirty-two of 34 (94.2%) pneumonia patients had respiratory failure and 15 of them died. Among the patients with CIP and pneumonia with acute respiratory failure, mortality was 46.9%. The mean time from poisoning to presentation at the emergency department was 213.4 min (SD 125.8, median 176.0). The mean time from poisoning to diagnosis of pneumonia

**Table 1** Demographic details of the patients with cholinesterase inhibitor poisoning

| | *n* = 155 |
|---|---|
| Age, years | 51.3 ± 16.8 |
| Gender (male/female) | 100/55 |
| Poison | |
| Carbamate, *n* (%) | 46 (29.7) |
| Organophosphate, *n* (%) | 109 (70.3) |
| Acute respiratory failure, *n* (%) | 92 (59.4) |
| Early onset pneumonia, *n* (%) | 34 (21.9) |
| ICU stay, days | 6.2 ± 7.4 |
| Hospital stay, days | 6.8 ± 8.2 |
| Death, *n* (%) | 31 (20) |
| Time to arrival in ED†, min | 213.4 ± 125.8 |
| Time to diagnosis of pneumonia‡, min | 1076.1 ± 1209.0 |
| Comorbidities, *n* (%) | |
| Diabetes mellitus | 22 (14.2) |
| Chronic lung disease | 9 (5.8) |
| Cerebrovascular disease | 4 (2.6) |
| Cardiovascular disease | 28 (18.1) |
| Liver disease | 9 (5.8) |
| Chronic renal disease | 3 (1.9) |

Values are mean ± SD unless otherwise indicated.
† Time from poisoning to arrival at the ED of the study hospital.
‡ Time from poisoning to diagnosis of pneumonia.
ED, emergency department; ICU, intensive care unit.

was 1076.1 min (SD 1209.0, median 336.0). The demographic and clinical details of the patients are summarized in Table 1.

## Early onset pneumonia in patients with cholinesterase inhibitor poisoning

Thirty-four patients developed pneumonia less than 5 days after admission. The pneumonia was assumed to be directly related to the CIP event. Charcoal contamination of sputum, yellowish sputum, acute respiratory failure, gastric lavage, intubation at peripheral hospitals, development of respiratory failure after gastric lavage or underlying cardiovascular disease, were features of patients with early onset pneumonia when compared with patients without pneumonia. Patients with early onset pneumonia were older, and had lower red blood cell acetyl cholinesterase and plasma pseudocholinesterase levels 48 h after arrival in the emergency department. These patients also had lower GCS scores, longer ICU and hospital stays and shorter times from poisoning to presentation at the emergency department. The clinical details of the patients with early onset pneumonia after CIP are shown in Table 2. Multivariate logistic regression analysis showed that acute respiratory failure (OR 12.10, 95% CI: 2.55–57.45), underlying cardiovascular disease (OR 3.02, 95% CI: 1.02–8.91), undergoing gastric lavage at peripheral hospitals (OR 6.23, 95% CI: 1.52–25.98) and respiratory failure in the study hospital after gastric lavage (OR 3.43, 95% CI: 1.17–10.0) were predictive factors for early onset pneumonia.

## Mortality in patients with cholinesterase inhibitor poisoning

The clinical parameters related to mortality in patients with CIP were analysed further. Comorbidities were similar between patients who survived and those who died (Table 3). Plasma pseudocholinesterase and red blood cell acetyl cholinesterase levels were significantly reduced in the patients who died. Lower GCS scores, cardiopulmonary resuscitation in the emergency department, acute respiratory failure, production of yellowish sputum, charcoal contamination of sputum, development of pneumonia less than 5 days after admission, high white blood cell counts and intubation at peripheral hospitals were all related to mortality. Multivariate logistic regression analysis showed that cardiopulmonary resuscitation (OR 23.58, 95% CI: 6.03–92.29), early onset pneumonia (OR 7.45, 95% CI: 2.02–27.50) and lower GCS scores (OR 1.26, 95% CI: 1.08–1.48) were predictive factors for mortality.

## Respiratory failure in patients with cholinesterase inhibitor poisoning

The clinical parameters related to respiratory failure in patients with CIP are shown in Table 4. Older patients and those with lower GCS scores, yellowish sputum, charcoal contamination of sputum and elevated white blood cell counts were more likely to develop respiratory failure. Multivariate logistic regression analysis showed that lower GCS scores (OR 1.34, 95% CI: 1.21–1.48), production of yellowish sputum (OR 8.37, 95% CI: 2.41–28.0) and charcoal contamination of sputum (OR 2.64, 95% CI: 1.02–6.84) were predictive factors for respiratory failure.

## Respiratory failure in patients with cholinesterase inhibitor poisoning who received gastric lavage at the study hospital

In order to clarify the relationship between patient consciousness during gastric lavage and respiratory failure, data on patients with CIP who underwent gastric lavage at the study hospital are presented in Table 5. Due to the retrospective study design, details of the timing of respiratory failure and gastric lavage at peripheral hospitals could not be obtained. However, the clinical parameters of patients with CIP, who underwent gastric lavage at the study hospital, were examined further. Thirty-three patients underwent gastric lavage at the study hospital. The times from poisoning to undergoing gastric lavage were shorter and GCS scores at lavage were lower in patients with respiratory failure than in those without respiratory failure; however, these two variables did

**Table 2** Clinical characteristics of patients with cholinesterase inhibitor poisoning, with or without early onset pneumonia

| | Early onset pneumonia ($n = 34$) | Without pneumonia ($n = 121$) | *P*-value |
|---|---|---|---|
| Age, years | 58.0 ± 16.4 | 49.4 ± 16.5 | <0.01 |
| Gender (male/female) | 23/11 | 77/44 | NS |
| Glasgow coma scale score | 6.2 ± 3.8 | 9.8 ± 5.4 | <0.001 |
| Cardiopulmonary resuscitation[†], *n* (%) | 9 (26.5) | 18 (14.9) | NS |
| Acute respiratory failure, *n* (%) | 32 (94.1) | 60 (49.6) | <0.001 |
| Yellowish sputum, *n* (%) | 17 (50) | 25 (20.7) | <0.01 |
| Carbamate, *n* (%) | 11 (32.4) | 35 (28.9) | NS |
| Organophosphate, *n* (%) | 23 (67.6) | 86 (71.1) | NS |
| Charcoal[‡], *n* (%) | 29 (85.3) | 78 (64.5) | <0.05 |
| Plasma pseudo-ChE1 (U/L)[§] | 2719.5 ± 1565.6 | 3231.5 ± 1681.5 | NS |
| Plasma pseudo-ChE2 (U/L)[¶] | 2785.2 ± 1223.1 | 3346.2 ± 1311.0 | <0.05 |
| RBC acetyl-ChE1 (U/L)[††] | 4216.5 ± 1772.5 | 5006.7 ± 1981.0 | <0.05 |
| RBC acetyl-ChE2 (U/L)[‡‡] | 4875.0 ± 1644.3 | 5541.3 ± 1214.2 | <0.05 |
| White blood cell count, $\times 10^9$/L | 16.57 ± 6.73 | 14.54 ± 7.53 | NS |
| Hospital stay, days | 11.7 ± 12.4 | 5.4 ± 6.0 | <0.001 |
| Intensive care unit stay, days | 11.0 ± 10.8 | 4.8 ± 5.4 | <0.001 |
| Gastric lavage at peripheral hospital, *n* (%) | 31 (91.2) | 91 (75.8) | <0.05 |
| Intubation at peripheral hospital, *n* (%) | 19 (55.9) | 44 (36.4) | <0.05 |
| Intubation after gastric lavage, *n* (%) | 13 (38.2) | 11 (9.1) | <0.001 |
| Time to ED[§§], min | 158.5 ± 81.7 | 228.9 ± 131.9 | <0.01 |
| Comorbidities, *n* (%) | | | |
| Diabetes mellitus | 5 (14.7) | 17 (14) | NS |
| Chronic lung disease | 2 (5.9) | 7 (5.8) | NS |
| Cerebrovascular disease | 1 (2.9) | 3 (2.5) | NS |
| Cardiovascular disease | 11 (32.4) | 17 (14) | <0.05 |
| Liver disease | 3 (8.8) | 6 (5) | NS |
| Chronic renal disease | 2 (5.9) | 1 (0.8) | NS |

Values are mean ± SD unless otherwise indicated.
[†] Patients received cardiopulmonary resuscitation before admission.
[‡] Charcoal contamination noted in sputum.
[§] Plasma pseudocholinesterase measured on arrival in the ED.
[¶] Plasma pseudocholinesterase measured 48 h after arrival in the ED.
[††] RBC acetyl cholinesterase measured on arrival in the ED.
[‡‡] RBC acetyl cholinesterase measured 48 h after arrival in the ED.
[§§] Time from poisoning to arrival in the ED of the study hospital.
ChE, cholinesterase; ED, emergency department; NS, not significant; RBC, red blood cell.

not predict respiratory failure in the multivariate logistic regression analysis. The number of patients with charcoal contamination of sputum, early onset pneumonia, and who were intubated after gastric lavage at the study hospital, were not different between the two groups. Four of 21 patients developed respiratory failure after undergoing gastric lavage. The average GCS score of these four patients at gastric lavage was 8.8 ± 1.0. Only one patient developed both pneumonia and respiratory failure after gastric lavage at the study hospital.

### Pneumonia pathogens in patients with cholinesterase inhibitor poisoning

Among the 34 patients with pneumonia, one was diagnosed with definite pneumonia, four were diagnosed with probable pneumonia and 29 were diagnosed with possible pneumonia. Fifty-eight pathogens were identified. The major pathogen was *Klebsiella pneumoniae* (32.8%), followed by *Staphylococcus aureus* (22.4%), *Acinetobacter baumannii* (13.8%), *Hemophilus influenzae* (8.6%) and *Pseudomonas aeruginosa* (8.6%) (Table 6).

## DISCUSSION

Organophosphate and carbamate cholinesterase inhibitors are widely used as insecticides in agriculture. Because of their ready availability and high toxicity, ingestion of cholinesterase inhibitors is one of the most frequent causes of poisoning in developing countries.[11,12] Mortality among patients with CIP ranges from 2.9% to 40% in those who receive

**Table 3** Clinical characteristics of the patients with cholinesterase inhibitor poisoning who survived or died

| | Survived ($n = 124$) | Died ($n = 31$) | *P*-value |
|---|---|---|---|
| Age, years | 49.8 ± 16.9 | 57.1 ± 15.1 | NS |
| Gender (male/female) | 84/40 | 16/15 | NS |
| Glasgow coma scale score | 10.4 ± 4.9 | 3.6 ± 3.0 | <0.001 |
| Cardiopulmonary resuscitation[†], *n* (%) | 6 (4.8) | 21 (67.7) | <0.001 |
| Acute respiratory failure, *n* (%) | 61 (49.2) | 31 (100) | <0.001 |
| Yellowish sputum, *n* (%) | 27 (21.8) | 15 (48.4) | <0.01 |
| Carbamate, *n* (%) | 36 (29) | 10 (32.3) | NS |
| Organophosphate, *n* (%) | 88 (71) | 21 (67.7) | NS |
| Charcoal[‡], *n* (%) | 80 (64.5) | 27 (87.1) | <0.05 |
| Early onset pneumonia, *n* (%) | 19 (15.3) | 15 (47.4) | <0.001 |
| Plasma pseudo-ChE1 (U/L)[§] | 3365.8 ± 1718.0 | 2132.7 ± 938.1 | <0.01 |
| Plasma pseudo-ChE2 (U/L)[¶] | 3372.5 ± 1372.9 | 2625.7 ± 780.7 | <0.05 |
| RBC acetyl-ChE1 (U/L)[††] | 5148.2 ± 1969.4 | 3574.1 ± 1325.0 | <0.01 |
| RBC acetyl-ChE2 (U/L)[‡‡] | 5542.5 ± 1250.9 | 4805.9 ± 1549.3 | NS |
| White blood cell count, $\times 10^9$/L | 13.60 ± 6.31 | 20.53 ± 8.81 | <0.001 |
| Hospital stay, days | 6.0 ± 6.5 | 10.1 ± 12.8 | NS |
| Intensive care unit stay, days | 5.4 ± 6.0 | 9.0 ± 10.9 | NS |
| Gastric lavage at peripheral hospital, *n* (%) | 100 (80.6) | 22 (71.0) | NS |
| Intubation at peripheral hospital, *n* (%) | 38 (30.6) | 25 (80.6) | <0.001 |
| Intubation after gastric lavage, *n* (%) | 20 (16.1) | 4 (12.9) | NS |
| Time to ED[§§], min | 218.0 ± 132.7 | 195.4 ± 92.8 | NS |
| Comorbidities, *n* (%) | | | |
| Diabetes mellitus | 16 (12.9) | 6 (19.4) | NS |
| Chronic lung disease | 8 (6.5) | 1 (3.2) | NS |
| Cerebrovascular disease | 2 (1.6) | 2 (6.5) | NS |
| Cardiovascular disease | 21 (16.9) | 7 (22.6) | NS |
| Liver disease | 7 (5.6) | 2 (6.5) | NS |
| Chronic renal disease | 2 (1.6) | 1 (3.2) | NS |

Values are mean ± SD unless otherwise indicated.
[†] Patient received cardiopulmonary resuscitation before admission.
[‡] Charcoal contamination noted in sputum.
[§] Plasma pseudocholinesterase measured on arrival in the ED.
[¶] Plasma pseudocholinesterase measured 48 h after arrival in the ED.
[††] RBC acetyl cholinesterase measured on arrival in the ED.
[‡‡] RBC acetyl cholinesterase measured 48 h after arrival in the ED.
[§§] Time from poisoning to arrival in the ED of the study hospital.
ChE, cholinesterase; ED, emergency department; NS, not significant; RBC, red blood cell.

intensive care.[13,14] In the present study, mortality was 20%. Early onset pneumonia is one of the predictive factors for mortality. Several studies have discussed the prevention and treatment of acute respiratory failure[15,16] but few studies have investigated pneumonia and the major pathogens in patients with CIP.

According to the literature, the incidence of pneumonia in patients with CIP ranges from 26% to 58%.[4,6] In the present study, only 34 of 155 (21.9%) patients with CIP had pneumonia and 32 (94%) had acute respiratory failure. The incidence of pneumonia was slightly lower than in other studies. In this study, the criteria for pneumonia were based on those of the *International Sepsis Forum Consensus Conference on Definitions of Infection in the Intensive Care Unit*, and included criteria for definite, possible or probable pneumonia. However, the strict criteria for the diagnosis of pneumonia did not appear to account for the lower incidence of pneumonia in this study. The lower incidence of pneumonia may be due to the retrospective study design or the exclusion of patients with late onset pneumonia after admission.

The present data showed that among the pneumonia patients, respiratory failure was more frequent among those who underwent gastric lavage at peripheral hospitals, and more patients developed respiratory failure after gastric lavage in the study hospital. However, there was no significant difference between those with or without pneumonia, in the numbers of patients who were intubated at peripheral hospitals. One explanation may be that there was no specialist toxicologist or standard treatment protocol at peripheral hospitals. Inadequate respiratory evaluation before and after gastric lavage may increase the incidence of pneumonia. In addition decontamination and toxicological treatment protocols should be implemented in peripheral hospitals.

**Table 4** Clinical characteristics of the patients with cholinesterase inhibitor poisoning, with or without acute respiratory failure

| | Patients with respiratory failure ($n = 92$) | Patients without respiratory failure ($n = 63$) | *P*-value |
|---|---|---|---|
| Age, years | 54.5 ± 16.4 | 46.6 ± 16.4 | <0.05 |
| Gender (male/female) | 57/35 | 43/20 | NS |
| Glasgow coma scale score | 6.4 ± 3.9 | 12.8 ± 4.8 | <0.001 |
| Yellowish sputum, *n* (%) | 38 (41.3) | 4 (6.3) | <0.001 |
| Carbamate, *n* (%) | 28 (30.4) | 18 (28.6) | NS |
| Organophosphate, *n* (%) | 64 (58.7) | 45 (71.4) | NS |
| Charcoal[†], *n* (%) | 73 (79.3) | 34 (30.2) | <0.01 |
| Plasma pseudo-ChE1 (U/L)[‡] | 2730.0 ± 1522.7 | 3687.4 ± 1712.6 | NS |
| Plasma pseudo-ChE2 (U/L)[§] | 3093.5 ± 1350.4 | 3412.4 ± 1232.6 | NS |
| RBC acetyl-ChE1 (U/L)[¶] | 4216.9 ± 1811.4 | 5733.6 ± 1825.3 | NS |
| RBC acetyl-ChE2 (U/L)[††] | 5098.3 ± 1521.1 | 5828.6 ± 874.5 | NS |
| White blood cell count, $\times 10^9$/L | 17.43 ± 7.69 | 11.41 ± 5.2 | <0.05 |
| Hospital stay, days | 8.1 ± 10.0 | 4.9 ± 4.1 | NS |
| Intensive care unit stay, days | 7.2 ± 8.8 | 4.6 ± 4.0 | NS |
| Gastric lavage at peripheral hospital, *n* (%) | 71 (77.2) | 51 (81.0) | NS |
| Time to ED[‡‡], min | 195.4 ± 113.8 | 239.7 ± 138.3 | NS |
| Comorbidities, *n* (%) | | | |
| Diabetes mellitus | 14 (12.9) | 8 (19.4) | NS |
| Chronic lung disease | 7 (6.5) | 2 (3.2) | NS |
| Cerebrovascular disease | 4 (1.6) | 0 (6.5) | NS |
| Cardiovascular disease | 21 (16.9) | 7 (22.6) | NS |
| Liver disease | 6 (5.6) | 3 (6.5) | NS |
| Chronic renal disease | 2 (1.6) | 1 (3.2) | NS |

Values are mean ± SD unless otherwise indicated.
[†] Charcoal contamination noted in sputum.
[‡] Plasma pseudocholinesterase measured on arrival in the ED.
[§] Plasma pseudocholinesterase measured 48 h after arrival in the ED.
[¶] RBC acetyl cholinesterase measured on arrival in the ED.
[††] RBC acetyl cholinesterase measured 48 h after arrival in the ED.
[‡‡] Time from poisoning to arrival in the ED of the study hospital.
ChE, cholinesterase; ED, emergency department; NS, not significant; RBC, red blood cell.

**Table 5** Clinical characteristics of the patients with cholinesterase inhibitor poisoning, with or without acute respiratory failure who underwent gastric lavage at the study hospital

| | Patients with respiratory failure ($n = 21$) | Patients without respiratory failure ($n = 12$) | *P*-value |
|---|---|---|---|
| Time from poisoning to lavage, min | 192.4 ± 79.5 | 277.5 ± 155.4 | <0.05 |
| GCS score during lavage at study hospital | 7.7 ± 4.3 | 15 | <0.001 |
| Charcoal contamination of sputum, *n* | 16 | 7 | NS |
| Early onset pneumonia, *n* | 3 | 0 | NS |
| Intubation after gastric lavage at study hospital, *n* | 4 | 0 | NS |

Values are mean ± SD or number of patients.
GCS, Glasgow coma scale; NS, not significant.

Early onset pneumonia, lower GCS scores and cardiopulmonary resuscitation were predictive factors for mortality in the present study. Davies *et al.* reported that GCS scores predicted outcomes in patients with acute organophosphate poisoning,[16] and the results from the present study are in keeping with this finding. Respiratory failure is another important cause of mortality,[4,7] and the present data showed that all the patients who died developed respiratory failure during hospitalization. As early onset pneumonia is a risk factor for mortality, physicians should identify the risk factors for pneumonia earlier, and thereby reduce morbidity.

Lower GCS scores, yellowish sputum and charcoal contamination of sputum were predictive factors for respiratory failure. Moll *et al.* reported that intubation

**Table 6** Pathogens isolated from patients with cholinesterase inhibitor poisoning and early onset pneumonia

| Pathogen | Number (%) |
|---|---|
| *Klebsiella pneumoniae* | 19 (32.8) |
| *Staphylococcus aureus* | 13 (22.4) |
| *Acinetobacter baumanni* | 8 (13.8) |
| *Pseudomonas aeruginosa* | 5 (8.6) |
| *Hemophilus influenzae* | 5 (8.6) |
| *Streptoccus pneumonia* | 1 (1.7) |
| Others | 7 (12.1) |
| Total | 58 (100.0) |

of patients was associated with a lower rate of aspiration pneumonia before administration of activated charcoal.[17] Hack *et al*. also reported loss of consciousness in a patient after aspiration of charcoal administered for gastrointestinal lavage.[18] In the present study, charcoal contamination of sputum occurred in 85.3% (29/34) of pneumonia patients, 79.3% (73/92) of patients with respiratory failure and 87.5% (28/32) of patients with both respiratory failure and pneumonia. Complications following CIP were associated with more frequent charcoal contamination of sputum.

There were no differences between patients with or without respiratory failure, in the numbers of patients undergoing lavage at peripheral hospitals. Among patients with both acute respiratory failure and pneumonia, 29 (90.6%) were diagnosed with pneumonia after intubation. It appeared that in most patients with pneumonia, respiratory failure developed before pneumonia. Although lavage procedures were related to the development of pneumonia, poor protection of the airways due to loss of consciousness and hypersecretion were key factors leading to the development of respiratory failure. However, physicians should be alert to the state of consciousness of patients and to sputum characteristics. This would help physicians to make decisions on early intubation.

Further analysis was performed on the 33 patients who underwent gastric lavage at the study hospital (Table 5). GCS scores at gastric lavage were higher in patients without compared with those with respiratory failure. However, small numbers of patients may be one of the reasons for the lack of statistical significance by logistic regression. Among the 13 pneumonia patients who developed respiratory failure in the study hospital after gastric lavage, only one had undergone gastric lavage at the study hospital. Careful evaluation of the patient's respiratory status and state of consciousness before gastric lavage would decrease the likelihood of complications following acute CIP.

The pathogens associated with pneumonia in patients with CIP were also investigated. The major pathogens isolated were *K. pneumoniae*, *H. influenzae*, *S. aureus*, *P. aeruginosa* and *A. baumannii*. *K. pneumoniae* is one of the most common pathogens causing community-acquired bacteraemic pneumonia in Taiwan,[19] accounting for 32%–34% of cases.[19,20] The results from the present study were in keeping with these findings. Retrospective review of the medical records of the pneumonia patients in the present study showed that they were all transferred to the study hospital from local hospitals after emergency management, including gastric lavage and administration of medications. Most patients were transferred to the emergency department after placement of an endotracheal tube. Whether such invasive procedures lead to local infection by nosocomial pathogens is not known, but they may increase the risk of nosocomial infections.[21] Infection by these pathogens should be considered before selection of empirical antibiotic treatment for the management of pneumonia in patients with organophosphate or carbamate poisoning.

There were some limitations to this study. First, because this was a retrospective study it was not possible to obtain detailed medical histories and referral sheets for patients transferred from peripheral hospitals. Second, the number of patients with pneumonia was small; hence the study did not show the actual distribution of pathogens in the environment. Nevertheless, the findings provided an indication of the characteristics of early onset pneumonia in patients with CIP and the empirical antibiotic treatment required in these patients.

In conclusion, pneumonia was a significant risk factor for mortality in patients with CIP. It also resulted in prolonged ICU and hospital stays. Implementation of treatment protocols at peripheral hospitals may improve the quality of care for patients with CIP and early onset pneumonia. In addition to aggressive management of patients with CIP who develop respiratory failure, careful respiratory evaluation before and after gastric lavage may help to decrease the incidence of early onset pneumonia in patients with CIP.

## REFERENCES

1 Yang CC, Wu JF, Ong HC *et al*. Taiwan National Poison Center: epidemiologic data 1985–1993. *J. Toxicol. Clin. Toxicol.* 1996; **34**: 651–63.
2 Gunnell D, Eddleston M. Suicide by intentional ingestion of pesticides: a continuing tragedy in developing countries. *Int. J. Epidemiol.* 2003; **32**: 902–9.
3 Eddleston M. Patterns and problems of deliberate self-poisoning in the developing world. *QJM* 2000; **93**: 715–31.
4 Lee P, Tai DY. Clinical features of patients with acute organophosphate poisoning requiring intensive care. *Intensive Care Med.* 2001; **27**: 694–9.
5 Senanayake N, Karalliedde L. Neurotoxic effects of organophosphorus insecticides. An intermediate syndrome. *N. Engl. J. Med.* 1987; **316**: 761–3.
6 Tsao TC, Juang YC, Lan RS *et al*. Respiratory failure of acute organophosphate poisoning. *Chest* 1990; **98**: 631–6.
7 Sungur M, Güven M. Intensive care management of organophosphate insecticide poisoning. *Crit. Care* 2001; **5**: 211–15.
8 Meuling WJ, Jongen MJ, van Hemmen JJ. An automated method for the determination of acetyl and pseudo cholinesterase in hemolyzed whole blood. *Am. J. Ind. Med.* 1992; **22**: 231–41.

9 Bartlett JG, Mundy LM. Community acquired pneumonia. *N. Engl. J. Med.* 1995; **333**: 1618–24.
10 Calandra T, Cohen J. International Sepsis Forum Definition of Infection in the ICU Consensus Conference. The International Sepsis Forum Consensus Conference on definitions of infection in the intensive care unit. *Crit. Care Med.* 2005; **33**: 1538–48.
11 Van der Hoek W, Konradsen F, Athukorala K *et al*. Pesticide poisoning: a major health problem in Sri Lanka. *Soc. Sci. Med.* 1998; **46**: 495–504.
12 Eddleston M, Phillips MR. Self-poisoning with pesticides. *BMJ* 2004; **328**: 42–4.
13 Emerson GM, Gray NM, Jelinek GA *et al*. Organophosphate poisoning in Perth, Western Australia, 1987–1996. *J. Emerg. Med.* 1999; **17**: 273–7.
14 De Silva HJ, Wijewickrema R, Senanayake N. Does pralidoxime affect outcome of management in acute organophosphate poisoning? *Lancet* 1992; **339**: 1136–8.
15 Eddleston M, Mohamed F, Davies JO *et al*. Respiratory failure in acute organophosphorus pesticide self-poisoning. *QJM* 2006; **99**: 513–22.
16 Davies JO, Eddleston M, Buckley NA. Predicting outcome in acute organophosphorus poisoning with a poison severity score or the Glasgow coma scale. *QJM* 2008; **101**: 371–9.
17 Moll J, Kerns W 2nd, Tomaszewski C *et al*. Incidence of aspiration pneumonia in intubated patients receiving activated charcoal. *J. Emerg. Med.* 1999; **17**: 279–83.
18 Hack JB, Gilliland MG, Meggs WJ. Images in emergency medicine. Activated charcoal aspiration. *Ann. Emerg. Med.* 2006; **48**: 522–31.
19 Chen CW, Jong GM, Shiau JJ *et al*. Adult bacteremic pneumonia: bacteriology and prognostic factors. *J. Formos. Med. Assoc.* 1992; **91**: 754–9.
20 Feldman C, Ross S, Mahomed AG *et al*. The aetiology of severe community-acquired pneumonia and its impact on initial empiric, antimicrobial chemotherapy. *Respir. Med.* 1995; **89**: 187–92.
21 American Thoracic Society Hospital-acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy, and preventive strategies. A consensus statement, American Thoracic Society, November 1995. *Am. J. Respir. Crit. Care Med.* 1996; **153**: 1711–25.