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Journal of Acute Medicine 2 (2012) 31–35

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Original Research

# Age as a predisposing factor of respiratory alkalosis in accidental carbon monoxide poisoning

Yung-Cheng Su [a], Chun-Chieh Chao [b], Tzong-Luen Wang [c,d], Chee-Fah Chong [c,d], Chien-Chih Chen [b,e,*]

[a] *Emergency Department, Buddhist Tzu Chi Dalin General Hospital, Chiayi County, Taiwan*
[b] *Department of Emergency Medicine, Zhong-Xiao Branch, Taipei City Hospital, Taipei, Taiwan*
[c] *Emergency Department, Shin-Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan*
[d] *School of Medicine, Fu Jen Catholic University, Taipei, Taiwan*
[e] *Division of Emergency Medicine, Keelung Hospital, Department of Health, Executive Yuan, Keelung, Taiwan*

Received 1 December 2011; accepted 9 April 2012
Available online 7 June 2012

**Abstract**

*Aims*: The purpose of this study was to determine the frequency of and identify the predisposing factors for respiratory alkalosis in patients with accidental carbon monoxide (CO) poisoning.
*Methods*: Patients presenting to the emergency department with accidental CO poisoning were retrospectively identified and divided into Group A (no respiratory alkalosis) and Group B (respiratory alkalosis). Charts were reviewed for neurologic status, various demographic factors, and laboratory data.
*Results*: A total 96 patients, 37 (38.5%) men and 59 (61.5%) women, were identified. Of these, the 58 (60.4%) patients without respiratory alkalosis were placed in Group A and the 38 (39.6%) patients with respiratory alkalosis were placed in Group B. Independent multivariate predictors of CO poisoning presenting with respiratory alkalosis were age [odds ratio (OR), 1.04; 95% confidence interval (CI), 1.01–1.08] and respiratory rate (OR, 1.16; 95% CI, 1.01–1.33). The rates of respiratory alkalosis in patients younger than 15 years, 15–29 years, 30–44 years, 45–59 years, and older than 59 years were 17.4%, 32.4%, 51.9%, 75%, and 75%, respectively ($p < 0.01$).
*Conclusions*: Respiratory alkalosis in the patients with CO poisoning is not an uncommon finding, and as age increases, the percentage becomes higher. When emergency physicians are faced with patients presenting with respiratory alkalosis of undetermined cause, CO poisoning should be taken into consideration, especially in the elderly.


*Keywords:* Age; Carbon monoxide; Poisoning; Respiratory alkalosis

## 1. Introduction

Carbon monoxide (CO) is a colorless, odorless, and tasteless gas that cannot be detected by human senses; however, intoxication can cause a great diversity of presentations, from headache, dizziness, nausea, diarrhea, or weakness, to more severe presentations such as altered states of consciousness and even death. Although the diagnosis can easily be made by examination of the carboxyhemoglobin (HbCO) level, the condition is often overlooked because of the nonspecific complaints and the unreliable exposure history.[1] Some studies about treatment decisions or the delayed sequelae of CO poisoning have been published,[2,3] but none mentioned clinical suspicion or diagnostic aids associated with objective physical findings in the emergency department (ED).

In our clinical experience, respiratory alkalosis is not an uncommon objective finding in patients presenting to the ED with CO poisoning. If no specific problems or history of exposure can be found, these patients may be mistakenly

* Corresponding author. Division of Emergency Department, Keelung Hospital, Department of Health, Executive Yuan, Number 268, Xin Second Road, Xinyi District, Keelung City 20147, Taiwan, ROC.
*E-mail address:* timshel119@gmail.com (C.-C. Chen).

2211-5587/$ - see front matter 
doi:10.1016/j.jacme.2012.04.001

diagnosed as having a non-urgent condition such as hyperventilation syndrome or anxiety. In a study by Myers and others,[4] there was poor correlation between pH and HbCO level in the initial arterial blood samples of victims with CO poisoning. Respiratory alkalosis is the most common acid-base abnormality observed in patients who are critically ill. When respiratory alkalosis is present, the problem may initially appear to be minor; however, if decompensation happens, the patient will deteriorate.[5] To the best of our knowledge, no previous study has examined the incidence of and predisposing factors for respiratory alkalosis in patients with accidental CO poisoning. The purposes of this study were to do so and to identify the clinical clues by which emergency physicians may suspect CO poisoning and then further diagnose and treat the condition.

## 2. Materials and methods

### 2.1. Study population and study design

This was a retrospective noninterventional study conducted in a 921-bed urban medical center with approximately 75,000 ED visits annually. All patients who presented to the ED between June1997 and May 2005 with the diagnosis of CO poisoning confirmed by an abnormal HbCO level were eligible for inclusion in the study. Patients were excluded from the study if arterial blood gases had not been determined in the ED, there was concomitant drug or alcohol use, or the poisoning was intentional. The study protocol was approved by our Institutional Review Board.

### 2.2. Data collections and definitions

In this study, CO poisoning was defined as an HbCO level greater than 5% in nonsmokers and greater than 10% in smokers. Alkalosis was defined as a pathologic state that caused or tended to cause an increase in blood pH (pH $>$ 7.44). Respiratory alkalosis was defined as alveolar hyperventilation leading to a primary decrease in the partial pressure of carbon dioxide ($PCO_2$). Detailed information about patients in the final cohort was obtained retrospectively after hospital discharge through medical record abstraction by one physician with extensive experience in chart review procedures. The following data were recorded for each patient: age, sex, comorbidities, arterial blood gas data, initial loss of consciousness or not, respiratory rate, lowest Glasgow Coma Scale score in the ED, lowest systolic blood pressure in the ED, highest heart rate in the ED, highest respiratory rate in the ED, blood urea nitrogen/creatinine ratio, arterial pH, $PCO_2$, bicarbonate ($HCO_3^-$), and HbCO level. Diabetes mellitus, hypertension, and coronary artery disease were recorded as comorbidities.

### 2.3. Data analysis and statistics

Patients were stratified into one of two groups based on the arterial blood gas findings: Group A, the nonrespiratory alkalosis group (pH $<$ 7.45) and Group B, the respiratory alkalosis group (pH $\geq$ 7.45 and $PCO_2 < 40$).

All analyses were performed with SPSS 10.0 (SPSS Inc, Chicago, Ill) for Windows. Continuous data were presented as medians (25th, 75th percentiles) and categorical variables as frequencies and percentages. Univariate comparisons between the two groups were made using Mann-Whitney and Wilcoxon tests for continuous variables and chi-square and Fisher's exact tests for categorical variables. The variables with a univariate comparison $p < 0.1$ were then included in a multiple logistic regression analysis of predisposing factors for respiratory alkalosis.

To confirm the findings that the high correlations among age, respiratory rate, and respiratory alkalosis in CO poisoning had been determined correctly in the study, an additional analysis determined by a selected cutoff-point of HbCO level was needed. An HbCO level of 25% is a conservative standard for hyperbaric oxygen therapy,[6] so we did the analysis using an HbCO level of 25%. The relationships among respiratory alkalosis, age, and respiratory rate were evaluated using a logistic regression model in both groups. Statistical significance was set at $p < 0.05$ (two tailed).

## 3. Results

During our study period, a total of 145 patients presented to the ED with confirmed CO poisoning. A total of 49 patients were excluded from the study because of absence of arterial blood gas data in the ED ($n = 11$), concomitant drug overdose or alcohol consumption ($n = 18$), and intentional causes ($n = 20$). The final study cohort consisted of 96 patients of whom 37 were men (38.5%) and 59 were women (62.5%). Their ages ranged from 3 to 84 years (median: 24.0). The cohort was divided into two groups according to the presence or absence of respiratory alkalosis on the initial arterial blood gas analysis: 58 (60.4%) patients were placed in Group A (nonrespiratory alkalosis) and 38 (39.6%) patients were placed in Group B (respiratory alkalosis). A flow diagram illustrating patient enrollment and group allocation is shown in Fig. 1. The arterial pH, $PCO_2$, $HCO_3^-$, and the general characteristics of the cohort are summarized in Tables 1and 2, respectively.

Univariate analysis was performed to compare Groups A and B (Table 2). The age of the patients with respiratory alkalosis was obviously older than that of the other group (median age, 36.0 vs. 20.5; $p < 0.01$). Preexisting comorbidities were more prevalent in the patients with respiratory alkalosis (13.2% vs. 1.7%; $p = 0.03$). The respiratory rates of the two groups were also different (18.0 vs. 20.0; $p = 0.02$). Other variables were not significantly different.

Multiple logistic regression modeling was then performed using the statistically significant univariate variables (Table 3). The presenting variables that were independently associated with patients with CO poisoning presenting with respiratory alkalosis were age [odds ratio (OR), 1.04; 95% confidence interval (CI), 1.01−1.08] and respiratory rate (OR, 1.16; 95% CI, 1.01−1.33). The preexisting comorbidities that were

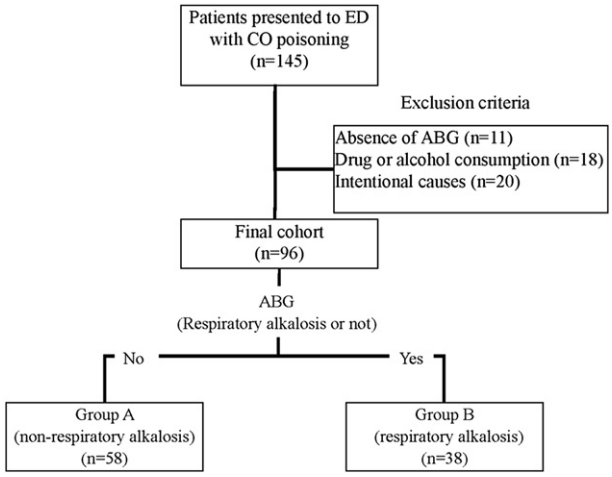


Fig. 1. Patient enrollment and group allocation. ABG = arterial blood gas; CO = carbon monoxide; ED = emergency department.

identified in the univariate analysis were not significant in the multivariate models.

We further compared the rate of respiratory alkalosis in patients with CO poisoning in different age groups by using chi-square tests for trend (Fig. 2). The rates of respiratory alkalosis for patients younger than 15 years, 15−29 years, 30−44 years, 45−59 years, and older than 59 years were 17.4%, 32.4%, 51.9%, 75%, and 75%, respectively ($p < 0.01$). Patients with CO poisoning were more likely to present with respiratory alkalosis as age increased.

An analysis of the relationships between age, respiratory rate, and respiratory alkalosis determined by an HbCO level of 25% was performed using a logistic regression model. A total of 25 (26%) patients had an HbCO level below 25% and 71 (74%) patients had a HbCO level above 25%. In the group with an HbCO level below 25%, the respiratory rate was an independent factor associated with respiratory alkalosis (OR, 1.15; 95% CI, 1.01−1.32); however, the age was an independent factor associated with respiratory alkalosis in the group with an HbCO level above 25% (OR, 1.03; 95% CI, 1.01−1.07).

## 4. Discussion

Previous studies have investigated the relationship between severity and arterial blood gas data in patients with CO poisoning. In the study by Myers and others,[4] no obvious correlation was found between initial pH and HbCO level; however, the HbCO level tended to be higher in the patients who presented with acidosis. They suggested that there might be a biphasic effect as a result of an increasing HbCO level on pH. An initial low HbCO level might cause patients to hyperventilate to compensate for the decrease in the oxygen-carrying capacity. A higher HbCO level might then exhaust the compensatory mechanisms and result in tissue anoxia and thus acidosis. In the study by Cevik and others,[7] a higher HbCO level and an adverse outcome were found to be related to acidosis, a decreased level of consciousness, tachycardia, high glucose and number of leukocytes. In the study by Turner and colleagues,[8] metabolic acidosis was a better indicator of the severity of CO poisoning than was the HbCO level, as the acidosis reflected tissue poisoning. In our study, we did not examine the relationship between disease severity and HbCO level, pH, $PCO_2$ or respiratory rate; however, we did find that there was no difference in the HbCO level, sex, loss of consciousness or blood pressure between the patients with and without respiratory alkalosis.

Table 1
Arterial pH, $PCO_2$, and $HCO_3^-$ of the Cohort.

| Characteristic | Total ($n = 96$) | Group A ($n = 58$) | Group B ($n = 38$) |
|---|---|---|---|
| pH, median | 7.43 | 7.41 | 7.49 |
| (25th, 75th percentiles) | (7.40, 7.47) | (7.38, 7.43) | (7.46, 7.53) |
| $PCO_2$, median | 31.7 | 33.7 | 27.3 |
| (25th, 75th percentiles) | (27.2, 35.4) | (30.4, 36.7) | (23.1, 32.0) |
| $HCO_3^-$, median | 21.8 | 22.3 | 20.5 |
| (25th, 75th percentiles) | (18.6, 23.7) | (19.0, 24.0) | (18.0, 23.2) |

$HCO_3^-$ = bicarbonate; $PCO_2$ = partial pressure of carbon dioxide.

In our study, 39.6% of patients with CO poisoning presented to the ED with respiratory alkalosis, which is not an uncommon finding. The predisposing factors that were independently associated with patients with CO poisoning presenting with respiratory alkalosis were respiratory rate and age. In the respiratory alkalosis group, the respiratory rate of patients tended to be faster than that of the other group and the age of the patients tended to be older. In addition to the definite linkage of respiratory rate and respiratory alkalosis,[9] it is known that $PO_2$ decreases gradually as age increases. The tolerance for hypoxia is relatively lower in the elderly when compared with that of younger people. As a result, the elderly tend to hyperventilate in order to compensate for the decrease in oxygen-carrying capacity in CO poisoning. In our study, the percentage of patients with respiratory alkalosis became higher as age increased, showing that elderly patients with CO poisoning were more likely to present with respiratory alkalosis.

High correlations among age, respiratory rate, and alkalosis may also occur in the general population, since people who cannot tolerate a low blood oxygen level may well present with similar findings. To confirm that the findings of high correlations among age, respiratory rate and respiratory alkalosis in CO poisoning had been analyzed correctly in this study, an analysis determined by an HbCO level of 25% was used. The respiratory rate was an independent factor associated with respiratory alkalosis in those with an HbCO level below 25%, but age was an independent factor associated with respiratory alkalosis in those with an HbCO level above 25%. Age was an independent predisposing factor for respiratory alkalosis in accidental CO poisoning, especially in those with an HbCO level above 25%.

How important is this finding for clinical practice? Acute or chronic exposure to CO can result in numerous symptoms,[10−12] and the death rate from unintentional CO poisoning is highest for adults older than 75 years of age.[10] However, the complaints

Table 2
General characteristics of the 96 patients and univariate comparisons between the two groups.

| Characteristic | Total ($n = 96$) | Group A ($n = 58$) | Group B ($n = 38$) | $p$ value |
|---|---|---|---|---|
| Age, median (25th, 75th percentiles), y | 24.0 (15.3, 39.3) | 20.5 (13.5, 43.5) | 36.0 (21.5, 43.5) | < 0.01 |
| Male sex, *n* (%) | 37 (38.5) | 24 (41.4) | 13 (34.2) | 0.48 |
| Comorbidities,[a] *n* (%) | 6 (6.3) | 1 (1.7) | 5 (13.2) | 0.03 |
| Diabetes, *n* (%) | 3 (3.1) | 1 (1.7) | 3 (7.9) | |
| Hypertension, *n* (%) | 3 (3.1) | 1 (3.4) | 2 (5.3) | |
| Coronary artery disease, *n* (%) | 2 (2.1) | 0 (0.0) | 2 (5.3) | |
| Loss of consciousness, *n* (%) | 35 (36.5) | 22 (37.9) | 13 (34.2) | 0.71 |
| GCS, median (25th, 75th percentiles), scores | 15.0 (15.0, 15.0) | 15.0 (15.0, 15.0) | 15.0 (15.0, 15.0) | 0.16 |
| RR, median (25th, 75th percentiles), breaths | 18.0 (17.0, 20.0) | 18.0 (16.0, 20.0) | 20.0 (18.0, 21.5) | 0.02 |
| HR, median (25th, 75th percentiles), beats | 99.0 (88.0, 112.8) | 103.0 (89.0, 119.0) | 96.0 (84.0, 107.0) | 0.12 |
| SBP, median (25th, 75th percentiles), mm Hg | 119 (100.0, 133.5) | 117.0 (102.5, 129.0) | 123.5 (97.0, 139.5) | 0.50 |
| Bun/Cr ratio, (25th, 75th percentiles) | 19.3 (13.7, 23.2) | 18.6 (11.4, 22.9) | 20.0 (14.0, 25.8) | 0.57 |
| HbCO, median (25th, 75th percentiles), % | 29.4 (24.2, 37.6) | 30.1 (26.2, 37.9) | 28.8 (18.8, 36.8) | 0.38 |

BUN = blood urea nitrogen; Cr = = creatinine; GCS = Glasgow coma scale; HbCO = carboxyhemoglobin; HR = heart rate; RR = respiratory rate; SBP = systolic blood pressure.
[a] One co-morbidity at least.

and symptoms of the elderly tend to be nonspecific, and a history of exposure is often difficult to retrieve; thus, the diagnosis is easily overlooked.[13] Other additional tools, such as an electrocardiogram have been advocated for physicians who suspect the possibility of CO poisoning.[14] Arterial blood gases, which are frequent checked in the ED, are usually used to evaluate the severity of numerous illnesses including CO poisoning.[4,7,8] In our study, we found that the patients with CO poisoning tended to present with respiratory alkalosis as their age increased. Emergency physicians cannot diagnose CO poisoning by arterial blood gases interpretation alone; an HbCO level is also needed.

Our study finding could be helpful in making the diagnosis of CO poisoning in the elderly. Under what circumstances should arterial blood gases be checked and what then will make emergency physicians think about CO poisoning? Shortness of breath is one common complaint of the elderly in ED visits. When patients present to the ED with shortness of breath or an altered state of consciousness, especially in the elderly, the arterial blood gases need to be checked. When the arterial blood gases reveal respiratory alkalosis, then CO poisoning should be taken into consideration, and emergency physicians need to elicit a history of exposure to CO. If an exposure history to CO is difficult to obtain, then the HbCO level should be checked, given the possibility of CO poisoning. If exposure to CO can be definitely excluded or the HbCO level is normal, then other causes should be taken into consideration.

Table 3
Independent predictors identified by multivariate analysis.

| Variable | β | OR (95% CI) | $p$ valve |
|---|---|---|---|
| Intercept | −4.51 | | |
| Age, y | 0.04 | 1.04 (1.01−1.08) | 0.04 |
| Comorbidities[a] | 0.49 | 1.64 (0.12−23.14) | 0.71 |
| RR | 0.15 | 1.16 (1.01−1.33) | 0.03 |

CI = confidence interval; OR = odds ratio; RR = respiratory rate.
[a] One comorbidity at least.

This study has some limitations. First, the quality of data obtained in a retrospective study is only as accurate as that which was recorded and stored. Second, $PO_2$ values were not considered in this study. This was due to patients receiving different concentrations of oxygen early in the ED visit before arterial blood gases were drawn, and the fraction of inspired oxygen was not recorded. Third, the study population was biased. Because our study was designed to examine the frequency of and identify the predisposing factors for respiratory alkalosis in patients with accidental CO poisoning, we excluded patients with intentional CO poisoning. We also excluded patients with concomitant drug or alcohol use, because these would influence the arterial blood gas interpretation. Fourth, medical treatments in the ED and the patients' outcomes and severity were not recorded so we cannot examine the correlations between disease severity and HbCO, pH, $PaCO_2$, or respiratory rate. Fifth, this was a single-center study and our database may not be representative of the general patient population in Taiwan.

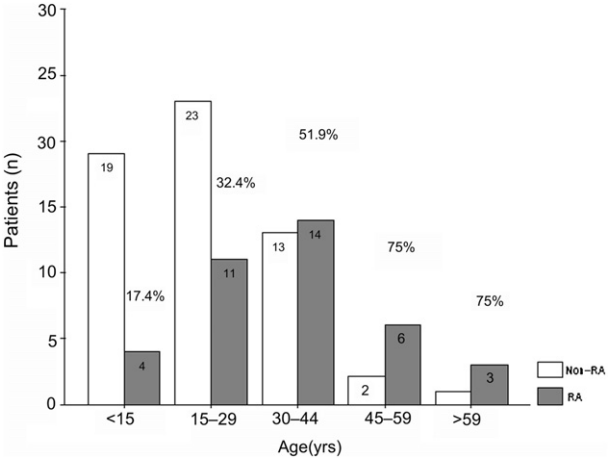


Fig. 2. Rate of respiratory alkalosis by age at intervals of 15 years; $p < 0.01$ (Chi-square test for trend). RA = respiratory alkalosis.

## 5. Conclusion

Our data suggest that respiratory alkalosis in patients with CO poisoning is not uncommon, and, as age increases, the likelihood becomes greater. When emergency physicians see patients who present with respiratory alkalosis of undetermined cause, then CO poisoning should be taken into consideration, especially in the elderly.

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