Acute carbon monoxide poisoning in Shandong, China: an observational study

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Abstract

Background: Carbon monoxide (CO) poisoning remains a major cause of accidental injuries and multiple studies have indicated that CO is also associated with significantly severe or long-term toxicity to the central nervous system. Given that CO poisoning causes serious morbidity and mortality, a better understanding of epidemiological features and clinical characteristics of acute CO poisoning in China is crucial.

Methods: We collected the clinical data of acute CO poisoning in patients between November 2019 and April 2020 across Shandong province, China and analyzed its characteristics focusing on the weekly amount and the severity of the confirmed cases.

Results: A total number of 21,088 acute CO poisoning cases were diagnosed. The overall incidence of acute CO poisoning was approximately 0.021%. On severity rankings, 63% of confirmed cases ($n = 13,378$) were mild, 27% ($n = 5635$) were moderate, and 10% ($n = 2075$) were severe. Interestingly, the coastal cities had more confirmed cases than the inland/suburban areas in Shandong. Meanwhile, the number of confirmed cases was negatively correlated with the local mean daily temperature ($P = 0.0167$).

Conclusions: Mild acute CO poisoning cases accounted for the majority of all confirmed cases during the winter of 2019. In Shandong province, which is located in east China, residents of the coastal cities are more susceptible to CO poisoning than residents of inland cities.

Keywords: Epidemiology; Acute carbon monoxide poisoning; Public health; Delayed neurological sequelae; Hyperbaric oxygen therapy

Introduction

Carbon monoxide (CO) poisoning remains a major cause of accidental injuries and may account for more than half of all fatal poisonings worldwide.[1] The non-occupational sources of acute CO poisoning include poorly maintained/ventilated home heating systems and cooking appliances in China.[2] Also, multiple studies have indicated that CO is associated with significantly more severe or long-term toxicity to the central nervous system than any other gas-related intoxications.[3-5] Given that CO poisoning causes serious morbidity and mortality, a better understanding of epidemiological features and clinical characteristics of acute CO poisoning is crucial.

Although the general status of the Chinese economy has skyrocketed in the last three decades, the development of the country's economy has not been very balanced. There has been rapid urbanization, and urban residents have relied much less on coal as a heating modality in winter compared to residents of rural areas. Nevertheless, the prevalence of CO poisoning in China remains remarkably high, especially given the country's largely rural population. Unlike other countries, where suicide and deliberate CO exposure during suicide is the main cause of CO poisoning,[6] inadequate maintenance of heating equipment and lack of adequate ventilation are the major non-occupational causes of CO poisonings in China. Residents of remote villages in northern China still use coal/charcoal as heating fuel in winter, with which insufficient combustion can easily lead to unintended CO gathering.

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Furthermore, in most urban areas, heating supply service (HSS) is highly available for most residents in winter, and the incidence of accidental CO poisoning is understandably much lower.[7]

Shandong is a coastal province with a temperate monsoon climate. As a big agriculture-based province, the rural population in Shandong is significantly larger than the urban ones. In this investigation, we conducted a weekly survey of the prevalence and severity of confirmed CO poisoning cases in Shandong province between November 2019 and April 2020, which was rarely reported as a provincial survey on acute CO poisoning.

Methods

Ethical approval

All studies included in the analyses reported here received ethics approval from the Shandong Medical Association Review Board.

Study design

We conducted a retrospective investigation of patients with acute CO poisoning who were admitted in order to receive hyperbaric oxygen (HBO) therapy in 16 districts of municipal cities in Shandong province between November 2019 and April 2020.

Data sources

Weekly data were collected from the HBO departments of hospitals in different districts via the HBO Medicine Branch of Shandong Medical Association. Once a week, the director of each city's HBO Medicine Branch collected the data on confirmed cases of three differentiated types of acute CO poisoning in their region.

Case definition

According to the diagnostic criteria for occupational acute CO poisoning (GBZ23–2002), we classified each case of CO poisoning into three types: mild, moderate, and severe.[8] Patients with mild CO poisoning showed clinical manifestations of headache, weakness, nausea, and vomiting and had arterial carboxyhemoglobin (COHb) level > 10%. Patients with moderate CO poisoning showed severe headache, irritability, impaired judgment, reduced awareness, etc, and had arterial COHb levels >30%. The patients with moderate CO poisoning recovered after rescue without obvious complications. Patients with severe CO poisoning showed signs of coma or deep coma, severe myocardial injury, respiratory failure, etc, and had arterial COHb levels >50%.

Statistical analysis

Data analysis was performed with GraphPad Prism software (version 5.0, GraphPad Software Inc., San Diego, CA, USA). Differences in proportion of acute CO poisoning were evaluated using two-way analysis of variance (ANOVA) with Bonferroni *post hoc-tests*, and $P < 0.05$ was considered statistically significant. Correlation analysis was used to examine the association between environmental temperature and the number of confirmed cases of acute CO poisoning. To correct for non-normality and small sample size, Spearman correlations were computed, and the level of significance for statistical testing was set to $\alpha = 0.05$.

Results

General characteristics

A total number of 21,088 cases of acute CO poisoning were diagnosed. Based on a general population of 101.5 million in Shandong province in 2020, the incidence of acute CO poisoning was about 0.021%.[9] As shown in Figure 1A, we observed two noteworthy increases in the number of confirmed cases. The first remarkable increase occurred during the third week of November 2019, while the second increase was a sharp peak that appeared on the third week of January 2020. As shown in Figure 1B, 63% of confirmed cases ($n = 13,378$) were mild, 27% ($n = 5635$) were moderate, and 10% ($n = 2075$) were severe. There were also two striking increases in the number of confirmed cases on the curve of mild type cases as shown in Figure 1B, which showed trends similar to those in Figure 1A.

Regional differences

The coastal cities of Qingdao and Yantai together had shared a larger number (>3000) of the confirmed cases than the other 14 municipal cities combined. In fact, the total number of confirmed cases for both Qingdao and Yantai was 6731 [32%, as seen in Supplementary Table 1, http://links.lww.com/CM9/A962 and Figure 2]. The total number of confirmed cases in the four coastal cities of Qingdao, Yantai, Rizhao, and Weihai ($n = 8827$) accounted for 42% of all cases. The number of confirmed cases (12,910, accounting for 61%) in the six cities of Qingdao, Yantai, Rizhao, Weihai, Linyi, and Weifang in the eastern region of Shandong province were more than that ($n = 8178$, accounting for 39%) of ten cities (Liaocheng, Dezhou, Jinan, Heze, Jining, Zibo, Dongying, Binzhou, Taian, and Zaozhuang) in the inland region of Shandong province. According to the results of the two-way ANOVA ofthe data (number of CO poisoning cases), there were significant differences among the 16 municipal cities in the number of CO poisoning cases ($P < 0.0001$).

The distribution of the confirmed cases of different types of CO poisoning was different across the 16 municipal cities [Supplementary Table 1, http://links.lww.com/CM9/A962]. There was no significant difference in the number of mild, moderate, or severe cases of CO poisoning among the cities Linyi, Dezhou, Zibo, Jinan, Heze, Zaozhuang, and Dongying ($P > 0.05$). There was no significant difference in the number of mild and moderate of CO poisoning cases among Qingdao, Liaocheng, Rizhao, Weifang, and Binzhou ($P > 0.05$), but there was a significant difference in the numbers of mild and severe cases of CO poisoning among these five cities ($P < 0.05$). In addition, there were significant differences in the number of mild and moderate cases

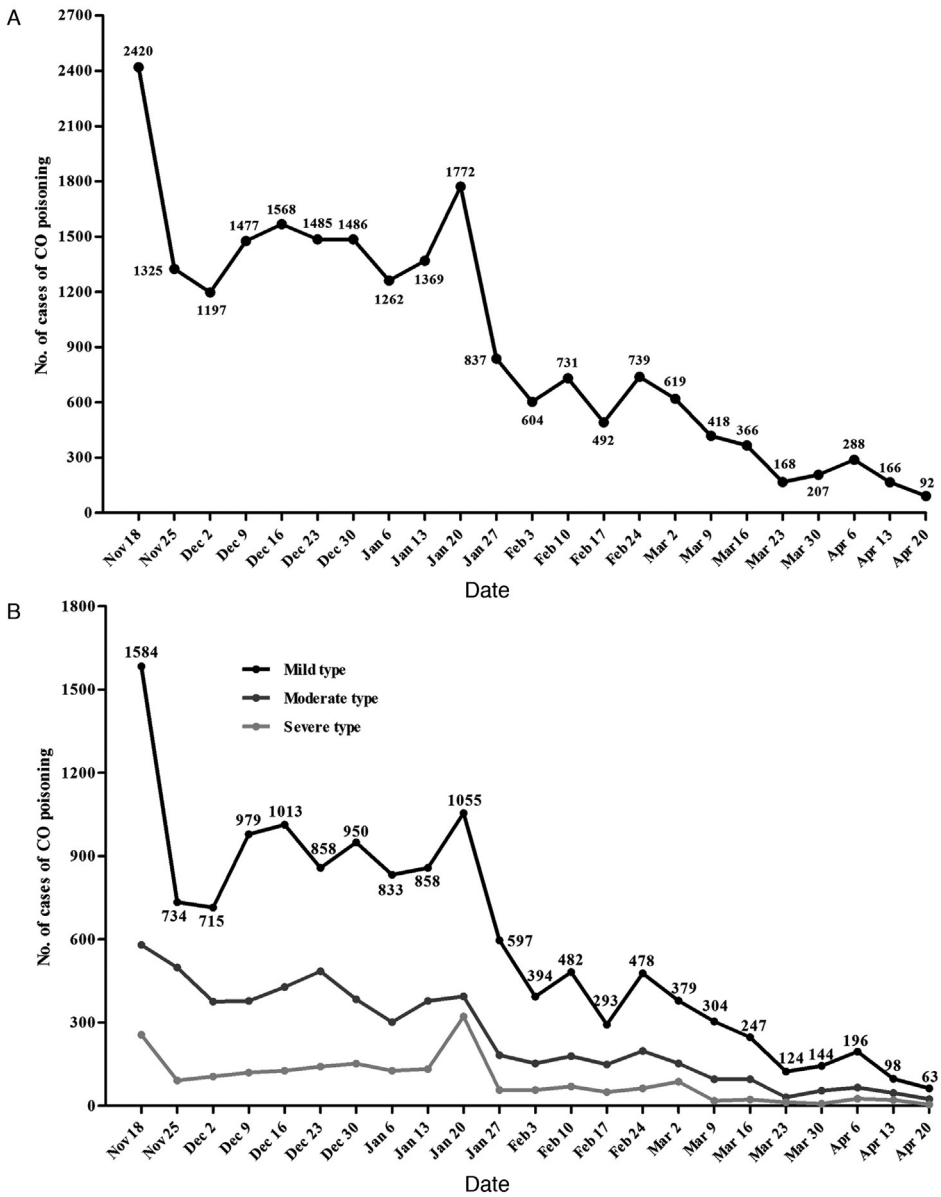

Figure 1: Provincial general characteristics of confirmed cases of acute CO poisoning. (A) The weekly number of total confirmed cases of acute CO poisoning. (B) Differences in distributions and characteristics of each type of acute CO poisoning. CO: Carbon monoxide.

of CO poisoning, mild and severe cases of CO poisoning in Yantai, Jining, Weihai, and Taian ($P < 0.01$). According to the results of two-way ANOVA with number of CO poisoning cases as the dependent variable, there were also significant differences among different types of CO poisoning ($P = 0.0111$).

Correlation analysis

We found that the number of confirmed cases between November and January ($n = 16{,}198$, 77%) was much larger than that from February to April ($n = 4890$, 23%). The incidence of CO poisoning changed with environmental temperature variance. According to the daily temperature management plan provided by the Shandong Meteorological Bureau, we drew a 6-month temperature curve [Supplementary Figure 1, http://links.lww.com/CM9/A962]. We examined Spearman correlations between mean daily temperature and number of confirmed cases of acute CO poisoning and found a significant negative correlation, indicating that a lower mean winter temperature was associated with increased incidence of acute CO poisoning [Figure 3].

Discussion

The most severe complication of acute CO poisoning is delayed neurological sequelae (DNS). DNS has long been a worldwide clinical concern because it leads to serious deterioration in a patient's quality of life, jeopardizes their independence, and eventually leads to an unavoidable disability, or even death.[10-13] Although most patients with mild CO poisoning could recover fully from the acute

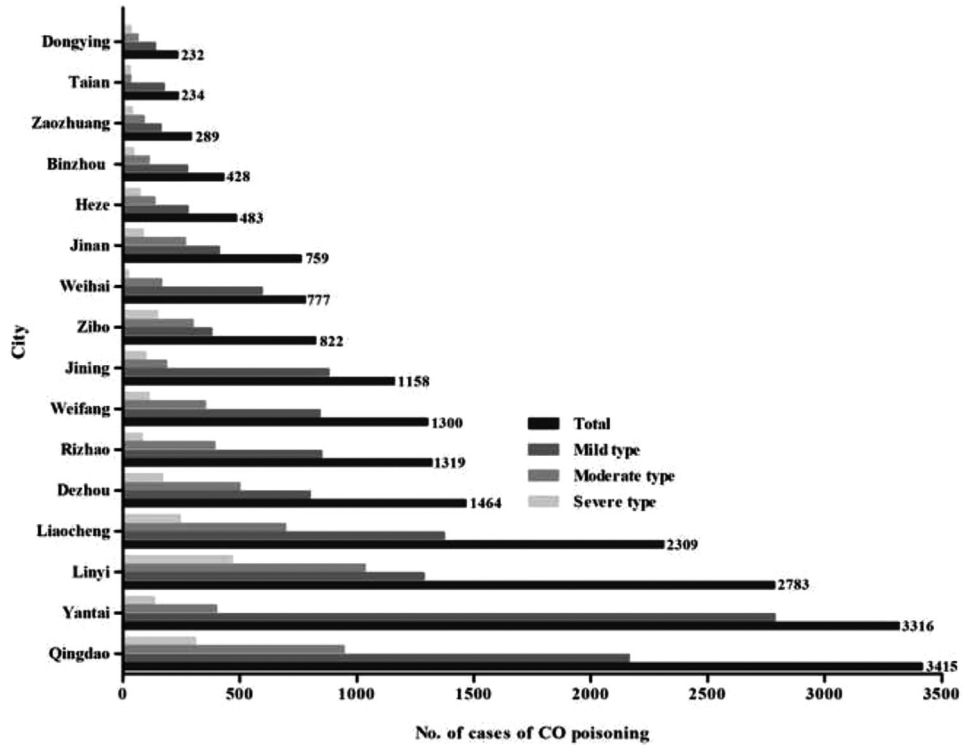

Figure 2: Regional differences in characteristics of acute CO poisoning in 16 municipal cities. CO: Carbon monoxide.

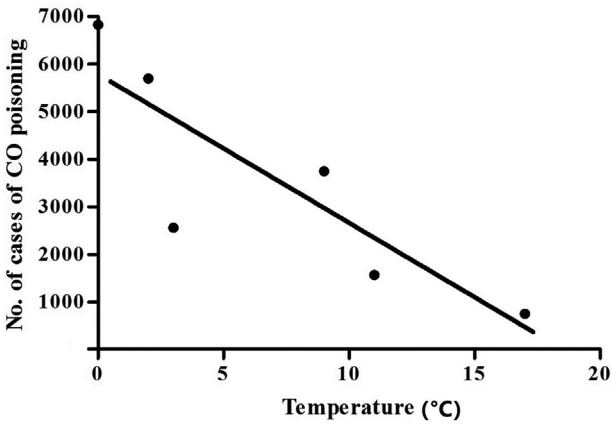

Figure 3: Correlation between environmental temperature and number of confirmed cases of acute CO poisoning (Spearman $r = -0.9429$, P value = 0.0167). Each value of temperature on the X-axis represents the mean daily temperature of each month. CO: Carbon monoxide.

phase, more than half of the patients with severe CO poisoning would develop a tragic DNS within 3 days to 6 weeks after CO poisoning onset.[14] Therefore, it is necessary for patients to go to the HBO department as early as possible, ideally within 24 h after CO exposure, for early emergency treatment and DNS prevention.[15]

Prior studies have shown that using HBO therapy in the acute phase of CO poisoning reduces immune-mediated neuropathology and can reduce the incidence of DNS.[15,16] It has been reported that a historical cohort study in which all patients with a diagnosis of CO poisoning managed in a regional hospital in Hong Kong from February 12, 2003 to November 8, 2013, was conducted. Of the clinical profiles of 93 patients analyzed, 24 patients who received HBO therapy at an earlier time did not develop the following DNS, which showed a 100% protective effect of HBO therapy against DNS in patients with severe CO poisoning. Loss of consciousness, low Glasgow Coma Scale score, intubation requirement, elevated troponin, and higher creatine kinase levels were possible prognostic factors for the development of DNS in patients with severe CO poisoning.[17]

A retrospective 6-year epidemiological study (2009–2014) reported an overall analysis of CO poisoning-related mortalities in China, which collected data provided by the forensics from nine districts of Wuhan, showing that a total of 131 incidents of CO poisoning that resulted in the death of 156 victims were collected, and 76 incident events (97 mortality in total) were classified as accidents, 49 incident events (51 deaths) were suicides, three incident events (four deaths) were homicides, one incident event (three deaths) was homicide-suicide, and one incident event (one death) was classified as undetermined. Coal or charcoal burning was found to be the major cause of the suicide CO poisoning-related death (67%), meanwhile fire-related accident was also the major cause of accidental CO poisoning's mortalities.[18]

In our investigation, malpractice or malfunctioning of the coal-burning stoves inside homes likely accounts for the majority of CO poisoning incidents in Shandong.

Therefore, community health centers or other grassroots medical facilities should provide more detailed instructions for residents that focus on the safe application of the home heating stoves.

In this study, the first remarkable increase in cases, which appeared during the third week of November 2019 at a time when a 7-month heating equipment halt had ended and an essential equipment renewal or maintenance should be carried out before reuse during the winter. However, due to the sudden drop in daily temperature in the winter of 2019, a large number of rural residents presumably rushed indoors to attend to the coal-based heating equipment directly, which resulted in a tragic rise in accidental CO poisonings. The second conspicuous increase we observed occurred during the third week of January 2020, when the daily minimum temperature was the lowest of the winter.[19] Furthermore, for the Chinese Lunar New Year, which was January 25th in early 2020, it is a solid fact that large numbers of college students and rural migrant workers returned to their rural hometowns for the Spring Festival Holidays, and the deadly combination of a closed environment and inadequately maintained heating equipment must have contributed greatly to the number of cases surging.

Another point worth mentioning is the proportion of acute CO poisoning types. There were 13,378 cases of the mild type, which accounted for more than half 63%) of all cases, consistent with the previous reports.[20]

Confirmed cases in the four coastal cities accounted for >40% of the total number of confirmed cases in Shandong province. Only three inland cities in the western region had over 1000 confirmed cases: 1158 in Jining, 1464 in Dezhou, and 2309 in Liaocheng. Last but not least, the number of cases of CO poisoning had a high correlation with seasonal colder weather,[21] which was consistent with the results of previous studies.[21-24]

This multi-center study of acute CO poisoning was the first provincial survey conducted in the last three decades in Shandong province. The frontline data provided by the 16 districts of municipal cities of Shandong province are considered highly reliable and representative. We presume that the larger number of confirmed cases in coastal cities mainly occurred because of regional disparities in economic level, medical conditions, and medical service availability, and all these advantages stood for a more percentage of data completion and more accountability of follow-up and bio-info statistics.

Shandong province is located in the northeastern part of China, adjacent to the Yellow Sea, where the climate is relatively moderate. It is also worth mentioning that the quality of Shandong's healthcare service is far better than average in China; therefore, the statistical data collected from the 16 cities we included should be considered representative for a well-off province.

Intriguingly, the HSS is not available in southern China, nor in rural and remote areas of northern China, and there may be more accidental CO poisoning cases in these areas.[2,25]

Our observations have certain limitations, and in the case of overall provincial economy status, medical service levels, and rural-urban differences, the collection of data indicating provincial disparities in CO poisoning in China was complicated; an overall long-term nation-based CO poisoning registration system should be guaranteed.

CO poisoning poses a significant public health burden. Systematic evaluation of data sources from a national registration system might assist in developing effective prevention strategies. The prevention of CO poisoning depends on reducing the source (insufficient combustion) or early detection. Public health interventions aimed at modification of health behaviors like using CO alarms indoors might prevent a large number of CO poisoning cases.

Limitations

This study lacks long-term follow-up. The mortality of the cases of acute CO poisoning we identified was not measured due to pre-hospital loss of follow-up. In addition, although data were collected from 16 cities, most of the patients came from suburban or rural areas. Therefore, patients who went to local primary hospitals for first aid or other treatment were not included in this study. We assume that the number of cases we identified was smaller than the actual number because of the incompleteness of our data collection procedure, which did not have the involvement of all frontline medical services.

Conclusions

In this study, mild acute CO poisoning cases accounted for the majority of all confirmed cases during the winter of 019. In Shandong province, which is located in east China, residents of the coastal cities are more susceptible to CO poisoning than residents of inland cities.

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Conflicts of interest

None.

References

1. Sircar K, Clower J, Shin MK, Bailey C, King M, Yip F. Carbon monoxide poisoning deaths in the United States, 1999 to 2012. Am J Emerg Med 2015;33:1140–1145. doi: 10.1016/j.ajem.2015.05.002.
2. Chen F, Ye Y, Wei Q, Chen J, Wu H, Yan Y, *et al*. Non-fire related carbon monoxide poisoning in Sichuan, China: a 9-year study (2008-2016). Iran J Public Health 2019;48:458–464. doi: 10.18502/ijph. v48i3.889.

3. Ernst A, Zibrak JD. Carbon monoxide poisoning. N Engl J Med 1998;339:1603–1608. doi: 10.1056/NEJM199811263392206.
4. Graber JM, Smith AE. Results from a state-based surveillance system for carbon monoxide poisoning. Public Health Rep 2007;122:145–154. doi: 10.1177/003335490712200203.
5. Zhang L, Sun Q, Xin Q, Qin J, Zhang L, Wu D, *et al*. Hyperbaric oxygen therapy mobilized circulating stem cells and improved delayed encephalopathy after acute carbon monoxide poisoning with up-regulation of brain-derived neurotrophic factor. Am J Emerg Med 2021;42:95–100. doi: 10.1016/j.ajem.2021.01.021.
6. Hampson NB. U.S. mortality due to carbon monoxide poisoning, 1999-2014. Accidental and Intentional Deaths. Ann Am Thorac Soc 2016;13:1768–1774. doi: 10.1513/AnnalsATS.201604-318OC.
7. Zhang Y, Yu B, Wang N, Li T. Acute poisoning in Shenyang, China: a retrospective and descriptive study from 2012 to 2016. BMJ Open 2018;8:e021881. doi: 10.1136/bmjopen-2018-021881.
8. Liu SD, Shen Q, Lv C, Zhang P, Yu H, Yang L, *et al*. Analysis of combined detection of N-terminal pro-B-type natriuretic peptide and left ventricular ejection fraction in heart function in patients with acute CO poisoning. Am J Emerg Med 2014;32:1212–1214. doi: 10.1016/j.ajem.2014.07.012.
9. Shandong Provincial Bureau of Statisyics. Main data of the seventh national census in Shandong Province. Shandong, China. 2021. Available from: http://tjj.shandong.gov.cn/art/2021/5/21/art_6293_10287509.html. [Accessed April 1, 2021]
10. Keim L, Koneru S, Ramos VFM, Murr N, Hoffnung DS, Murman DL, *et al*. Hyperbaric oxygen for late sequelae of carbon monoxide poisoning enhances neurological recovery: case report. Undersea Hyperb Med 2018;45:83–87. doi: 10.22462/01.02.2018.11.
11. Hsiao CL, Kuo HC, Huang CC. Delayed encephalopathy after carbon monoxide intoxication - long-term prognosis and correlation of clinical manifestations and neuroimages. Acta Neurol Taiwan 2004;13:64–70.
12. Pepe G, Castelli M, Nazerian P, Vanni S, Del Panta M, Gambassi F, *et al*. Delayed neuropsychological sequelae after carbon monoxide poisoning: predictive risk factors in the Emergency Department. A retrospective study. Scand J Trauma Resusc Emerg Med 2011;19:16. doi: 10.1186/1757-7241-19-16.
13. Ide T, Kamijo Y. Myelin basic protein in cerebrospinal fluid: a predictive marker of delayed encephalopathy from carbon monoxide poisoning. Am J Emerg Med 2008;26:908–912. doi: 10.1016/j. ajem.2007.11.021.
14. Weaver LK, Hopkins RO, Chan KJ, Churchill S, Elliott CG, Clemmer TP, *et al*. Hyperbaric oxygen for acute carbon monoxide poisoning. N Engl J Med 2002;347:1057–1067. doi: 10.1056/NEJMoa013121.
15. Ning K, Zhou YY, Zhang N, Sun XJ, Liu WW, Han CH. Neurocognitive sequelae after carbon monoxide poisoning and hyperbaric oxygen therapy. Med Gas Res 2020;10:30–36. doi: 10.4103/2045-9912.279981.
16. Wang W, Cheng J, Zhang J, Wang K. Effect of hyperbaric oxygen on neurologic sequelae and all-cause mortality in patients with carbon monoxide poisoning: a meta-analysis of randomized controlled trials. Med Sci Monit 2019;25:7684–7693. doi: 10.12659/MSM.917065.
17. Chan MY, Au TTS, Leung KS, Yan WW. Acute carbon monoxide poisoning in a regional hospital in Hong Kong: historical cohort study. Hong Kong Med J 2016;22:46–55. doi: 10.12809/hkmj144529.
18. Li F, Chan HCO, Liu S, Jia H, Li H, Hu Y, *et al*. Carbon monoxide poisoning as a cause of death in Wuhan, China: a retrospective six-year epidemiological study (2009-2014). Forensic Sci Int 2015;253:112–118. doi: 10.1016/j.forsciint.2015.06.007.
19. Bando M, Miyatake N, Kataoka H, Kinoshita H, Tanaka N, Suzuki H, *et al*. Relationship between air temperature parameters and the number of deaths stratified by cause in Gifu Prefecture, Japan. Healthcare (Basel) 2020;8:35. doi: 10.3390/healthcare8010035.
20. Kim JH, Lim AY, Cheong HK. Trends of accidental carbon monoxide poisoning in Korea, 1951-2018. Epidemiol Health 2020;42:e2020062. doi: 10.4178/epih.e2020062.
21. Iqbal S, Clower JH, King M, Bell J, Yip FY. National carbon monoxide poisoning surveillance framework and recent estimates. Public Health Rep 2012;127:486–496. doi: 10.1177/003335491212700504.
22. Centers for Disease Control and Prevention (CDC). Unintentional non-fire-related carbon monoxide exposures - United States, 2001-2003. MMWR Morb Mortal Wkly Rep 2005;54:36–39. doi: 10.1001/jama.293.10.1183.
23. Yari M, Fouladi N, Ahmadi H, Najafi F. Profile of acute carbon monoxide poisoning in the west province of Iran. J Coll Physicians Surg Pak 2012;22:381–384.
24. Roca-Barceló A, Crabbe H, Ghosh R, Freni-Sterrantino A, Fletcher T, Leonardi G, *et al*. Temporal trends and demographic risk factors for hospital admissions due to carbon monoxide poisoning in England. Prev Med 2020;136:106104. doi: 10.1016/j.ypmed.2020.106104.
25. Xue J, Sun Q, Wang Y, Gao G, Shi L, Yu T. Features of carbon monoxide poisoning in China. Iran J Public Health 2013;42:1192–1193.

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