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Review

Carbon monoxide intoxication: What we know

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ABSTRACT

Carbon monoxide (CO) is a toxic, color-, taste- and odorless gas with fatal consequences if undetected. Intoxication caused by CO is frequent possibly leading to a high morbidity and mortality. The disease involves multiple organ systems without a typical clinical presentation. The clinical picture is furthermore unrelated to levels of carboxyhemoglobin — the routine biomarker. Therefore the diagnosis and treatment can be very demanding. This article in detail reviews epidemiology, symptoms, diagnosis and the therapy of this multidisciplinary challenge.

Contents

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1. Epidemiology

Carbon monoxide (CO) is a gas, which by its nature is colorless, odorless and tasteless, making it an invisible threat. It arises from the incomplete burning of hydrocarbons. Its affinity to hemoglobin molecules is roughly 240 times higher than that of oxygen (O_2) [1], leading when present to the formation of carboxyhemoglobin by replacing the bounded O_2 [2]. Once inhaled CO leads to tissue hypoxia primarily effecting areas of high blood flow and oxygen demand [3]. The affinity of CO to myoglobin is also 60 times greater than that of O_2 causing cardiac depression and potentially hypotension [4]. However, the main pathomechanism has not proven to be the reduction of the oxygen-carrying capacity caused by the increased carboxyhemoglobin forming. The toxic effect is the result of CO binding to cytochrome oxidase and inhibiting the electron transport chain [5]. Death certificates from 1999 to 2004 in the United States recorded CO intoxication as a contributing cause of death in 16,447 cases. During the same period CO intoxication alone accounted for 439 deaths per year [6]. According to estimations 40,000 people per year require medical attention due to CO intoxication in the United States [7]. Reviewing the data on worldwide injuries and deaths after poisoning, CO intoxication is the most common cause [8]. Sources causing accidental CO poisoning are open fires (42%), work-related exposure in industry (26%) and faulty furnaces (19%). Motor vehicles only explain a small proportion (4%), of which 88% however are the result of a suicidal attempt [9]. The high morbidity and mortality stand face to face with the risk of oversight due to non-specific symptoms and difficulties in detection [10]

2. Symptoms

CO poisoning causes a variety of symptoms of which nausea (40%), headache (46%), dyspnea (20%) and tachycardia (41%) seem to be the most common. Vertigo and vomiting are furthermore described [9,11]. Specific cardiovascular effects include electrocardiographic QT prolongation, myocardial ischemia, low blood pressure, ventricular arrhythmia and in rare cases atrial thrombus [12,13]. CO poisoning can also lead to left ventricle dysfunction with systolic and diastolic impairment [14]. Moreover, multiple neurological and psychological disorders are associated with CO intoxication such as status epilepticus, polyneuropathy, Korsakoff syndrome, MS-like syndrome, dementia, Parkinson's syndrome, psychosis, depression and kleptomania [15–17]. In addition, symptoms involving the central nervous system can lead to hallucinations, dizziness, confusion, seizures and at a maximum extent to respiratory arrest [18,19]. These enumerations highlight that the clinical presentation is unspecific and complex involving multiple organ systems. Therefore, the diagnosis can easily be overlooked or misdiagnosed possibly leading to coma and death at worst [10]. The comparison of two case reports by Grieb et al. clearly emphasizes the difficulties in everyday clinic life: the first patient was a fireman working in a silo who reported chest pain and nausea, then became somnolent and collapsed. The physical examination showed neurological deficits and paresthesia of the upper legs as well as rosy complexion and livid coloration. A CO poisoning was suspected in consideration of the symptoms and work environment. Slight but not significant ST elevations in the initial electrocardiography (ECG) were explained as transient ischemia compatible with CO intoxication. After hyperbaric oxygen therapy and extubation in stable condition the man still complained about severe chest pain. The diagnosis of a myocardial infarction (MI) was then correctly made based on an elevated Troponin level and a second ECG with significant ST elevations [20]. In comparison the second patient an older man presented with chest pain, palpations and inner agitation. His medical history included type II diabetes, nicotine and alcohol abuse and schizophrenic psychosis. The physical examination showed a sufficient general health, however an ECG indicated ST elevations. The leading diagnosis of a MI was ruled out via clinical chemistry. Only on second admission a week later with identical symptoms the correct diagnosis was found. The man had an CO poisoning from a defective furnace in his garden cottage [20]. CO intoxication successfully mimics other diseases and therefore is a differential diagnosis to always bear in mind.

3. Diagnosis

To detect a CO intoxication the percentage of COHb is measured. Arterial blood gas tests are the most reliable source. An advantage is the pre-clinical determination via pulse CO-oximetry which is competent possible with the suitable equipment [21]. A normal ratio of carboxyhemoglobin to hemoglobin is up to 5%, in smokers up to 9% [22]. However, COHb measurement alone is an insufficient marker for assessing the severity of disease. A case report on two patients with almost equal COHb levels showed major differences in presentation and severity of symptoms as well as course of disease [23]: the patients, a young male and female both healthy, nonsmokers and without significant medical history had been exposed to the same source of CO for approximately the same amount of time causing similar COHb levels (34.7% vs. 38%). The male presented somnolent, spontaneously breathing and reactive to verbal stimuli (Glasgow Coma Scale 13). He recovered quickly after receiving oxygen and was fully orientated to all qualities. He felt minor nausea but no further symptoms. ECG, serum analysis and chest x-ray showed no abnormalities. He received hyperbaric oxygen therapy without complications, remained free of symptoms and left the hospital the next day against medical advice [23]. The female was unconscious and gasping (GCS: 3) and required direct intubation and ventilation with 100% O_2. She initially only showed tachycardia but also became hypotonic needing treatment. Her ECG was normal, serum analysis only showed elevated hepatic enzymes however the chest x-ray revealed severe toxic lung edema. She received hyperbaric oxygen therapy without complications but had to remain intubated for a total of 43 h. The lung edema declined and after extubation she presented no neurologic deficits but needed further oxygen support. She left the hospital after 4 days. This comparison furthermore emphasizes the lacking correlation of COHb levels with the severity of symptoms and the

prognosis [15,24]. In addition, it has been demonstrated that COHb levels also do not correlate with the duration of inpatient treatment. On the other hand a significant inverse correlation between the initial GCS and the duration of inpatient stay has been revealed. Along with it an association between the duration of inpatient treatment and elevated leukocyte numbers, CRP serum concentration and the occurrence of lung infiltrates has been published. COHb is a helpful parameter supporting the initial diagnosis of CO poisoning. To judge the severity of disease further examinations are needed. GCS, leucocyte count, CRP serum concentration and pulmonary infiltrates on chest x-ray are promising tools [9]. In case of suspected CO intoxication the investigation should also include a complete blood count, a liver function test as well as the determination of electrolyte, urea and glucose levels [25–27]. Some studies suggest a correlation between measured lactate blood levels and loss of consciousness and convulsion in children. This parameter is used as a tool to decide for hyperbaric oxygen treatment [28]. Especially in burn victims with possible smoke inhalation injuries a fiberoptic bronchoscopy can be useful to judge erythema, edema and ulceration. Furthermore, it is a meaningful tool to perform airway management during an ICU stay [29,30]. The most important measurements and parameters for diagnosing and treating CO intoxication are summarized in Table 1.

4. Therapy

Due to the large spectrum of symptoms a critical management of CO intoxications is recommended. This includes an inpatient treatment in a specialized clinic, a detailed medical history and physical examination. Furthermore, the vital parameters such as heart rate, blood pressure, percutaneous oxygen saturation and blood gas analysis should be monitored continuously. Intubation and ventilation with 100% O_2 is required in patients with respiratory insufficiency [9,23].

If there is a preclinical suspicion of CO intoxication emergency staff should administer high levels of oxygen (e.g. high-flow oxygen, reservoir face mask, 100% oxygen in terms of artificial air way) [31,32]. It is essential to focus on ventilation and perfusion and establish an appropriated monitoring as stated above (ECG, blood pressure, measurement of oxyhemoglobin and if available carboxyhemoglobin). To assess the neurological status immediately, GCS is the appropriate tool even preclinically [9,18,19]. If possible the circumstances of exposure have to be determined (duration, source, other injured patients) and documented for further inpatient hospital therapy. In case of a suicide attempt toxicologic labor investigations have to be considered [18].

The half-life of COHb under standard atmospheric conditions is 4–8 h and can be reduced to 2 h under administration of 100% O_2. Due to the fact that carbon monoxide may have severe effects on the fetus, pregnant women are treated for longer periods with oxygen insufflation [30]. The greatest lowering to 30 min can be achieved under hyperbaric oxygen therapy at 3 atm of pressure [2]. Nevertheless, hyperbaric oxygen therapy is under debate as some studies criticize the insufficiently proven benefit of a routine use in the treatment of CO poisoning [2,33,34]. However, many authors argue that the majority of patients benefit from hyperbaric oxygen therapy [34] and a convincing advantage is the effective minimization of delayed neurological sequelae, cerebral edema and pathological central nervous system changes [35,36]. Possible side effects of HBO treatment are pneumothorax, decompression sickness, gas embolism and middle ear barotrauma. Bessereau et al. report about up to 13.6% of barotrauma auris in patients [37]. In 2002 Weaver and colleagues published in The New England Journal of Medicine results of a double-blinded, randomized trial regarding cognitive sequelae after acute carbon monoxide poisoning to compare the effects of HBO versus NBO. Six weeks after CO-poisoning neurological pathologies detected with neuropsychological testing revealed a significantly lower rate in the hyperbaric-oxygen group (25 vs. 46.1%; $p=0.007$). There are multiple different designs of HBO procedures. Weaver et al., as the only study to show a positive effect in a double-blinded, randomized trial, used an initial session of 150 min (75 min of

Table 1 – Most important parameters for diagnosing and treating CO-intoxication.

Parameters	Comment
Carboxyhemoglobin	- Initial diagnosis of co-intoxication [9,21] - Preclinical use with percutaneous co-oximetry [21] - No correlation to duration of inpatient treatment, severity of symptoms, prognosis [9,15,24]
Oxyhemoglobin	- Respiratory arrest is a possible symptom of CO-intoxication [18,19]
Lactate blood level	- Tissue hypoxia [27] - Correlation to time of co-exposure and severity [25] - Tool to decide for HBO treatment in children [28]
Leucocytes	- Correlation between elevated leucocytes and duration of inpatient treatment [9]
C-reactive protein	- Correlation between increased CRP and duration of inpatient treatment [9]
Chest x-ray	- Lung infiltrates, lung edema [9] - Correlation between pulmonary infiltrates and severity [9]
Glasgow-Coma-Scale	- Possible symptoms: dizziness, confusion, seizures [18,19] - Inverse correlation to inpatient stay and severity [9]
Electrocardiography	- Possible heart disorder e.g. tachycardia, QT prolongation, myocardial ischemia, ventricular arrhythmia [9,11–13]
Bronchoscopy (if inhalation injury is suspected)	- Degree of erythema, edema, ulceration [29,30]

3atm+75min of 2atm) following two sessions of 120min (2atm) [38].

There even is a study by Annane et al. from 2011 which shows a lower recovery rate after two HBO sessions compared to one HBO session in comatose patients (trial B). This led to a premature termination of the trial. Additionally, recovery rates in patients with transient loss of consciousness (trial A) were close to even (61% versus 58%) so that this arm was discontinued as well. The authors concluded that HBO therapy is not superior to NBO therapy [39].

Buckley et al. included six randomized trials with a large heterogeneity regarding different treatment regimes, follow-ups and biases in a systematic review involving 1361 patients. The pooled analysis revealed no statistical significance between NBO and HBO therapy. In conclusion routine HBO treatment is not recommended but may be beneficial for patients with severe poisoning [40].

Therefore, a hyperbaric oxygen therapy is recommended for patients with neurological deficits, respiratory insufficiency or a COHb level >15% [23].

Recovery after acute CO-intoxication depends on the development of sequelae. Those can develop immediately (persistent neurological sequelae — PNS) or weeks later (delayed neurological sequelae — DNS) and can be permanent [31]. Signs and symptoms can have a great variety and can be non-specific. It is recommended to treat symptoms with cognitive, psychiatric, vocational, speech, occupational and physical rehabilitation. Therefore, a long-term follow up after hospital discharge is required [18].

5. Conclusion

Carbon monoxide intoxication is one of the most common inhalative poisoning worldwide which can lead to high morbidity and mortality involving multiple organ systems. Due to its variety of clinical presentations and lack of reliable blood tests with correlation to the clinical outcome it remains a multidisciplinary challenge. Therapy of CO intoxication depends on variable factors. Even the benefit of hyperbaric oxygen therapy is still under current debate. Carbon monoxide intoxication is a differential diagnosis to always bear in mind and treat thoroughly.

Conflict of interest

All authors declare no conflict of interest.

REFERENCES

[1] Barret L, Danel V, Faure J. Carbon monoxide poisoning, a diagnosis frequently overlooked. J Toxicol Clin Toxicol 1985;23(4–6):309–13.

[2] Silver S, Smith C, Worster A. Should hyperbaric oxygen be used for carbon monoxide poisoning? C J E M 2006;8(January (1)):43–6.

[3] Ilano AL, Raffin TA. Management of carbon monoxide poisoning. Chest 1990;97(January (1)):165–9.

[4] Nelson LH. Carbon monoxide. Goldfrank's toxicologic emergencies. 7th ed. New York: McGraw-Hill; 2002. p. 1689–704.

[5] Goldbaum LR, Ramirez RG, Absalon KB. What is the mechanism of carbon monoxide toxicity. Aviat Space Environ Med 1975;46(October (10)):1289–91.

[6] MMWR. Carbon monoxide related deaths United States, 1999–2004. MMWR Morb Mortal Wkly Rep 2007;56(50):1309–12.

[7] Hampson NB. Emergency department visits for carbon monoxide poisoning in the Pacific Northwest. J Emerg Med 1998;16(5):695–8.

[8] Thom SR. Hyperbaric-oxygen therapy for acute carbon monoxide poisoning. N Engl J Med 2002;347(14):1105–6.

[9] Grieb G, Simons D, Schmitz L, Piatkowski A, Grottke O, Pallua N. Glasgow Coma Scale and laboratory markers are superior to COHb in predicting CO intoxication severity. Burns 2011;37:610–5.

[10] Tellez J, Fajardo A. Carbon monoxide contamination: an environmental health problem. Rev Salud Publica (Bogota) 2006;8(January–April (1)):108–17.

[11] Garland H, Pearce J. Neurological complications of carbon monoxide poisoning. Q J Med 1967;36:445–55.

[12] Oikarinen L, Toivonen L, Viitasalo M. Electrocardiographic measures of ventricular repolarisation dispersion in patients with coronary artery disease susceptible to ventricular fibrillation. Heart 1998;79:554–9.

[13] Onvlee-Dekker IM, De Vries AC, Ten Harkel AD. Carbon monoxide poisoning mimicking long-QT induced syncope. Arch Dis Child 2007;92:244–5.

[14] Ozyurt A, Karpuz D, Yucel A. Effects of acute carbon monoxide poisoning on ECG and echocardiographic parameters in children. Cardiovasc Toxicol 2017;17(July (3)):326–34.

[15] Brown KL, Wilson RF, White MT. Carbon monoxide-induced status epilepticus in an adult. J Burn Care Res 2007;28:533–6.

[16] Roohi F, Kula RW, Mehta N. Twenty-nine years after carbon monoxide intoxication. Clin Neurol Neurosurg 2001;103:92–5.

[17] Gurlek Yuksel E, Taskin EO, Yilmaz Ovali G, Karacam M, Esen Danaci A. Case report: kleptomania and other psychiatric symptoms after carbon monoxide intoxication. Turk Psikiyatri Derg 2007;18:80–6.

[18] Weaver LK. Clinical practice. Carbon monoxide poisoning. N Eng J Med 2009;360(March (12)):1217–25.

[19] Shochat, Guy N. Toxicity, Carbon Monoxide. emedicine. (17 February 2009). http://emedicine.medscape.com/article/819987-overview.

[20] Grieb G, Simons D, Piatkowski A, Altiok E, Eppstein RJ, Bernhagen J, et al. Carbon monoxide intoxication versus myocardial infarction: an easy diagnosis? Burns 2011;37:e29–31.

[21] Piatkowski A, Ulrich D, Grieb G, Pallua N. A new tool for the early diagnosis of carbon monoxide intoxication. Inhal Toxicol 2009;21(13):1144–7.

[22] Ford MD, Delaney KA, Ling LJ, Erickson T, editors. Clinical toxicology. WB Saunders Company; 2001 p. 1046. ISBN 0-7216-5485-1.

[23] Grieb G, Groger A, Bozkurt A, Stoffels I, Piatkowski A, Pallua N. The diversity of carbon monoxide intoxication: medical courses can differ extremely—a case report. Inhal Toxicol 2008;20:911–5.

[24] Ferguson KL, Su M. Clinical complexity of carbon monoxide poisoning. Am J Cardiol 2007;100:1184–5.

[25] Sokal JA, Kralkowska E. The relationship between exposure duration, carboxyhemoglobin, blood glucose, pyruvate and lactate and the severity of intoxication in 39 cases of acute carbon monoxide poisoning in man. Arch Toxicol 1989;57:196–9.

[26] Sokal JA. The effect of exposure duration on the blood level of glucose pyruvate and lactate in acute carbon monoxide intoxication in man. J Appl Toxicol 1985;5:395–7.

[27] Buehler JH, Berns AS, Webster JR, Addington WW, Cugell DW. Lactic acidosis from carboxyhemoglobinemia after smoke inhalation. Ann Intern Med 1975;82:803–5.
[28] Damlapinar RD, Arikan FI, Sahin S. Lactate level is more significant than carboxihemoglobin level in determining prognosis of carbon monoxide intoxication of childhood. Pediatr Emerg Care 2016;32(June (6)):377–83.
[29] Cancio LC. Airway management and smoke inhalation injury in the burn patient. Clin Plast Surg 2009;36(4)555–67, doi:http://dx.doi.org/10.1016/j.cps.2009.05.013 PMid:19793551.
[30] Mlcak RP, Suman OE, Herndon DN. Respiratory management of inhalation injury. Burns 2007;33(1)2–13, doi:http://dx.doi.org/10.1016/j.burns.2006.07.007 PMid:17223484.
[31] Ernst A, Zibrak JD. Carbon monoxide poisoning. N Engl J Med 1998;339:1603–8.
[32] Weaver LK, Howe S, Hopkins R, Chan KJ. Carboxyhemoglobin half-life in carbon monoxide-poisoned patients treated with 100% oxygen at atmospheric pressure. Chest 2000;117:801–8.
[33] Lindenmann J, Matzi V, Kaufmann P, Krisper P, Maier A, Porubsky C, et al. Hyperbaric oxygenation in the treatment of life-threatening isobutyl nitrite-induced methemoglobinemia — a case report. Inhal Toxicol 2006;18:1047–9.
[34] Sinkovic A, Smolle-Juettner FM, Krunic B, Marinsekz M. Severe carbon monoxide poisoning treated by hyperbaric oxygen therapy — a case report. Inhal Toxicol 2006;18:211–4.
[35] Stoller KP. Hyperbaric oxygen and carbon monoxide poisoning: a critical review. Neurol Res 2007;29:146–55.
[36] Buckley NA, Isbister GK, Stokes B, Juurlink DN. Hyperbaric oxygen for carbon monoxide poisoning: a systematic review and critical analysis of the evidence. Toxicol Rev 2005;24(2):75–92.
[37] Bessereau J, Tabah A, Genotelle N, Français A, Coulange M, Annane D. Middle-ear barotrauma after hyperbaric oxygen therapy. Undersea Hyperb Med 2010;37(July–August (4)):203–8.
[38] 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(October (14)):1057–67.
[39] Annane D, Chadda K, Gajdos P, Jars-Guincestre MC, Chevret S, Raphael JC. Hyperbaric oxygen therapy for acute domestic carbon monoxide poisoning: two randomized controlled trials. Intensive Care Med 2011;37(March (3)):486–92.
[40] Buckley NA, Juurlink DN, Isbister G, Bennett MH, Lavonas EJ. Hyperbaric oxygen for carbon monoxide poisoning. Cochrane Database Syst Rev 2011;(April (4)):CD002041.