Neurological Impacts from Carbon Monoxide Poisoning

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Carbon monoxide (CO) has been well established as an acute and chronic toxicant. This substance usually arises from incomplete combustion and can occur in a variety of environmental and occupational situations [1,2]. In general, the largest number of “localized” CO poisoning events occur at the time of a disaster [3,4]. The variety of symptoms, organ systems impacted and types of events associated with this toxicant are unique [1]. Historically, toxicity from this agent has focused on the blood and respiratory system particularly related to carboxyhemoglobin (COHb). Reports in the literature commonly suggest a relationship between symptoms and COHb levels [1,5]. However, recent investigations have shown no practical relationship between clinical symptoms and COHb, which may be a result of when COHb measurements are obtained [5,6]. Some chemicals, like methylene chloride (Dichloromethane-DCM), have been shown to be “metabolized” in the liver to CO resulting in poisoning [7]. Thus, sources of CO poisoning are not restricted to events involving incomplete combustion and could be a result of skin absorption.

CO poisoning during the ten year period 1979-1988 was reported to have resulted in 56,133 deaths in the US [8]. One of the major problems with non-lethal CO events is that it mostly goes unrecognized and symptoms are often generic and considered by many to be erroneously characterized as another pathogenic disease state. Iqbal et al., [4] reported that 30% of CO poisoning cases are diagnosed correctly with 43% identified as food poisoning. This study suggests CO poisoning will not likely be identified when it results from low-level exposure, resulting in a large number of un-reported cases. What has been recently recognized are delayed effects of CO poisoning which can arise after an acute occurrence [9]. These recognized delayed events do not include CO poisoning that actually may be chronic in nature, which will most likely be unidentified or not “diagnosed” [10]. It appears that little information exists regarding chronic CO poisoning [11], with neurological effects being common in those exposed, but poorly recognized [9,10]. This lack of recognition is likely due to the variability in symptomology [12] and a lack of understanding regarding neurological impacts [10,13,14].

The mechanism of injury by CO is varied. The primary mechanism is thought to be through a hypoxia-induced event due to CO binding to hemoglobin in the blood. CO can also bind to other proteins, such as myoglobin. COHb does cause the oxygen dissociation curve to shift to the left, which is likely a major component of acute events [1]. Other mechanisms, which are more often categorized, possibly incorrectly, as delayed effects, include the release of excitatory amino acids, activation of leukocytes in the creation of free radicals resulting in lipid peroxidation, formation of peroxynitrite and oxidation (during re-oxygenation) of various proteins and nucleic acids [9]. Neurological impacts from CO poisoning may be seen in 50% of those exposed. These neurological effects may not be observed immediately and be delayed in onset (delayed neurological sequelae–DNS) [9]. Much of these biochemical (molecular) impacts are observed as inflammation on the physiological/anatomical level [10].

The physiological/molecular relationship with CO appears to be important as a co-morbidity factor associated with the actual occurrence of CO poisoning [13]. However, careful analysis of outcomes from CO poisoning, especially when examining long-term effects, is needed because some reports in the literature are erroneous, as seen in cardiac consequences [5]. Historically, CO poisoning was thought to create a risk of future cardiological issues which has been shown to be inaccurate [5]. Other physiological/molecular events, as associated with DNS, are not considered in most CO poisoning cases [10].

An unforgotten, and in some ways not well recognized, impact of CO poisoning is neurological damage [1,9,10]. Neurological
effects from CO are well known in the literature, but do not appear to be commonly evaluated when a person is reported as being exposed. Observed neurological effects can be delayed and often occur after the patient is discharged [9]. One issue with generalizing neurological reports from CO events is a result of the wide variety of “symptoms/signs” and disease events noted in the literature [10,14]. A Table provides a partial list of neurological-related symptoms/signs that have been reported in the literature in association with CO poisoning events. Depending on the publication, neurological effects can be seen in the time range (days) of 2-40 [14], 2-12 [9], 14-45 [15], and 56 or more (possibly months) [10,13], which are categorized as DNS. Risk factors for DNS include “advanced” age (greater than 72.5 years) and early time onset of symptoms since the CO event [10].

Neurological effects of CO poisoning are considered by some to be common, although mostly overlooked as a clinical consequence in initial evaluations, yet frequently result in poor patient outcome [20]. In many cases, neurological effects can result from low dose CO exposures and commonly exhibit irreversible consequences [21]. Neurological effects can be categorized as acute or chronic, with chronic events identified in the literature as DNS [22]. However, some can be in either categorization, such as in the case of hearing or vision loss [17,20,21]. The mechanisms of neurological impact and DNS from CO are not clearly known, but appear to be related to “cerebral vascular autoregulation”, accumulation of toxic-metabolites or by-products (metabolic changes and free radicals), and abnormalities in gray/white matter/globus pallidus (including pallidoreticular pathway) [22-24].

It has been suggested that CO can result in damage to substantia nigra resulting in a Parkinson-type disease state [18]. Even with hyperbaric oxygen therapy (HBO), DNS have been shown to occur [18]. Thus, metabolic disturbances from CO poisoning may not be readily correctable, notably on a molecular level (i.e., HBO), suggesting monitoring of exposed patients is necessary well after acute symptoms have subsided [18,20,23]. These findings are supported by animal studies using magnetic resonance spectroscopy where metabolic changes have been demonstrated even after acute CO poisoning [24]. Even though these are acute occurrences, such information suggests chronic CO exposure may result in neurological events which are almost completely unrecognized and when observed often are attributed to other pathological “contributors” [25,26].

For some DNS and related events, such as hearing loss, there may be a synergistic (potentiation) effect with CO and other causative factors (e.g. noise exposure, ototoxic agents) [21,27]. Most fail to recognize that this agent is a hazard for hearing loss, specifically in the occupational environment; although, documented reports of CO poisoning and loss of hearing are well established in the literature [21,28,29]. The potential mechanism of this effect is thought to be due to hypoxia of “sensitive” auditory tissue [29]. Hearing loss has also been reported when exposure to methylene chloride occurred [30]. The occurrence and reports of hearing loss from CO exposure demonstrates how wide impacts can be from this agent and the lack of recognition regarding the potential for disease causation. This poor understanding may be even more evident concerning low exposure concentrations. The number of CO poisoning cases, specifically associated with DNS, is likely much higher than reported in the literature due to a poor understanding of all possible symptoms [3,4,9,10].

Table 1 Neurological events reported in the literature from CO “exposure” (poisoning) [14-20].

<table>
<thead>
<tr>
<th>Sign/Symptoms (event)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic stroke</td>
<td>Lin et al. [14]</td>
</tr>
<tr>
<td>Dementia*</td>
<td>Nager and O’Connor [15]</td>
</tr>
<tr>
<td>Amnesia*</td>
<td>Nager and O’Connor [15]</td>
</tr>
<tr>
<td>Psychosis*</td>
<td>Nager and O’Connor [15]</td>
</tr>
<tr>
<td>Paralysis*</td>
<td>Nager and O’Connor [15]</td>
</tr>
<tr>
<td>Generalized chorea (delayed encephalopathy)</td>
<td>Sung et al. [16]</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>Mehrparvar et al. [17]</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>Chang et al. [18]</td>
</tr>
<tr>
<td>Cerebrovascular ischemia</td>
<td>Kara et al. [19]</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>Duncan and Gumpert [20]</td>
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<tr>
<td>Photophobia</td>
<td>Duncan and Gumpert [20]</td>
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References


