ORIGINAL ARTICLE

Structural Findings in the Brain MRI of Patients with Acute Carbon Monoxide Poisoning

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Abstract

Background: Carbon monoxide (CO) poisoning may lead to hypoxic/anoxic injury and eventually ischemic encephalopathy. Magnetic resonance imaging (MRI) has a well-recognized role in assessment of the severity of brain damage caused by CO poisoning. In this study, we aimed to present and analyze the structural abnormalities in the brain MRI and especially in diffusion weighted MRI (DWI) images in a series of patients with acute CO poisoning.
Methods: This cross-sectional observational study was performed on patients with moderate to severe CO poisoning admitted to Mashhad Medical Toxicology Center of Imam Reza Hospital, Mashhad, Iran, during autumn and winter 2013. After stabilization, patients underwent brain MRI. T1 weighted, T2 weighted and FLAIR images in sagittal, axial and coronal sections, and DWI in axial sections were performed for each patient.
Results: Eighteen patients (77.8% men) were enrolled in this study with median age of 29.5 years. Eleven patients (61.1%) had abnormal MRI signals and in 7 cases no abnormality or nonspecific abnormalities were detected. The most common involved region in brain MRI was white matter (38.9%) followed by globus pallidus (33.3%). Patients with signal abnormality in brain MRI had significantly longer duration of exposure to CO compared to those without signal changes (10.6 ± 6.2 h vs. 3.4 ± 2.8 h, P = 0.011). Nine patients had restricted diffusion in DWI. Patients with restricted diffusion in DWI had also longer duration of exposure to CO compared to patients with normal DWI (12.1 ± 5.5 h vs. 3.5 ± 2.9 h, P = 0.001).
Conclusion: The white matter and globus pallidus were the most common affected regions in brain following acute CO poisoning. Signal abnormalities and restricted diffusion in MRI were correlated with duration of exposure to CO but not with the carboxyhemoglobin levels.

Keywords: Brain; Carbon Monoxide; Magnetic Resonance Imaging; Poisoning

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INTRODUCTION

Carbon monoxide (CO) is a common cause of accidental poisoning in low and middle income countries (1-3). CO poisoning is also a potential threat to public health during environmental disasters (4). CO is a non-irritant, colorless and odorless gas produced by incomplete combustion of carbonated substances (3,4). CO poisoning mostly occurs due to inadequate ventilation when non-standard heating equipment is used (4,5). CO enters blood circulation and forms carboxyhemoglobin (COHb). High affinity of hemoglobin with CO in COHb leads to hypoxic/anoxic injury and eventually ischemic encephalopathy (5). Furthermore, it has also been claimed that delayed encephalopathy due to CO poisoning results from its effects on mitochondrial oxidative phosphorylation (5).

Bilateral abnormalities in the globus pallidus and pars reticulata of the substantia nigra are reportedly common sequels of CO poisoning in brain that may occur immediately (6,7). Two possible reasons have been suggested for the selective vulnerability of these areas to CO poisoning: (a) these areas have the highest iron content and the CO binds directly to the heme iron, (b) poor anastomotic blood supply of these areas that can be easily affected by the hypoxic-hypotension process (8,9). These sequels appear as low attenuations in computed tomography (CT) scan of the brain (10), and low signal intensity in T1 weighted images of brain magnetic resonance imaging (MRI). On the contrary, high signal intensity is seen in T2 weighted images and fluid attenuation inversion recovery (FLAIR) modality. Patchy peripheral enhancement may also be seen in contrast mediated images (11). Nevertheless, some studies suggest that white matter involvement and brain edema following CO poisoning are more common than involvement of globus pallidus (9,10). Cytotoxic edema manifests with water diffusion restriction in diffusion weighted MRI (DWI) (9).

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The caudate nucleus, putamen, thalamus, periventricular white matter, subcortical white matter, cerebral cortex, hippocampus and rarely cerebellum can also be involved in CO poisoning (8,9,12).

MRI has a well-recognized role in assessment of the severity of brain damage caused by CO poisoning. DWI is an MRI modality which is highly sensitive in detecting small and early cerebral ischemic changes. In this study, we aimed to present and analyze the structural abnormalities in brain MRI and especially in DWI images in a series of patients with acute CO poisoning.

METHODS

This cross-sectional observational study was performed on patients with CO poisoning admitted to Mashhad Medical Toxicology Center (MTC) of Imam Reza Hospital, Mashhad, Iran, during autumn and winter 2013. In MTC, which is a specialized ward for treatment of poisoned patients, 25 to 35 cases of CO poisoning are admitted annually (1).

On admission, COHb level was measured by a UV/VIS-Spectrophotometer 550 SE (Perkin Elmer Co., MA, USA). The level of toxicity was evaluated according to the clinical manifestations. Patients with moderate to severe toxicity were included in this study. Moderate CO poisoning denotes patients with confusion, syncope, chest pain, dyspnea, weakness, tachycardia, tachypnea or rhabdomyolysis while severe CO poisoning implies patients with palpitations dysrhythmia, hypotension, myocardial ischemia, cardiac arrest, respiratory arrest, non-cardiogenic pulmonary edema, seizures or coma (13). Reduced consciousness was considered as Glasgow coma scale equal or less than 14. Patients who refused to give consent, had previous structural abnormalities of brain, were contraindicated to undergo MRI and had history of substance abuse were excluded.

After stabilization, patients underwent brain MRI (Siemens 1.5T Symphony, Siemens, Germany). T1 weighted (TR: 400-500, TE: 8, Slice thickness: 5mm), T2 weighted (TR: 3300-3500, TE: 94-118) and FLAIR images (TR: 3300, TE: 15) in sagittal, axial and coronal sections and DWI in axial sections were performed for each patient. DWI was performed in b value 1: 0, b value 2: 500, and b value 3: 1000 with noise level: 40, band width: 952Hz/px, echo spacing: 1.13 ms, TR: 3300-3500 and TE: 94-118. All scans were interpreted by an experienced neuroradiologist. Signal changes in different brain regions including subcortical and periventricular areas, centrum semiovale, cortical areas, hippocampus, basal ganglia, white matter and the cerebellum were assessed. Any area of increased signal intensity in the T2 and FLAIR sequences was considered as abnormal. Moreover, in DWI sequences any area of high signal intensity in b = 500 and b = 1000 which shows signal loss in apparent diffusion coefficient maps were considered as abnormal.

The study was approved by the ethics committee of the Mashhad University of Medical Sciences (MUMS). Informed consent was taken from all patients or their relatives (if they were below age of consent or were unconscious). Patients were waived from the MRI costs.

Demographic features, cause and length of exposure to CO, length of reduced or loss of consciousness, clinical manifestations and MRI findings were recorded into pre-designed checklists. Length of exposure to CO was measured by taking history from patients after regaining consciousness and their relatives as well. The length of reduced consciousness was also obtained by history taking and measured from the time the patient felt confused or their relatives found them unconscious to the time-point that the patient regained consciousness either at home or in the hospital. Collected data were analyzed using SPSS version 11.5 (SPSS Inc., Chicago, IL). Student's t test was used to compare the means of normally distributed variables in 2 categories, and for non-normal variables Mann-Whitney U test was used. P values of less than 0.05 were considered to be statistically significant.

RESULTS

Eighteen patients with moderate to severe acute carbon monoxide poisoning were enrolled in this study, which of them 14 patients (77.8%) were men. Median age of patients was 29.5 (range: 0.4-64) years. Eleven patients were poisoned due to inadequate ventilation and faulty heaters and 7 patients due to indoor fire or incomplete combustion. Mean (± SD) period of exposure was 7.8 ± 6.1 hours and mean COHb level was 11.8 ± 4.9% (range: 10-25%).

None of the patients needed cardiopulmonary resuscitation. The most common clinical manifestation of patients was decreased level of consciousness in 16 patients (88.9%) for which the median length of reduced consciousness was 3 (range: 0-72) hours. Other common clinical findings were headache, confusion and drowsiness (Table 1).

Patients underwent MRI from 12 to 80 hours post-admission (mean (± SD) = 36.1 ± 22.2 h). Eleven patients (61.1%) had abnormal MRI signals and in 7 cases no abnormality or nonspecific abnormalities were detected (two patients had nonspecific abnormalities in the white matter). The most common involved region in brain MRI was white matter (38.9%) followed by globus pallidus (33.3%) (Table 2). In figure 1, bilateral involvement of globus pallidus with signal changes in T2 weighted and FLAIR sequences is shown. There was no significant association between

Table 1. Clinical manifestations of patients (no. = 18)

Clinical manifestations	No. (%)
Reduced consciousness	16 (88.9)
Headache	12 (66.7)
Confusion	12 (66.7)
Drowsiness	12 (66.7)
Chest pain	6 (33.3)
Tachycardia	6 (33.3)
Nausea/vomiting	5 (27.8)
Dyspnea	5 (27.7)
Seizure	1 (5.6)

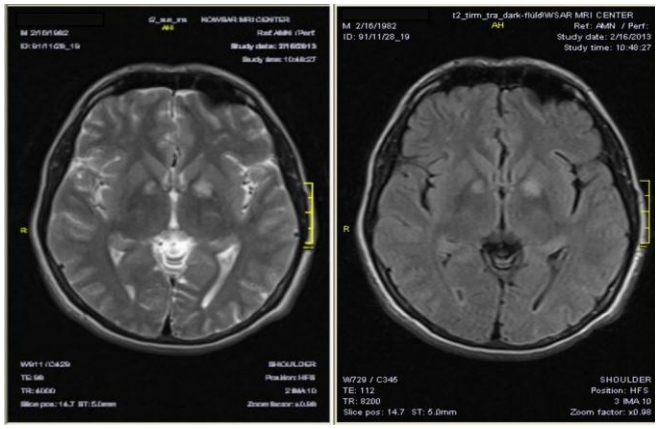

Figure 1. T2 weighted and FLAIR sequences of MRI of a 35-year-old man with carbon monoxide poisoning which show bilateral symmetrical signal changes in globus pallidus

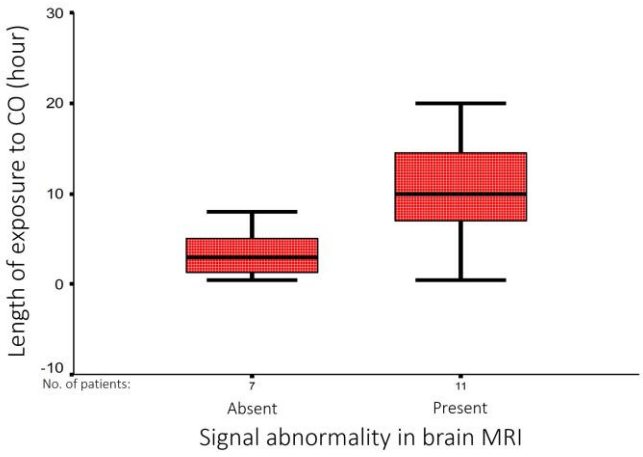

Figure 2. Difference of length of exposure to carbon monoxide (CO) between patients with signal abnormality in brain MRI and patients with normal MRI.

Table 2. Distribution of involved regions in brain MRI (no. = 18)

Involved regions	NO. (%)
White matter	7 (38.9)
Centrum semiovale	4 (22.2)
Subcortical area (global hypoxia)	2 (11.1)
Periventricular area	1 (5.6)
Globus pallidus	6 (33.3)
Cortical area	1 (5.6)
Cerebellum	1 (5.6)

signal abnormalities and age, sex, COHb level, elapsed time between admission and MRI, clinical manifestations and length of reduced consciousness. Patients with signal abnormality in brain MRI had significantly longer duration of exposure to CO compared to those without signal changes (10.6 ± 6.2 h vs. 3.4 ± 2.8 h, P = 0.011) (Figure 2).

In DWI images, nine patients who had abnormal MRI findings (9 of 11, 81.8%) showed restricted diffusion in involved areas, representing acute ischemia caused by acute CO poisoning. In figure 3, involvement of the centrum semiovale along with restricted diffusion is shown. Figure 4 depicts bilateral symmetrical subcortical involvement with restricted diffusion indicating global hypoxia.

There was no statistically significant association between DWI findings and levels of COHb or duration of reduced consciousness; although the p value was close to being significant for the latter (P = 0.074). As shown in figure 5, patients with restricted diffusion in DWI had longer duration of exposure to CO compared to patients with normal findings in DWI (12.1 ± 5.5 h vs. 3.5 ± 2.9 h, P = 0.001).

DISCUSSION

To our knowledge, this was the first study on the structural brain damages of CO poisoning which was done on Iranian patients. In this study, we found that white matter and globus pallidus were the most common involved regions in brain following CO poisoning. In a case presentation by Sener, symmetrical hyper-intense white matter changes in DWI, reflecting the cytotoxic edema, of a 9-year-old girl, 12 hours after CO poisoning, was reported (14). On the follow-up MRI, 16 days post-exposure, prominent basal ganglia lesions with no further white matter changes were found (14). Kinoshita et al. reported a case with restricted diffusion in the globus pallidus and substantia nigra in MRI in an early phase of CO poisoning (9). O'donnell et al. in a study on 19 CO poisoned patients showed that the most common affected site in brain was globus pallidus followed by periventricular and centrum semiovale regions of the white matter, cerebral cortex and hippocampus (6). They also reported involvement of cerebellum in two patients who were severely exposed to CO and died. They concluded that the extent of involved areas in early brain imaging might correlate with clinical outcome of the patient (6). In another report, in an unconscious 32-year-old woman with COHb level of 23%, bilateral hypodense lesions in the globus pallidus and upper bilateral white matter lesions in both hemispheres in computed tomography (CT) scan, and attenuated signal in globus pallidus and white matter in T2 weighted and FLAIR sequences, along with restricted diffusion in DWI were found (15). Similarly, Stephen et al. reported symmetrical signal changes in white matter of both cerebellar hemispheres, but with a normal CT scan in a 78-year-old woman (16). They emphasized that MRI is more sensitive than CT scan in acute CO poisoning (16).

Some studies have claimed that DWI is more sensitive for structural abnormalities caused by CO poisoning when compared with other MRI modalities (9,14). In this respect, in a study by Teksam et al. representing MRI findings in two patients, subtle changes in parietal subcortical white matter was found on FLAIR sequences, while DWI was

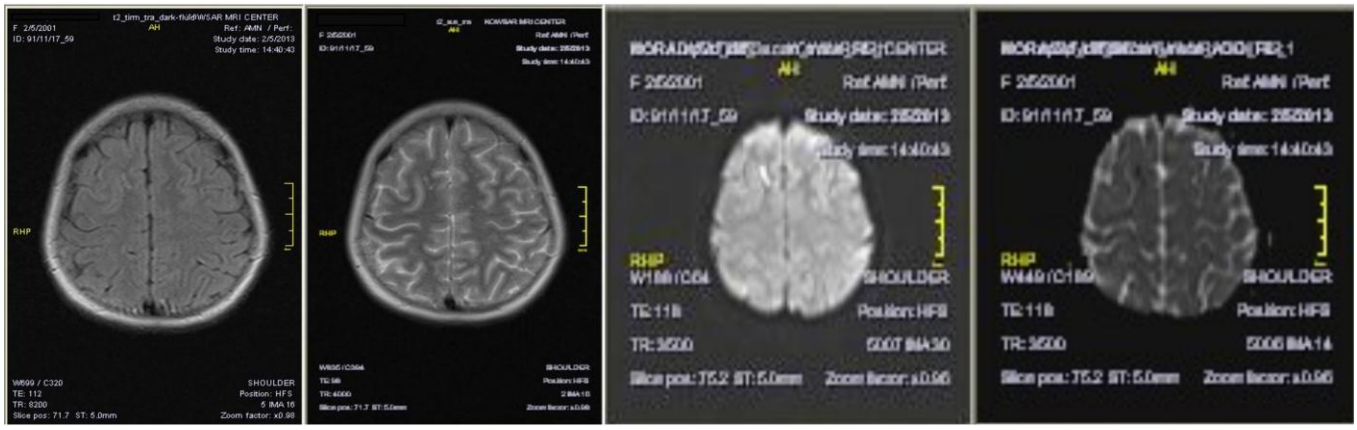

Figure 3. Left to right: axial FLAIR, T2 weighted, b = 1000 and ADC map images of a 12-year-old girl with carbon monoxide poisoning which show signal changes in the right sided centrum semiovale with restricted diffusion

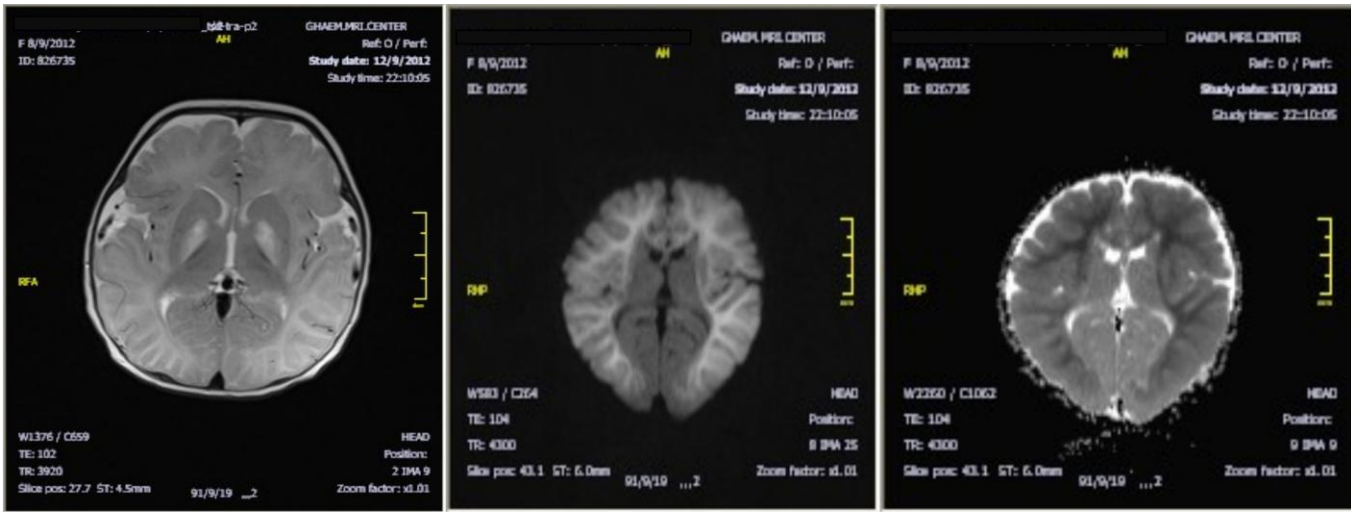

Figure 4. T2 weighted and DWI sequences of a 5-month-old boy with carbon monoxide poisoning which show symmetrical signal changes in the subcortical white matter of both hemispheres (global hypoxia)

able to demonstrate prominent subcortical and white matter changes and abnormal signal in the right frontal area in the same patient (17).

The most common affected site in brain due to CO toxicity in several reports is the globus pallidus. Other basal ganglia may occasionally be affected (11). Chang et al. found that in delayed encephalopathy due to CO poisoning, bilateral symmetric high signal intensities in centrum semiovale and periventricular white matter with decreased water diffusion are present. These two areas are the most common white matter lesions (18). It has been proved that white matter demyelination is responsible for late neuropsychiatric complications of CO poisoning (18,19). In addition, it has been claimed that lesions of globus pallidus does not clinically correlate with patient's clinical findings; however, diffuse white matter involvement can be a good index of clinical status and outcome (20).

Parkinson et al. in a prospective study on 73 patients found that the severity of CO poisoning is not associated with white matter lesions although lesions in the centrum semiovale are associated with later cognitive impairments (21). They also concluded that although COHb levels are associated with loss of consciousness, they do not correlate with white matter hyperintensities and cognitive sequels (21). Similarly, we found no significant relationship between structural abnormalities in brain and COHb level. In the present study, we found that duration of exposure to CO is correlated to development of structural abnormalities in brain. Likewise, Pavese et al. in a prospective study on 30 patients showed that the clinical status and lesions in brain correlate with the duration of altered consciousness and duration of exposure to CO, but not with the levels of COHb (22).

Hypoxia and hypotension are the two main underlying

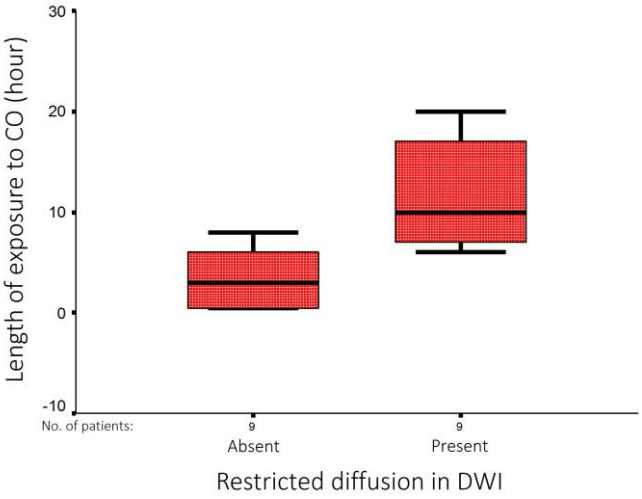

Figure 5. Difference of length of exposure to carbon monoxide (CO) between patients with restricted diffusion in DWI and patients with normal DWI.

causes of brain damages due to CO toxicity (5,8). Nevertheless, CO can directly affect cellular respiratory function by inhibition of mitochondrial metabolism. It can also provoke immunological reactions resulting in progressive demyelination in the white matter (5). The most sensitive parts of brain to hypoxia include cerebral cortex, the white matter, the basal nuclei, and Purkinje cells of the cerebellum (8). Regions with relatively poor vascularization such as the globus pallidus may be more vulnerable to hypoxic events especially during periods of hypotension (8). These facts support the greater involvement of globus pallidus and the white matter in the present study. In addition, it can be concluded that prolongation of hypoxic events is able to more compromise the viability of brain structures, the fact that was also established in our study. However, hippo-campus and reticular nucleus of thalamus are other known hypoxia-sensitive structures in the brain (23), which were not affected in our study. This may indicate that the mechanism of brain injuries in CO poisoning is slightly different from other causes of hypoxic events.

LIMITATIONS

The relatively small sample size can be considered as the main limitation of this study. Moreover, the length of exposure to CO and length of reduced consciousness were estimated by taking history from the patients or their relatives, which in some cases might be inaccurate.

CONCLUSION

The white matter and globus pallidus were the most common affected regions in brain following acute CO poisoning. Signal abnormalities and restricted diffusion in MRI were correlated with duration of exposure to CO but not with the COHb levels.

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Conflict of interest: None

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