Utilizing Cerebral Perfusion Scan and Diffusion-tensor MR Imaging to Evaluate the Effect of Hyperbaric Oxygen Therapy in Carbon Monoxide-induced Delayed Neuropsychiatric Sequelae—A Case Report and Literature Review

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Abstract-

Purpose: Detection of regional cerebral blood flow (rCBF) and/or brain magnetic resonance imaging (MRI) has been used to investigate functional defect of brain caused by carbon monoxide (CO) poisoning. In this report, we attempted to demonstrate the correlation of changes in brain single-photon emission computed tomography (SPECT) and diffusion-tensor MR image (DTI) with functional improvement of severe delayed neuropsychiatric sequelae (DNS) after CO intoxication during the treatment of hyperbaric oxygen therapy (HBOT).

Case Report: The patient had normal activities of daily life after he recovered from acute CO poisoning. One month later, he presented symptoms of declined cognitive functioning, aphasia, apraxia, dysphagia, muscle rigidity, urine and fecal incontinence. After one course of HBOT, these symptoms improved significantly and the patient could regain most of his previous functioning. The patient’s improvement was evidenced by increased rCBF in Brodmann areas 7, 8, 11 and 40, as well as higher mean fractional anisotropy (FA) value of DTI.

Conclusion: Although the efficacy of HBOT in DNS patients is still needed to be evaluated in large clinical study, these data suggest that HBOT may be the choice to improve DNS efficiently and shorten the duration of suffering with favorable outcome.

Key Words: Carbon monoxide poisoning; Hyperbaric oxygen therapy (HBOT); Delayed neuropsychiatric sequelae (DNS); Regional cerebral blood flow (rCBF); Single-photon emission computed tomography (SPECT); Diffusion-tensor MR image (DTI).

Acta Neurol Taiwan 2015;24:57-62

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Received December 4, 2014. Revised February 2, 2015. Accepted March 3, 2015.

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INTRODUCTION

Carbon monoxide (CO) is an odorless and colorless gas. The affinity of hemoglobin for CO is over 200 times of its affinity for oxygen. CO can displace oxygen from hemoglobin easily\(^{(1)}\). CO has the toxic effect of tissue hypoxia and produces various systemic and neurological complications\(^{(2)}\). The principal treatment for acute carbon monoxide poisoning is oxygen treatment. Hyperbaric oxygen therapy (HBOT) is often recommended for patients with acute carbon monoxide poisoning, especially when they have lost consciousness or have severe poisoning\(^{(3)}\). Some people who survived the insult of acute CO intoxication might develop neuropsychiatric sequelae after a lucid interval from days to weeks, usually within one month\(^{(2)}\). Delayed neuropsychiatric sequelae (DNS) are estimated to occur in 10 to 30 percent of victims, but the reported incidence varies widely. Various symptoms of DNS mainly involve cognitive change, parkinsonism, urinary and fecal incontinence, dementia, and psychosis\(^{(4)}\).

Although the neuropathological findings of DNS are characterized by necrosis of the bilateral globi pallidi and diffused white matter myelinopathy, it is reasonable to evaluate rCBF in patients with DNS who have higher cortical dysfunction based on the abnormal findings of rCBF in acute CO poisoning\(^{(5,6)}\). Furthermore, there is no current effective treatment for DNS. Here we presented a case of severe DNS treated by HBOT with favorable outcome. The results of Tc-99m ethyl cysteinate dimmer (Tc-99m ECD) of brain single photon emission computed tomography (SPECT) also demonstrated the correlation between clinical situation and imaging findings, especially in bilateral orbitofrontal area, supramarginal gyrus, somatosensory associated cortex and frontal eye fields\(^{(7)}\).

CASE REPORT

The 30-year-old male had attempted suicide by burning charcoal and was found unconscious in the morning. He was taken to the emergency room of a local hospital where the level of carboxyhemoglobin was 38.5%. The patient was treated with 100% normobaric oxygen therapy. Due to unavailable HBO facility, he was transferred to the medical center in the afternoon.

At presentation to the emergency room, his carboxyhemoglobin level was dropped to 3.7% after a period of 100% normobaric oxygen therapy. Other laboratory tests revealed CK, 4323 U/L; CK-MB, 46 U/L; Troponin-I, 1.24 ng/mL. ECG showed normal sinus rhythm. He was admitted under the impression of acute CO intoxication and rhabdomyolysis. HBOT (2.5 ATA for 120 min) was arranged immediately. Magnetic resonance imaging (MRI) of brain showed hyperintense change of the bilateral globus pallidi. After 10 sessions of HBOT, he was discharged with mild depressive symptom.

However, his condition deteriorated quickly 1 month later with symptoms of declined cognitive functioning, aphasia, apraxia, dysphagia, muscle rigidity, urine and fecal incontinence. He could not talk, walk, eat, response to any stimulation and even displayed decorticate-like posture with bed-ridden. Therefore, he was admitted to neurology ward again under the impression of delayed neuropsychiatric sequelae of CO intoxication. Brain MRI showed diffuse hyperintensity of the bilateral hemispheric white matters consistent with changes of delayed

![Figure 1. Brain MR image obtained with FLAIR sequence before HBOT (a) and six weeks after HBOT (b) shows resolution of diffuse white matter change. The brain diffusion tensor MRI obtained before (c) and after (d) hyperbaric oxygen therapy. (b) The values of fractional anisotropy of the six regions of interest on the bilateral centrum semiovale are higher than their correspondents in (c).]
leukoencephalopathy as a result of prior CO injury (Fig. 1a). The bilateral globus pallidi had central necrosis with cavity changes. Meanwhile, the fractional anisotropy (FA) values of diffusion tensor imaging (DTI) were also measured by manually placing six uniform ovoid regions of interest on the bilateral centrum semiovale (Fig. 1c). The average FA value was 0.287. The EEG reported general encephalopathy with slow waves. Mini-Mental State Examination (MMSE) was unable to take because of his demented status and aphasia. The initial brain SPECT showed decreased Tc-99 ECD uptake in the bilateral orbitofrontal areas, somatosensory associated cortex, frontal eye fields and supramarginal gyrus. (Fig. 2a).

In addition to supportive treatment, HBOT (2.5 ATA for 120 min) was scheduled once a day, 5 days a week, immediately after admission. After 20 sessions of HBOT, Tc-99m ECD cerebral perfusion SPECT with SPM2 analysis demonstrated markedly decreased uptake in Brodmann area 11, 40, 7 and 8 before HBOT (a), after HBOT (b) by glass brain view. 3D rendering view(c) displayed the correlated abnormal areas of regional hypoperfusion before HBOT (red areas), after HBOT (green areas). There was much improvement with only few areas of hypoperfusion within the previous hypoperfusion areas (yellow areas) as compared with all the abnormal regions.

Figure 2. Tc-99m ECD cerebral perfusion SPECT with SPM2 analysis demonstrated markedly decreased uptake in Brodmann area 11, 40, 7 and 8 before HBOT (a), after HBOT (b) by glass brain view. 3D rendering view(c) displayed the correlated abnormal areas of regional hypoperfusion before HBOT (red areas), after HBOT (green areas). There was much improvement with only few areas of hypoperfusion within the previous hypoperfusion areas (yellow areas) as compared with all the abnormal regions.
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The patient was discharged after total 40 sessions of HBOT. At the time of discharge, he could walk without assistance, obey command and communicate with other people. Urine and fecal incontinence was also improved. The result of MMSE performed 22 days after discharge was 26/30.

Brain MRI and DTI were undertaken again at our out-patient department. Although the result of conventional MRI remained the same as previous report (Fig. 1b), the mean FA value of DTI with the same size and location on the bilateral centrum semiovale was 0.332 (Fig. 1d), which was higher than the value before HBOT.

DISCUSSION

Coma is an indication for HBOT in acute CO poisoning. In this case, the patient was unconscious when he was found with high level of carboxyhemoglobin. Although his condition was stabilized after 10 sessions of HBOT, pallidal injury had been observed on brain MRI. The globus pallidus was the most frequently injured area during the first week after acute CO poisoning because of their high oxygen consumption. Emergent HBOT within 24 hours appeared to reduce the risk of cognitive sequelae after acute CO poisoning. However, the efficacy of hyperbaric oxygen for the prevention of neurological sequelae is still uncertain. In this case, HBOT didn’t prevent the patient from developing DNS.

On the patient’s second admission, he exhibited typical symptoms of DNS. DNS, characterized by the symptoms and signs, had been described in early 1940’. However, recent studies indicated DNS might be correlated with pathological changes in the brain subsequently caused by CO poisoning. The brain MRI of our patient revealed that not only globus pallidi which had been injured in the acute stage but diffused cerebral white matter were involved. White matter myelinopathy could be associated with decreased mental processing speed, decline in executive functioning, balance and gait abnormalities, which are characters of DNS. Most white matter lesions consist of reversible myelin injuries rather than irreversible necrosis and axonal destruction.

DTI can evaluate the magnitude and the directionality of water diffusion in tissue. Normal myelinated white matter tracts have higher degree of FA because they are highly directional. If the myelination or axonal integrity is disrupted, the FA can be expected to decrease. DTI had been applied in the study of neuropsychiatric symptoms caused by CO intoxication. Our patient’s FA of white matter was higher after HBOT, which also suggested that the process of myelin damage could be reversed by HBOT.

Wu et al. had reported the findings of the Tc-99m ECD SPECT correlated well with the clinical outcome and could be used for evaluating rCBF of the basal ganglia and cerebral cortex in acute CO poisoning. Cerebral vascular changes may be the possible cause of hypoperfusion in patients with CO poisoning. Therefore, the Tc-99m ECD brain SPECT was arranged to detect abnormal regional cerebral blood flow on his second admission with DNS. The Tc-99m ECD brain SPECT of the patient, before HBOT, showed significantly decreased Tc-99m ECD uptake in the bilateral orbitofrontal area (Brodmann area 7), supramarginal gyrus (Brodmann area 8), somatosensory associated cortex (Brodmann area 11) and frontal eye fields (Brodmann area 40). These areas involve the different functions including planning, reasoning, decision making, reading both in regards to meaning and phonology, visuomotor coordination such as in reaching to grasp an object, as well as planning complex movements. The rCBF changes could correlate well with his symptoms of DNS. We were also interested in the topographical changes of rCBF between pre- and post-treatment. After HBOT, although all the symptoms of DNS got improved,
he had normal functions of perception, execution and eyeball movement, but had relatively slow response to motor tasks. His functional improvement was compatible with increased Tc-99m ECD uptake in Brodmann areas 11, 40 and normal rCBF in Brodmann areas 7, 8 of the following brain SPECT.

From literature review, only few studies reported therapeutic effect of HBOT on DNS. Myers et al. reported 10 patients with specific neurological sequelae included headaches, irritability, personality changes, confusion, and loss of memory. These recurring symptoms resolved rapidly with hyperbaric oxygen therapy (10). Lo et al. and Chang et al. reported 6 patients and 9 patients received HBOT to treat DNS with good response (13, 16). Compared with those cases reported in the previous studies, the patient’s condition in this study was much worse. He had symptoms of urine and fecal incontinence, akinetic mutism and declined cognitive functioning. The imaging findings of brain SPECT and MRI also showed that the patient suffered from extensive brain damage, including cerebral cortex, sub-cortical nuclei, globus pallidus and cerebral white matter. In such severe condition, the patient could regain most of his previous functions after HBOT in two months. Later on, he rode the motorcycle back to our OPD at the end of the 3-month follow-up period.

The pathological changes of DNS occur mainly during the reperfusion phase when lipid peroxidation occurs (10). In considering acute CO poisoning as a hypoxia/reoxygenation disease, in which free radicals were produced in an inflammatory-like cascade, HBO was found to prevent brain lipid peroxidation by inhibiting β2 integrin-mediated neutrophil adhesion to brain microvasculature (17). Thom et al. also demonstrated in the rat model that HBO inhibits the CO-induced structural alterations in myelin basic protein as well as the associated inflammatory response and learning abnormalities (18). HBO might be an effective therapeutic modality to reduce the free radical-driven injury. Certainly, searching for CO-induced DNS animal models will be the future direction to explore the clear mechanism of HBOT in DNS.

In this case, the patient recovered from severe DNS in only 2 months, which was shorter than average duration of one year needed to recover from DNS (4). Considering the severity of this patient, HBOT could reduce the duration of suffering and help the patient to regain his previous functions. We are the first to utilize brain SPECT and DTI evaluating the clinical benefit of HBOT in CO-induced DNS. Definitely, the proper design of clinical trial is essential for formal application of HBOT to the patients with CO-induced DNS.

ACKNOWLEDGEMENTS

This study was supported in part by the The-Tzer Group for Human Medical Research Foundation and Cardinal Tien Hospital (CTH-100-1-2A01, CTH-101-1-2B15). The authors thank Ms. M-S Hsu, S-F Dei and Mr. J-S Lan for technical support and help in operating the hyperbaric oxygen chamber.

REFERENCES

8. Ernst A, Zibrak JD. Carbon monoxide poisoning. N

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