Seizure during hyperbaric oxygen therapy for carbon monoxide toxicity: a case series and five-year experience.

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SEIZURE DURING HYPERBARIC OXYGEN THERAPY FOR CARBON MONOXIDE TOXICITY: A CASE SERIES AND FIVE-YEAR EXPERIENCE

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□ **Abstract—Background: Hyperbaric oxygen (HBO) therapy is recommended to reduce the delayed neurologic sequelae resulting from carbon monoxide (CO) toxicity. Although HBO is generally well tolerated, there exists a risk of seizure in all patients that may be increased in patients with predisposing factors including: fever, hypothermia, prior seizure, or brain injury. Case Report: We present two cases of patients without known risk factors who experienced seizures associated with HBO therapy during treatment for CO toxicity. Conclusion: This facility's 5-year experience and a review of the germane literature are also presented to elucidate the risk factors and incidence of seizures in patients treated with HBO for CO toxicity.**

□ **Keywords—hyperbaric oxygen; carbon monoxide; poisoning; seizure; structure fire; oxygen toxicity**

INTRODUCTION

Carbon monoxide (CO) toxicity is the most common form of poisoning, resulting in approximately 40,000 emergency department (ED) visits annually. In 2002, there were 15,904 reports to the American Association of Poison Control Centers Toxic Exposures Surveillance System, with approximately 2600 receiving hyperbaric oxygen therapy (HBO). Reported death rates from severe CO poisoning range from 31 to 3800 annually, with one-third to four-fifths described as accidental (1–4).

HBO therapy is currently recommended to potentially ameliorate delayed neurologic sequelae resulting from severe CO toxicity. Although HBO is generally well tolerated, seizures do rarely occur. The risk of seizure is traditionally thought to be increased in patients with predisposing factors, including fever, hypothermia, anxiety, prior seizure, and traumatic brain injury. Additionally, higher HBO treatment pressures and longer therapy duration are known to increase the risk of seizures due to central nervous system (CNS) oxygen toxicity, but seizure may also result from CNS injury from CO alone. Both higher pressures and longer durations are required for effective treatment of emergent conditions such as CO poisoning, decompression sickness, and air embolism. We report two cases of HBO-associated seizures that occurred in patients without known predisposing seizure risk factors, who were being treated for CO poisoning.

CASE REPORTS

Case 1

A 54-year-old woman was found unresponsive in her apartment during a structure fire. The patient was started

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Table 1. Historical Review of Seizure Incidence during Hyperbaric Oxygen Therapy as Reported in the Literature

Study	Number of Treatments	Number of Seizures (%)	Indications*	Comments
Hart, 1987 (5)	Not reported	44 (0.008%)	All	Includes emergent indications (i.e., CO toxicity)
Davis, 1989 (6)	52,758	5 (0.009%)	All	2 centers
Sloan et al., 1990 (7)	297	14 (4.7%)	CO	CO only, mean COHgb 38%, 88% > 25%
Welslau, 1996 (8)	107,264	16 (0.15%)	All	19 centers, rates: 0.011%–0.055% (+CO)
Hampson et al., 1996 (4)	900	16 (1.8%)	CO	CO only, 2 centers, rates 0.3%–3.02%
Plafki, 2000 (9)	11,376	4 (0.035%)	Non	2 centers
Weaver, 2002 (10)	152	0 (0%)	CO	CO only
Hampson and Atik 2003 (11)	20,328	6 (0.030%)	Non	Emergent indications excluded; O_2: hood
Yildiz et al., 2004 (12)	80,679	2 (0.002%)	All	648 treatments for CO without seizures; O_2: mask
Yildiz et al., 2004 (13)	36,500	3 (0.008%)	All	Includes emergent indications, no CO seizures
Hampson et al., 2006 (2)	30	0 (0%)	CO	CO only
Sanders et al., 2008 (present study)	5972	2 (0.033%)	All	All indications, all seizures with CO (1.7% of CO)

* Indications included in study: All = all indications; CO = CO toxicity only; Non = non-emergent cases, excludes CO, AGE, DCS.
CO = carbon monoxide; COHgb = carboxyhemoglobin.

on high-flow oxygen by emergency medical services (EMS) personnel and transported to an outside hospital. Initial ED serum carboxyhemoglobin (COHgb) level was 17.3%, and ethanol was 164 mg/dL. Additional laboratory tests included normal complete blood count, electrolytes, glucose, and troponin I. Given the history of altered mental status and elevated COHgb, she was transferred to this facility for HBO therapy. Before HBO therapy, the patient regained consciousness and was asymptomatic, with normal vital signs and physical examination, in our ED. The patient was prescribed three treatments of 100% oxygen at 2.8 atmospheres for 90 min each. Within 45 min of the start of HBO therapy, the patient experienced a 2-min-long grand mal seizure. HBO therapy was discontinued and, after supportive measures, the patient recovered uneventfully and was discharged within 24 h.

Case 2

A 65-year-old man, while using an outdoor cooking grill to heat his camper, called EMS after he was unable to arouse his granddaughter. Local EMS recognized this as a probable CO poisoning. The child was brought to another facility and released. The grandfather, however, was brought to our facility breathing 100% oxygen via non-rebreather mask. ED serum COHgb level was 32.9% and the patient had unremarkable vital signs, physical examination, electrocardiogram, glucose, and troponin I. He was prescribed three treatments of 100% oxygen at 2.8 atmospheres for 90 min each. After 50 min of the initial HBO treatment, he suffered a 3-min-long grand mal seizure. HBO was discontinued and he recovered uneventfully and was discharged within 24 h without incident.

HISTORICAL REVIEW

The primary HBO nurse at our facility maintains a running log of treatment numbers, indications, and adverse reactions. A summary of this information was obtained via electronic mail, and re-formatted into Tables 1 and 2. All HBO treatments at this facility between January 1, 2003 and December 31, 2007 were included. A literature review of seizures during HBO treatment was also performed utilizing the keywords: HBO, seizure, CO, carbon monoxide, and hyperbaric. These data were then included in Table 1, and specific details put into Table 2 to examine other factors that may contribute to the seizure risk.

The two reported patients were the only ones treated with HBO therapy at this facility during the last 5 years who experienced a seizure. Out of 5972 total treatments, there were 171 for CO exposure. Thus, the seizure incidence was 0.033% for all treatment indications and 1.2% for patients treated for CO exposure. Our review of the medical literature revealed a 0.008% rate of seizure in those treated with HBO for non-CO conditions (106,158 treatments, 8 seizures) and a 1.45% rate of seizures in CO-poisoned patients treated with HBO (2200 treatments, 32 seizures; Table 1).

DISCUSSION

Central nervous system oxygen toxicity causing grand mal seizures was first described in 1878 by Paul Bert in France. Through his diving physiology research, he noted that oxygen toxicity produces self-limited, isolated seizures, rather than a recurrent "epileptiform" disorder. Although oxygen toxicity may contribute to seizures in HBO-treated CO-poisoned patients, the CO poisoning must also play a role, because the seizure risk increases substantially in CO-poisoned patients compared to non-poisoned patients exposed to the same or greater oxygen

Table 2. Details of Seizing Patients in Selected Studies Listed in Table 1

Study	Treatment Details	Case #	Age (Years)	Indication for Therapy	Time of Seizure: Treatment, Period, Minute	Comments
Sanders et al., 2008*	M1, 2.8 ATA, Continuous O_2 90 min	1	54	CO	Treatment #1, 45 min	Discontinued therapy
		2	65	CO	Treatment #1, 50 min	Discontinued therapy
Yildiz et al., 2004 (12,13)	M2, 2.4 ATA O_2 25 min 3× periods, AB, Mask	1	22	NHW	Treatment #31,	Anti-convulsants, fatal status-epilepticus
		2	14	CI	Treatment #14,	Respiratory arrest preceded seizure 20 add treatments w/o reoccurrence
	M2, 2.8 ATA O_2 25 min 3× periods, AB, Mask	3	48	DCS	Treatment #1,	—
Hampson and Atik, 2003 (11)	M2, 2.36 ATA O_2, AB, Hood	1	85	NHW	Treatment #1, 3rd O_2 period	Completed 18 more treatments w/o reoccurrence
		2	67	DRI	Treatment #25, 2nd O_2 period	Completed 10 more treatments w/o reoccurrence
		3	62	DRI	Treatment #4, 3rd O_2 period	40 treatments 6 months earlier
		4	69	STSG	Treatment #1, 1st O_2 period	Discontinued therapy
		5	54	DRI	Treatment #21, 2nd O_2 period	—
		6	77	DRI	Treatment #16, 3rd O_2 period	Completed 29 more treatments, w/o reoccurrence
Hampson et al., 1996 (4)	M2, 2.36 or 2.45 ATA	1		CO	Treatment #1, 45 min	Continued O_2, 90 min total
	M2, 2.8 ATA, AB	1-9		All CO	All Txt #1, 15, 16, 18, 22, 23,44, 46, 58, 69 min	7 patients had therapy aborted
						9 patients continued after 15-min airbreak
						1 had recurrent seizure, aborted therapy
	M2, 3.0/2.0 ATA, AB	10-15		All CO	All Txt #1, 18, 23, 32, 35, 40,46 min	6 patients received diazepam

* Unpublished data, from a personal communication.
CO = carbon monoxide; NHW = non-healing wound; DRI = delayed radiation injury; STSG = compromised split thickness skin graft; CI = crush injury; DCS = decompression sickness; M1 = monoplace chamber; M2 = multiplace chamber; AB = airbreaks.

pressures (Table 1). CO exposure by itself is a known risk factor for seizures, with seizure rates of 1–6% reported in severe exposures (4,7).

A review of the literature regarding HBO-associated seizures was performed (Table 1). Although a comparison of the data is difficult because these studies utilize different HBO protocols, equipment, and diving criteria, seizure rates in those treated specifically for CO toxicity ranged from 0–4.7%. Although the highest rates seen were in the studies specifically looking at the CO-poisoned subjects, even within this group there is a substantial range cited. We did not find a relationship between seizure risk and chamber size, oxygen delivery systems, or treatment protocols (Table 2).

Potential reasons for the different rates of seizure within this group may be the differences in study design or whether the study included emergent indications for HBO treatment. Some authors excluded diving-related indications, whereas others included all emergent indications (11–13). Also, the severity of the CO exposure may have differed between studies. When the treatment protocols and equipment used in the two studies in which no seizures occurred are examined, there is no particular feature unique to either group (10,11). Both multiplace and monoplace facilities as well as mask and hood delivery devices are represented. Although some of these studies utilized air breaks, the seizures listed in Table 1 occurred regardless of their use. In fact, many patients did not reach the first air break before seizing.

The pathophysiology of HBO-associated seizures for CO toxicity has not been fully elucidated (3,14–16). Sloan et al. provided the most comprehensive review of 297 CO-poisoned patients before, during, and after HBO treatment (7). These patients experienced a high mortality rate (6%), and complications such as seizure did occur with a high frequency. Although 17 deaths occurred during or after HBO treatment, 16 patients sustained their first cardiac arrest *before* treatment with HBO. Other than those who seized, no patient had a decreasing level of consciousness after arrival in the ED. Eighteen grand mal and five focal seizures occurred in these patients. Interestingly, of those patients experienc-

ing grand mal seizures, 50% experienced them before HBO treatment (7). With two recurrences during therapy, only 7 of the 18 grand mal seizures had a first occurrence during therapy, and none after therapy; thus, the role of HBO as a cause of seizure in these cases must be questioned.

Part of our review included a comparison of the timing of seizure occurrence relative to HBO therapy onset. All of the CO-associated seizures (18/18, 100%) occurred during the first treatment, whereas only 2 of 8 seizures (25%) occurred during the first HBO treatment for all non-CO-related seizures (Table 2). This may indicate that there is indeed no interaction between HBO and the CNS insult of CO toxicity and that these seizures would have occurred regardless of treatment modality. If this is true, then the lack of repetitive-dive seizure is most likely the result of successful treatment.

Although there is apparent overlap of the pathophysiology of both oxygen toxic seizures and CO-induced seizures, the time of occurrence was different in the cases reviewed (Table 2) (3,14–16). Unfortunately, there is no clinically reliable way to distinguish the two types of seizures. In cases of severe CO poisoning (i.e., those at greatest risk for CO-induced seizure), HBO is indicated, and these patients will be exposed to a level of oxygen that puts them at risk for oxygen-induced seizure. Our data do not allow us to determine whether HBO increases the risk of seizure in CO-poisoned patients or whether the risk of seizures is simply the result of the CO poisoning.

Although the seizures in our cases did interrupt patient therapy, they were self-limited, and the patients experienced no adverse effects. This is consistent with the majority of patients who experience HBO-induced seizures, with only 2 of the 110 patients suffering additional seizures (Table 2) (7,12). Given the low overall incidence of seizures, and the ease with which these seizures have been treated (i.e., removal from HBO), the situation does not warrant prophylaxis, just awareness.

CONCLUSION

HBO therapy is commonly and safely used in the treatment of CO toxicity to help prevent delayed neurologic sequelae. There is an increasing body of evidence to support a low, but substantially increased risk of seizure in the CO-poisoned patient before and during the first HBO session. Although these seizures are often self-limited, the treating physician must be aware of and prepared for the risk of seizure, even in the absence of obvious risk factors. This risk, however, should not dissuade the emergency physician from ordering this important therapy when needed.

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