Yonsei University Wonju College of Medicine
Department of Emergency Medicine

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Seizure during Hyperbaric Oxygen Therapy: Experience at a Single Academic Hospital in Korea

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Disclosure information

- I have no relevant financial relationships with commercial interests to disclose.
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1. Introduction

- If performed at centers with adequate accreditation, hyperbaric oxygen therapy (HBO_2) is safe and well tolerated.

- However, it is associated with several side effects.
  - Because of its therapeutic mechanism, oxygen toxicity may occur, which can affect several organs of the body as well as the central nervous system (CNS).
  - CNS oxygen toxicity is characterized by various neurologic symptoms ranging from twitching of the face to seizures.

- Although generalized tonic-clonic seizures are rare, with an occurrence rate of 0.002% (1 in 40,340 treatments) – 0.279% (1 in 358 treatments) of all indications, this side effect is the most severe, unless appropriately managed.

- However, in countries such as Korea where hyperbaric medicine is still in the developmental stage, clinicians at most HBO_2 centers currently do not have the relevant experience and knowledge in this regard and are not well prepared for handling seizures that may occur during HBO_2.

- Therefore, this study aimed to identify the frequency of seizures occurring as a side effect of HBO_2 at an HBO_2 center with certified clinicians; this center was located in a tertiary academic hospital in Korea.
  - Furthermore, all seizure cases were reviewed.

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2. Materials and methods

Study design and setting

- This was a prospectively collected registry-based observational study (October 2016 - December 2019) in a tertiary academic hospital located at a suburban area in Wonju, Republic of Korea.

- The study protocol was approved by the institutional review board of Wonju Severance Christian Hospital (approval number: CR319163).

- The need for informed consent was waived since the study was retrospective and observational in nature.

Operation of the HBO_2 center

- As a division of the Department of Emergency Medicine, the HBO_2 center is managed by five board-certified emergency physicians.
  - Four emergency physicians had completed the educational program "Introduction to Hyperbaric Medicine and Wound Care," approved by the UHMS.
  - One emergency physician had completed the educational course approved by the Diving Medical Advisory Committee (DMAC) and the European Diving Technology Committee (EDTC).
  - One hyperbaric physician, one nurse, and one emergency medical technician were usually administered per day.
  - Gas-related technicians managed the facilities at the HBO_2 center.
- Our center currently
  - One multiplace chamber (each capable of holding 10 persons) + three monoplace chambers (IBEX Medical Systems, Seoul, Korea).

- Because of the limited human resources, the IA was not always able to accompany the patient into the multiplace chamber during each HBO_2 session until May 2020.
  - However, if patients were being treated for the first time or were critically ill, an IA always accompanied them into the chamber.
  - In addition, the IA entered the chamber during treatment if the patient complained of abnormal symptoms.

- When patients were treated in a monoplace chamber,
  - The hyperbaric physician, nurse, and emergency medical technician were stationed adjacent to the monoplace chamber, and cautiously observed the patient.

- For cases of acute CO poisoning and central retinal artery occlusion,
  - Initial compression was set to 2.8 atmospheres absolute (ATA) for 45 min with one air-break (5 minutes), followed by 2 ATA for 60 min.

- For diabetic foot ulcers, delayed radiation injuries, crushing injuries, acute thermal burns, compromised grafts and flaps, refractory osteomyelitis, idiopathic sudden sensory neural hearing loss, Buerger's disease, and additional treatments for CO poisoning,
  - 2 ATA was administered for 90 min.

- The United States (US) Navy Treatment Table 5
  - Decompression sickness (DCS) type I

- The US Navy Treatment Table 6
  - DCS type II and AGE

Data collection and definition

- The demographic and medical data of all patients who underwent HBO_2 at the center during the study period,
  - Age, sex, source of first referral, presence of IA during HBO_2 therapy, total number of HBO_2 sessions, and indication for HBO_2.
  - For patients with seizures,
    - Age, sex, indication for HBO_2 treatment, comorbidities, mental status of the patient at the initial visit, and HBO_2 protocol.
    - Seizure-related variables included
      - Time from the start of HBO_2 to seizure onset, type of seizure, and duration and management of seizure.

Statistical analysis

- Continuous variables were presented as median and minimum–maximum values, and categorical variables were presented as frequency and percentage values. Categorical data were compared using Fisher's exact test. All statistical analyses were carried out using the Statistical Package for the Social Sciences version 25 software (IBM Corp., Armonk, New York, United States of America (USA)).

3. Results

Table 1: General characteristics of all patients who received HBO_2 therapy during the study period

	Total (N=1,308)
Age	50 (1-91)
Male (%)	795 (60.8%)
First referral	
Emergency department	750 (57.3%)
Consultation upon admission	410 (31.3%)
Outpatient department	148 (11.4%)
Total number of HBO_2 sessions	3 (1-114)
Indications	
CO poisoning	547 (41.8%)
Decompression sickness	187 (14.3%)
Non-healing wound	163 (12.5%)
ISSHL	139 (10.6%)
Compromised grafts and flaps	80 (6.1%)
Delayed radiation injury	57 (4.4%)
Diabetic foot ulcer	52 (4.0%)
Central retinal artery occlusion	36 (2.8%)
Acute thermal burn	11 (0.8%)
Buerger's disease	10 (0.7%)
Peripheral arterial disease	8 (0.6%)
AGE	7 (0.5%)
Gas gangrene	6 (0.5%)
Refractory osteomyelitis	5 (0.4%)

Data are presented as median (minimum–maximum) and frequency (percentage).

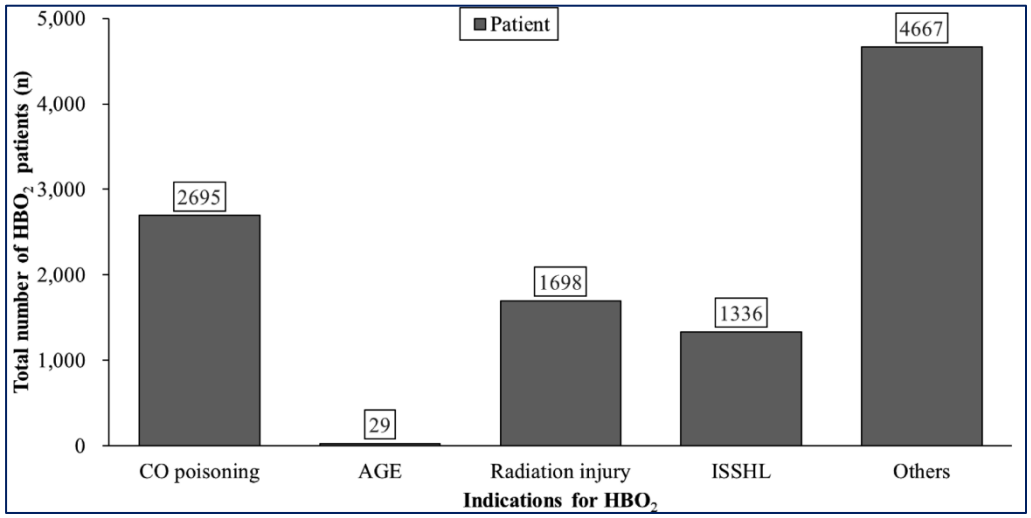
10,425회 치료

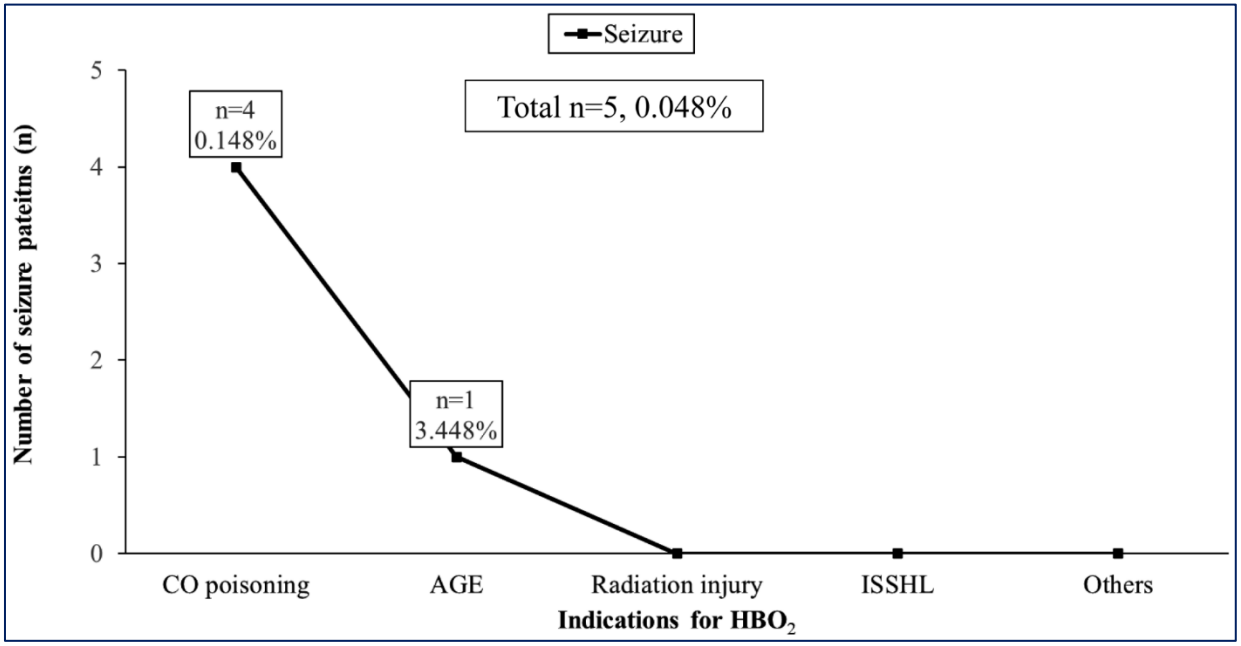
Table 2: Data of the five patients who presented with seizures during HBO_2 treatment

	Total (n=5)
Age (years)	52 (37-64)
Male	4 (80%)
Seizure onset from the start of HBO_2 session (min)	45 (38-234)
Mental deterioration at ED presentation	5 (100%)
Glasgow Coma Scale	6.0 (4.0 – 8.0)
Indication for HBO_2	
CO poisoning	4 (80%)
AGE	1 (20%)

Patient #	Age/sex	Indication	Treatment protocols	Comorbidities	Presence of IA	Seizure session #	Seizure onset from the start of HBO/ Pressure at seizure	Patient's status during seizure episode
1	50/M	CO	M2, 2.8/2.0 ATA for 135 min	No	Yes	4[t]	45 min/2.8 ATA	Ambulatory (mask use)
2	52/M	CO	M2, 2.8/2.0 ATA for 135 min	No	Yes	5	39 min/2.8 ATA	Ambulatory (mask use)
3	64/F	AGE	M2, 2.8/2.0 ATA for 285 min	No	Yes	1	234 min/2.8 ATA	ETI under sedation*
4	59/M	CO	M2, 2.8/2.0 ATA for 135 min	DM, HTN	Yes	1	63 min/2.8 ATA	ETI under sedation*
5	37/M	CO	M2, 2.0 ATA for 110 min	No	Yes	3	38 min/2.0 ATA	ETI under sedation*

Data are presented as median (minimum–maximum) and frequency (percentage).


Patient
Total number of HBO2 patients (n)
5,000
4,000
3,000
2,000
1,000
0
2695
29
1698
1336
4667
CO poisoning
AGE
Radiation injury
ISSHL
Others
Indications for HBO2


Seizure
Total n=5, 0.048%
Number of seizure pateitns (n)
5
4
3
2
1
0
n=4
0.148%
n=1
3.448%
CO poisoning
AGE
Radiation injury
ISSHL
Others
Indications for HBO2

4. Discussion

- To the best of our knowledge, this study is the first to report the frequency of HBO_2-related seizures in Korea.

- We conducted a literature review of previous publications on the occurrence of seizures during HBO_2 between 1989 and 2019.
  - The frequency rate of seizures during HBO_2 ranged from 0.002% (1 in 40,340 treatments) to 4.7% (1 in 21 treatments).

- The frequency of HBO_2-related seizures varied among studies because each HBO_2 center may not have similar settings,
  - Including the equipment used and the HBO_2 protocol followed.
  - Compared with previous studies, our study revealed a similar frequency rate in terms of all indications and CO poisoning, and a slightly higher rate in AGE.

Table 3: Frequency of seizures during HBO_2 therapy as reported in previous peer-reviewed publications

Study	Number of Treatments	Number of seizures (%, frequency)	Indications	Number of participating centers
Costa et al. 2019[13]	188,335	43 (0.023%, 1:4380)	All	Single center
Sherlock et al. 2018[21]	96,670	38 (0.039%, 1:2544)	All	Eight centers
Jokinen-Gordon et al. 2017[18]	1,529,859	267 (0.017%, 1:5730)	None	More than 400 centers
Hadanny et al. 2016[14]	64,614	7 (0.011%, 1:9231)	All	Single center
Heyboer et al. 2014[17]	23,328	11 (0.047%, 1:2121)	All	Single center
Seidel et al. 2013[20]	4,357	7 (0.16%, 1:622)	All	Three centers
Banham 2011[12]	41,273	25 (0.061%, 1:1651)	All	Single center
Sanders et al. 2009[19]	5,972	2 (0.033%, 1:2986)	All	Single center
Weaver 2006[24]	90	1 (1.111%, 1:90)	DCS, AGE	Single center
Wilkinson et al. 2005[10]	6,084	17 (0.279%, 1:358)	All	Single center
Smerz 2004[23]	2,166	14 (0.646%, 1:155)	DCS	Single center
Yildiz et al. 2004[26]	36,500	3 (0.008%, 1:12167)	All	Single center
Yildiz et al. 2004[9]	80,679	2 (0.002%, 1:40340)	All	Two centers
Hampson and Atik 2003[15]	20,328	6 (0.03%, 1:3388)	None	Single center
Plafki et al. 2000[8]	11,376	4 (0.035%, 1:2844)	None	Two centers
Hampson et al. 1996[16]	900	16 (1.778%, 1:56)	CO	Two centers
Welslau and Almeling 1996[25]	107,264	16 (0.015%, 1:6704)	All	Nineteen centers via survey
Sloan et al. 1989[22]	297	14 (4.7%, 1:21)	CO	Single center
Kim et al. 2020 (Present)	10,425	5 (0.048%, 1:2085)	All	Single center

*Indications: All, all indications; Non, non-emergent indications; HBO_2, hyperbaric oxygen; DCS, decompression sickness; AGE, arterial gas embolism;

- The frequency of HBO_2-related seizures was the highest in CO poisoning. This phenomenon may be attributed to the fact that CO poisoning causes neuronal toxicity and associated metabolic changes, resulting in a lower threshold for seizures.

- As regards AGE, only one patient had an HBO_2-related despite being intubated and sedated with lorazepam.
  - A prolonged HBO_2 protocol based on the US Navy Table 6.
  - However, seizures in AGE patients may not necessarily occur due to HBO_2, because AGE by itself increases the risk of seizures.

- For some indications such as CO poisoning and AGE, emergency HBO_2 performed in a timely manner has been recommended.
  - Under such circumstances, unexpected adverse events related to HBO_2 are likely to occur, and appropriate steps for their management should be taken by the IA present inside the chamber.
  - If the HBO_2 facility does not have a multiplace chamber or an IA, the medical staff should consider transferring critically ill patients to another HBO_2 facility that is suitable for the treatment of critically ill patients.
  - Regarding monoplace chamber,
    - A back-up system that converts oxygen in the monoplace chamber into air in an emergency situation should be present in the monoplace chamber.

- This study had several limitations.
  - First, the study design was retrospective. Moreover, some data were missing, and not all relevant assessment parameters could be included.
  - Second, the sample size of the included patients was small because the study was limited to a single center. However, we evaluated all treated patients to reduce possible bias.
  - Third, there was no specific information about HBO_2-treated patients prior to October 2016.

5. Conclusions

- Compared with previous studies, our study revealed a similar frequency rate in terms of all indications and CO poisoning, and a slightly higher rate in AGE.

- CO poisoning and AGE are usually treated using higher pressures, which is a potential reason for the higher seizure frequency in these cases.

- Therefore, if clinicians plan to operate a hyperbaric center in a country like Korea, where acute CO poisoning is frequently observed, they should be prepared for the possible occurrence of seizures during HBO_2.

Thank you
for Your Attention !!!