2020 4회 대한고압의학회

2020.11.20

Cerebral white matter lesions on diffusion-weighted images and delayed neurological sequelae after carbon monoxide poisoning: A prospective observational study

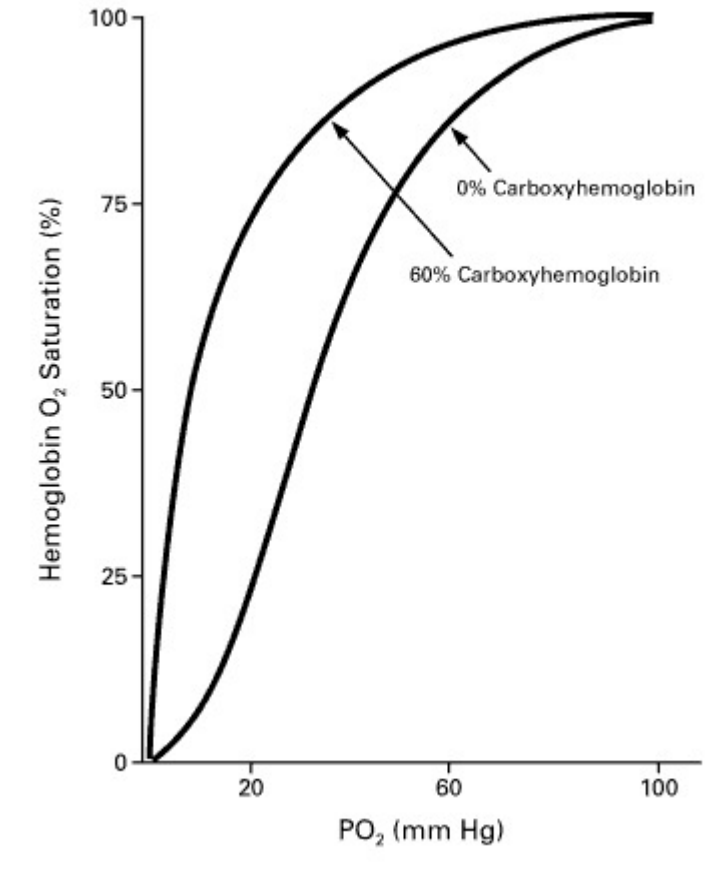
Sang Un Nah[1], Sungwoo Choi[1], Han Bit Kim[1],Jungbin Lee[2], Sun-uk Lee[3], Young Hwan Lee[1], Sangsoo Han[1],Gi Woon Kim[1], Hoon Lim[1]

1 Department of Emergency Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, Korea
2 Department of Radiology, Soonchunhyang University Bucheon Hospital, Bucheon, Korea
3 Department of Neurology, Korea University Medical Center, Seoul 02841, Korea

Introduction

CO has 250 times greater affinity for hemoglobin than oxygen

this process can damage the brain and heart etc.
(which are vulnerable to ischemia)



Introduction

- Delayed neurological sequelae (DNS)

  → caused by CO poisoning

  → occur 2d ~ 6wks later

- Symptoms of DNS

1. insomnia
2. headache
3. dizziness
4. Parkinson-like syndrome
5. movement disorder
6. conscious disorder
7. mood disorder
8. memory disorder

Introduction

The pathophysiological results of CO poisoning in the brain

1. apoptosis
2. abnormal inflammatory responses
3. ischemia–reperfusion injury

→cause ischemic brain tissue damage and demyelination

Introduction

MRI diffusion-weighted images (DWIs)

→one of the best ways to present acute ischemic brain lesions

Previous studies

→ white matter hyperintensities and hippocampal atrophy were usually found

→ the putamen, thalamus, and caudate nucleus in T2-weighted and FLAIR images

→ globus pallidus

Various brain lesions can be found in CO poisoning

Investigation of relationship between

acute brain lesion on MRI (ABLM) & occurrence of DNS

Method (Participant Selection)

●Inclusion criteria

→ August 2016 to July 2019.

→ who had adequate history or physical examination after CO Poisoning

→ measured carboxyhemoglobin (COHb) values
> 5% in non-smokers and >10% in smokers

→ consented to hyperbaric oxygen (HBO) therapy.

● Exclusion criteria

→ < 18 years of age

→ refused HBO therapy

→ refused MRI

→ discharged against medical advice

→ lost to follow-up

→ neurological deficits persisting at discharge from the ED

→ were transferred from another hospital 24 h after exposure

Method (HBO Therapy Protocol)

- HBO therapy was delivered

→ initial COHb was ≥25% (COHb ≥15% in pregnant women),
→ history of loss of consciousness
→ presence of neurological abnormalities
→ apparent cardiac injury
(abnormal electrocardiogram or elevation of troponin I)

- HBO therapy was applied in a monochamber

→ conducted in three sessions at intervals of 6–12 h within a day.

Method (Clinical and Laboratory Assessments)

- Collected data

→ Demographic data
→ Medical comorbidities
→ Vital signs
→ Glasgow coma scale (GCS)
→ CO exposure time
→ Intentionality of poisoning
→ Symptoms
→ Laboratory results

- DNS

Patients visited the emergency department 1 month later

Telephone interviews
2 weeks and 3 months after discharge

Method (Imaging analysis)

Scheduled for MRI scans within 2 days of visiting the ED

Categorized MRI

1. Patterns
(globus pallidus, diffuse lesions and focal lesions for asymmetric focal lesions)

2. Location
(cortex, white matter, deep nucleus, brainstem, and cerebellum)

3. Region
(frontal, parietal, temporal, occipital, insular, hippocampus, corpus callosum, splenium, internal capsule, centrum semiovale, periventricular white matter, globus pallidus, putamen, caudate, thalamus, and cerebellum)

Method (Statistical analysis)

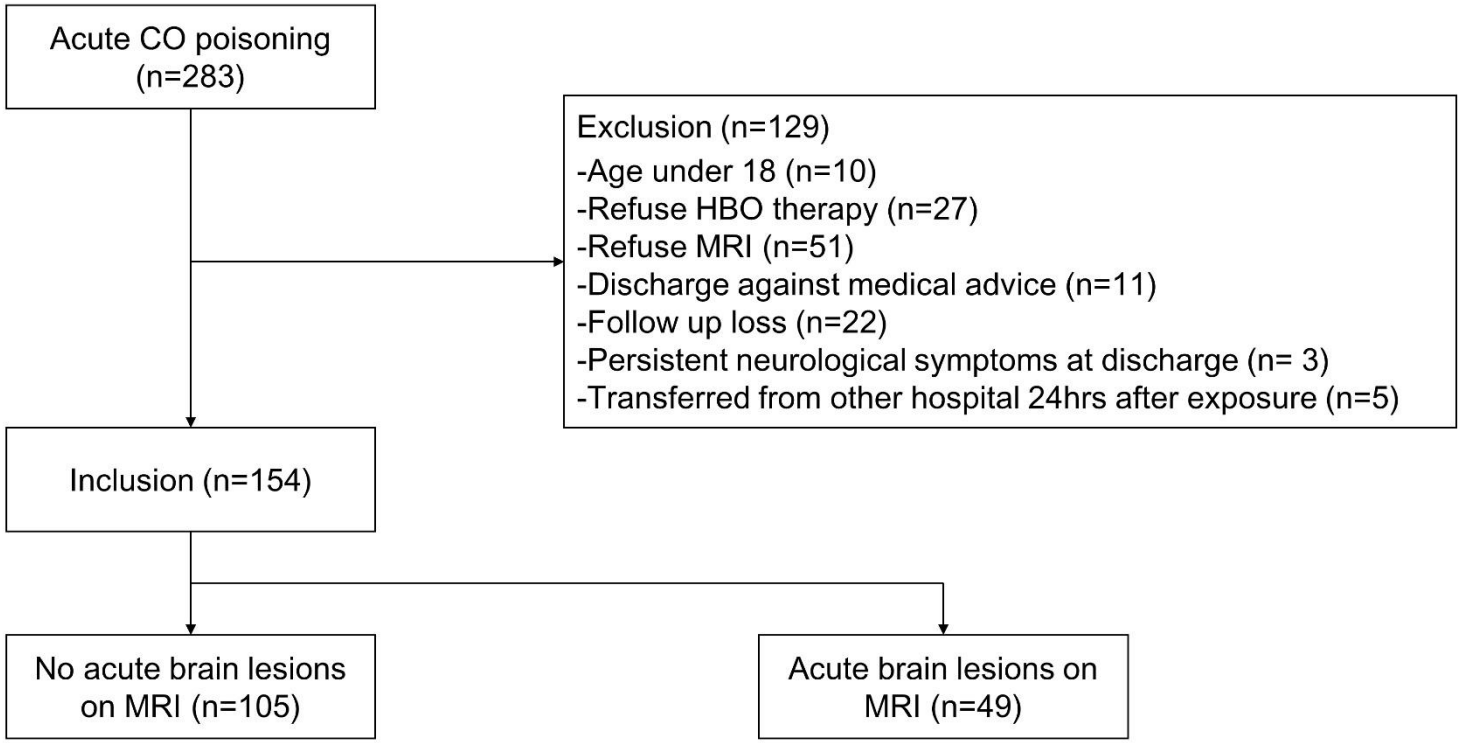
Categorical variables
→Fisher's exact test and the chi-squared test

Continuous variables
→ Mann–Whitney test

Logistic regression modeling
→ Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were also calculated, and two-tailed p-values < 0.05 were considered statistically significant

To avoid multicollinearity problems
→ Model 1 ~ 4 (multivariable analysis)

Results


Acute CO poisoning
(n=283)
Exclusion (n=129)
-Age under 18 (n=10)
-Refuse HBO therapy (n=27)
-Refuse MRI (n=51)
-Discharge against medical advice (n=11)
-Follow up loss (n=22)
-Persistent neurological symptoms at discharge (n= 3)
-Transferred from other hospital 24hrs after exposure (n=5)
Inclusion (n=154)
No acute brain lesions on MRI (n=105)
Acute brain lesions on MRI (n=49)

Results

Table 1. Comparison of baseline characteristics between the non-DNS and DNS groups.

	Non-DNS (n = 124)	DNS (n = 30)	p-Value
Age, year	40 (29–50.3)	44 (35–55)	0.171
Male, n (%)	82 (66.1)	19 (63.3)	0.940
BMI (kg/m^2)	23.3 (21.0–25.5)	22.8 (21.0–25.4)	0.769
Comorbidities (%)			
Hypertension	9 (7.3)	3 (10.0)	0.902
Diabetes	2 (1.6)	0 (0)	>0.999
Vital signs			
Systolic BP, mmHg	130 (113.5–140)	130 (111.3–143.8)	0.744
Diastolic BP, mmHg	80 (70–90)	80 (70–90)	0.847
Heart rate, BPM	92.5 (78–105)	92 (78.5–100)	0.734
Respiratory rate, BPM	20 (18.8–20)	20 (18–20)	0.215
Body temperature, °C	36.8 (36.5–37.2)	36.9 (36.5–37.5)	0.516
O_2 saturation, %	98 (97–98)	97.5 (95–98)	0.155
Initial GCS	15 (12–15)	12.5 (6.3–15)	0.004
Exposure time, min	150 (60–315)	360 (90–480)	0.072
Time from exposure to MRI, h	32 (21–48)	43 (24–78)	0.175
Current smoking (%)	60 (50)	15 (51.7)	>0.999
Cause of exposure (%)			0.124
Accidental	41 (33.1)	5 (16.7)	
Intentional	83 (66.9)	25 (83.3)	
Symptoms (%)			
Headache	16 (12.9)	2 (6.7)	0.524
Loss of consciousness	31 (25)	9 (30)	0.743
Chest pain	2 (1.61)	0 (0)	>0.999
Dizziness	16 (12.9)	1 (3.3)	0.239
Dyspnea	5 (4.0)	0 (0)	0.586
Laboratory findings			
COHb, %	6.0 (2.8–11.8)	9.3 (4.2–16.7)	0.139
CRP, mg/dL	0.11 (0.1–0.4)	0.23 (0.1–0.8)	0.077
Lactate, mg/dL	2.1 (1.5–3.9)	2.9 (1.8–4.1)	0.690
Troponin I, ng/mL	0.1 (0.1–0.3)	0.1 (0.1–0.3)	0.942
Ethanol, mg/dL	1.5 (1.0–7.1)	1.2 (0.7–4.2)	0.222
Outcomes			
Onset of DNS, day	-	27 (18–30)	-
ABLM (%)	31 (25)	18 (60)	0.001

Results

Table 2. Lesion distribution according to the development of DNS in patients with ABLM.

	No. (%)		
	Non-DNS	DNS	*p*-Value
Pattern			
Globus pallidus lesion	16 (16.2)	11 (36.7)	0.031
Diffuse lesion	13 (13.1)	10 (33.3)	0.024
Focal lesion	5 (5.1)	7 (23.3)	0.007
Region			
Frontal	5 (5.1)	1 (3.3)	>0.999
Parietal	5 (5.1)	3 (10)	0.387
Temporal	2 (2.0)	4 (13.3)	0.026
Occipital	2 (2.0)	4 (13.3)	0.026
Insular	0 (0)	0 (0)	
Hippocampus	3 (3.0)	1 (3.3)	>0.99
Corpus callosum	3 (3.0)	2 (6.7)	0.330
Splenium	2 (2.0)	1 (3.3)	0.551
Internal capsule	1 (1.0)	0 (0)	>0.999
Centrum semiovale	3 (3.0)	1 (3.3)	>0.999
Periventricular white matter	1 (1.0)	2 (6.7)	0.135
Globus pallidus	16 (16.2)	9 (30)	0.157
Putamen	1 (1.0)	3 (10)	0.039
Caudate	1 (1.0)	0 (0)	>0.999
Thalamus	2 (2.0)	1 (3.3)	0.551
Midbrain	0 (0)	0 (0)	
Pons	0 (0)	0 (0)	
Medulla	0 (0)	0 (0)	
Cerebellum	4 (4.0)	1 (3.3)	>0.999
Location			
Cortex	6 (6.1)	4 (13.3)	0.240
White matter	5 (5.1)	9 (30)	<0.001
Deep nucleus	24 (24.2)	13 (43.3)	0.073
Brainstem	0 (0)	0 (0)	
Cerebellum	4 (4.0)	1 (3.3)	>0.999

When multiple lesions appeared in one person, the numbers were aggregated in duplicate. Abbreviations: DNS, delayed neurological sequelae; ABLM, acute brain lesion on magnetic resonance imaging.

Results

Table 4. Factors associated with the development of DNS in multivariable analysis.

	Multivariable Analysis			
	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)
Initial GCS	0.864 (0.760–0.983)	0.882 (0.767–1.014)	0.859 (0.755–0.978)	0.849 (0.745–0.967)
Exposure time, min	1.002 (1.001–1.004)	1.003 (1.001–1.004)	1.003 (1.001–1.005)	1.003 (1.001–1.004)
ABLM	2.242 (0.864–5.821)			
Globus pallidus (P)		1.160 (0.364–3.695)		
Diffuse (P)		2.728 (0.948–7.850)		
Focal (P)		2.564 (0.527–12.477)		
Temporal (R)			1.229 (0.109–13.868)	
Occipital (R)			5.643 (0.440–72.543)	
Putamen (R)			2.223 (0.115–43.033)	
White matter (L)				6.741 (1.843–24.660)

P = 0.097

P = 0.004

Discussion

- In our study
  Low GCS score
  Long exposure time
  White matter lesion on MRI (OR, 6.741)

- Previous studies
  Old age, CO exposure time, cardiac arrest, initial neurological abnormalities, GCS, brain imaging abnormalities, and biochemical indicators (e.g., neuron-specific enolase, CRP, lactic acid)

- Impossible or inaccurate to gather an initial GCS or medical history
  1. Have impaired consciousness (or co-ingestion drugs)
  2. Uncooperative with the medical staff

  →To predict DNS, objective factors other than GCS or history taking were needed

Discussion

- Biochemical indicators

Troponin I

→ Increased troponin I indicates reduced blood supply to the brain

→ perhaps is too specific to myocardial injury compared with other predictors

C-reactive protein

→ controversial in previous studies

Discussion

- Brain CT
  → no correlation with the occurrence of DNS

- Electroencephalography and single-photon emission computed tomography (SPECT)
  → only useful in monitoring efficacy of treatment

Discussion

- Brain MRI

  Both acute and chronic phases

  → cerebral cortex, white matter, hippocampus, globus pallidus, and cerebellum

- Recent studies

  lesions on MRI(DWIs) can predict DNS

  → Moon et al. White matter lesion on MRI (within 7 days)

  → Jeon et al. ABLM and DNS significantly associated (within 1 day)

  → but differences in the locations or patterns of MRI lesions

  <u>no correlations with DNS</u>

Conclusion & Limitation

Predictor of DNS

1. Lower GCS score
2. Higher exposure time
3. Presence of ABLM in white matter

→ White matter lesions on MRI & DNS

Limitation

1. A single-center study
2. Did not reveal how these lesions were related to patient symptoms (e.g., gait disorder, cognitive disorder)
3. ABLMs are different over time
(hyperintense signal can be seen on DWIs up to 7 days after the injury)