ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

The Ultrasound Examination of the Optic Nerve Sheath Diameter in the Patients Presenting with Carbon Monoxide Poisoning: A pilot study

Karbonmonoksit Zehirlenmesi ile Başvuran Hastalarda Optik Sinir Kılıf Çapının Ultrasonografi ile İncelenmesi: Pilot Çalışma

Emel Altintas[1], Sertac Guler[1], Hayri Ramadan[1]

[1]*Ankara Training and Research Hospital, Department of Emergency Medicine, Ankara, Turkiye*

ABSTRACT

Aim: *In carbon monoxide poisoning, hypoxia results in neuronal damage and death of brain cells. It is considered that cerebral edema occurs consequently, with an associated increase in intracranial pressure. The present study evaluates the presence of increased intracranial pressure using the measurement of optic nerve sheath diameter by ultrasonography in patients presenting with carbon monoxide poisoning.*

Material and Method: *Twenty-eight patients diagnosed with carbon monoxide poisoning after presenting to the emergency department underwent the bilateral measurement of optic nerve sheath diameter by ultrasonography. In addition, the patient's demographic data, laboratory results, stage of the poisoning, and optic nerve sheath diameters were recorded.*

Results: *The median optic nerve sheath diameter on the right and left sides was greater than 5 mm. The optic nerve sheath diameter of the right and the left eye was significantly higher in patients with severe carbon monoxide poisoning than in those with moderate and mild poisoning.*

Conclusion: *The optic nerve sheath diameter measurement can be used to evaluate increased intracranial pressure in patients with carbon monoxide poisoning.*

Keywords: carbon *monoxide poisoning; elevated intracranial pressure; ultrasonography; optic nerve sheath diameter*

ÖZET

Amaç: *Karbon monoksit zehirlenmesinde hipoksi nöronal hasara ve beyin hücrelerinin ölümüne neden olur. Sonuç olarak, kafa içi basıncında ilişkili bir artışla birlikte beyin ödeminin meydana geldiği düşünülmektedir. Bu çalışmada karbonmonoksit zehirlenmesi ile başvuran hastalarda ultrasonografi ile optik sinir kılıf çapı ölçümü kullanılarak kafa içi basınç artışının varlığı değerlendirilmiştir.*

Materyal ve Metot: *Acil servise başvurduktan sonra karbon monoksit zehirlenmesi tanısı alan 28 hastaya ultrasonografi ile bilateral optik sinir kılıf çapı ölçümü yapıldı. Hastaların demografik verileri, laboratuvar sonuçları, zehirlenme evresi ve optik sinir kılıf çapları kaydedildi.*

Bulgular: *Sağda ve solda median optik sinir kılıf çapı 5 mm'den büyüktü. Sağ ve sol gözde optik sinir kılıf çapları şiddetli karbon monoksit zehirlenmesi olan hastalarda orta ve hafif zehirlenmesi olanlara göre anlamlı olarak daha yüksekti.*

Sonuç: *Karbonmonoksit zehirlenmesi olan hastalarda optik sinir kılıf çapı ölçümü kafa içi basınç artışının varlığını değerlendirmede kullanılabilir.*

Anahtar Kelimeler: *karbon monoksit zehirlenmesi; kafa içi basınç artışı; ultrasonografi; optik sinir kılıf çapı*

Introduction

Carbon Monoxide is an odorless and colorless gas. Carbon Monoxide poisoning results in hypoxia, cellular death, and death[1]. The symptoms are associated with the brain and heart, which are most sensitive to hypoxia. The patients may present to the emergency department with headache, weakness, chest pain, shortness of breath, seizures, and consciousness impairment[2].

The increase in intracranial pressure can be caused by various mechanisms such as venous obstruction, increased blood and brain volumes, mass effect, and

İletişim/Contact: *Emel Altıntaş, Ankara Training and Research Hospital, Department of Emergency Medicine, Ankara, Türkiye* •
Tel: *0554 598 2714* • ***E-mail:*** *emelaltintas61@gmail.com* • ***Geliş/Received:*** *17.11.2021* • ***Kabul/Accepted:*** *18.01.2023*

ORCID: *Emel Altıntaş, 0000-0003-4487-5661* • *Sertaç Güler, 0000-0002-6266-6145* • *Hayri Ramadan, 0000-0002-5018-152X*

cerebral edema. Intracranial pressure increases in many conditions, such as hydrocephalus, traumatic brain injury, intracerebral and subarachnoid hemorrhage, and ischemic stroke. The symptoms include headache, nausea, vomiting, consciousness impairment, and Cushing reflex[3].

In carbon monoxide poisoning, hypoxia has been reported to be the most critical mechanism for brain damage. In addition, animal studies have reported that increased cerebral blood flow leads to the loss of consciousness[4]. The brain areas often involved in carbon monoxide poisoning are basal ganglia (globus pallidus), hippocampus, white matter, cortex, cerebellum, corpus callosum, and hypoxia resulting in neuronal damage and death[5]. The authors consider that cerebral edema occurs consequently, with an associated increase in intracranial pressure. The increase in intracranial pressure can be measured by various interventional methods. However, in recent years, ultrasonography's optic nerve sheath diameter measurement has become a non-invasive method to determine increased intracranial pressure[6–8]. The present study aims to evaluate the presence of increased intracranial pressure using the measurement of optic nerve sheath diameter by ultrasonography in patients presenting with carbon monoxide poisoning.

Material and Method

The present study was carried out in a tertiary emergency department with an average annual visit number of 360.000. The study was conducted after ethics committee approval had been granted. Patients started after the ethics committee's approval and the study ended when the number of patients in the sample size is completed. After receiving 1-hour theoretical and applied training with a certificate on ultrasonographic measurement of optic nerve sheath diameter, pilot measurements were made on both eyes of 10 patients, including five positive patients (with increased optic nerve sheath diameter due to pathologies such as intracranial hemorrhage, ischemic cerebrovascular accident) and five negative patients. The measurements were only made by the emergency medicine specialist involved in the study. The study included the patients aged 18 years and older with a blood carbon monoxide level of higher than 10% and a time interval of no more than one hour after being diagnosed with carbon monoxide poisoning.

The stage of carbon monoxide poisoning was determined as follows[1].

1- Mild poisoning: COHb >10% without clinical signs and symptoms

2- Moderate poisoning: COHb >10% with mild signs and symptoms [headache, lethargy, fatigue]

3- Severe poisoning: COHb >20–25% with a loss of consciousness, confusion, or findings of cardiac ischemia

The measurement of optic nerve sheath diameter was made as follows. The patients were placed in a supine position with 20 degrees horizontal angle. Tegaderm medical dressing was placed on the eye to avoid contact of the eyelid with ultrasound gel. The Tegaderm dressing was covered with an ultrasound gel with an insonation depth of 5–8 cm. The ultrasound probe was placed on the temporal region of the eyelid. The angle of the probe was adjusted to visualize the entrance of the optic nerve. A two-dimensional image was used, and the diameter of the optic nerve sheath was measured electronically in 3 mm behind the globe with a perpendicular axis to the optic nerve. Fujifilm-Sonosite FC-1 brand ultrasound device and a high-frequency (10 mHz) linear probe were used in the measurement. Two measurements were made for each eye, and the average of the two measurements was recorded.

Exclusion criteria:

1. Conditions resulting in an increased optic nerve sheath diameter a-Not accompanied by increased intracranial pressure: Optic neuritis, optic nerve trauma, arachnoid cyst of the optic nerve, anterior orbital or cavernous sinus mass b-Accompanied by increased intracranial pressure: A mass or a space-occupying lesion in the central nervous system, pseudotumor cerebri, decreased cerebrospinal fluid (CSF) resorption (cerebral venous sinus thrombosis, subarachnoid hemorrhage, meningitis, inflammatory conditions), increased CSF production (tumors), ventricular system obstruction, cerebral edema, encephalitis, craniostenosis)
2. Unstable patients for ocular ultrasonography
3. The patients with eyelids ineligible for ultrasonography
4. Conditions where ultrasound operator is not available

5. Pregnant patients
6. The patients who did not give consent to participate in the study.
7. Patients who are not in the first hour of admission to the emergency department

Sample size: H1 hypothesis of the study; The optic nerve sheath diameter measurement of carbonmonoxide poisoning is >5 mm. Our hypothesis is one-sided. When this alpha error was calculated as 0.05 and the power 80% standardized effect size was calculated as 0.5, the number of samples was calculated as 25. Since there may be 10% data loss, it is planned to take a total of 28 patients.

Demographic data of patients suffering from carbon monoxide poisoning, laboratory results, exposure to carbon monoxide gas, stage of poisoning and optic nerve sheath diameters were recorded.

IBM Statistical Package for Social Sciences (SPSS) program version 22.0 (IBM, *Chicago*, USA) statistical software package was used in the statistical analysis. A Shapiro-Wilk test was used to test whether the variables were normally distributed. In order to determine whether the optic nerve sheath diameter measurement of the patients with carbon monoxide poisoning was larger than the population median, the non-parametric single-sample test, the sign test, was used. The median value of 5 mm was taken to evaluate the optic nerve sheath diameter in patients with carbon monoxide poisoning[9]. A Kruskal-Wallis test was used to compare numeric variables between more than two independent groups without normal distribution. A p-value of less than 0.05 was considered statistically significant.

Results

The study included 28 participants. A total of 33 patients were diagnosed with carbon monoxide poisoning during the study period. One patient was unstable (cardiac arrest) to undergo the measurement of optic nerve sheath diameter by ultrasonography, one patient was pregnant, and three other patients were excluded due to the unavailability of an ultrasound operator. Demographic data of the patients are presented in Table 1.

A median optic nerve sheath diameter of the right and left eyes greater than 5 mm was found to be significant (the sign test, p <0.001) (Table 2).

Table 1. *The characteristics of patients with carbon monoxide poisoning*

Age	48.07±18.75	
	Number	%
Gender		
Female, n, %	15	53.6
Duration of exposure		
<6 hours, n, %	19	67.9
6–12 hours, n, %	7	25
12–24 hours, n, %	2	7.1
Stage		
Mild, n, %	1	3.6
Moderate, n, %	16	57.3
Severe, n, %	11	39.1
Symptom		
Nausea-vomiting, n, %	13	32.5
Headache, n, %	11	27.5
Dizziness n, %	7	17.5
Syncope, n, %	5	12.5
Chest pain, n, %	2	5
Loss of consciousness, n, %	2	5
Treatment		
100% oxygen n, %	18	64.3
100% oxygen+Hyperbaric Oxygen n, %	8	28.6
100% oxygen+Hyperbaric Oxygen with Intubation n, %	2	7.1
Laboratory parameters		Median (IQR)
WBC uL	28	9.96 (8.31–12.85)
Creatinine mg/dl	28	0.82 (0.68–1.07)
Lactate mmol/L	25	2.7 (1.55–3.55)
CK-MB uq/L	28	1.74 (1.14–4.18)
Troponin uq/L	28	10.05 (4.43–14.46)
CO Hb %	28	18.5 (14.05–28.85)

Table 2. *Optic nerve sheath diameter measurements of patients with carbon monoxide poisoning*

	Median (IQR), mm	p value
Right eye optic nerve sheath diameter	5.8 (5.5–6.3)	<0.001*
Left eye optic nerve sheath diameter	6.0 (5.2–6.3)	<0.001*

*The sign test was used with a median value of 5 mm.

A statistically significant difference was found in median optic nerve sheath diameters of the left and right eye between carbon monoxide poisoning stages (Kruskal-Wallis, p=0.027, and p=0.043, respectively) (Table 3). In paired comparisons of the groups, optic nerve sheath diameters of the left and right eyes were significantly higher in patients with severe carbon monoxide poisoning than the patients with mild and moderate poisoning.

Table 3. *Optic nerve sheath diameter measurements of the right and left eye according to the stage of carbon monoxide poisoning*

	Right eye optic nerve sheath diameter, mm	p value	Left eye optic nerve sheath diameter, mm	p value
Mild n=1	4.4	0.317	5.2	0.317
Moderate n=16	5.5 (5.4–5.9)	0.003**	5.7 (5.1–6.2)	0.001**
Severe n=11	6.2 (5.8–6.5)	0.003**	6.3 (5.9–7.0)	0.003**
p value	0.027*		0.043*	

*A Kruskal-Wallis test was used.
** The sign test was used with median value of 5 mm.

Discussion

In this study, it was determined that the optic nerve sheath diameter measurement in patients with carbon monoxide poisoning was larger than the population median. It was determined that the median of optic nerve sheath diameter measurement in the patients with the severe stage was larger than those in the moderate stage. We concluded that there is an increase in optic nerve sheath diameter in carbon monoxide poisoning.

The mortality rate is higher among the patients with acute brain injury after sustaining carbon monoxide poisoning, and the development of acute brain injury is associated with blood carbon monoxide levels, but no association exists with the symptoms[5]. Late neuropsychiatric symptoms are associated with secondary brain damage occurring 2–40 days after carbon monoxide poisoning and are encountered in approximately 15–30% of successfully treated patients[10,11]. Carbon monoxide poisoning remains a significant health problem as it results in death in the short term and various neurological sequels in the long term due to brain damage.

The optic nerve sheath diameter measurement by ultrasonography has come into use as a non-invasive method in recent years to determine an increase in intracranial pressure[6–8]. It was reported emergency medicine physicians without previous ultrasound education could accurately detect pathological conditions on ocular ultrasound after gain an experience of 15–75 attempts[12]. The optic nerve sheath diameter has also been evaluated according to the types of ischemic stroke and increased values have been reported in all types of ischemic stroke, the values being higher in the patients with more extensive ischemic area[13]. The increase in intracranial pressure has always been attributed to widespread cerebral edema[14–16].

In the present study, the optic nerve sheath diameter was significantly higher when tested against a median value of 5 mm. The authors consider that an increase in intracranial pressure is associated with increased blood volume caused by anoxia and the development of cytotoxic cerebral edema due to ischemia[3].

It was reported that the extent of brain damage on computed tomography (CT) and magnetic resonance imaging (MRI) scans are associated with prognosis in the patients with carbon monoxide poisoning[17,18]. In the present study, optic nerve sheath diameters were significantly higher in the patients with severe carbon monoxide poisoning than the patients with mild and moderate poisoning. The presence of three or more lesions in the white matter on MRI scans or a lesion in the initial diffusion MRI scans has been identified as the independent predictor of delayed neuropsychiatric symptoms[19–21].

The authors suggest that an increase in intracranial pressure can be estimated and monitored by the measurement of optic nerve sheath diameter, as the detection of increased intracranial pressure is essential to determine the severity of the condition and to prevent secondary brain damage[3]. Also, the patients with intracranial lesions on initial MRI studies have a poorer prognosis. However, the use of MRI scans in all patients is not cost-effective, and not all patients (with implanted cardioverter/defibrillator, platinum implantation) are eligible to undergo MRI.

The increase in intracranial pressure estimated by optic nerve sheath diameter measurement in carbon monoxide poisoning is considered to cause symptoms. Based on the relationship between optic nerve sheath diameter and the severity of carbon monoxide poisoning, the authors of the present manuscript suggest that further studies must be conducted to evaluate whether optic nerve sheath diameter could be used as a parameter to monitor the outcomes of the treatment and whether the measurement of optic nerve sheath diameter could predict delayed neurological sequels.

Limitations

The sources of carbon monoxide gas responsible for the poisoning in the present study, the patients were not specified. No comparison was made between the optic nerve sheath diameter and CT/MRI findings.

No other measurement was made for intracranial pressure increase except ONSD measurement. The link between the increase in intracranial pressure and the measurement of ONSD has been accepted in principle. We do not have a control group to compare and no control measurement after treatment. Due to these limitations, this study is a pilot study.

Also, no comparison was made between the optic nerve sheath diameter and mortality/late neurological sequels.

Conclusion

Increased intracranial pressure can be estimated by measuring optic nerve sheath diameter in patients presenting with carbon monoxide poisoning. The optic nerve sheath diameter is greater in patients with severe poisoning.

References

1. Smollin C, Olson K. Carbon monoxide poisoning (acute). BMJ Clin Evid. 2010;2010.
2. Eichhorn L, Thudium M, Jüttner B. The Diagnosis and Treatment of Carbon Monoxide Poisoning. Dtsch Arztebl Int. 2018;115(51-52):863–870.
3. Saria MG, Kesari S. Increased Intracranial Pressure: The Use of an Individualized Ladder Approach. Seminars in oncology nursing. 2021:151133.
4. Chung-Ping Lo, Shao-Yuan Chen, Kwo-Whei Lee, Wei-Liang Chen, Cheng-Yu Chen et al. Brain injury after acute carbon monoxide poisoning: early and late complications. AJR Am J Roentgenol 189(4):W205-211.
5. Kavak N, Doğan B, Sultanoğlu H, Kavak RP, Özdemir MJKD. Clinical and Magnetic Resonance Imaging Findings of Patients with Acute Carbon Monoxide Poisoning.12(3):443-50.
6. Girisgin AS, Kalkan E, Kocak S, Cander B, Gul M, et al. The role of optic nerve ultrasonography in the diagnosis of elevated intracranial pressure. Emerg Med J. 2007;24(4):251–4.
7. Robba C, Santori G, Czosnyka M, Corradi F, Bragazzi N, et al.Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. Intensive Care Med. 2018;44(8):1284–1294.
8. Miller MT, Pasquale M, Kurek S, White J, Martin P, et al. Initial head computed tomographic scan characteristics have a linear relationship with initial intracranial pressure after trauma. J Trauma. 2004;56(5):967–72.
9. Major R, Girling S, Boyle A. Ultrasound measurement of optic nerve sheath diameter in patients with a clinical suspicion of raised intracranial pressure. Emerg Med J. 2011;28(8):679–81. doi:10.1136/emj.2009.087353.
10. Nah S, Choi S, Kim HB, Lee J, Lee SU, et al. Cerebral White Matter Lesions on Diffusion-Weighted Images and Delayed Neurological Sequelae after Carbon Monoxide Poisoning: A Prospective Observational Study. Diagnostics (Basel, Switzerland). 2020;10(9).
11. Han S-T, Bhopale VM, Thom SR. 2007. Xanthine oxidoreductase and neurological sequelae of carbon monoxide poisoning. Toxicol Lett. 170(2):111–115.
12. Blaivas M, Theodoro D, Sierzenski PR. A study of bedside ocular ultrasonography in the emergency department. Academic emergency medicine: official journal of the Society for Academic Emergency Medicine. 2002;9(8):791–9.
13. Gökcen E, Caltekin İ, Savrun A, Korkmaz H, Savrun Ş T, et al. Alterations in optic nerve sheath diameter according to cerebrovascular disease sub-groups. The American journal of emergency medicine. 2017;35(11):1607–11.
14. Ropper AH, Shafran B. Brain edema after stroke. Clinical syndrome and intracranial pressure. Arch Neurol. 1984;41:26–9.
15. Schwab S, Schwarz S, Spranger M, Keller E, Bertram et al. Moderate hypothermia in the treatment of patients with severe middle cerebral artery infarction. Stroke. 1998;29:2461–6.
16. Morley NC, Berge E, Cruz-Flores S, Whittle IR. Surgical decompression for cerebral oedema in acute ischaemic stroke. Cochrane Database Syst Rev. 2002;3: CD003435.
17. O'Donnell P, Buxton PJ, Pitkin A. The magnetic resonance imaging appearances of the brain in acute carbon monoxide poisoning. Clin Radiol. 2000; 55(4):273–280.
18. T Miura, M Mitomo, R Kawai, K Harada. CT of the brain in acute carbon monoxide intoxication: characteristic features and prognosis. Am J Neuroradiol. 1985; 6(5):739–742.
19. Jeon S-B, Sohn CH, Seo D-W, Oh BJ, Lim KS, et al.2018. Acute brain lesions on magnetic resonance imaging and delayed neurological sequelae in carbon monoxide poisoning. JAMA Neurol. 75(4):436–443.
20. Kim YS, Cha YS, Kim MS, Kim HJ, Lee YS, et al. The usefulness of diffusion-weighted magnetic resonance imaging performed in the acute phase as an early predictor of delayed neuropsychiatric sequelae in acute carbon monoxide poisoning. Human & experimental toxicology. 2018;37(6):587–95.
21. Kokulu K, Mutlu H, Sert ET. 2020. Serum netrin-1 levels at presentation and delayed neurological sequelae in unintentional carbon monoxide poisoning. Clin Toxicol (Philadelphia, Pa). 58(12):1313–1317.