Submitted: 10 December, 2024 Accepted: 05 March, 2025 Published: 08 July, 2025 DOI:10.22514/sv.2025.103

Open Access
Signa Vitae

ORIGINAL RESEARCH

High-flow nasal cannula oxygen versus conventional oxygen therapy in a rat model of severe carbon monoxide toxicity

Sumeyye Cakmak[1,*], Gul Sahika Gokdemir[2], Mehmet Tahir Gokdemir[3], Ozgur Sogut[4], Revsa Evin Canpolat Erkan[5]

[1]Department of Emergency Medicine, Bakırkoy Dr. Sadi Konuk Training and Research Hospital, University of Health Sciences, 34147 İstanbul, Türkiye
[2]Department of Physiology, Faculty of Medicine, Mardin Artuklu University, 47200 Mardin, Türkiye
[3]Department of Emergency Medicine, Faculty of Medicine, Mardin Artuklu University, 47200 Mardin, Türkiye
[4]Department of Emergency Medicine, Haseki Training and Research Hospital, University of Health Sciences, 34093 İstanbul, Türkiye
[5]Department of Biochemistry, Faculty of Medicine, Dicle University, 21280 Diyarbakır, Türkiye

***Correspondence**
sumeyye.cakmak@sbu.edu.tr
(Sumeyye Cakmak)

Abstract

Background: This study compared the efficacy of high-flow nasal cannula (HFNC) oxygen therapy with conventional oxygen therapy (COT) using a simple face mask for clearing carbon monoxide (CO) from the bloodstream in a rat model of severe CO poisoning. **Methods**: Twenty-eight male Wistar rats were assigned to four groups: severe CO intoxication treated with HFNC, a sham group (no intoxication or treatment), severe CO intoxication treated with COT, and a control group with severe CO intoxication receiving no treatment. Their arterial blood gas and metabolic parameters were analyzed and compared to determine treatment effectiveness. **Results**: Significant differences were observed among the groups in terms of carboxyhemoglobin (COHb), pH, bicarbonate (HCO_3), hemoglobin, sodium (Na), potassium (K), calcium (Ca), glucose and lactate levels. Both treatment groups had lower COHb and lactate levels compared to the untreated control group, with COHb clearance being significantly higher in the HFNC group than in the COT group (20.33% $\pm$ 3.58% *vs.* 41.17% $\pm$ 6.49%; $p < 0.001$). Additionally, pH levels were higher in the HFNC group than in the COT group (7.32 $\pm$ 0.07 *vs.* 7.27 $\pm$ 0.05; $p = 0.486$). **Conclusions**: HFNC oxygen therapy was found to be more effective than COT in promoting CO elimination and improving arterial blood gas parameters, indicating its potential as a superior treatment strategy for severe CO poisoning.

Keywords

Carbon monoxide poisoning; Carboxyhemoglobin; High-flow nasal cannula; Conventional oxygen therapy; Arterial blood gas

1. Introduction

Acute carbon monoxide (CO) poisoning is a serious toxicological condition and a leading cause of poisoning-related mortality worldwide. In the United States alone, approximately 50,000 individuals seek emergency medical care annually due to CO poisoning. CO is a colorless, odorless, tasteless and non-irritating gas produced by the incomplete combustion of carbon-containing substances. The initial symptoms of CO poisoning, including headache, dizziness and nausea, are often nonspecific, making early diagnosis challenging. In severe cases, prolonged exposure can result in unconsciousness and death, while long-term complications include neurological deficits, left ventricular dysfunction and cardiac arrhythmias [1–7].

The management of severe CO poisoning involves early detection and appropriate oxygen therapy to facilitate CO elimination and prevent complications. In patients with neurological symptoms, it is recommended to perform an electrocardiogram (ECG) and assess cardiac ischemia biomarkers within the first 6 hours.

CO exerts its toxic effects by binding to hemoglobin (Hb) with an affinity over 200 times greater than that of oxygen, leading to a significant reduction in oxygen-carrying capacity and subsequent tissue hypoxia. The rapid elimination of CO is essential to prevent neurological and cardiovascular complications, and standard treatment approaches include the use of 100% normobaric oxygen (NBO_2) and hyperbaric oxygen therapy (HBOT), both of which accelerate CO dissociation from Hb. The half-life of carboxyhemoglobin (COHb) is approximately 320 minutes in individuals breathing ambient air [8–10], but this decreases to 71 minutes with 100% oxygen administered via a non-rebreather mask and is further reduced to 20 minutes with HBOT [10].

High-flow nasal cannula (HFNC) oxygen therapy has gained increasing attention as a treatment for acute respiratory failure due to its ability to deliver humidified oxygen at high flow rates through a soft nasal cannula [11]. Unlike standard nasal cannulas, which provide a maximum flow rate of 6 liters per minute, HFNC can deliver up to 60 liters per minute, ensuring

a higher fraction of inspired oxygen (FiO_2) and improved alveolar ventilation. Additionally, HFNC generates a positive pressure effect that synchronizes with the patient's inspiratory effort, thereby enhancing oxygenation and increasing the partial pressure of oxygen (PaO_2) [12]. This technique also facilitates more effective carbon dioxide (CO_2) clearance compared to conventional oxygen therapy (COT) by reducing rebreathing and providing higher oxygen flow rates [12]. Recently, HFNC has been introduced as an alternative to oxygen delivery via a simple face mask for patients with hypoxemia [13]. However, limited studies have evaluated its role in CO poisoning. Existing clinical data suggest that HFNC is more effective than COT in reducing COHb levels in patients with CO poisoning, but further investigation is needed to establish its efficacy in this setting [14–16].

However, no experimental studies have directly compared the efficacy of HFNC and COT delivered via a simple face mask in the management of CO poisoning. To address this gap, this study evaluated the effectiveness of HFNC oxygen therapy compared to COT in facilitating CO clearance from the bloodstream using a severe CO toxicity rat model.

2. Materials and methods

Twenty-eight adult male Wistar albino rats (300–350 g) were purchased from the Experimental Animal Center at Dicle University, housed under specific pathogen-free conditions at a controlled temperature of 24 °C with a 12-hour light/dark cycle, and fed a standard diet and given unrestricted access to food and water. All experimental procedures adhered to the European Community Council Directive and were approved by the local animal ethics committee.

The rats were randomly assigned to four groups, each consisting of seven animals. Group 1 included rats with severe CO intoxication treated with HFNC oxygen therapy. Group 2 served as the sham group and was neither exposed to CO nor treated. Group 3 comprised rats with severe CO intoxication treated with COT, while Group 4 included rats with severe CO intoxication that received no treatment (control group).

Rats in the sham group were placed in a 45-liter plastic chamber and exposed to ambient air for 30 minutes. CO intoxication was induced following the method described by Gokdemir GS *et al.* [17]. The CO exposure protocol was selected based on a literature review to achieve an acute COHb level of 80% while minimizing mortality [18–20]. A pilot study determined that exposure to 4000 ppm CO at a flow rate of 3 L/min for 30 minutes was the most effective in inducing severe CO toxicity and was therefore applied to the experimental groups.

After exposure, the remaining rats were placed in a 45-liter plastic chamber and subjected to a 3000-ppm CO–air mixture for 30 minutes using a 101CO cylinder supplied by HABAŞ, administered at a flow rate of 4 L/min (Fig. 1A). After CO exposure, the rats that were still conscious were randomly allocated to three treatment subgroups. The COT group received oxygen at 10 L/min via a simple face mask, ensuring an oxygen concentration of more than 50%. The control group remained in ambient air for 30 minutes without oxygen supplementation (Fig. 1B). For HFNC oxygen delivery, a BMC NC10 nasal cannula (small size, yellow designation) and an HFNC device (BMCH-80 series, BMC Medical Co., Ltd., Beijing, China) were used (Fig. 2). The device settings were adjusted for temperature, flow rate and FiO_2 according to the physiological condition of the rats. To improve tolerance to high oxygen flow, the initial flow rate was set at 30 L/min and increased stepwise to 60 L/min over 10 minutes. The HFNC group received 100% humidified and heated oxygen at a maximum flow rate of 60 L/min (Fig. 2).

The rats were anesthetized via an intraperitoneal injection of 30 mg/kg ketamine hydrochloride (Ketalar; 08699844771904, Eczacıbaşı, Istanbul, Turkey) and 5 mg/kg xylazine (Rompun, 2% solution; 724089483584, Bayer, Leverkusen, NRW, Germany). A midline abdominal incision was made, and a 1-mL blood sample was collected from the left ventricle of the heart using a specialized blood gas syringe. The sample was immediately analyzed for COHb levels using a blood gas analyzer (ABL800, Radiometer, Copenhagen, Denmark). Arterial blood gas parameters, including pH, bicarbonate (HCO_3), Hb and COHb levels, were measured along with metabolic parameters such as sodium (Na), potassium (K), calcium (Ca), glucose and lactate levels. The treatment outcomes were compared with those of the control and sham groups to assess therapeutic efficacy. At the end of the experiment, the rats were euthanized using an overdose of midazolam anesthesia. An additional 5 mL of blood samples were collected in yellow-capped biochemistry tubes for further liver function analysis. Liver tissue specimens were excised from both the left and right lobes. The right lobe was stored at −80 °C for oxidative stress analysis, while samples from the left lobe were fixed in 10% neutral buffered formalin for histological and immunohistochemical evaluation.

The data were analyzed using SPSS version 20.0 (IBM Corp, Armonk, NY, USA). Results were expressed as mean ± standard deviation (SD), minimum and maximum values or as absolute numbers and percentages where appropriate. Comparisons between two groups were conducted using the Student's *t*-test, while multiple-group comparisons were performed using one-way analysis of variance (ANOVA) followed by Tukey's *post hoc* test. A p-value < 0.05 was considered statistically significant.

3. Results

Table 1 presents the comparison of arterial blood gas parameters, electrolytes and metabolites among the treated (HFNC and COT) and non-treated (sham and control) groups. Significant differences can be observed in mean COHb, pH, HCO_3, Hb, Na, K, Ca, glucose and lactate levels across all groups. In addition, both treatment groups (HFNC and COT) demonstrated significantly lower COHb and lactate levels compared to the control group.

As shown in Table 2, COHb levels were significantly lower in the HFNC group than in the control group (20.33% ± 3.58% *vs.* 89.84% ± 1.96%; $p < 0.001$). Lactate levels were also significantly reduced in the HFNC group (3.79 ± 0.41 *vs.* 7.81 ± 1.58 mmol/L; $p = 0.002$). Similarly, the COT group exhibited significantly lower COHb (41.17% ± 6.49% *vs.* 89.84% ± 1.96%; $p < 0.001$) and lactate (5.06 ± 0.99 *vs.*

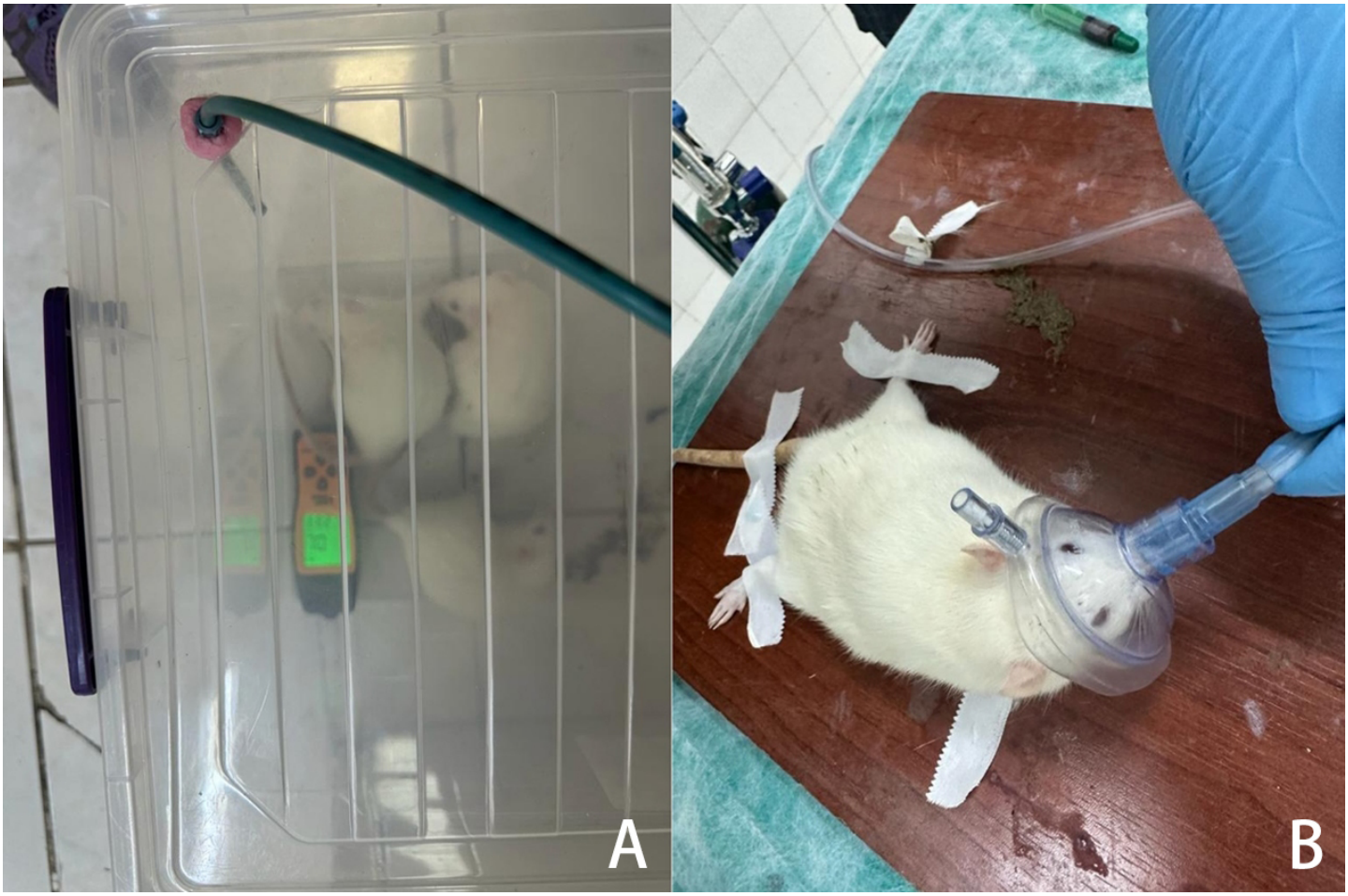

FIGURE 1. Carbon monoxide exposure and oxygen therapy in a rat model. (A) Rats at exposed to severe carbon monoxide poisoning in a plastic chamber; (B) A rat receiving COT with an oxygen flow rate of 10 L/min for 30 minutes via a simple face mask.

FIGURE 2. A rat receiving HFNC oxygen therapy with an oxygen flow rate of 60 L/min for 30 minutes.

TABLE 1. Comparison of arterial blood gas parameters, electrolytes and metabolite levels among the groups.

Parameters	HFNC group (n = 7)	Sham group (n = 7)	COT group (n = 7)	Control group (n = 7)	
	Mean ± SD (Min–Max)	Mean ± SD (Min–Max)	Mean ± SD (Min–Max)	Mean ± SD (Min–Max)	*p**
pH	7.32 ± 0.07 7.25–7.38	7.40 ± 0.05 7.35–7.44	7.27 ± 0.05 7.22–7.32	7.20 ± 0.06 7.15–7.25	<0.001
COHb (%)	20.33 ± 3.58 17.02–23.64	0.71 ± 0.35 0.39–1.04	41.17 ± 6.49 35.17–47.17	89.84 ± 1.96 88.03–91.66	<0.001
Lactate (mmol/L)	3.79 ± 0.41 3.40–4.17	1.83 ± 0.29 1.56–2.10	5.06 ± 0.99 4.14–5.97	7.81 ± 1.58 6.35–9.28	<0.001
Hb (g/dL)	12.29 ± 1.08 11.29–13.28	13.79 ± 0.49 13.33–14.24	12.61 ± 0.56 12.10–13.13	13.65 ± 0.92 12.69–14.61	0.003
K (mEq/L)	4.59 ± 0.54 4.09–5.08	3.20 ± 0.24 2.98–3.42	5.06 ± 0.92 4.21–5.91	6.40 ± 1.37 4.96–7.84	<0.001
Ca (mg/dL)	0.59 ± 0.17 0.44–0.75	0.79 ± 0.08 0.72–0.86	0.63 ± 0.12 0.51–0.74	0.95 ± 0.24 0.70–1.20	0.002
Na (mEq/L)	153.00 ± 4.90 148.40–157.60	146.40 ± 2.10 144.40–148.40	148.40 ± 6.80 142.20–154.70	144.80 ± 4.20 140.50–149.20	0.029
Glucose (mg/dL)	150.10 ± 12.50 138.60–161.70	89.90 ± 9.00 81.50–98.20	178.90 ± 42.40 139.60–218.10	224.70 ± 26.40 200.30–249.20	<0.001
HCO_3 (mmol/L)	18.40 ± 1.00 17.40–19.30	23.20 ± 0.90 22.40–23.90	17.10 ± 1.90 15.30–18.90	20.00 ± 2.04 17.50–22.50	<0.001

Note: Data are expressed as numbers, percentages, mean and standard deviation (SD) or minimum and maximum values.
**One-way ANOVA.*
HFNC group: Severe CO intoxication treated with high-flow nasal cannula oxygen therapy (HFNC); Sham group: No CO intoxication, no treatment; COT group: Severe CO intoxication treated with conventional oxygen therapy (COT); Control group: Severe CO intoxication without treatment; COHb: Carboxyhemoglobin; HCO_3: Bicarbonate; Na: Sodium; K: Potassium; Ca: Calcium; Hb: hemoglobin.

TABLE 2. Subgroup analysis.

Parameter	HFNC *vs.*			Sham *vs.*		COT *vs.*
	Sham	COT	Control	COT	Control	Control
	p	*p*	*p*	*p*	*p*	*p*
pH#	0.062	0.486	0.004	0.002	<0.001	0.100
COHb*	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Lactate*	<0.001	0.055	0.002	<0.001	<0.001	0.013
Hb#	0.009	0.865	0.025	0.050	0.990	0.116
K*	0.001	0.658	0.078	0.006	0.008	0.247
Ca#	0.134	0.982	0.003	0.255	0.279	0.006
Na#	0.078	0.311	0.027	0.864	0.933	0.547
Glucose#	0.001	0.197	<0.001	<0.001	<0.001	0.016
HCO_3#	<0.001	0.488	0.327	<0.001	0.011	0.023

*#Tukey's HSD, *Games–Howell post hoc test.*
HFNC: High-flow nasal cannula oxygen therapy; COT: Conventional oxygen therapy; COHb: Carboxyhemoglobin; HCO_3: Bicarbonate; Na: Sodium; K: Potassium; Ca: Calcium; Hb: hemoglobin.

7.81 ± 1.58 mmol/L; $p = 0.013$) levels compared to the control group.

A direct comparison between the HFNC and COT groups further demonstrated the superior efficacy of HFNC in CO clearance. The HFNC group had significantly lower COHb levels than the COT group (20.33% ± 3.58% *vs.* 41.17% ± 6.49%; $p < 0.001$). Additionally, the pH levels were numerically higher in the HFNC group (7.32 ± 0.07 *vs.* 7.27 ± 0.05; $p = 0.486$), although this difference was not statistically significant. Moreover, no significant differences were observed between the HFNC and COT groups in terms of lactate ($p = 0.055$) or HCO_3 ($p = 0.488$) levels, as detailed in Table 2.

These findings highlight the effectiveness of HFNC in lowering COHb levels and maintaining better pH values, suggesting its potential advantage over COT for CO elimination in this experimental model.

4. Discussion

HFNC oxygen therapy is a noninvasive respiratory support technique that offers several advantages over conventional oxygen delivery methods. Its effectiveness depends on the flow rate, which remains a subject of investigation, particularly in patients with acute exacerbations of chronic obstructive pulmonary disease (COPD). Previous studies have reported that HFNC at flow rates exceeding 30 L/min provides the most accurate fraction of FiO_2 [21]. Recently, a study compared HFNC at flow rates of 30 and 50 L/min with noninvasive ventilation in patients with COPD exacerbations to determine its efficacy and safety [22].

Despite its increasing use in clinical practice, no experimental studies have directly compared HFNC with COT for the management of CO poisoning. This study is the first to evaluate the efficacy of HFNC oxygen therapy in facilitating CO elimination in a rat model of severe CO toxicity. CO exerts its toxic effects by binding to Hb with an affinity significantly higher than that of oxygen, leading to tissue hypoxia. Prompt administration of oxygen therapy is essential to displace CO from Hb, restore oxygen delivery to tissues and mitigate CO's toxic effects.

COT is typically administered using a bag-valve-mask device to deliver high concentrations of oxygen; however, achieving a consistent FiO_2 of 100% with this approach remains a challenge. In contrast, HFNC therapy can deliver up to 100% humidified and heated oxygen at flow rates of up to 60 L/min, with adjustable room air intake to maintain a stable and higher FiO_2 than COT [23]. The ability to control these parameters independently ensures more precise oxygen delivery, leading to improved clinical outcomes. Beyond its capacity for FiO_2 regulation, HFNC provides several physiological benefits. For instance, it generates positive end-expiratory pressure (PEEP) in the lower airways, which functions similarly to continuous positive airway pressure by preventing alveolar collapse during exhalation [24] and enhances alveolar recruitment, thereby increasing the available surface area for gas exchange [24, 25]. Additionally, HFNC reduces anatomical dead space, increases lung volumes, and promotes alveolar recruitment, collectively improving alveolar ventilation [25]. Although HFNC therapy offers the advantages of PEEP generation, improved oxygenation and enhanced patient comfort and compliance, it has certain limitations, particularly in individuals with compromised respiratory function [26]. Moreover, one of the primary drawbacks is its relatively high cost compared to low-flow nasal cannulas, as well as the requirement for specialized training to initiate and manage therapy. Other potential limitations include its unsuitability for patients with altered consciousness, facial injuries, excessive secretions with an increased risk of aspiration or hemodynamic instability [27].

A randomized controlled trial investigating HFNC oxygen therapy in patients with CO poisoning found no significant reduction in the half-life of COHb (fCOHb $t_{1/2}$) compared to NBO_2 therapy. However, the study suggested the potential benefits of HFNC in maintaining stable fCOHb $t_{1/2}$ values and enhancing COHb clearance in cases of mild CO poisoning compared to standard NBO_2 therapy [28]. Similarly, Akkan *et al.* [29] analyzed 81 patients with acute CO intoxication and reported no significant difference in CO elimination rates between HFNC and COT during the first 60 minutes of treatment. In contrast, a study of 33 patients with acute CO poisoning demonstrated that HFNC resulted in shorter fCOHb $t_{1/2}$ values than a non-rebreather face mask, suggesting that HFNC may be as effective as HBOT in promoting CO elimination [14]. A retrospective analysis of 71 patients with acute CO poisoning further confirmed that HFNC effectively reduced fCOHb $t_{1/2}$ values [15]. Similarly, Tomruk *et al.* [16] reported that HFNC therapy achieved greater reductions in COHb levels than COT. Overall, these findings are consistent with the results of the present study, which demonstrated that HFNC oxygen therapy was superior to COT in reducing COHb levels.

Plasma lactate levels are commonly elevated in CO poisoning due to impaired oxygen delivery and the resulting shift to anaerobic metabolism. A strong positive correlation has been reported between lactate and COHb levels, reflecting the severity of CO-induced hypoxia [30]. In this study, all groups exposed to CO exhibited increased lactate concentrations. The control group, which experienced severe CO intoxication without treatment, had significantly higher mean COHb and lactate levels than the sham group, which was not exposed to CO (COHb: 89.84% ± 1.96% *vs.* 0.71% ± 0.35%; $p < 0.001$; lactate: 7.81 ± 1.58 *vs.* 1.56 ± 2.10 mmol/L; $p < 0.001$). These findings indicate the pronounced physiological impact of untreated CO poisoning. In addition, treatment with HFNC and COT resulted in significantly lower COHb and lactate levels compared to the untreated control group. Although the difference did not reach statistical significance, mean lactate levels were lower in the HFNC group than in the COT group (3.79 ± 0.41 *vs.* 5.06 ± 0.99 mmol/L; $p = 0.055$). This trend suggests that HFNC may provide more effective lactate clearance, potentially due to its higher oxygen delivery and improved ventilation.

This study has several limitations that should be acknowledged. First, the small sample size (n = 7 rats/group) reduces statistical power, which may limit the generalizability of the results. Additionally, the use of a rat model introduces inherent limitations, as physiological responses to CO toxicity in rodents may not fully translate to human pathophysiology,

thereby restricting the direct applicability of the findings to clinical practice. Second is the absence of long-term outcome data, as the study focused solely on immediate physiological changes following treatment, and this may have limited the ability to determine the sustained effects of HFNC oxygen therapy and its potential advantages over COT in managing CO poisoning. Furthermore, the study might have been underpowered to definitively establish the superiority of HFNC in enhancing CO clearance. Thus, further well-designed clinical trials with larger sample sizes and long-term follow-up are necessary to comprehensively evaluate the efficacy of HFNC oxygen therapy in both acute and chronic CO poisoning.

5. Conclusions

In this experimental model of severe CO intoxication, HFNC oxygen therapy demonstrated greater efficacy in improving arterial blood gas parameters compared to COT. HFNC treatment resulted in significantly lower COHb levels and higher pH values, suggesting enhanced CO clearance in severe CO toxicity. These findings indicate that HFNC may be a more effective therapeutic approach for managing severe CO poisoning and support the potential of HFNC as an alternative treatment strategy, particularly in patients presenting with severe CO poisoning. However, further research, including studies with larger sample sizes and clinical trials in human subjects, is necessary to confirm its effectiveness and feasibility in clinical practice.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on request from the corresponding author.

AUTHOR CONTRIBUTIONS

SC, OS, MTG—conceptualization. SC, OS, MTG, GSG, RECE—methodology. SC, RECE, GSG—investigation. SC—writing–original draft preparation. SC, OS, MTG, GSG—writing–review and editing. OS—supervision. All authors have read and agreed to the published version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The experimental procedures adhered to ethical guidelines outlined in the European Community Council Directive (86/609/EEC) and were approved by the local animal ethics committee for experimental animals of Dicle University (Ethical approval no: 3; date: 30 November 2023).

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Childs J, Fischbach A, Smirnov A, Farinelli B, Bühl T, Franco W, *et al*. Extracorporeal membrane oxygenators with light-diffusing fibers for treatment of carbon monoxide poisoning: experiments, mathematical modeling, and performance assessment with unit cells. Lasers in Surgery and Medicine. 2023; 55: 590–600.

[2] Zazzeron L, Franco W, Anderson R. Carbon monoxide poisoning and phototherapy. Nitric Oxide. 2024; 146: 31–36.

[3] Hanley ME, Patel PH. Carbon monoxide toxicity. StatPearls: Treasure Island (FL). 2023.

[4] Buboltz JB, Robins M. Hyperbaric treatment of carbon monoxide toxicity. StatPearls: Treasure Island (FL). 2023.

[5] Lin MS, Lin CC, Yang CC, Weng SC, Wang SM, Chen CY, *et al*. Myocardial injury was associated with neurological sequelae of acute carbon monoxide poisoning in Taiwan. Journal of the Chinese Medical Association. 2018; 81: 682–690.

[6] Gao H, Chen C, Zhao X, Zhao L, Zheng X, Sun H, *et al*. Correlation between rats hippocampal ATP content and delayed encephalopathy after acute carbon monoxide poisoning. Neuropsychiatric Disease and Treatment. 2023; 19: 329–336.

[7] Baharara H, Ghasemi H, Samadi S, Roohshad B, Jomehzadeh V, Ravankhah Moghaddam K, *et al*. The effect of preconditioning agents on cardiotoxicity and neurotoxicity of carbon monoxide poisoning in animal studies: a systematic review. Drug and Chemical Toxicology. 2023; 46: 256–270.

[8] Fischbach A, Wiegand SB, Zazzeron L, Traeger L, di Fenza R, Bagchi A, *et al*. Veno-venous extracorporeal blood phototherapy increases the rate of carbon monoxide (CO) elimination in CO-poisoned pigs. Lasers in Surgery and Medicine. 2022; 54: 256–267.

[9] Fischbach A, Traeger L, Farinelli WA, Ezaka M, Wanderley HV, Wiegand SB, *et al*. Hyperbaric phototherapy augments blood carbon monoxide removal. Lasers in Surgery and Medicine. 2022; 54: 426–432.

[10] Buckley NA, Juurlink DN. Carbon monoxide treatment guidelines must acknowledge the limitations of the existing evidence. American Journal of Respiratory and Critical Care Medicine. 2013; 187: 1390.

[11] Oczkowski S, Ergan B, Bos L, Chatwin M, Ferrer M, Gregoretti C, *et al*. ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. European Respiratory Journal. 2022; 59: 2101574.

[12] Zhao H, Wang H, Sun F, Lyu S, An Y. High-flow nasal cannula oxygen therapy is superior to conventional oxygen therapy but not to noninvasive mechanical ventilation on intubation rate: a systematic review and meta-analysis. Critical Care. 2017; 21: 184.

[13] Spoletini G, Alotaibi M, Blasi F, Hill NS. Heated humidified high-flow nasal oxygen in adults: mechanisms of action and clinical implications. Chest. 2015; 148: 253–261.

[14] Ozturan IU, Yaka E, Suner S, Ozbek AE, Alyesil C, Dogan NO, *et al*. Determination of carboxyhemoglobin half-life in patients with carbon monoxide toxicity treated with high flow nasal cannula oxygen therapy. Clinical Toxicology. 2019; 57: 617–623.

[15] Yesiloglu O, Gulen M, Satar S, Avci A, Acehan S, Akoglu H. Treatment of carbon monoxide poisoning: high-flow nasal cannula versus non-rebreather face mask. Clinical Toxicology. 2021; 59: 386–391.

[16] Tomruk O, Karaman K, Erdur B, Armagan HH, Beceren NG, Oskay A, *et al*. A new promising treatment strategy for carbon monoxide poisoning: high flow nasal cannula oxygen therapy. Medical Science Monitor. 2019; 25: 605–609.

[17] Gokdemir GS, Seker U, Demirtas B, Taskin S. Effects of acute carbon monoxide poisoning on liver damage and comparisons of related oxygen

therapies in a rat model. Toxicology Mechanisms and Methods. 2024; 34: 845–854.

[18] Rezaee R, Sheidary A, Jangjoo S, Ekhtiary S, Bagheri S, Kohkan Z, *et al*. Cardioprotective effects of hesperidin on carbon monoxide poisoned in rats. Drug and Chemical Toxicology. 2021; 44: 668–673.

[19] Penney DG, Helfman CC, Dunbar JC III, McCoy LE. Acute severe carbon monoxide exposure in the rat: effects of hyperglycemia and hypoglycemia on mortality, recovery, and neurologic deficit. Canadian Journal of Physiology and Pharmacology. 1991; 69: 1168–1177.

[20] Bor-Kucukatay M, Atalay H, Karagenc N, Erken G, Kucukatay V. The effect of carbon monoxide poisoning on hemorheological parameters in rats and the alterations in these parameters in response to three kinds of treatments. Clinical Hemorheology and Microcirculation. 2010; 44: 87–96.

[21] Rittayamai N, Phuangchoei P, Tscheikuna J, Praphruetkit N, Brochard L. Effects of high-flow nasal cannula and non-invasive ventilation on inspiratory effort in hypercapnic patients with chronic obstructive pulmonary disease: a preliminary study. Annals of Intensive Care. 2019; 9: 122.

[22] Haciosman O, Ergenc H, Az A, Dogan Y, Sogut O. A high-flow nasal cannula versus noninvasive ventilation in acute exacerbations of chronic obstructive pulmonary disease. The American Journal of Emergency Medicine. 2025; 87: 38–43.

[23] Sotello D, Rivas M, Mulkey Z, Nugent K. High-flow nasal cannula oxygen in adult patients: a narrative review. The American Journal of the Medical Sciences. 2015; 349: 179–185.

[24] Ramnarayan P, Richards-Belle A, Drikite L, Saull M, Orzechowska I, Darnell R, *et al*.; FIRST-ABC Step-Up RCT Investigators and the Paediatric Critical Care Society Study Group. Effect of high-flow nasal cannula therapy *vs* continuous positive airway pressure therapy on liberation from respiratory support in acutely ill children admitted to pediatric critical care units: a randomized clinical trial. JAMA. 2022; 328: 162–172.

[25] Grasselli G, Calfee CS, Camporota L, Poole D, Amato MBP, Antonelli M, *et al*. ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. Intensive Care Medicine. 2023; 49: 727–759.

[26] Di Mussi R, Spadaro S, Stripoli T, Volta CA, Trerotoli P, Pierucci P, *et al*. High-flow nasal cannula oxygen therapy decreases postextubation neuroventilatory drive and work of breathing in patients with chronic obstructive pulmonary disease. Critical Care. 2018; 22: 180.

[27] Segovia B, Velasco D, Jaureguizar Oriol A, Díaz Lobato S. Combination therapy in patients with acute respiratory failure: high-flow nasal cannula and non-invasive mechanical ventilation. Archivos de Bronconeumología. 2019; 55: 166–167.

[28] Kim YM, Shin HJ, Choi DW, Kim JM, Lee SW, Jeong SH, *et al*. Comparison of high-flow nasal cannula oxygen therapy and conventional reserve-bag oxygen therapy in carbon monoxide intoxication: a pilot study. The American Journal of Emergency Medicine. 2020; 38: 1621–1626.

[29] Akkan S, Uyanik Ö. Comparing high-flow nasal oxygen therapy and normobaric oxygen therapy on the treatment of carbon monoxide poisoning. Medizinische Klinik, Intensivmedizin und Notfallmedizin. 2024; 119: 214–219. (In German)

[30] Doğan NÖ, Savrun A, Levent S, Günaydın GP, Çelik GK, Akküçük H, *et al*. Can initial lactate levels predict the severity of unintentional carbon monoxide poisoning? Human & Experimental Toxicology. 2015; 34: 324–329.

How to cite this article: Sumeyye Cakmak, Gul Sahika Gokdemir, Mehmet Tahir Gokdemir, Ozgur Sogut, Revsa Evin Canpolat Erkan. High-flow nasal cannula oxygen versus conventional oxygen therapy in a rat model of severe carbon monoxide toxicity. Signa Vitae. 2025; 21(7): 111-117. doi: 10.22514/sv.2025.103.