TNF-ALPHA AND IL-10 ARE HERALDING NEUROLOGICAL COMPLICATIONS FROM CO POISONING

Enrico Camporesi, MD, FUHM

UHMS 2014

St Louis

TNF-alpha as a biomarker for neurological severity in acute Carbon Monoxide (CO) poisoning

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Florida Gulf-to-Bay ANESTHESIOLOGY

BACKGROUND

Carbon monoxide (CO) poisoning can result in mild-to-severe cardiac, neurologic, and other systemic complications. In severe CO intoxication, hyperbaric oxygen therapy (HBOT) may reduce neurologic sequelae (1). Traditionally, carboxyhemoglobin (COHb) serves as an index of exposure severity and duration, but post-treatment COHb does not correlate with patient outcomes. While early CO-induced cardiotoxicity can be identified with serum natriuretic peptides, neurologic injury cannot be similarly predicted.

METHODS

In this study, we evaluated biomarkers in 30 consecutive adult patients admitted with CO poisoning for HBOT at a single facility (Vaio Hospital; Parma, Italy) from 10/2013 - 12/2013. Intubated and comatose patients were excluded. HBOT was initiated within a few hours post-exposure and performed at 2.8 atmospheres absolute (ATA) O2 for 30 minutes followed by 2.5 ATA O2 for 60 minutes. As part of a standing research protocol approved by our regional safety committee, 10 mL venous blood samples were obtained at admission and immediately post-HBOT for standard venous blood gas data, COHb, interleukin (IL)-6, IL-8, IL-10, C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), neuron-specific enolase, and S100B protein. Seven healthy adult volunteers served as controls from whom identical measures were obtained. Neurologic evaluations were performed at arrival and daily until discharge. Follow-up telephone interviews were completed at 10, 20, and 30 days after HBOT.

RESULTS

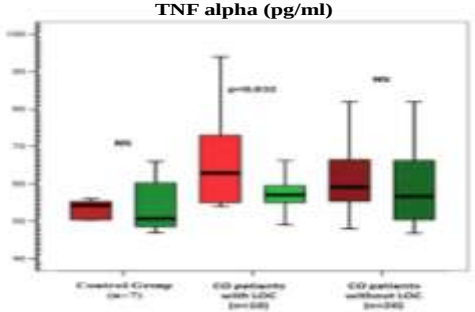
Neurologic symptoms were observed at HBOT initiation in 5 patients: 4 with confusion and malaise and 1 with headache. Although 10 patients had transient loss of consciousness, all patients were conscious at the start of HBOT. All neurologic symptoms resolved after 1 HBOT without long-term sequelae on follow-up. After HBOT, COHb levels were significantly decreased in all patients (3.8% vs 26.8%, p = 0.01). In controls, low COHb levels without significant changes were found.
Significant decreases were seen in IL-10 and TNF-α levels after HBOT between groups (Table 1 for TNF-α; IL-10 data are similar but not shown). When further evaluating the 10 patients with transient loss of consciousness, TNF-α and IL-10 levels were significantly higher at admission and reduced after HBOT as compared to controls. Conversely, these measures were not significantly different in the 20 patients without loss of consciousness (Figure 1). No significant differences were seen in the remaining markers.

Table 1. TNF-alpha Values in Controls and Carbon Monoxide Poisoning Patients Before and After Hyperbaric Oxygen Therapy

	Before	After
Controls (n=7)	55.2 pg/mL (13.1)	54.4 pg/mL (26)
HBO patients (n=30)	67.5 pg/mL (30.5)#	63.3 pg/mL (27.8)*

Data are depicted as mean (1 SD).
significantly different from Controls Before, p<0.01 by unpaired t-test;
* significantly different from Before treatment for HBO patients: p<0.03 by Wilcoxon two-tailed signed-rank test

TNF alpha (pg/ml)



CONCLUSION

Previous toxicology data from CO poisoning patients found that acute inflammatory modulation may mediate neurologic toxicity (2). Our data suggests that a rapid decrease in TNF-α and IL-10 levels after HBOT may predict resolution of neurologic symptoms. From our findings, we propose further study of TNF-α monitoring in CO poisoning patients as a marker of neurologic complications, especially if residual symptoms persist after HBOT.

REFERENCES

1) Weaver LK. Clinical practice. Carbon monoxide poisoning. N Engl J Med,2009;360:1217.
2)Thom SR: Plasma biomarkers in CO Poisoning, Clin Tox, 2010; 48: 47.

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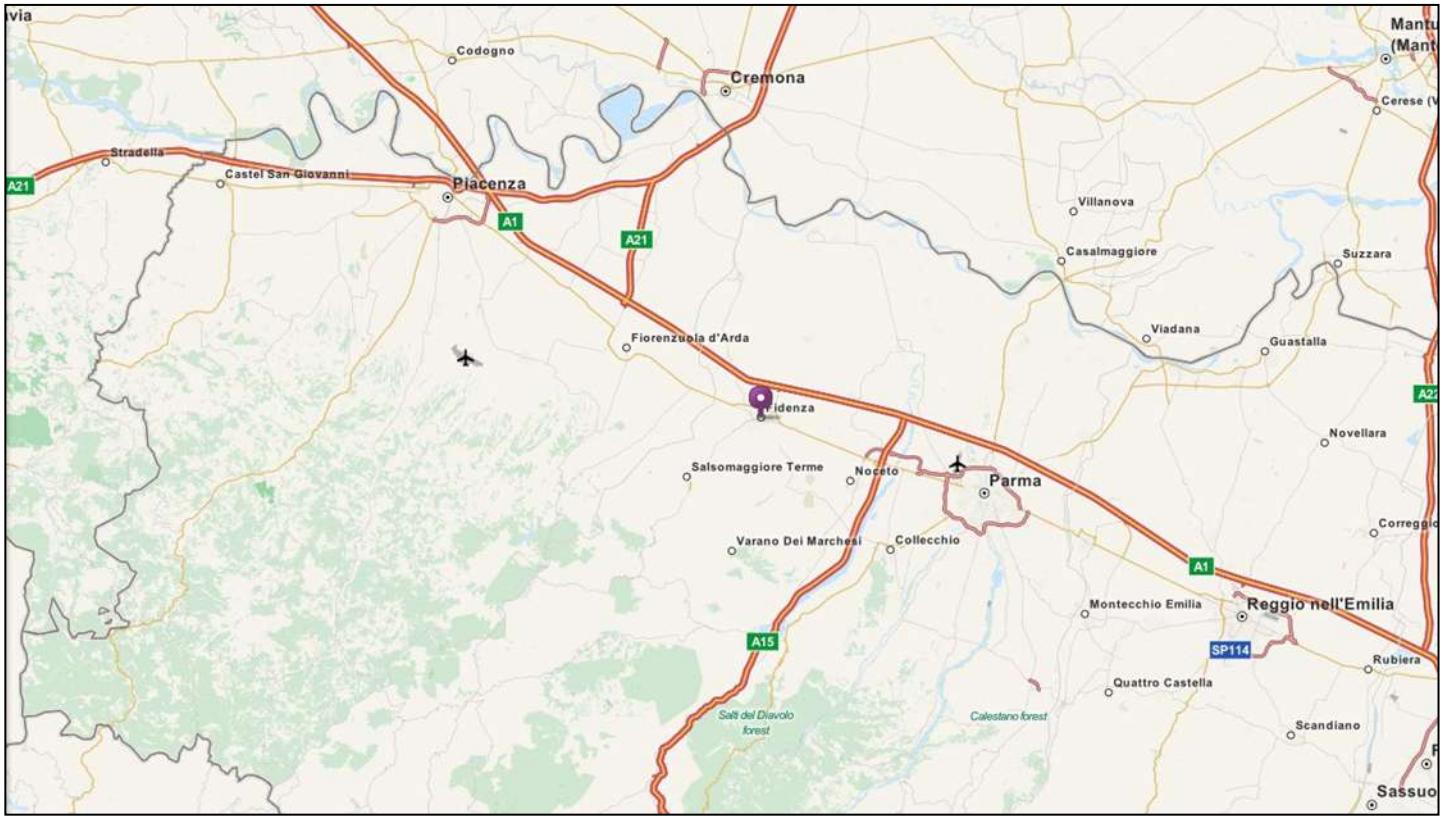

New Train Station

Ospedale di Vaio

Multiplace Hyperbaric Unit

Prof. Vezzani

2012

Concise Clinical Review

Practice Recommendations in the Diagnosis, Management, and Prevention of Carbon Monoxide Poisoning

Neil B. Hampson[1], Claude A. Piantadosi[2], Stephen R. Thom[3], and Lindell K. Weaver[4]

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CO intoxication: cardiac and neurological complications

Carbon monoxide (CO) poisoning can result in mild-to-severe **cardiac, neurologic**, and other systemic complications. In severe CO intoxication, hyperbaric oxygen therapy (HBOT) may reduce neurologic sequelae

Traditionally, **carboxyhemoglobin (COHb)** serves as an index of **exposure severity and duration**, but post-treatment COHb does not correlate with patient outcomes

While early CO-induced **cardiotoxicity** can be identified with **serum natriuretic peptides**, neurologic injury cannot be similarly predicted

Cardiac Markers

Clinical Biochemistry 45 (2012) 1278–1285

Contents lists available at SciVerse ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Review

Pathophysiology, clinics, diagnosis and treatment of heart involvement in carbon monoxide poisoning ☆

Giuseppe Lippi [a,*], Gianni Rastelli [b], Tiziana Meschi [c], Loris Borghi [c], Gianfranco Cervellin [d]

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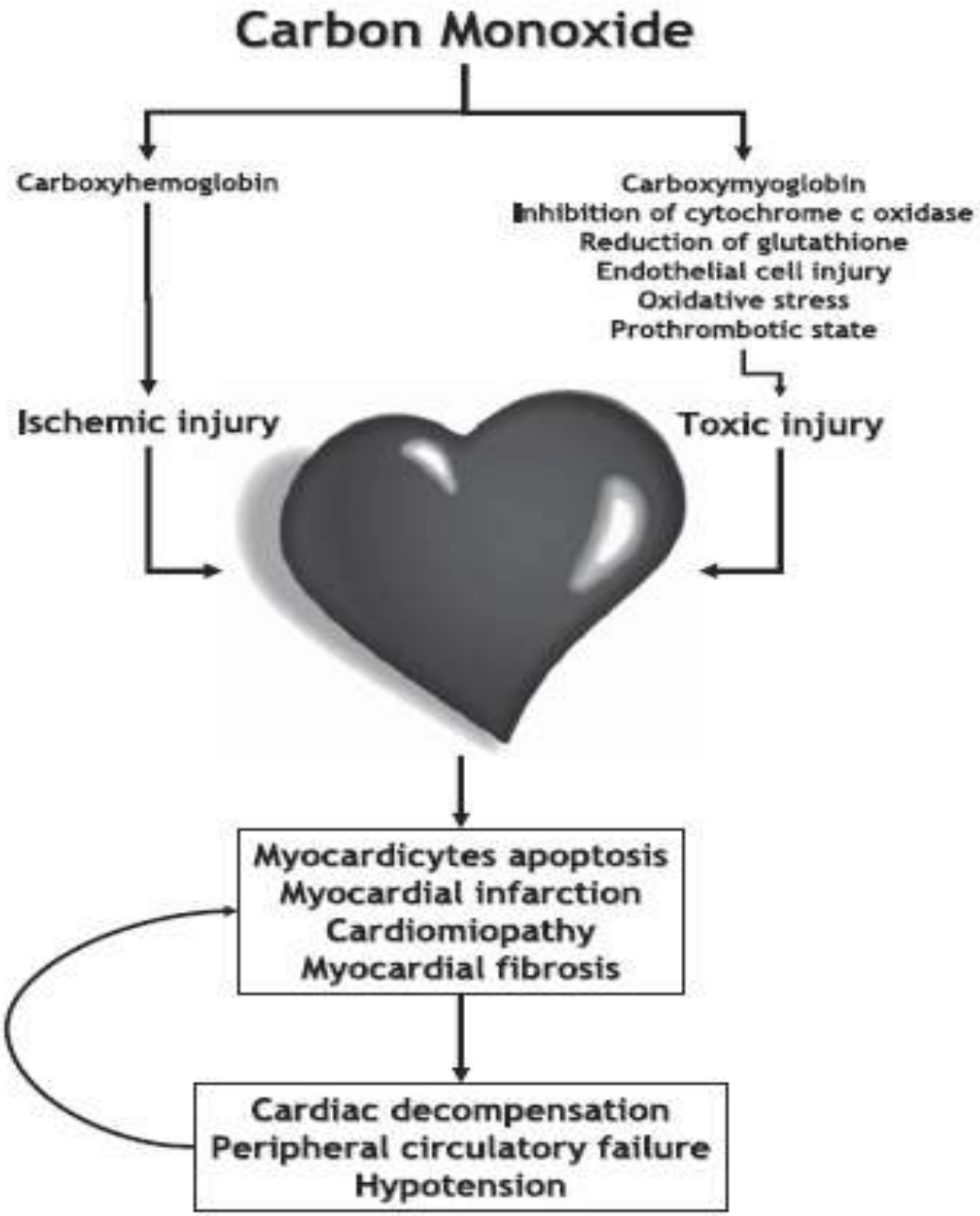

Fig. 1. Pathophysiology of myocardial injury in carbon monoxide intoxication.

New EKG diagnostic criteria

American Journal of Emergency Medicine 31 (2013) 1651–1655

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Original Contribution

A new marker for myocardial injury in carbon monoxide poisoning: T peak–T end

Nazire Belgin Akilli, MD [a,*], Emine Akinci, MD [a], Hakan Akilli, MD [b], Zerrin Defne Dundar [c], Ramazan Koylu, MD [a], Mustafa Polat, MD [a], Basar Cander, MD [c]

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Tp-e

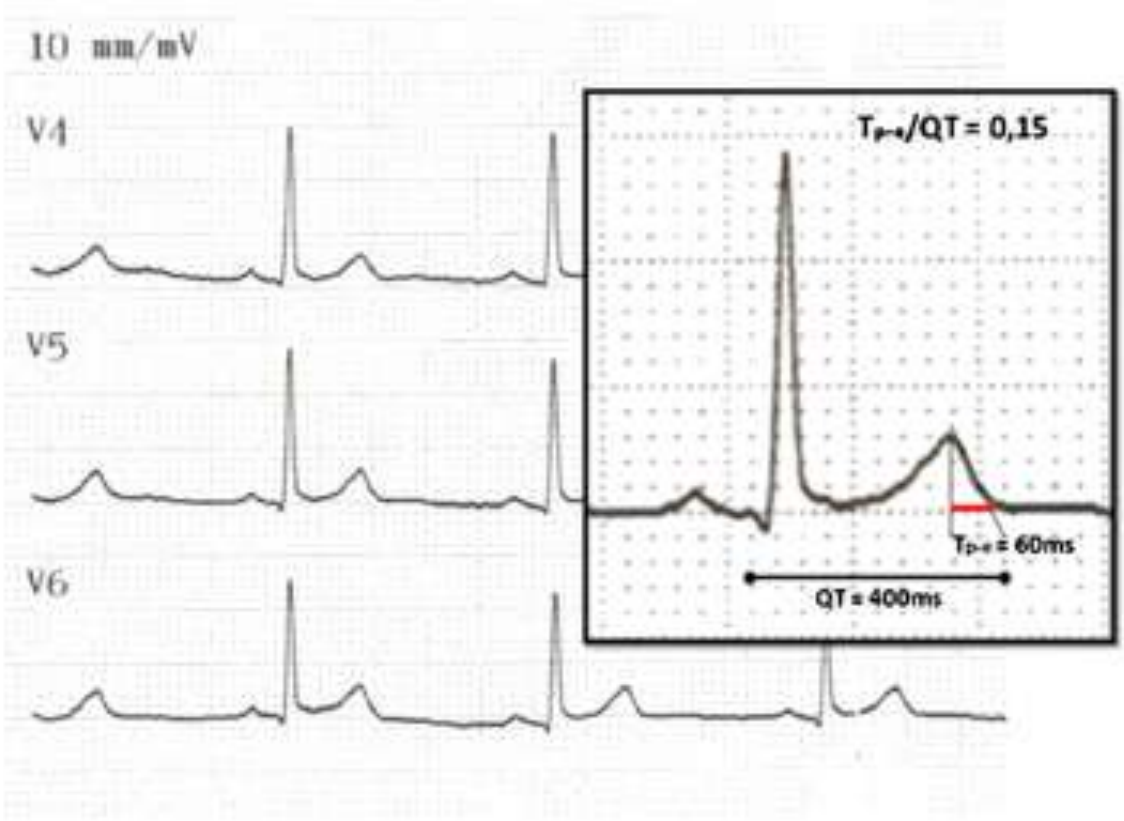

Fig. 1. Measurement of Tp-e via the tangent method.

Serum BNP

Inhalation Toxicology, 18:155–158, 2006

ISSN: 0895-8378 print / 1091-7691 online
DOI: 10.1080/08958370500305885

Taylor & Francis
Taylor & Francis Group

Serum Levels of NT-ProBNP as an Early Cardiac Marker of Carbon Monoxide Poisoning

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Other Plasma Biomarkers

Clinical Toxicology (2010) **48**, 47–56

ISSN: 1556-3650 print / 1556-9519 online
DOI: 10.3109/15563650903468209

informa
healthcare

ARTICLE

Plasma biomarkers in carbon monoxide poisoning

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Stratification of Risk: LOC

"A prospective study involving use of objective neuropsychological testing is planned as this will be necessary to assess whether variations in plasma proteins provide an objective method for stratifying CO poisoning severity

A major clinical challenge is to identify at-risk patients among those who do not suffer overt loss of consciousness. This would aid clinical decisions on treatment and provide an objective method to compare patients in clinical research"

METHODS

In this study, we evaluated biomarkers in **30 consecutive adult patients** admitted with CO poisoning for HBOT at a single facility **(Vaio Hospital; Parma, Italy)** from 10/2013 - 12/2013

Intubated and comatose patients were excluded. HBOT was initiated within a few hours post-exposure and performed at **2.8 atmospheres absolute (ATA) O_2 for 30 minutes followed by 2.5 ATA O_2 for 60 minutes**

Methods: Blood Samples and Biomarkers

As part of a **standing research protocol** approved by our regional safety committee,

10 mL venous blood samples were obtained **at admission and immediately post-HBOT** for standard venous **blood gas** data, **COHb**, interleukin **(IL)-6, IL-8, IL-10**, C-reactive protein **(CRP),** tumor necrosis factor-alpha **(TNF-α)**, neuron-specific **enolase**, and **S100B** protein

Patients and Volunteers in Vaio

- 10 pt lost consciousness (LOC)
- 20 pt did not lose consciousness
- 7 normal volunteers: no intoxication

- Parameters were compared, before vs. after HBO treatment, with Wilcoxon two-tailed signed rank test

Pt Follow-up Telephone Interviews

- Neurologic evaluations were performed at arrival and daily until discharge. Follow-up telephone interviews were completed at
- **10, 20, and 30 days** after HBOT

RESULTS

Neurologic symptoms were observed at HBOT initiation in 5 patients: 4 with confusion and malaise and 1 with headache

10 patients had transient loss of consciousness, all patients were conscious at the start of HBOT. All neurologic symptoms resolved after 1 HBOT without long-term sequelae on follow-up

COHb

- After HBOT, COHb levels were significantly reduced in all patients

  (26.8% vs. 3.4% , p = 0.01)

Pt with LOC had slightly higher COHb presenting values:

but not significantly different from Pt without LOC

In controls, low COHb levels without significant changes were found

Patient Characteristics, Mean Values

	M/F	Age	Pre % COHb	Post % COHb	Time to HBO (hr)
LOC	5/5	41.8	26.8	3.8	6.0
No LOC	10/10	43.1*	23.1*	5.8*	4.7*

*Non-significant

Serum Markers:

- Significant decreases were seen in IL-10 and TNF-α levels after HBOT between groups (Table 1 for TNF-α; IL-10 data are similar but not shown).

All Pooled CO Patients

Table 1. TNF-alpha Values in Controls and Carbon Monoxide Poisoning Patients Before and After Hyperbaric Oxygen Therapy (pg/mL)

	Before	After
Controls (n=7)	55.2 (13.1)	54.4 (26)
HBO patients (n=30)	67.5 (30.5)#	63.3 (27.8)*

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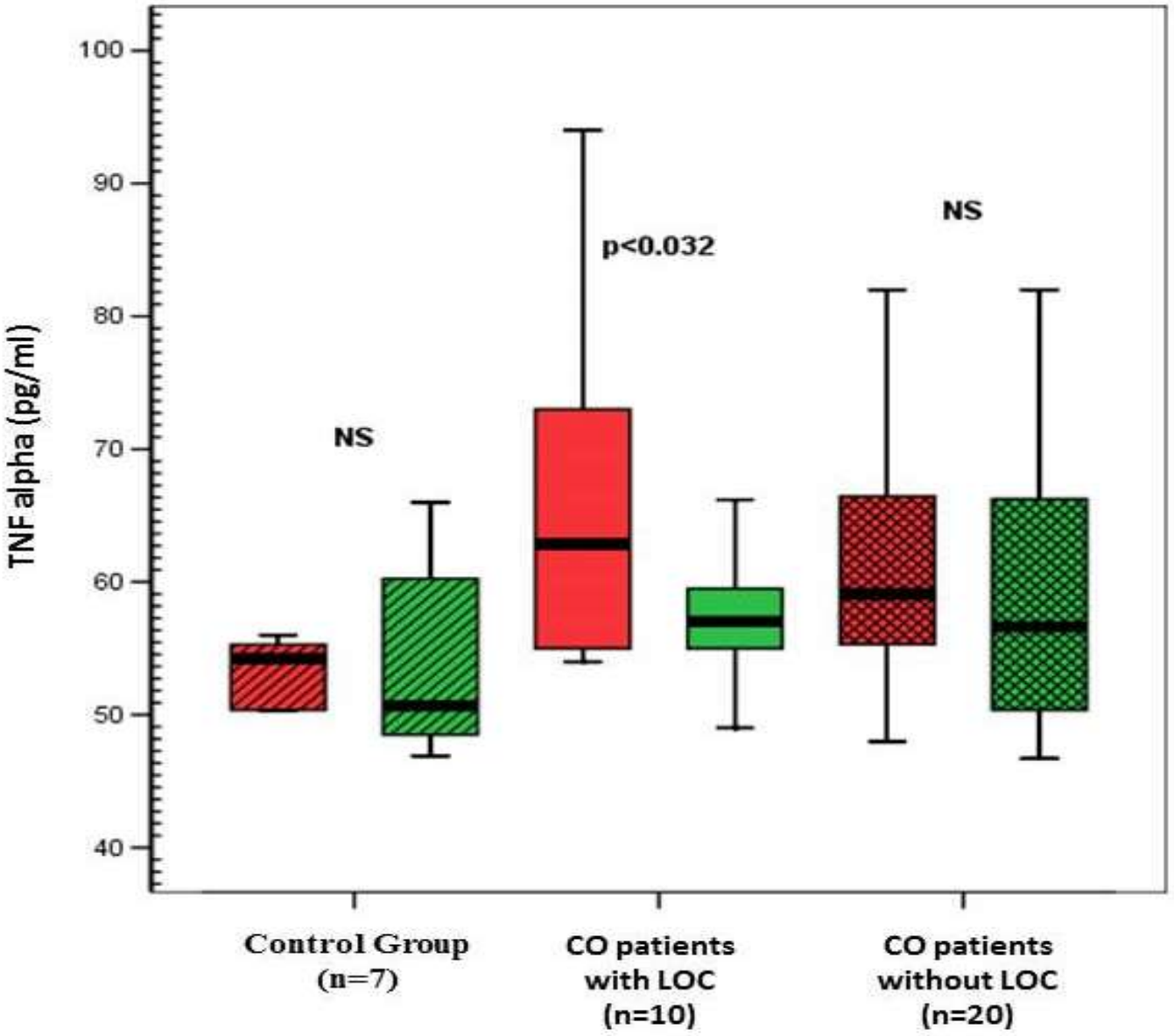
significantly different from Controls Before, $p < 0.01$ by unpaired t-test;
* significantly different from Before treatment for HBO patients: $p < 0.03$ by Wilcoxon two-tailed signed-rank test

TNF-alpha and IL-10

- When further evaluating the 10 patients with transient loss of consciousness, **TNF-α and IL-10 levels were significantly higher at admission and reduced after HBOT as compared to controls**. Conversely, these measures were not significantly different in the 20 patients without loss of consciousness (*Figure 1*).

TNF-alpha in all subjects



No other differences:

- No significant differences were seen in the remaining markers, comprising enolase and SB100 protein

Significant Reduction after HBO

- Previous toxicology data from CO poisoning patients found that **acute inflammatory modulation** may mediate neurologic toxicity

- Our data suggests that a rapid decrease in TNF-α and IL-10 levels after HBOT may predict resolution of neurologic symptoms.

Suggestion

- From our findings, we propose further study of TNF-α monitoring in CO poisoning patients as a marker of neurologic complications, especially if residual symptoms persist after HBOT.

LIMITATION

- None of these pt died
- Moderate intoxication
- Suspicion that these mediators might HERALD
- Not a Proof

Additional Limiting Factors:

- Short delay to tx
- Fast response
- Many small ER and hospitals

SUMMARY:

- **Inflammatory meditators**, IL-10 and TNF-alpha, were significantly **elevated** upon admission to HBOT in patients who suffered from LOC after CO intoxication

- Both biological markers where **significantly reduced after HBOT** and recovery

- We propose to use these markers as indicators of recovery from neurological symptoms.