Yonsei University Wonju College of Medicine
Department of Emergency Medicine

일산화탄소 중독의 치료
-기타 치료 중심 근거-

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Disclosure information

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

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1. Major review journals

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Carbon Monoxide Poisoning

Lindell K. Weaver, M.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

A 39-year-old female executive has a several-month history of fatigue, headache, and memory lapse. Multiple specialists have performed evaluations, but no diagnosis has been established. During a period of feeling worse than usual, she called a friend, who arrived at the residence to find the woman semicomatose and called 911. The patient was given supplemental oxygen and transported to the emergency department, where she is alert and has nonfocal findings on examination. Her carboxyhemoglobin level is 18%. How should she be treated? What is the expected outcome?

Weaver, L. K. (2009). N Engl J Med 360(12): 1217-1225.

Other Therapy

- Inflammation caused by carbon monoxide results in tissue injury.
- Whether anti-inflammatory therapy or the use of other neuroprotective interventions, such as induced hypothermia, could improve outcomes after poisoning is unknown.

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]

[1]Virginia Mason Medical Center, Seattle, Washington; [2]Duke University Medical Center, Durham, North Carolina; [3]University of Pennsylvania Medical Center, Philadelphia, Pennsylvania; and [4]Intermountain Medical Center, Salt Lake City, Utah

Hampson, N. B., et al. (2012). Am J Respir Crit Care Med 186(11): 1095-1101.

No recommendation for other treatment except for HBO

CONCISE CLINICAL REVIEW

Carbon Monoxide Poisoning: Pathogenesis, Management, and Future Directions of Therapy

Jason J. Rose[1,2], Ling Wang[1,2], Qinzi Xu[1], Charles F. McTiernan[1], Sruti Shiva[1,3,4], Jesus Tejero[1,2], and Mark T. Gladwin[1,2]

[1]Pittsburgh Heart, Lung, Blood and Vascular Medicine Institute, [2]Division of Pulmonary, Allergy, and Critical Care Medicine, School of Medicine, [3]Department of Pharmacology and Chemical, and [4]Center for Metabolism and Mitochondrial Medicine, University of Pittsburgh, Pennsylvania

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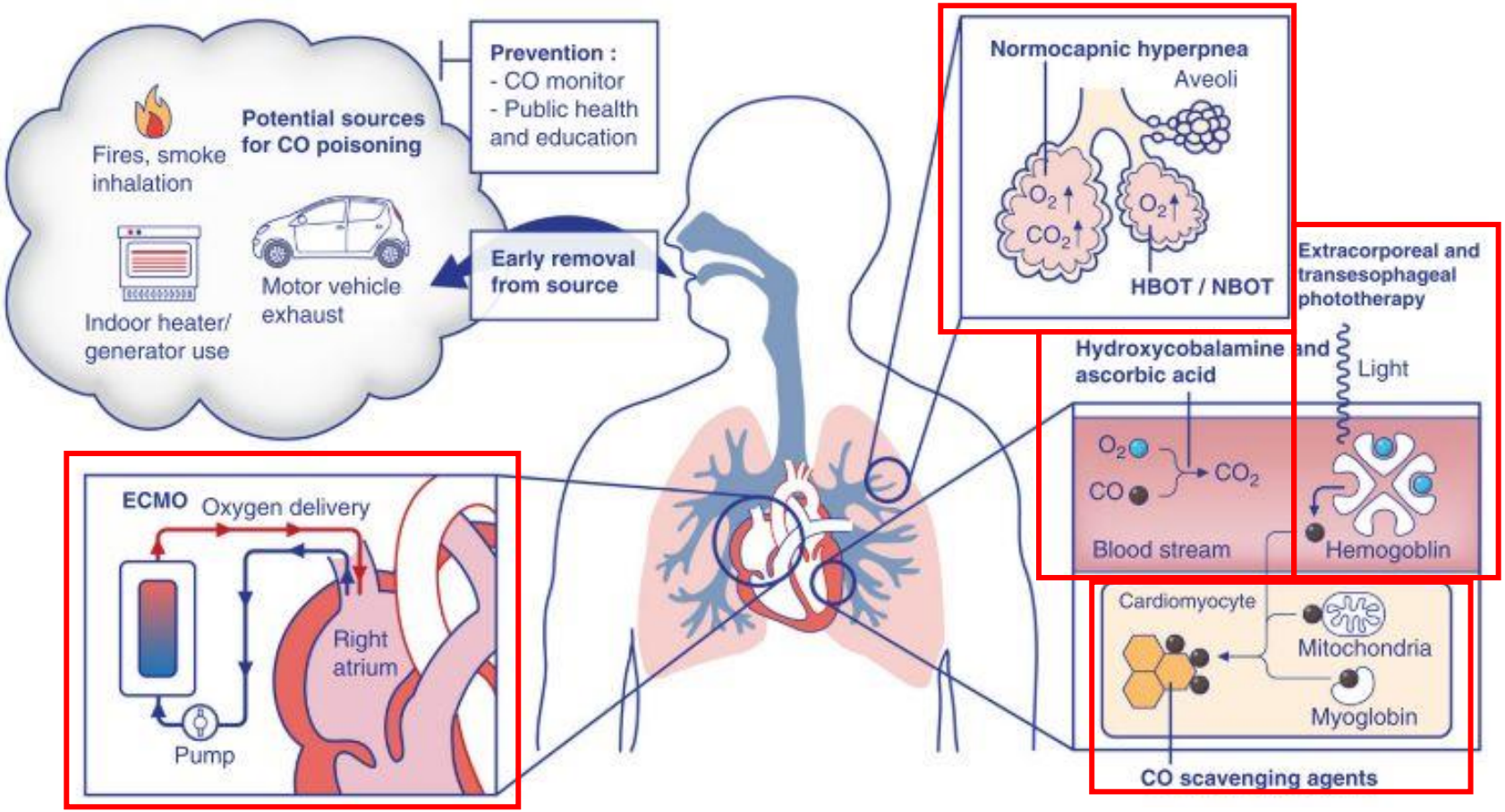
Rose, J. J., et al. (2017). Am J Respir Crit Care Med 195(5): 596-606.

Nonpharmacologic + pharmacologic options

Although none has demonstrated improved neuorocognitive outcomes, many show promising early results and should be further studied.



Alternative Strategies for Treating Carbon Monoxide Poisoning Targeting Downstream Effects

Agent (Ref. No.)	Species	Effect
Inflammation		
Allopurinol (110)	Rats	Reduced neuronal death, reduced expression of proinflammatory markers, and improved performance in Morris water maze
Corticosteroids plus amifostine (111)	Rats	Reduced lipid peroxides
Methylprednisolone plus memantine (112)	Humans	Case report: reversed delayed neurocognitive deficits that appeared at Week 3 by Week 12
Ketamine (113)	Rats	Reduced cerebral edema, blood lactate levels, and improved survival
Oxidative stress		
Hydrogen sulfide (114)	Rats	Improved cognitive function, reduced apoptosis and inflammatory response, decreased oxidative damage in brains
Fructose-1,6-diphosphate (115)	Mice	Reduced impairment of memory function, improved mortality
Magnesium sulfate (116)	Rats	Protective versus oxidative damage in cerebrum
Cardiac dysfunction		
Levosimendan (117)	Humans	Case report: improved ejection fraction in stunned myocardium
Atenolol (118)	Rats	Pretreatment associated with increased contraction band necrosis
Nimodipine (115)	Mice	Decreased impairment of memory function and improved mortality rate
Verapamil (113)	Rats	No improvement in survival, blood pressure, blood lactate, or cerebral edema

2. Recent papers

Check for updates

Unsolicited Review

Human and Experimental Toxicology
1–8
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Current and research therapies for the prevention and treatment of delayed neurological syndrome associated with carbon monoxide poisoning: A narrative review

B del Moral-Barbudo[1], R Blancas[1,2], D Ballesteros-Ortega[1,3], M Quintana-Díaz[1,4] and Ó Martínez-González[1,2]

Del Moral-Barbudo, B., et al. (2020). Hum Exp Toxicol 39(6): 765-772.

Effects of Adjunctive Therapeutic Hypothermia Combined With Hyperbaric Oxygen Therapy in Acute Severe Carbon Monoxide Poisoning

Sun Ju Kim, MD[1]; Stephen R. Thom, MD, PhD[2]; Hyun Kim, MD, PhD[1,3]; Sung Oh Hwang, MD, PhD[1]; Yoonsuk Lee, MD[1,3]; Eung Joo Park, MS[4]; Seok Jeong Lee, MD[5]; Yong Sung Cha, MD[1,3]

Kim, S. J., et al. (2020). Crit Care Med 48(8): e706-e714.

The mechanisms underlying HBO effects

1) Reversal of cytochrome binding
2) Preservation of ATP
3) Adaptive/protective oxidative stress response through increased HO-1, upregulation and modulation of various antioxidant enzymes, and induction of heat shock protein
4) Reduced MPO activity
5) Reduced leukocyte adhesion, inhibition of immune response, and blocking of XD conversion to XO
6) Prevention of brain lipid peroxidation
7) Muted adduct formation and blocked inflammatory response to altered MBP
8) Decreased HIF-1 expression
9) Reduced necrosis and protection from apoptosis

The mechanisms underlying TH effects

1) Decreased cerebral metabolism
2) Reduced mitochondrial dysfunction and improved energy homeostasis
3) Reduced excessive free radical production
4) Mitigated reperfusion injury
5) Depressed immune response and proinflammatory reaction
6) Improved ion homoeostasis
7) Reduced apoptosis
8) Fever can adversely affect neurologic outcome in various types of neurologic injuries, while TH can control fever.

TABLE 2. Outcome Data for the No-Therapeutic Hypothermia and Therapeutic Hypothermia Groups

Variables	No-TH ($n = 16$)	TH ($n = 21$)	p
GDS			
1 mo	7.0 (3.0–7.0)	5.0 (1.0–7.0)	0.078
Favorable outcome (GDS, 1–3)	1 (6.3)	7 (33.3)	0.104
Poor outcome (GDS, 4–7)	15 (93.8)	14 (66.7)	
6 mo	7.0 (2.0–7.0)	3.0 (1.0–7.0)	0.015
Favorable outcome (GDS, 1–3)	2 (12.5)	11 (55.0)	0.008
Poor outcome (GDS, 4–7)	14 (87.5)	9 (45.0)	
Improvement in GDS score at 6 mo than at 1 mo	3 (18.8)	13 (65.0)	0.006
Carbon monoxide–related mortality	4 (25.0)	4 (19.0)	0.705

GDS = Global Deterioration Scale, TH = therapeutic hypothermia.

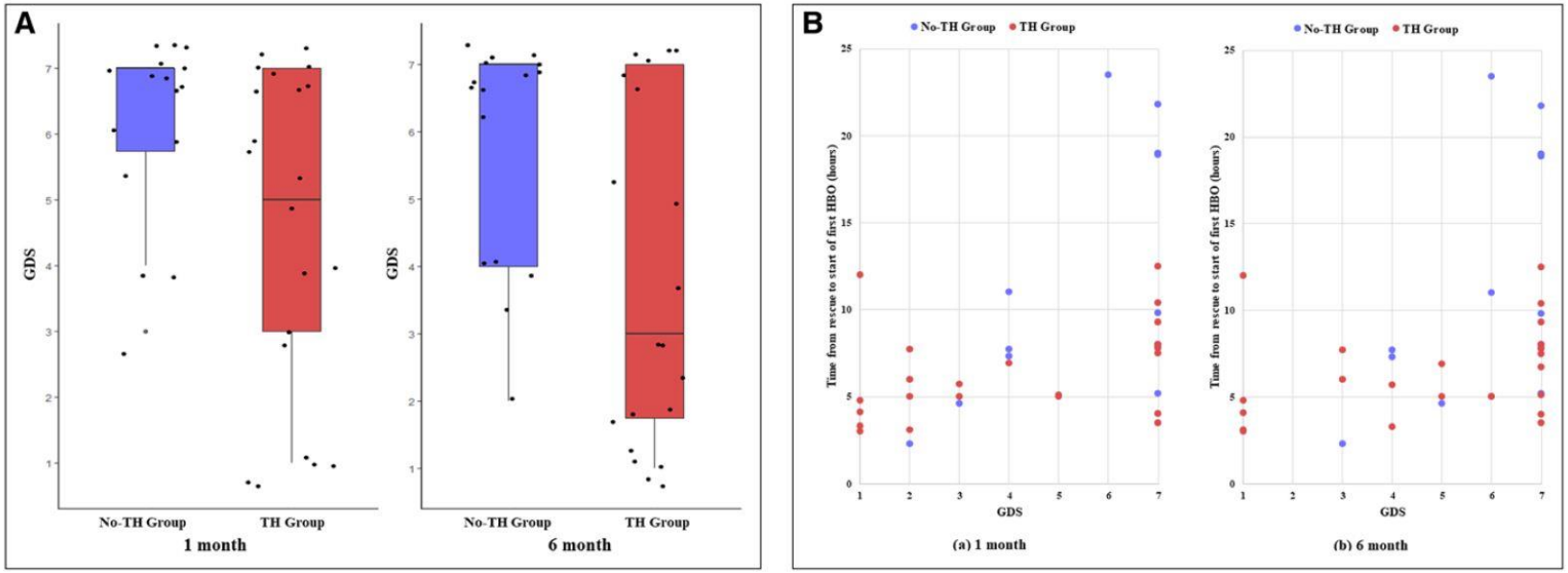


Figure 3. Comparison of Global Deterioration Scale (GDS) (**A**) and time from rescue to the start of the first hyperbaric oxygen therapy (HBO) (**B**) between no-therapeutic hypothermia (TH) and TH groups.

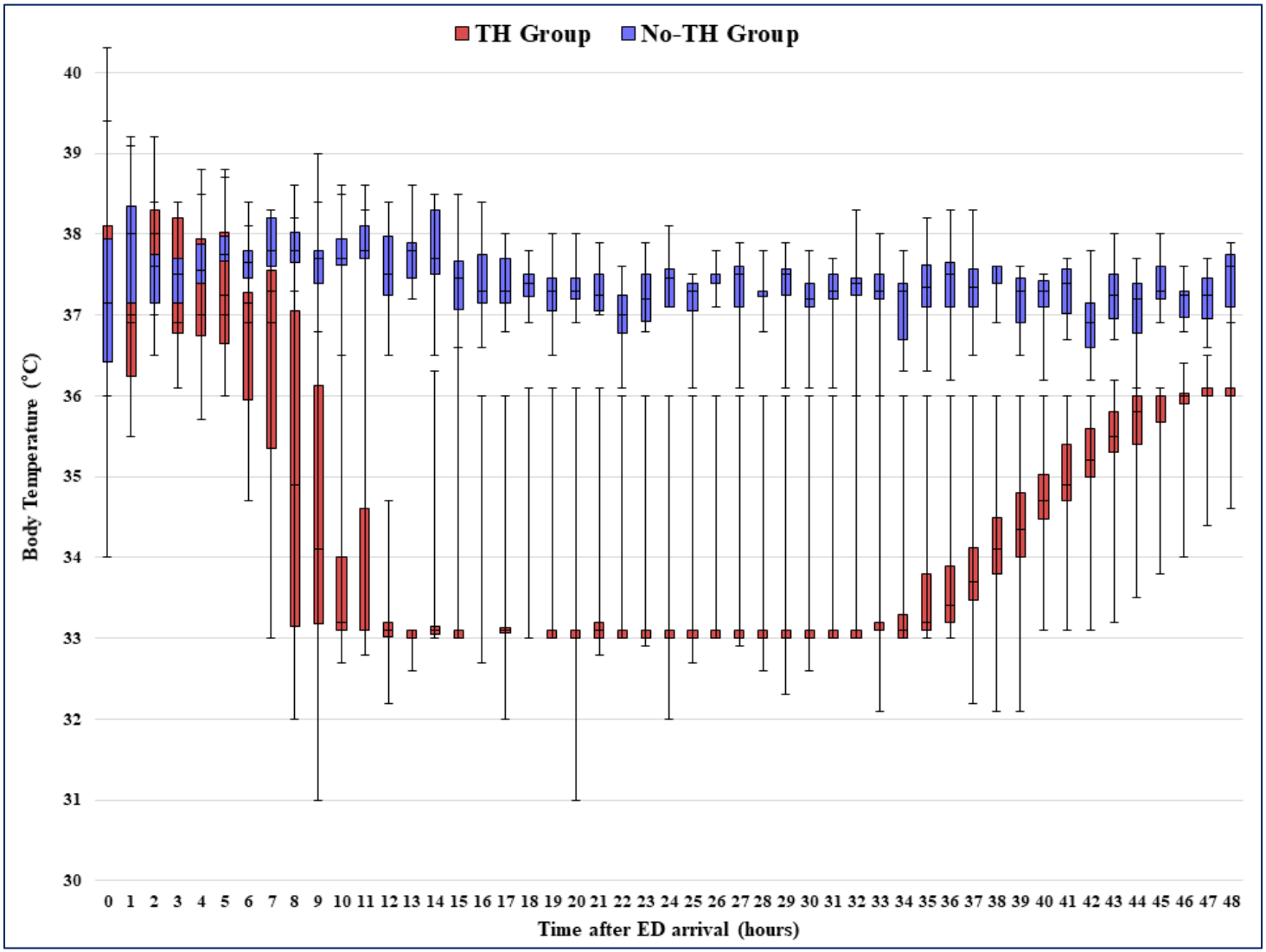
Supplemental Table 2. Baseline characteristics and outcome data in patients who received HBO within 6 h (A) and over 6 h (B) after rescue

(A)

GDS			
1 month	7.0 (3.0 – 7.0)	4.0 (1.0 – 7.0)	0.069
Favorable outcome (GDS 1-3)	1 (20.0)	5 (45.5)	0.588
Poor outcome (GDS 4-7)	4 (80.0)	6 (54.5)	
6 months	7.0 (2.0 – 7.0)	3.0 (1.0 – 5.0)	0.027
Favorable outcome (GDS 1-3)	2 (40.0)	9 (69.2)	0.245
Poor outcome (GDS 4-7)	3 (60.0)	2 (18.2)	
Improvement in GDS score at 6 months than at 1 month	2 (40.0)	10 (90.9)	0.063
CO-related mortality	3 (60.0)	0 (0.0)	0.018

(B)

GDS			
1 month	7.0 (4.0 – 7.0)	7.0 (1.0 – 7.0)	0.973
Favorable outcome (GDS 1-3)	0 (0.0)	2 (20.0)	0.214
Poor outcome (GDS 4-7)	11 (100)	8 (80.0)	
6 months	7.0 (4.0 – 7.0)	7.0 (1.0 – 7.0)	0.824
Favorable outcome (GDS 1-3)	0 (0.0)	2 (22.2)	0.189
Poor outcome (GDS 4-7)	11 (100)	7 (77.8)	
Improvement in GDS score at 6 months than at 1 month	1 (9.1)	3 (33.3)	0.285
CO-related mortality	1 (9.1)	4 (40.0)	0.149


TH Group
No-TH Group
Body Temperature (°C)
40
39
38
37
36
35
34
33
32
31
30
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48
Time after ED arrival (hours)

3. Conclusion

There is no approved treatment in acute CO poisoning except for HBO.

Where to from here?

More basic work:

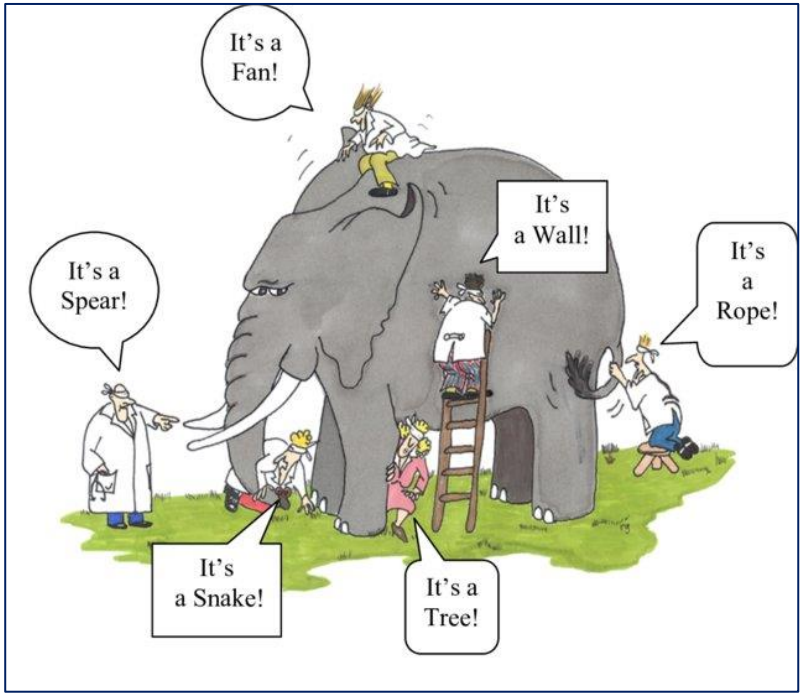
"What's the opposite of 'Eureka'?"

- Further research on the pathophysiology of ACOP should be needed to develop new treatments.

- International collaboration

Clinical Trials:

More well designed



Thank you
for Your Attention !!!