



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 70265

**Title:** Hydrogen inhalation promotes recovery of a patient in persistent vegetative state from intracerebral hemorrhage: A case report and literature review

**Provenance and peer review:** Unsolicited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05467628

**Position:** Peer Reviewer

**Academic degree:** MBBS

**Professional title:** Doctor, Research Fellow

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-08-10

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-08-10 15:11

**Reviewer performed review:** 2021-08-20 07:48

**Review time:** 9 Days and 16 Hours

|                           |   |
|---------------------------|---|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |



|                                 |   |
|---------------------------------|---|
| <b>Peer-reviewer statements</b> | Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous<br>Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No |
|---------------------------------|---|

### **SPECIFIC COMMENTS TO AUTHORS**

This is an interesting case report of hydrogen gas inhalation promoting the recovery of an 11-year-old boy with persistent vegetative state. I have the following comments in no particular order:

1. Please do not consider that the journal reviewers do not look at the uploaded files. CARE checklist has been filled in a manner as if to simply do away with a formality. Please re-upload with correctly filled checklist with page and line number.
2. Please write imaging findings properly. Authors write 'X ray shadows on CT'. This is not technically correct.
3. Please remove this line from the conclusion: "High-concentration of hydrogen gas inhalation may be an effective intervention for PVS and the recovery of other brain dysfunction caused by ICH" --> This case report does not allow us to make this conclusion. The main conclusion is: "Phase 1 Clinical trials are needed to explore the safety and efficacy of hydrogen gas inhalation in persistent vegetative state."
4. Kindly make the corresponding change in both main text and abstract.
5. Figure 2 the scale is incorrect. Some units are separated by one month and some units are separated by just 15 days (but have equal distance between them). Kindly redraw to scale.
6. Wrong statement here: "In brief, these clinical observations suggested the potential effects of high concentration hydrogen gas inhalation on consciousness recovery, and muscle tone, locomotor function, and other health conditions were significantly improved in this patient with ICH-induced PVS." Please change to: "In brief, these clinical observations suggested a possible beneficial role of high concentration hydrogen gas inhalation on consciousness recovery, and muscle tone, locomotor function in this patient with ICH-induced PVS."



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**Reviewer's code:** 05221155

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Taiwan

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-08-10

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-08-11 23:32

**Reviewer performed review:** 2021-08-24 09:00

**Review time:** 12 Days and 9 Hours

|                           |   |
|---------------------------|---|
| <b>Scientific quality</b> | <input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |



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|-------------------------------------|---|
| <b>Peer-reviewer<br/>statements</b> | Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous<br>Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No |
|-------------------------------------|---|

### **SPECIFIC COMMENTS TO AUTHORS**

This report presents a successful treatment using high-dose hydrogen gas in a child who was diagnosed as persistent vegetative state for two months. The use of molecular hydrogen in the complementary treatment of neurological disorder has been proven by a large number of pre-clinical studies. The neuroprotective effects of molecular hydrogen are attributed to its anti-oxidative and anti-inflammatory property. A clinical trial further demonstrated its therapeutic effects in patients with SAH. However, the standard usage of gas hydrogen are limited to 1~4 % in concentration due to the explosive property of high-dose gas hydrogen. The authors hypothesized that high-dose hydrogen gas (66.7%) may be benefit to VGS patients. The idea may come from a study which indicated that higher dose of hydrogen gas (40%) showed therapeutic effects on ischemic stroke animal models. Nevertheless, this case is the first reported PVS case who responded to high-dose hydrogen gas treatment, thus, provides a clue for the connection between bench and bedside. Case reports with more cases or randomized control trials using the same strategy for the treatment of stroke patients who develop PVS lately may be a direction to provide the evidences of safety and efficacy in the future. The case presentation is comprehensive but the words are a little bit too lengthy for a case report.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-08-10

**Reviewer chosen by:** Jing-Jie Wang (Online Science Editor)

**Reviewer accepted review:** 2021-10-20 10:09

**Reviewer performed review:** 2021-10-20 10:21

**Review time:** 1 Hour

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|---------------------------|---|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Peer-reviewer</b>      | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous   |



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statements

Conflicts-of-Interest: [ ] Yes [Y] No

### **SPECIFIC COMMENTS TO AUTHORS**

The manuscript has been revised but the same issue of overreach remains present. Authors continue to use over reaching statements in their manuscript. When reviewer points to an issue of overreach and asks you to make one change in one place, then it is the authors' responsibility to make corresponding change at other places as well. This manuscript CANNOT HAVE ANY LANGUAGE that is taken to mean "hydrogen gas is effective for VGS treatment". This is a wrong conclusion and having this published will make authors and journal editors be seen as having insufficient quality control. This manuscript's language needs to be toned down at all places. Phrases like "suggests a possible role" " may have some effect which needs further investigation" "more evidence is needed" "no conclusive therapeutic evidence" should be used. 1. The first page of revised manuscript file below title section states: "Hydrogen Ameliorates Persistent Vegetative State" \_ WRONG CONCLUSION. 2. "Core tip: This case indicates that inhalation of hydrogen maybe may be an effective intervention candidate for patients with loss of consciousness." - please tone down further. 3. "Accumulated clinical and experimental biomedical evidence in a variety of models of different diseases HAS PROVEN that molecular hydrogen, administered either through gas inhalation or aqueous solution consumption, can act as a scavenger to selectively alleviate ROS and exert potent cellular protective effects." - Kindly change to "has suggested". These studies are in animals. No RCT exists.