

Peer Review File

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Reviewer Comments

Comment 1: Lines 160 – 164: Not too sure if this is guideline driven or opinion of the authors. Please quote a journal why you have chosen this protocol. If this is an expert opinion, then why this approach was made. They quoted a journal stating that the safe range for iNO therapy is 5-40 ppm. But the consensus guideline “Inhaled nitric oxide therapy in neonates and children: reaching a European consensus” by Macrae et al mentioned “Four published studies have reported dose-response data for this group of babies. All four studies suggest that a maximal beneficial effect of iNO is already seen at concentrations of less than 30 ppm. Further increases of iNO (to 80–100 ppm) do not appear to result in further improvement of oxygenation above that achieved at 20–30 ppm.”

Reply 1: Many thanks for your comment. What we did not mention in the original text is that the initial dose of NO was 20 ppm, and the oxygenation status of the child was not improved after half an hour. Therefore, we adjusted the dose to 40 ppm. After realizing that the oxygenation and hemodynamics of the child were improved, we decided to maintain the therapeutic dose.

Changes in the text: We added some instructions.(see Page 03, line 67-69)

Comment 1a: Not too sure if this 40ppm iNO had likely predisposed the child to have methemoglobinemia. Maybe a justification should have been made in the last sentence of that paragraph.

Reply 1a: Many thanks for your comment. Before diagnosis, we ruled out other possible causes of methemoglobinemia in this child.

Changes in the text: We added some exclusionary diagnosis.(see Page 04, line 84-85)

Comment 2: Line 76 seems to be too broad. They mentioned in the discussion that they have mentioned G6PD is normal but didn't mention in the clinical story nor hemolytic markers such as LDH, Haptoglobin and total bilirubin.

Reply 2: Many thanks for your comment. As mentioned in the discussion section, methylene blue is ineffective in patients with G6PD deficiency and may even cause hemolysis. Since this was an emergency, we tested the patient's G6PD levels and administered methylene blue before the results returned. After that, the G6PD, LDH, Haptoglobin and total bilirubin levels were normal. Fortunately, the patient's hypoxia was relieved, and no hemolysis occurred. We have added explanations in the case.

Changes in the text: We added some explanations in the case section.(see Page 04-05, line 88-91)

Comment 2a: Did they do an ultrasound of the lung to make sure its aeriated and no pleural effusion causing the low O2 saturation. Or perhaps it was done but omitted in the report as it is not indicated in this case?

Reply 2a: We performed bedside ultrasound and chest radiographs to rule out possible causes of hypoxia, including tracheal tube position, pneumothorax, pleural effusion, and pulmonary edema. Due to the length of the article, it was not mentioned in the case.

Changes in the text: We added some explanations .(see Page 04, line 81-82)

Comment 3: Lines 138 regarding Co-oximeter, is this used with the patient as well? If so, please correlate. If not, then perhaps please put ideally or good to mention.

Reply 3: Many thanks for your comment. Since Co-oximeter is not available in our facility, it is recommended as a noninvasive and reliable monitoring method for oxygen saturation in patients treated with NO.

Changes in the text: We added some explanations in the discussion section.(see Page 07, line 143-145)

Comment 4: Lines 113 - 133 this too complicated and barely decipherable for a clinician. Recommend summarizing or use simple terms. Maybe use connection adjectives like: "furthermore, in addition, or however". Some sentences seems to disconnect as it was quoted from reference #10 then reference #8.

Reply 4: Many thanks for your comment. We have revised the relevant expression, please review it again.

Changes in the text: We have revised the relevant expression.(see Page 06-07, line 122-137)

5. Overall paper is well written. Figures are impressive.

Reply 5: Thank you very much for your comments.

Other comments/ edits are attached in the review document.