

Letters to the Editor

Letter to the Editor: "Nitrogen Wash Out to Inhaled Nitric Oxide"

Dear Editor,

We want to congratulate and acknowledge the work done by Manzar et al. regarding their study entitled "Nitrogen Wash Out to Inhaled Nitric Oxide." This compelling case study underscores the importance of careful consideration in managing pneumothorax in newborn infants. Although a customary practice, the nitrogen washout method using 100% oxygen warrants caution, as demonstrated by the development of pulmonary hypertension in the presented case.

The comprehensive exploration of maternal and birth history provides crucial context, enriching the reader's comprehension of the case. The authors provided detailed documentation of the hospital course, including diagnostic procedures and treatment interventions, which deeply imbues the narrative and promotes learning. Incorporating pertinent literature, such as the study by Shireen et al. and insights into the mechanism of nitrogen washout and its potential pitfalls, further enhances the discussion. Moreover, the discourse on hyperoxia-induced pulmonary hypertension, supported by recent research findings, strengthens the argument for prudent oxygen administration in neonatal pneumothorax cases.

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While the discussion adeptly connects the case study findings to existing literature, a deeper exploration of potential mechanisms underlying the observed effects of nitrogen washout would be beneficial. Additionally, elucidating procedural cautions to avoid neonatal pneumothorax during nitrogen washout procedures would enhance comprehension of best practices. For healthcare professionals, this study stimulates reflection on current practices and raises awareness of potential complications associated with hyperoxia therapy.

We want to provide further commentary and ask questions about the study. The study presents a valuable case regarding the management of pneumothorax in a newborn infant. It is significant to discuss the use of nitrogen washout and the subsequent development of pulmonary hypertension due to hyperoxia as it adds to the existing literature on this topic. As 100% oxygen is commonly used, it is crucial to include potential complications from its use, such as the development of pulmonary hypertension, as eloquently addressed in the case report by Manzar et al. However, our question to the authors is how the development of pulmonary hypertension occurred due to treating the pneumothorax with 100% oxygen. Multiple variables could be involved, and pulmo-

nary hypertension is a complex phenomenon. According to the Pulmonary Hypertension Association, there are 5 Groups of Pulmonary hypertension, with the types further categorized by the World Health Organization (WHO) (1). Further characterizing the group and type of pulmonary hypertension would allow readers to understand its manifestation from 100% oxygen use.

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Furthermore, it would be helpful if the authors outline the pathophysiology of the development of pulmonary hypertension following treatment. Doing so while factoring in other variables and ruling out other differential diagnoses would better clarify the relationship between pulmonary hypertension and the treatment of pneumothorax with the nitrogen washout method. Outlining the pathophysiology in this case report is especially important because some literature shows that using 100% oxygen could benefit patients with pulmonary hypertension since it can lead to pulmonary vasodilation, increased cardiac output, and decreased peripheral vascular resistance (2). Explaining the reasoning behind the development of pulmonary hypertension would clarify the cause-and-effect relationship between pulmonary hypertension and the use of the nitrogen washout method, as there is some current literature that refutes what the case report concludes—doing so while including other treatment options as alternatives to 100% oxygen would educate practitioners and provide other options for optimal medical management of pneumothorax.

"Outlining the pathophysiology in this case report is especially important because some literature shows that using 100% oxygen could benefit patients with pulmonary hypertension since it can lead to pulmonary vasodilation, increased cardiac output, and decreased peripheral vascular resistance (2)."

In addition to 100% oxygen being useful, other studies show it can also have no benefit. In a study by Clark et al., researchers found no clinically significant advantages to using 100% oxygen versus targeted oxygen saturation levels in managing pneumothorax (3). Longer exposures to elevated oxygen levels increased the risk of toxicity and further prolonged the need for oxygenation. As men-

tioned before, it is interesting that 100% oxygen has been commonly used for so long in frequent practice despite growing evidence that it may not necessarily resolve a pneumothorax versus other measures, where, in some cases, it may even lead to complications. It asks if other possibilities and studies have been conducted to assess alternative management methods. Therefore, we ask a second question to address whether other studies are conducted to assess alternative management for pneumothorax.

“In aiming for conservative management of pneumothorax, oxygen levels can be catered towards different values based on factors such as symptoms and physical examination findings to help guide the properly targeted oxygen levels instead of resorting to 100% oxygenation in all instances while further reducing potential complications associated with using 100% oxygen.”

We further suggest expanding on the caution of using 100% oxygen to manage pneumothorax. In a study by Shaireen et al., researchers evaluated different methods and levels of oxygenation in neonates regarding the resolution of pneumothorax. Their study, 21% FiO₂, >60% FiO₂, and <60% FiO₂, found no significant difference between each supplemental oxygen parameter in the resolution of pneumothorax (4). This further lends credence to findings that 100% oxygen is not necessarily required in managing a neonatal pneumothorax. Additionally, in a later study done in 2023 by Jouneau et al., researchers aimed to create guidelines for managing primary spontaneous pneumothorax. The study stated that even large pneumothorax (>30%) could see benefits in low-flow oxygen therapy (2-4 L per minute) that was associated with an increased rate of resolution (5). In aiming for conservative management of pneumothorax, oxygen levels can be catered towards different values based on factors such as symptoms and physical examination findings to help guide the properly targeted oxygen levels instead of resorting to 100% oxygenation in all instances while further reducing potential complications associated with using 100% oxygen.

Addressing management while including other sources to support the study by Manzar et al. would clarify why the 100% oxygen method may not be the best choice for optimal management.

Another valuable point to address is retinopathy of prematurity (ROP), an adverse effect of using high oxygen levels. When babies are born prematurely, they may need extra oxygen to help them breathe. However, high oxygen levels can damage the developing blood vessels in the retina. This can lead to abnormal blood vessel growth, which is the hallmark of ROP. ROP is typi-

cally staged from 1 to 5, with stage 5 being the most severe. In the initial stages of ROP, there may be no symptoms. However, as the disease progresses, a baby may develop a detached retina, Cloudiness in the cornea, Cataracts, or Glaucoma (6). Considering this, it is worthwhile for the authors Manzar et al. to discuss why high oxygen levels should not be used when considering a pneumothorax, especially in a premature infant, rather than the term infant described in the case.

“In conclusion, while the study by Manzar et al. offers valuable insights into pneumothorax management, further research and discussion are warranted to optimize neonatal care and minimize adverse outcomes associated with oxygen therapy. Describing what procedural precautions should be implemented to avoid neonatal pneumothorax during the nitrogen washout procedure would help understand better practices.”

In conclusion, while the study by Manzar et al. offers valuable insights into pneumothorax management, further research and discussion are warranted to optimize neonatal care and minimize adverse outcomes associated with oxygen therapy. Describing what procedural precautions should be implemented to avoid neonatal pneumothorax during the nitrogen washout procedure would help understand better practices. We encourage future studies to explore alternative oxygenation methods and delve deeper into the pathophysiology of pulmonary hypertension development post-treatment. Overall, your manuscript will contribute meaningfully to the literature on neonatal respiratory care.

References:

1. “Types of Pulmonary Hypertension: The Who Groups.” *About Pulmonary Hypertension*, Pulmonary Hypertension Association, 13 Dec. 2023, phassociation.org/types-pulmonary-hypertension-groups/.
2. Roberts, David H., et al. “Oxygen therapy improves cardiac index and pulmonary vascular resistance in patients with pulmonary hypertension.” *Chest*, vol. 120, no. 5, Nov. 2001, pp. 1547–1555, <https://doi.org/10.1378/chest.120.5.1547>.
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4. Shaireen, H., Rabi, Y., Metcalfe, A. *et al.* Impact of oxygen concentration on time to resolution of spontaneous pneumothorax in term infants: a population based cohort study. *BMC Pediatr* 14, 208 (2014). <https://doi.org/10.1186/1471-2431-14-208>
5. Jouneau, S., Ricard, JD., Seguin-Givelet, A. *et al.* SPLF/SMFU/SRLF/SFAR/SFCTCV Guidelines for the management of patients with primary spontaneous pneumothorax. *Ann. Intensive Care* 13, 88 (2023). <https://doi.org/10.1186/s13613-023-01181-2>
6. Retinopathy of prematurity and oxygen therapy: A changing relationship. Bueno, M., *et al.* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3740273/>

Mona Singh, OSMIII, Andy Ngo, OSMIII, Priya Kishore, OSMIII, Geoffrey Lo, OSMIII

Dear Mona Singh, OSMIII, Andy Ngo, OSMIII, Priya Kishore, OSMIII, Geoffrey Lo, OSMIII,

Thank you for your thoughtful and comprehensive letter regarding the study by Manzar *et al.*, "Nitrogen Wash Out to Inhaled Nitric Oxide." Your engagement and detailed analysis contribute significantly to the ongoing discussion of optimal management strategies for neonatal pneumothorax, and we appreciate your efforts to highlight both the strengths and areas for further exploration in the study.

"Your commendation of the study's detailed documentation and contextual background is well noted. The comprehensive approach taken by Manzar *et al.* indeed enriches our understanding of the complexities involved in managing such critical cases. The meticulous documentation of maternal and birth history, along with the thorough description of the hospital course, including diagnostic procedures and treatment interventions, provides a robust framework for understanding the clinical decisions made in this case."

Your commendation of the study's detailed documentation and contextual background is well noted. The comprehensive approach taken by Manzar *et al.* indeed enriches our understanding of the complexities involved in managing such critical cases. The meticulous documentation of maternal and birth history, along with the thorough description of the hospital course, including diagnostic procedures and treatment interventions, provides a robust framework for understanding the clinical decisions made in this case. This level of detail is invaluable for practitioners and researchers alike, as it allows for a deeper comprehension of the case's nuances and facilitates learning.

Your insights on the potential mechanisms and the need for a deeper exploration into the pathophysiology of pulmonary hypertension (PH) induced by 100% oxygen are valuable. Pulmonary hypertension is a complex and multifaceted condition with various underlying mechanisms that require careful delineation. By categorizing the type of PH according to the Pulmonary Hypertension Association and WHO classifications, the study could provide a clearer picture of the specific pathophysiological processes involved. This would not only enhance the clarity and applicability of the findings but also contribute to a more precise understanding of the relationship between oxygen therapy and the development of PH in neonatal patients.

"Providing specific procedural cautions and best practices would be immensely beneficial for healthcare professionals managing similar cases. This would not only help in avoiding potential complications but also ensure that the treatment protocols are safe and effective. The inclusion of such guidelines would enhance the study's utility and impact, making it a more valuable resource for clinicians."

Additionally, your request for more detailed procedural guidelines to prevent neonatal pneumothorax during nitrogen washout underscores the need for practical recommendations that can be directly applied in clinical settings. Providing specific procedural cautions and best practices would be immensely beneficial for healthcare professionals managing similar cases. This would not only help in avoiding potential complications but also ensure that the treatment protocols are safe and effective. The inclusion of such guidelines would enhance the study's utility and impact, making it a more valuable resource for clinicians.

The discussion you bring up regarding alternative oxygenation strategies, supported by evidence from Clark *et al.*, Shaireen *et al.*, and Jouneau *et al.*, adds a crucial dimension to the debate on using 100% oxygen in treating neonatal pneumothorax. The contrasting evidence on the efficacy and safety of 100% oxygen therapy versus other approaches is essential for fostering a nuanced understanding of the best practices. This highlights the importance of individualized patient care and the need for ongoing research to optimize treatment protocols. The evidence you present suggests that lower concentrations of oxygen may be equally effective, if not more beneficial, in resolving pneumothorax while minimizing the risk of complications associated with hyperoxia.

Your emphasis on the potential risks of high oxygen levels, such as retinopathy of prematurity (ROP), further underscores the necessity for cautious oxygen administration, particularly in premature infants. ROP is a significant concern in neonatal care, and the potential for high oxygen levels to exacerbate this condition cannot be overlooked. Your call for the authors to discuss why high oxygen levels should not be used in treating pneumothorax, especially in premature infants, is well-founded. Including this discussion would provide a more comprehensive understanding of the risks associated with high oxygen therapy and help guide

more prudent clinical practices.

Furthermore, your letter raises important questions about the pathophysiology of PH following 100% oxygen therapy. The call for a detailed explanation of how PH develops in the context of treating pneumothorax with 100% oxygen is crucial. Understanding the underlying mechanisms is essential for clinicians to make informed decisions about treatment strategies. By elucidating the pathophysiological pathways and considering other variables that could contribute to the development of PH, the study could provide clearer insights into the cause-and-effect relationship between oxygen therapy and PH. This would also help in ruling out other differential diagnoses and ensuring that the observed effects are accurately attributed to the treatment method used.

“The contrasting findings in the literature regarding the benefits and risks of 100% oxygen therapy further highlight the need for careful consideration of alternative management strategies. The study by Clark et al., which found no significant advantages to using 100% oxygen compared to targeted oxygen saturation levels, suggests that there may be safer and equally effective ways to manage pneumothorax.”

The contrasting findings in the literature regarding the benefits and risks of 100% oxygen therapy further highlight the need for careful consideration of alternative management strategies. The study by Clark et al., which found no significant advantages to using 100% oxygen compared to targeted oxygen saturation levels, suggests that there may be safer and equally effective ways to manage pneumothorax. Similarly, the findings by Shaireen et al. and Jouneau et al. support the notion that lower concentrations of oxygen can be effective in resolving pneumothorax and may reduce the risk of oxygen toxicity. These studies collectively call into question the traditional reliance on 100% oxygen and suggest that more conservative approaches may be preferable.

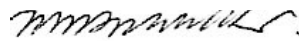
Your letter also underscores the importance of expanding on the caution of using 100% oxygen to manage pneumothorax. By referencing studies that evaluated different methods and levels of oxygenation in neonates, you provide a broader context for understanding the potential risks and benefits of various oxygenation strategies. This evidence supports the need for guidelines that recommend targeted oxygen levels based on individual patient factors rather than a one-size-fits-all approach. Such guidelines would help reduce the potential complications associated with high oxygen therapy and promote safer, more effective management of pneumothorax in neonates.

Finally, your suggestion to explore other treatment options for pneumothorax is particularly relevant. The current evidence indicates that there may be viable alternatives to 100% oxygen therapy that could offer similar benefits without the associated risks. Encouraging further research into these alternatives could lead to the development of more refined and effective treatment protocols, ultimately improving patient outcomes.

In conclusion, your letter provides a rich, multifaceted perspective on the study by Manzar et al. and raises important questions that warrant further research and discussion. We encourage the authors to consider these insights in their future work to refine and enhance neonatal respiratory care practices. Your contributions help drive the field forward, promoting a deeper understanding and better clinical outcomes for our youngest patients. Thank you for your valuable input and for engaging in this critical dialogue.

Best regards,

Sincerely,



Mitchell Goldstein, MD, MBA, CML

Editor in Chief



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Erratum (Neonatology Today April, 2024)

We regret that there was an author's name missing in "Case Report: Neonatal Intraventricular Hemorrhage in E. coli K1 Meningitis." Nobel Enayati, OSMIII was missing from the list of authors. This will be corrected in the PDF available on-line

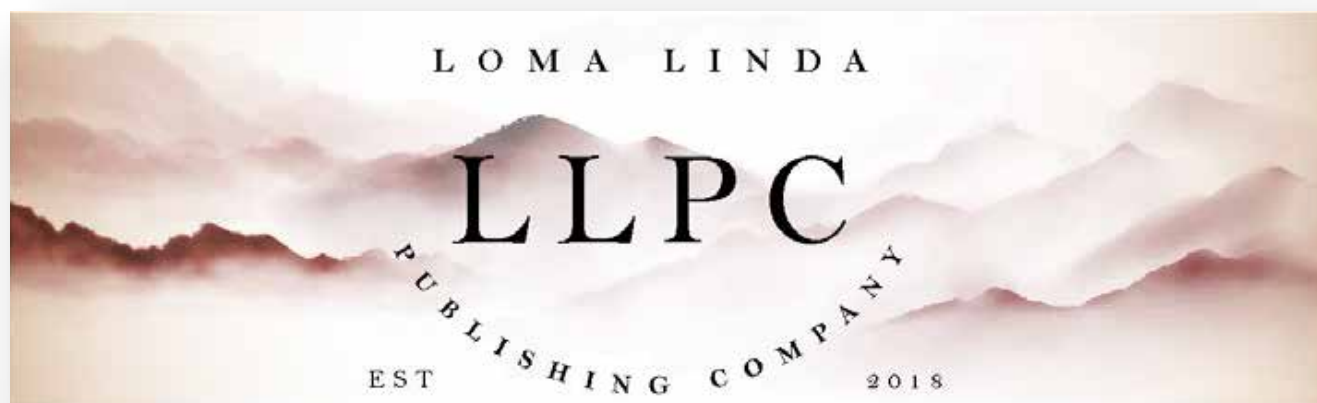
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