Medicina Intensiva 48 (2024) 180–182

medicina intensiva

http://www.medintensiva.org/en/

LETTER TO THE EDITOR

Expanding the evidence: A brief updated analysis of short-term mortality in conservative oxygen therapy versus liberal oxygen therapy in intensive care unit patients

Ampliando la evidencia: breve análisis actualizado de la mortalidad a corto plazo en la oxigenoterapia conservadora frente a la oxigenoterapia liberal en pacientes de unidades de cuidados intensivos

Dear Editor,

Medical research and clinical decision-making are based on the constant evolution of scientific evidence. In this context, the publication of meta-analyses and systematic reviews is essential to provide guidance to health care professionals. The recently published study, ''Conservative versus liberal oxygen therapy in relation to all-cause mortality among patients in the intensive care unit: a systematic review of randomized controlled trials with meta-analysis and trial sequential analysis''[1] provides a valuable analysis of the medical literature current available up to the date of its analysis, and sheds light on the implications of oxygen therapy in patients at the ICU setting. However, the ever-evolving nature of medical research has given us a new opportunity to expand and enrich its conclusions. The aim of this article is to present a brief updated analysis—including additional studies recently published—to provide a more comprehensive and up-to-date view of short-term mortality in conservative oxygen vs liberal oxygen therapy in patients at the ICU setting.

To identify the new relevant studies that should be added to this updated analysis, a search was conducted in the Cochrane Plus database. The search was conducted using its advanced search panel, and specific criteria were applied to guarantee the inclusion of relevant articles. The following English search terms were used: ''liberal oxygen therapy'' and ''conservative oxygen therapy.'' A temporal filter was applied to include only studies published over the past 3 years to ensure the inclusion of the most recent evidence available. Also, the search was limited to clinical trials to guarantee the quality and relevance of the studies selected for this updated analysis. The search strategy was conducted systematically, following Cochrane Plus guidelines and adhered to best practices available in medical literature review. The studies identified through this process underwent a selection and evaluation process, and those that met the inclusion criteria were considered for further analysis in this article.

Short-term mortality was defined as a clinical outcome: studies reporting on 28-day mortality rates were included by default, as this timeframe is a commonly accepted indicator of early clinical outcomes in critically ill patients. However, aware of the fact that some studies may have included 30-day mortality rate assessments, we decided to include this data too, considering that the 30-day timeframe is consistent with a short-term outcome in the context of critically ill patients at the ICU setting.

A total of 9 randomized clinical trials were analyzed including 6 studies analyzed in Li et al.'s work[1] and 3 new trials: Nafae et al.'s study,[2] and the post hoc analysis data of patients with sepsis from the ICU-ROX trial,[3] and the ICONIC trial.[4] These 9 trials included a total of 5216 patients admitted to the ICU. The results did not show a significantly lower all-cause mortality rate in the short-term with the use of conservative oxygen therapy (OR, 0.97; 95%CI, 0.86–1.09 in the common effects model; OR, 0.88; 95%CI, 0.71–1.09 in the random effects model) (Fig. 1).

The results indicate moderate variability (I^2 of 44.81%) that cannot be attributed to simple sampling error. This heterogeneity, referring to differences among studies in terms of population, design, or outcome measurement, requires careful consideration when interpreting the results. We did not find any statistically significant evidence either to support the lack of heterogeneity ($P > 0.05$) (Fig. 1). Fig. 2 shows the funnel plot of effect size against precision in a scatterplot. The funnel plot exhibits a tilt toward the left, which could be indicative of potential publication bias where studies with negative results are not disclosed. Girardis et al.'s

DOI of original article: https://doi.org/10.1016/j.medin.2023.10.013

https://doi.org/10.1016/j.medine.2023.11.010

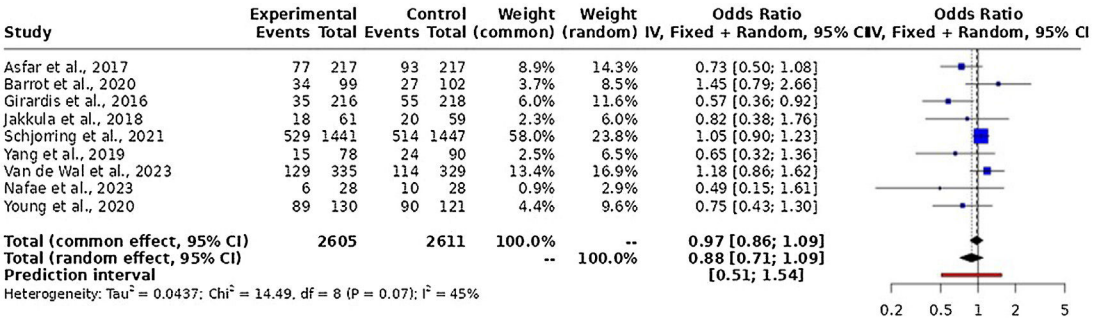

Figure 1 Forest plots comparing short-term mortality of conservative vs liberal oxygen therapy.

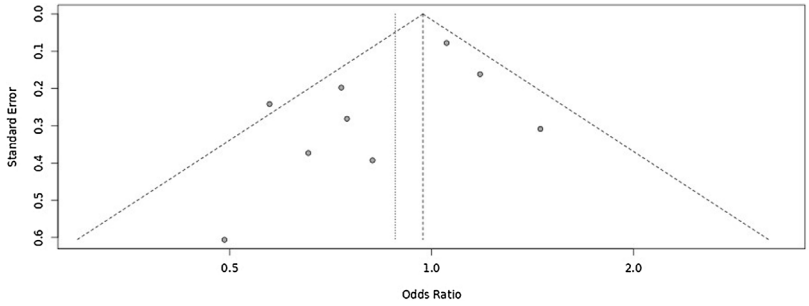

Figure 2 Funnel plot of effect size vs precision in a scatterplot.

work[5] deviates from the general shape of the funnel (outlier).

These results just do not clarify the debate of whether patients ventilated in the ICU setting with liberal oxygen therapy are genuinely at risk of developing hyperoxia and lung damage. It is hypothesized that oxidative stress following the production of reactive agents with oxidant properties could be an important mechanism in the development of lung damage, inducing phenomena such as apoptosis of the alveolar epithelium and changes to cellular functions, especially at mitochondrial level.[6,7] Although the prolonged use of a high fraction of inspired oxygen has historically been associated with potential detrimental effects on the lungs—mainly mild injuries such as atelectasis and hyperoxic bronchitis—a characteristic diffuse alveolar damage has not been found yet.[8]

The question of whether hyperoxia and lung damage are legitimate concerns in patients on liberal oxygen therapy at the ICU setting remains a matter of discussion and requires a more detailed evaluation and understanding.[9]

Despite the moderate variability seen, our analyses support the need for a cautious approach when extrapolating the conclusions of individual studies to a broader context, thus recognizing that differences seen among studies can have an impact on the results and should be considered in future research and clinical practices.

Conflict of interest

None of the authors declared any conflicts of interest at the completion of this study.

Funding

This manuscript received no funding.

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