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LETTER TO THE EDITOR

Non-invasive mechanical ventilation and high-flow oxygen therapy in the COVID-19 pandemic: the value of a draw☆

Ventilación mecánica no invasiva y oxigenoterapia de alto flujo en la pandemia COVID-19: el valor de un empate

Dear Editor:

We have read the consensus document of the SEMICyUC, published in your journal, regarding noninvasive ventilatory support in adults with acute respiratory failure (ARF) due to COVID-19.[1] The document states that «extrapolating the evidence in *de novo* ARF (sic)», high-flow oxygen therapy (HFO) would be the first-choice modality. Noninvasive ventilation is established as the second option in the event of insufficient patient response in the absence of immediate intubation criteria. This recommendation is based on two literature references. The first[2] is the interim guidance of the World Health Organization (WHO), which positions HFO and NIV at the same level (yellow traffic light, conditional recommendation), since both therapies «should be used only in selected patients with hypoxemic respiratory failure». Curiously, in Remark 3, the WHO states that «compared with standard oxygen therapy», HFO reduces the need for intubation. This observation is based on the European/American clinical practice guide.[3] However, this guide, in Question 5 on de novo ARF, explains that «the primary endpoint of intubation was not significantly different» in the FLORALI-REVA trial,[4] and is not able to establish any recommendation because the evidence is of low quality.

The second reference is the FLORALI-REVA study.[4] This was a clinical trial involving three cohorts (HFO, NIV and conventional oxygen), and with the proportion of patients requiring intubation as the primary endpoint. A statistical power of 80% in identifying a relevant difference (defined as 20%) in the frequency of intubation was calculated for this purpose. No statistically significant differences in the primary endpoint were recorded. In the rest of the study, analyses were made of *post hoc* comparisons between groups of patients, with Cox regression models to explain the primary endpoint and mortality. Both analyses could be biased: no adjustment for multiple comparisons was made, no model with time-dependent variables (HFO and NIV were interchanged) was used, and there may have been over-adjustment. They consequently could only serve to generate hypotheses that would have to be confirmed by future trials.

However, the SEMICyUC document does not cite a clinical trial[5] specifically designed (power 80%) to detect a relevant decrease (now defined as 30%) in the intubation rate. In the mentioned study, NIV versus standard oxygen therapy was seen to significantly reduce the intubation rate in patients with *de novo* hypoxemic ARF. This experiment has not been replicated, though the preliminary data on the experience with COVID-19 in China appear to confirm its results. With a beta-binomial model, using an *a priori* non-informative construct, the probability that the intubation rate is lower with NIV versus HFO was 0.9993 (difference in rates = 0.444; 95%CI = 0.097−0.706).[6]

The current health emergency situation requires full dedication on the part of intensivists, but also a rational distribution of the available resources. If we seek to avoid intubations, perhaps NIV and HFO should be positioned at the same level as first choice option. The WHO has done so.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Living evidence for SARS-CoV-2☆

Evidencia viva frente al SARS-CoV-2

Dear Editor,

The current health crisis due to the SARS-CoV-2 pandemic has triggered a need for answers that exceeds the actual capacity of producing scientific knowledge. Very few landmark studies on COVID-19 have been completed to this date, and those with preliminary results published provide very low levels of evidence. Under the current situation of uncertainty, the wise thing to do is to be cautious when it comes to interpreting the evidence available and avoid making rush decisions that may be more detrimental than beneficial.[1] But, do we have such evidence available for an adequate management of COVID-19? The Chinese experience can help us solve the problems we have been having to deal with at the ICU setting in record time and with serious limitations in the human resources and equipment available.[2] Consensus documents are also very important since they provide an agile and effective support to all the healthcare professionals while admitting that reviews and updates may be necessary based on the epidemiological situation of the pandemic, and changes necessary in the therapeutic alternatives used.[3]

On the other hand, different research working groups have been publishing protocols, and preprints that adds to the amount of currently available reports in the repositories (SSRN and medRxiv) that have not been approved during the review process. What this tells us is that we should be very cautious about this information. Table 1 shows the different sources of scientific information and the number of entries found with search terms relative to COVID-19/SARS-CoV-2 as of April 10, 2020. Results are significantly larger in unarbitrated references.

Also, to this point, the scientific evidence available on this topic is still associated with low levels of evidence. Most of the 586 findings obtained through Pubmed are comments, letters to the editor, and editorials. No meta-analyses, clinical trials or observational studies have been found (Fig. 1).

The so-called «living systematic review» is a tool that helps in the decision-making process in the daily routine clinical practice with the highest level of evidence and the capacity to solve the problem of the ongoing publication of new data. It is based on a systematic review of the scientific literature available while leaving the review window open to add new evidence as it becomes available. Also, this can lead to changes in the recommendations made based on new data that may have appeared.[4] Several international groups are working on this type of living evidence that may provide an easy and updated answer to the problems found in the management of COVID-19 by combining methodological rigor and new technologies.[5]

This pandemic has taught us quite a few lessons. One of them is that scientific knowledge needs to be spread fast and on an ongoing basis to provide timely answers to the doubts and questions physicians may have during their routine clinical practice. In a changing and specific environment like the ICU setting, this premise may be considered an interesting strategy to be developed through the so-called «living systematic review».

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