Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Medicina Intensiva 45 (2021) 506–509

medicina intensiva

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

LETTERS TO THE EDITOR

High-flow oxygen therapy in acute hypoxemic respiratory failure secondary to COVID-19 pneumonia☆

Oxigenoterapia de alto flujo en insuficiencia respiratoria aguda hipoxémica secundaria a neumonía por COVID-19

Dear Editor,

We have been reading with great interest the scientific letter written by González-Castro et al. concluding that high-flow oxygen therapy (HFOT) is not an effective therapy, in clinical or economic terms, to treat acute hypoxemic respiratory failure due to SARS-CoV-2-induced pneumonia.[1] As far as we know, statements like this should be taken with caution due to the limitations of the analysis.

Oxygen therapy is one of the main pillars for the management of this particular entity. To this date, multiple techniques have become available including the use of high-flow nasal cannulae (HFNC) that also optimize the conditions of the gas administered (temperature, humidity) with a more reliable FiO_2.[2] Physiologically speaking, it offers some attractive advantages and is very well-tolerated.[2] Additionally, HFOT is versatile and can be used in the emergency room or in general rooms. This is an important advantage especially when the resources or beds available at the intensive care unit setting are scarce. Different consensus documents and clinical practice guidelines from various scientific societies advocate for the use of HFOT.[3,4] Some controversial issues here are the risk of aerosolization and its impact on the rates of intubation and mortality.[2]

A meta-analysis conducted before the pandemic confirmed that HFOT reduces the need for increasing ventilatory support including invasive mechanical ventilation.[5] However, uncertainty surrounds COVID-19-induced pneumonia due to the heterogeneity of the studies conducted on several aspects reported. Therefore, no valid conclusions can be drawn to this date on this regard (Table 1).

Therefore, the retrospective nature of the study and its small sample do not let us draw any conclusive statements yet. However, we should reflect on the data provided from a different angle. Only 20 patients (30% of the population) received HFOT. A total of 12 of these patients (60%) did not need to be escalated to ventilatory support and had shorter ICU and hospital stays. Also, no deaths were reported. No information on cost-effectiveness in this population has been disclosed. In our opinion, this situation cannot be considered a failure whatsoever.

On the other hand, when patients who remained «unresponsive and required invasive ventilation» were studied, the HFOT was implemented with further delay, they were older patients with more comorbidities, and worse oxygenation indices prior to the indication for HFOT, which makes us wonder:

1. Would an earlier implementation of HFOT increase its effectiveness?
2. Does HFOT affect all patients the same way or is it more beneficial for certain subgroups of patients?
3. Does awake prone positioning plus HFOT increase the effectiveness of this oxygenation technique?

On the other hand, the protocols of initiation and withdrawal of HFOT are heterogeneous across the world, but they have not been universally validated yet. Our preliminary experience (data still unpublished) in 2 regions and in different countries is encouraging, especially regarding the association between HFOT and the awake prone positioning through the implementation of clinical guidelines or protocols since hospital admission. For all these reasons, we believe it is important to conduct well-designed studies to shed light on all these issues.

☆ Please cite this article as: Godoy DA, Graneros N, Oyarzabal L, Murillo-Cabezas F. Oxigenoterapia de alto flujo en insuficiencia respiratoria aguda hipoxémica secundaria a neumonía por COVID-19. Med Intensiva. 2021;45:506–508.

Table 1 Series that used HFOT (without the prone positioning) to treat COVID-19-induced pneumonia. One study (published in Chinese) and case reports were excluded.

Author-references	Country	Number of patients	Protocol	Moment when the HFOT was started	HFOT parameters	Rates of intubation and mechanical ventilation
Wang Ann Intensive Care 2020; 10: 37	China	17	No	N/A	Flow: 30–60 lpm T: 87.8 °F–98.6 °F FiO_2: titulated SpO_2 > 93%	41%
Cancelliere Ther Adv Respir Dis 2020; 14: 1–10	Italy	5	No	After COT and CPAP failure	Flow: 40 lpm T: 87.8 °F FiO_2: 0.6, titulated SpO_2: 94%–98%	0%
Geng Heart Lung 2020; 49: 444–445	China	8	No	2: admission 6: 4.5 days after admission	FiO_2: 1	0%
Blez Intensive Care Med 2020; 46: 2094—2095	France	30	No	Admission	Flow: 60 lpm FiO_2: 1, titulated SpO_2 > 92%	53.3%
Lalla S Afr Med J 2020; 110: 12941	South Africa	7	No	Admission	N/A	14.3%
Demoule Am J Respir Crit Care Med 2020; 7: 1039–1042	France	146	No	Within the first 24 h	Flow: ≥50 lpm	56% on day 28 of disease progression
Gonzalez-Castro Med Intensiva 2021	Spain	20	No	Mean of 11 days after admission	Flow: 60 lpm FiO_2: 0.9, titulated SpO_2 > 95%	40%
Godoy (unpublished data) 2021	Argentine	73	Yes	Mean of 11 days after admission	Flow: 60 lpm T: 87.8 °F–98.6 °F FiO_2: 1, titulated Sat > 92%	44%

COT, conventional oxygen therapy; CPAP, continuous positive airway pressure; FiO_2, fraction of inspired oxygen; HFOT, high-flow oxygen therapy; lpm, liters per minute; N/A, non-applicable; SpO_2, oxygen saturation; T, temperature.

References

1. González-Castro A, Fito EC, Fernández A, Acha PE, Borregian JCR, Peñasco Y. Oxigenoterapia de alto flujo en el tratamiento de la neumonía por SARS-CoV-2. Medicina Intensiva. 2021, http://dx.doi.org/10.1016/j.medin.2020.12.004.
2. Raoof S, Nava S, Carpati C, Hill NS. High-flow, noninvasive ventilation and awake (nonintubation) proning in patients with coronavirus disease 2019 with respiratory failure. Chest. 2020;158:1992–2002, http://dx.doi.org/10.1016/j.chest.2020.07.013.
3. Cinesi Gómez C, Peñuelas Rodríguez Ó, Luján Torné M, Egea Santaolalla C, Masa Jiménez JF, García Fernández J, et al. Clinical consensus recommendations regardingnon-invasive respiratory support in the adult patient with acute respiratory failure secondary to SARS-CoV-2 infection. Med Intensiva. 2020, http://dx.doi.org/10.1016/j.medin.2020.03.005.
4. Rochwerg B, Einav S, Chaudhuri D, Mancebo J, Mauri T, Helviz Y, et al. The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. Intensive Care Med. 2020;46:2226–37, http://dx.doi.org/10.1007/s00134-020-06312-y.
5. Agarwal A, Basmaji J, Muttalib F, Granton D, Chaudhuri D, Chetan D, et al. High-flow nasal cannula for acute hypoxemic respiratory failure in patients with COVID-19: systematic reviews of effectiveness and its risks of aerosolization, dispersion, and infection transmission. Can J Anaesth. 2020;67:1217–48, http://dx.doi.org/10.1007/s12630-020-01740-2.

D.A. Godoy[a,b,*], N. Graneros[b], L. Oyarzabal[b], F. Murillo-Cabezas[c]

[a] *Unidad de Cuidados Neurointensivos, Sanatorio Pasteur, Catamarca, Argentina*
[b] *Unidad de Terapia Intensiva, Hospital Carlos G. Malbran, Catamarca, Argentina*
[c] *Departamento de Medicina, Universidad de Sevilla, Sevilla, Spain*

* Corresponding author.
E-mail address: dagodoytorres@yahoo.com.ar (D.A. Godoy).

2173-5727/

The need for rigorous analysis of the effectiveness and efficiency of high flow oxygen therapy during the SARS-CoV-2 pandemic☆

La necesidad de un análisis riguroso de la efectividad y eficiencia de la terapia de oxigeno de alto flujo durante la pandemia por SARS-CoV-2

Dear Editor:

We wish to take the opportunity the editor of this journal gives us to make a few remarks on the response[1] given to the scientific letter ''High-flow oxygen therapy in the treatment of SARS-CoV-2 pneumonia''.[2]

In the first place, in our analysis, and in the context of hypoxemic acute respiratory failure due to SARS-CoV-2-induced pneumonia, ''the optimal decision was the use of the high-flow nasal cannula (HFNC) strategy followed by invasive mechanical ventilation (IMV) in cases of failed HFNC''. Our letter says it clearly, and we believe that the chances that this strategy is more effective compared to the control one are 0.965. However, this difference was not statistically significant, which is why with our we could not rule out the null hypothesis. Contrary to what the authors say in their response to our letter we could not confirm ''(...) that high-flow oxygen therapy is not an effective therapy in clinical terms'', because this would have been like saying that the hypothesis is null, and our study was not statistically powered to determine such a thing.

Secondly, the authors of the comments to our letter indicate that our second conclusion is that the HFNC also is not cost-effective either (sic). We believe they are referring to the fact that, in our analysis, we claim that HFNC does not seem an effective therapy because the ''incremental cost-effectiveness ratio (ICER) is €219,294 for every discharge from the intensive care unit (ICU)''. And please let us stand by this conclusion, and on the fact that it seems necessary to perform a more solid analysis to confirm the economic impact of such strategy in terms of cost-effectiveness.

We do not think these statements contradict the scientific evidence collected in the metanalysis conducted by Agarwal et al.[3] In this metanalysis, HFNC is compared to conventional oxygen therapy. Also, the results obtained in the most rigorous analysis (the one with fewer chances of bias) only found (like we did) a statistically non-significant difference (RR, 0.87; 95%CI, 0.75–1.01; $P = .06$; heterogeneity: $P = .84$). Using a beta-binomial conjugate Bayesian model from a non-informative aprioristic distribution in addition to the data provided by the authors' table we can estimate (with a 95% credibility) that, according to the scientific literature on this issue, the chances of HFNC failure are somewhere between 0.422 and 0.533 (median, 0.477). Nearly the same chances we have when we toss a coin into the air, but with all the cost derived from treatment.

Funding

None whatsoever.

Conflicts of interest

The authors declared no conflicts of interest whatsoever.

References

1. Godoy DA, Graneros N, Oyarzabal L, Murillo-Cabezas F. Oxigenoterapia de alto flujo en insuficiencia respiratoria aguda hipoxemica secundaria a neumonía por Covid-19. Med Intensiva. 2021, http://dx.doi.org/10.1016/j.medin.2021.02.003.
2. González-Castro A, Cuenca Fito E, Fernandez-Rodriguez A, Escudero Acha P, Rodríguez Borregán JC, Peñasco Y. High flow oxygen therapy in the treatment of SARS-CoV-2 pneumonia. Med Intensiva. 2021;18, http://dx.doi.org/10.1016/j.medin.2020.12.004.
3. Agarwal A, Basmaji J, Muttalib F, Granton D, Chaudhuri D, Chetan D, et al. Highflow nasal cannula for acute hypoxemic respiratory failure in patients with COVID-19: systematic reviews of effectiveness and its risks of aerosolization, dispersion, and infection transmission. Can J Anaesth. 2020;67:1217–48, http://dx.doi.org/10.1007/s12630-020-01740-2.

☆ Please cite this article as: González-Castro A, Medina A, Modesto i Alapont V, Cuenca-Fito E, Fernandez-Rodríguez A, Peñasco Y. La necesidad de un análisis riguroso de la efectividad y eficiencia de la terapia de oxigeno de alto flujo durante la pandemia por SARS-CoV-2. Med Intensiva. 2021;45:508–509.