Do we have scientific evidence about the effect of hypoxaemia on cognitive outcome in adult patients with severe acute respiratory failure?

Bernhard Holzgraefe, Anders Larsson & Laura Von Kobyletzki

To cite this article: Bernhard Holzgraefe, Anders Larsson & Laura Von Kobyletzki (2018) Do we have scientific evidence about the effect of hypoxaemia on cognitive outcome in adult patients with severe acute respiratory failure?, Upsala Journal of Medical Sciences, 123:1, 68-70, DOI: 10.1080/03009734.2018.1433255

To link to this article: https://doi.org/10.1080/03009734.2018.1433255
LETTER TO THE EDITOR

Do we have scientific evidence about the effect of hypoxaemia on cognitive outcome in adult patients with severe acute respiratory failure?

Dear Editor,

Survivors of acute respiratory failure (ARF) treated with invasive mechanical ventilation (IMV) only or IMV in combination with extracorporeal membrane oxygenation (ECMO) can suffer from mental disorders later on, especially from cognitive impairment (1). It was suggested that long-term cognitive impairment could be caused by hypoxaemia, which is a common condition during the course of severe ARF in adult patients (2,3). To shed some light on this matter we performed a systematic literature search. We included cohort studies, nested case-control studies, or randomized controlled trials that evaluated associations between hypoxaemia and cognitive function and the effect of ECMO during the course of ARF on cognitive functioning. Hypoxaemia was defined as a haemoglobin oxygen saturation (SaO2) < 94%. Only studies performed in adult patients who were treated with IMV with or without ECMO were included. Study eligibility was independently assessed by two reviewers (authors B.H., L.K.) as were primary selected studies extracted using a standardized form. Full details on our methodology have been included in our protocol registration on the International Prospective Register of Systematic Reviews (PROSPERO 2016: CRD42016045447) and as

Figure 1. PRISMA 2009 flow diagram.

Supplemental data for this article can be accessed here.
supplemental materials (Search strategy, available online). The search in Medline, EMBASE, Cochrane, and PsychInfo was finalized on 26 August 2016.

A total of 2606 articles were found. After removal of 781 duplicates, 1825 titles and abstracts were screened (Preferred Reporting Items for Systematic Reviews and Meta-Analyses, PRISMA 2009; Figure 1) (4). Thirty papers were identified for full-text assessment. We could not identify any study that met the inclusion criteria. However, four case series and two longitudinal studies without comparison to an unexposed control group investigating study questions similar to the current study were found (see Search Strategy, available online).

A seventh case series, which was published online in October 2016, was added after the database search (Supplementary Tables 1–3, available online). Two studies showed some evidence that arterial oxygen saturation below 90% might be associated with cognitive impairment (studies 22 and 24, Supplementary Tables 1–3, available online). One study found a correlation between the duration of desaturation and cognitive outcome at 1-year follow-up and another study at discharge but not at 1- and 2-year follow-up. The patients in these studies were mechanically ventilated and without ECMO treatment. One study including patients with ECMO treatment did not find an association between hypoxaemia and cognitive impairment (study 25, Supplementary Tables 1–3, available online).

Our observations highlight a dearth of evidence on the association of hypoxaemia during the course of ARF with or without ECMO and cognitive function, with not a single study fulfilling our eligibility criteria. The case series found conflicting results. This was in line with the first International Study of Postoperative Cognitive Dysfunction, which did not find any association between hypoxaemia and cognitive dysfunction (5).

The occurrence of hypoxaemia is a common feature in severe ARF and other conditions with severely impaired pulmonary gas exchange. Hypoxaemia is defined as haemoglobin oxygen saturation below the normal value. The term ‘normoxaemia’ is defined as a PaO₂ of 10.7–13.3 kPa (80–100 mmHg) or a SaO₂ of >94% at sea level (6). On the other hand, the term hypoxia describes a lack of oxygen at the cellular level. The terms hypoxaemia and hypoxia are often mixed up, but it is important to keep in mind that they describe two different situations. Hypoxaemia may not lead to cellular hypoxia per se because the physiological compensation of reductions in oxygen saturation might maintain capillary oxygen content at an adequate level (7), which seems to be the most important factor for sufficient cerebral oxygenation (8). Tissue hypoxia is usually caused by an ischemic event, i.e. cerebral infarction. Therefore, in our view, it is unlikely that hypoxaemia per se will lead to tissue hypoxia as long as organ perfusion is preserved. Attempts to maintain normoxaemia during treatment with mechanical ventilation with or without ECMO in patients with hypoxaemic respiratory failure are associated with a risk of serious complications, e.g. ventilator-induced lung injury (9) and cerebral haemorrhage (10). This risk could even out the potential benefit of increasing blood oxygen saturation. Thus, it is important to clarify whether hypoxaemia is associated with decreased cognitive function.

Our observations highlight a knowledge gap on this issue. From low-evidence data we cannot exclude that hypoxaemia could negatively influence cognitive function at discharge from hospital in patients treated with only mechanical ventilation. Hence, we conclude that future high-quality studies are needed to explore this question.

Disclosure statement

The authors report no conflicts of interest.

Acknowledgements

The authors thank librarians Susanne Gustafsson and Carl Gornitzki, Karolinska Institutet University Library, for their invaluable work in the development and performance of the search strategy and the search.

Funding

This work was funded by Vetenskapsrådet [K2015-99X -22731-01-4].

References

1. Chiumello D, Coppola S, Froio S, Gotti M. What’s next after ARDS. Long-term outcomes. Respir Care. 2016;61:689–99.
2. Hopkins RO, Weaver LK, Pope D, Orme JF, Bigler ED, Larson LV. Neuropsychological sequelae and impaired health status in survivors of severe acute respiratory distress syndrome. Am J Respir Crit Care Med. 1999;160:50–6.
3. Hopkins RO, Weaver LK, Collingridge D, Parkinson RB, Chan KJ, Orme JF Jr. Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. Am J Respir Crit Care Med. 2005;171:340–7.
4. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6:e1000097.
5. Moller JT, Cluitmans P, Rasmussen LS, Houx P, Rasmussen H, Canet J, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. Lancet. 1998;351:857–61.
6. Kratz A, Lewandrowski KB. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Normal reference laboratory values. N Engl J Med. 1998;339:1063–72.
7. Finch CA, Lenfant C. Oxygen transport in man. N Engl Med. 1972;286:407–15.
8. Hoiland RL, Bain AR, Rieger MG, Bailey DM, Ainslie PN. Hypoxaemia, oxygen content, and the regulation of cerebral blood flow. Am J Physiol Regul Integr Comp Physiol. 2016;310:R398–413.
9. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med. 2015;372:747–55.
10. Allen S, Holena D, McCunn M, Kohl B, Sarani B. A review of the fundamental principles and evidence base in the use of extracorporeal membrane oxygenation (ECMO) in critically ill adult patients. J Intensive Care Med. 2011;26:13–26.
