CRITICAL CARE

LETTER

How to assess the dangers of hyperoxemia: methodological issues

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See related research by Bellomo *et al.*, http://ccforum.com/content/15/2/R90

We read with interest the paper by Bellomo and colleagues [1] in the previous issue of *Critical Care*. We agree with the authors' final conclusion that there should not be a deliberate policy to decrease the fraction of inspired oxygen (FiO_2) in the absence of accurate and reliable oximetry. In the developed world, accurate and reliable oximetry and blood gas results are ubiquitous in ICU settings, the context of their study. However, we have issues with the methods used to come to the conclusion that hyperoxaemia has only a weak relationship with mortality.

If one wishes to show no association of hyperoxemia with outcomes, the best approach is to pick the lowest level of arterial partial pressure of oxygen (PaO_2). By analogy, if one wished to assess the risk of speeding prior to traffic accidents, one would not look at the lowest speed or the speed at impact; one would, ideally, look at peak speed or average speed. Kilgannon and colleagues [2] used the first blood gas measurement in the ICU and found that hyperoxemia (PaO_2 of at least 300 mm Hg) was associated with increased risk of death in the hospital. de Jonge and colleagues [3] looked at mean PaO_2 of mechanically ventilated patients in the first 24 hours in ICUs and also reported an increased risk of death in patients with hyperoxemia.

We are also concerned that the conclusion of the study relates to hyperoxemia when defined as a PaO_2 of greater than 400 mm Hg whereas the study objective was to analyze the risk of death if the PaO_2 was at least 300 mm Hg. We understand that the authors did find excess mortality in their intended study group (and in those with a PaO_2 of greater than 200 mm Hg) even after adjustment for illness severity. We are concerned that their negative conclusion is based on a different (and smaller) *post hoc* subset of patients with a PaO_2 of greater than 400 mm Hg. By contrast, Kilgannon and colleagues [4] re-analyzed their data and reported a clear dose response with lowest hospital mortality in the PaO_2 range of 60 to 99 mm Hg and they reported a 24% increase in mortality risk for every 100 mm Hg increase in PaO_2.

Authors' response

Rinaldo Bellomo, Michael Bailey and Alistair Nichol (on behalf of the Study of Oxygen in Critical Care Group)

We thank O'Driscoll and Howard for their letter. We share the view that pulse oximetry monitoring in cardiac arrest patients is desirable. However, we wish to emphasize that our methods simply sought to replicate those of Kilgannon and colleagues [2] given the characteristics of our national database. The view that the PaO_2 associated with the highest A-a gradient [1] is a poorer marker of the chance of exposure to hyperoxemia than the first blood gas measurement [2] was not supported by our findings. In a sample of 100 patients with detailed arterial blood gas information, the worst PaO_2 was significantly more representative of mean PaO_2 than was the first PaO_2 in the ICU (P <0.0001 for the first 24, 48, or 72 hours), as reported in our paper. In terms of the speeding analogy, the slowest speed achieved by a driver tells us a lot more about his or her mean speed (the speed that may well matter the most) than does the highest speed in the first 10 minutes. Moreover, our conclusions were not based on the lack of effect at a PaO_2 of greater than 400 mm Hg (a parameter chosen by Kilgannon and colleagues [2]) but on a considered assessment of all observations. We advise caution in over-interpreting data from a study in which no adjustment for illness severity was possible and more than 30% of data were missing [1]. Similarly, the study of de Jonge and colleagues [3] requires validation. We are currently conducting such an

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investigation. Irrespective of views and interpretations, we believe it is high time to investigate oxygen therapy in a more systematic fashion. We have begun to do so [1,5,6] and intend to persevere.

Abbreviations

ICU, intensive care unit; PaO_2, arterial partial pressure of oxygen.

Competing interests

BRO'D is co-chair of the British Thoracic Society Guideline Development group for Emergency Oxygen therapy.

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