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LETTER TO THE EDITOR

Debating pharmacological options for dyspnoea relief; the need for full, accurate and balanced critical appraisal of the evidence

To the editor,

We read with interest the review on strategies to relieve dyspnoea in patients with advanced chronic respiratory disease by Ambrosino and Fracchia.[1] Given the clinical need for pharmacological options for dyspnoea relief, we would like to comment on some important aspects that we feel merit further clarification.

The review comments on inhaled furosemide as a potential drug for relieving dyspnoea and refers to our RCT in healthy volunteers[2] which showed significant relief of experimentally-induced air hunger. The review stipulates that this was ''*a finding not confirmed later even at higher doses*.''[3] The comment is misleading, implying that higher-dose studies were completed subsequent to ours and that the findings were incongruous. Our study[2] was published *after* the higher-dose studies. The controlled delivery of 80 mg *was* associated with greater air hunger relief[3] compared to what we found with uncontrolled delivery of 40mg (mean ± SE: −17 ± 3 versus −11 ± 5%VAS). However, the greater relief in the higher-dose study was offset by a larger placebo effect (−13 ± 4 versus −2.5 ± 4%VAS). The enhanced placebo effect in the higher-dose study can be explained by differences in study design.

While there is high variability in dyspnoea relief in all published studies of inhaled furosemide, there is potential for it to form a viable treatment option for the most unpleasant form of dyspnoea if the sources of variability are unravelled. Potential sources of variability include, i) site of drug deposition in the lungs ii) rate of extinction from the lungs iii) lack of information on the quality of dyspnoea rated and iv) use of a dyspnoea model that is not focussed on 'air hunger'. More research with inhaled furosemide is justified given that it is safe, inexpensive and underpinned by a defined physiological mechanism of action.

The discussion by Ambrosino and Fracchia on the use of opioids for dyspnoea relief is also misleading and fails to paint a balanced picture. The authors have ignored the opioid crisis that has killed over ¾ million Americans since 1999.[4] They have not considered the absence of long-term studies of opioid efficacy or safety.[5] In most people, opioid efficacy is high in the short term but diminishes over 6 weeks to 3 months. The resultant dose escalation increases risk of adverse events with no improvement in symptoms.[5] We suggest extreme caution is necessary for prescription of opioid medication for breathlessness because, i) opioids increase risk for death in people with lung conditions,[4] ii) people with anxiety/depression are more likely to have diminished opioid response to pain,[5] and breathlessness,[6] but also are more likely to have problems with dependency and failure to wean off opioids.

Finally the author's assertion that ¨*Relief of dyspnoea [...] is a human right*ëchoes sentiments expressed in the mid 1980′s that were used to justify using opioids for all kinds of pain,[7] leading to the opioid crisis we are in today. It is preposterous to portray those who harbour legitimate concerns about opioid safety as human rights violators when the debate is not fuelled by a balanced appraisal of the evidence.

Statement of ethics

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Author contributions

All authors contributed equally to this correspondence.

Conflict of interest

None.

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