Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnea: a double-blind, randomized controlled trial

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Question: In patients with life-limiting illness and refractory dyspnea, what is the effectiveness of oxygen compared with room air delivered by nasal cannula for relief of breathlessness?

Design: Randomized controlled trial. ClinicalTrials.govNCT00327873, Current Controlled Trials ISRCTN67448752.

Allocation: Concealed.*

Blinding: Blinded (patients, clinicians, and {clinical research nurses}†).

Follow-up period: 7 days.

Setting: Outpatient pulmonary, oncology, and primary care clinics in Australia, USA, and the UK.

Patients: 239 patients > 18 years of age (mean age 74 y, 62% men) who had PaO2 > 7.3 kPa and refractory dyspnea related to life-limiting illness (≥ 3 on Medical Research Council categorical dyspnea scale at rest or with negligible exertion), had received maximum treatment for underlying disease, were expected to survive for ≥ 1 month, and were receiving stable medications the previous week. Exclusion criteria were eligibility for long-term oxygen therapy; history of hypercarbic respiratory failure with oxygen; anemia, hypercarbia, or cognitive impairment; smoking; or respiratory or cardiac event in the past 7 days.

Intervention: 7 days of oxygen (n = 120) or room air (n = 119) delivered by a concentrator and nasal cannula at a continuous rate of 2 L/min. Patients were asked to use the concentrator for ≥ 15 h/d.

Outcomes: Main outcome was “breathlessness right now” (rating scale from 0 to 10, 10 = “breathlessness as bad as you can imagine,” assessed twice daily). Based on a sample size of 240, the study would have 80% power to detect a 1-point difference in breathlessness (α = 0.05).

Patient follow-up: 88% of patients completed all 7 days of assessments.

Main results: Oxygen and room air did not differ for morning or evening breathlessness (Table).

Conclusion: Oxygen and room air delivered by nasal cannula did not differ for relief of breathlessness in patients with life-limiting illness and refractory dyspnea.

Strengths:
- Good study design with strong concealment and intent to treat analysis.
- The randomized groups did not differ in causes of dyspnea, opioid use, performance status, or baseline oxygenation.
- This is in a way a pivotal study showing that high enrollment and high completion rates are feasible in palliative medicine setting.

Weaknesses:
- Only one flow rate of oxygen was tested (2L/min), which could be seen as under treating.
- This study was conducted in an outpatient setting, with relatively stringent exclusion criteria, which reduces its applicability across the board.
- The definition of refractory dyspnea was not well supported by the basic assessment scale used. The length of the study was only 7 days.

Relevance to palliative care: Although this study raises an important clinical question it is not necessarily groundbreaking and practice changing in context of tertiary palliative care (TPCU). It would be hard to extrapolate this data to a TPC unit, or any patient with end-stage dyspnea and associated comorbidities. It could, however, apply to a primary care management of outpatients with dyspnea; it is not unreasonable to think about benefit of home oxygen therapy, as well as costs associated, before prescribing it.