Oxygen and the airways

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The best things carried to excess are wrong (Charles Churchill (saturist) 1731–1764)

The use of oxygen for the management of patients with acute breathlessness, irrespective of cause, is well established in medical practice. The perception of benefit, even in the absence of measurement of oxygenation, and concerns over adverse outcomes from severe hypoxaemia have driven the use of high-concentration oxygen therapy over many years with little regard to possible harmful effects. While there have been many advocates for the cautious use of oxygen in chronic obstructive pulmonary disease (COPD) as a result of its propensity to promote hypercarbia, liberal use in asthma appears universal. This approach pervades student teaching through medical texts, even when there is significant respiratory input into the publication and extends to recent evidence-based guidelines on both asthma management and oxygen usage. The recently published British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) guidelines recommend administration of oxygen for acute exacerbations of asthma, stating ‘Many patients with acute severe asthma are hypoxaemic. Supplementary oxygen should be given urgently to hypoxaemic patients, using a face mask, Venturi mask or nasal cannulae with flow rates adjusted as necessary to maintain \( \text{SpO}_2 \) of 94–98%’, advice that is allocated a moderate to low level of evidence. Furthermore, they emphasise the use of oxygen therapy even in the absence of information on oxygenation, recommending that the ‘Lack of pulse oximetry should not prevent the use of oxygen’. Use of oxygen according to these recommendations is likely to result in a high fractional inspired oxygen, as ‘In hospital, ambulance and primary care, nebulised \( \beta_2 \) agonist bronchodilators should preferably be driven by oxygen’, noting ‘A flow rate of 6 l/min is required to drive most nebulisers’. The recently published BTS guidelines on emergency oxygen use are more circumspect on use without measurement of oxygenation, stating that there is no benefit from oxygen administration in non-hypoxic patients and emphasising that administration should be based on, and monitored by, objective measures.

The relationship between oxygen concentrations and airway diseases, particularly the impact on ventilatory responses, has been of interest for many years. As early as 1979, investigations were being carried out on the impact of hyperoxia in asthma, by measuring specific airway conductance during exercise-induced bronchoconstriction and comparing patients with asthma who had bilateral carotid body resection with those having intact carotid bodies. Oxygen breathing during exercise markedly attenuated the post-exercise bronchospasm in patients with asthma who had intact carotid bodies, but had no significant effect in those without carotid bodies, unrelated to changes in end-tidal partial pressure of carbon dioxide. The authors concluded that oxygen attenuates exercise-induced bronchospasm in patients with asthma through its action on the carotid bodies. Further reassurance on the safety of oxygen in asthma came in 1991, when bronchial reactivity to methacholine under normoxic and hyperoxic conditions was studied in a double-blind study involving nine patients with asthma. The provocative concentrations that caused a 20% fall in \( \text{FEV}_1 \) while breathing 21% and 100% oxygen were 0.18 mg/ml (range 0.06–5.73) and 0.25 mg/ml (range 0.07–8.49), respectively. These were not significantly different, allowing the investigators to conclude that 100% oxygen does not affect bronchial reactivity in asthma.

These studies seem to have been accepted as evidence that hyperoxia did not have an impact on asthma, yet a number of cases were reported in the literature suggesting that there may be cause for concern over oxygen use in asthma under some circumstances. Although these reports did not appear to alarm the medical fraternity, the broader asthma community seemed more concerned about hypercarbia in asthma. Internet postings noted ‘A study was done in 1963 and written up in the New England Journal of Medicine [a very prestigious medical journal], where people were forced to breathe as deeply as they could for 15 minutes. After 15 minutes of deep breathing the level of oxygen had DROPPED greatly in the blood, and the CO\(_2\) level had increased. So always remember—you're lungs are a gas mixing chamber. They work best when you have the right mix of gases in them—just like the carburettor of a car’. Yet some medical practitioners did question the role of oxygen in cases of acute severe asthma, particularly those presenting in primary care. They reported that a systematic review was not feasible as there had never been a randomised controlled trial of oxygen use in acute severe asthma, so they opted to present a narrative literature review. They went on to state that in acute severe asthma, nebulisation of \( \beta_2 \) agonist therapy in primary care and in the community was rational and could save lives, urging the BTS to review this issue when it updated its guidelines.

It was not until 2003 that the first controlled trial to investigate the effects of hyperoxia in patients with acute severe asthma was reported. Seventy-four patients were randomised to receive 28% or 100% oxygen for 20 min. The administration of 100% oxygen significantly increased arterial carbon dioxide pressure (PaCO\(_2\)) compared with 28% oxygen, especially in those with PaCO\(_2\) greater than 40 mm Hg before oxygen treatment. Supporting these observations, in this issue of the journal, Perrin et al report on findings that provide high-level evidence based on which recommendations have been made for oxygen administration in acute asthma. They report a randomised study comparing the effect of high-concentration oxygen delivered at 8 l/min via a face mask with oxygen titrated to achieve oxygen saturations of 93–95% in acute exacerbations of asthma presenting to an emergency department. Transcutaneous CO\(_2\) pressure (PtCO\(_2\)) was used to measure the effect of the interventions, with the proportion of patients having a rise in PtCO\(_2\) ≥4 mm Hg at 60 min being significantly greater in the high concentration oxygen group when compared with the titrated group. The investigators concluded that
high-concentration oxygen therapy causes a clinically significant increase in PtCO2 and they recommended the use of a titrated oxygen regime in the treatment of severe asthma. These results mirror those of a similar study performed recently in patients with COPD. In this randomised, controlled, prehospital study, participants allocated to titrated oxygen therapy were significantly less likely to have respiratory acidosis (mean difference in pH 0.12; SE 0.05; p = 0.01; n = 58) or hypercapnoea (mean difference in PaCO2 33.6 mm Hg; SE 16.3; p = 0.02; n = 59) than patients receiving high-concentration oxygen. Treatment with titrated oxygen was also associated with a 58% reduction in mortality, the primary outcome in this study.

As asthma and COPD are prevalent diseases in the Western world, and acute exacerbations of either are associated with an increased risk of death, it is behelden to health professionals to ensure that they do not contribute to this outcome. We now have strong evidence to support the BTS guidelines on emergency oxygen use, which recommend that it be approached in the same way as any other drug, recognising that adverse outcomes may eventuate from either inappropriately low or high concentrations. Should the guidelines be revised in the light of this new evidence to better align recommendations with the philosophy of keeping arterial oxygen saturations ‘within the target saturation range’ that aim to ‘achieve normal or near-normal oxygen saturation’ and move away from any suggestion that high-concentration oxygen should be administered in the absence of objective evidence of a physiological need? With the advent of low-cost portable oxygen saturation monitors, surely it is time we followed the guideline exhortations to measure the fifth vital sign, as in the words of Willy Wonka ‘it’s the only way if you want it just right’.

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