Nebulisers for chronic obstructive pulmonary disease

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Definition of chronic obstructive pulmonary disease

In this paper the term “chronic obstructive pulmonary disease” (COPD) is used as defined in the forthcoming British Thoracic Society guidelines for the management of COPD (1997) as a chronic slowly progressive disorder characterised by airways obstruction (reduced forced expiratory volume in one second (FEV₁) and ratio of FEV₁ to forced vital capacity (FVC)) which does not change markedly over several months. Most of the lung function impairment is fixed, although some reversibility can be produced by bronchodilator (or other) therapy.

The guidelines indicate that, in practice, a diagnosis of COPD requires a history of chronic progressive symptoms such as cough, wheeze and/or breathlessness without intervening periods of “wellness”, usually a cigarette smoking history of more than 20 pack years, and objective evidence of airways obstruction (ideally verified by spirometric testing) that does not return entirely to normal with treatment.

Acute exacerbations of COPD

Current clinical practice is based largely on tradition rather than on careful clinical trials. Although patients with COPD are considered to have relatively static lung function, most have some reversibility and peak flow will often show a modest rise during the first few days in hospital. For example, Rebuck et al found that, in 51 patients with COPD, the mean peak flow increased from 701/min to 951/min (36% rise) 90 minutes after treatment with a nebulised bronchodilator, and a later study reported a rise of 19% in mean peak flow from 113 l/min to 134 l/min in 47 patients with COPD after nebulised bronchodilator treatment. These studies demonstrate that patients with acute exacerbations of COPD can respond to high doses of bronchodilator drugs.

Several studies have suggested that patients with acute asthma or COPD may respond better to treatment with a β agonist given by nebuliser than by metered dose inhaler. However, other authors have suggested that treatment with a metered dose inhaler (given through a spacer device) may be as effective as nebulised treatment in the acute situation. It is difficult to compare these results directly as the patient groups and inhaler devices were different and most studies have contained relatively small numbers of patients, making it difficult to draw definite conclusions about the difference between treatments. However, it is generally agreed that the bronchodilation obtained is largely a reflection of the dose of bronchodilator administered rather than the mode of administration. It is therefore unlikely that treatment with either a nebuliser or a metered dose inhaler will give superior results for most patients provided similar doses are given to the lungs by each device. The question therefore becomes one of convenience and cost.

For low dose bronchodilator therapy—for example, 100–400 µg salbutamol or terbutaline—treatment with a metered dose inhaler is more convenient whilst a nebuliser can deliver higher doses more easily. A nebuliser has the further advantage of being independent of effort or breathing pattern when a patient is distressed. This means that a patient can begin nebulised treatment using a mask or a mouthpiece while the medical attendant can continue with other tasks. The use of a metered dose inhaler in this situation would require the medical attendant (or respiratory therapist or nurse) to stand by the patient and supervise or administer multiple doses of treatment, possibly more than 20, at one minute intervals. Breathless patients are less likely to be able to inspire slowly or breathe hold for optimum lung deposition from a metered dose inhaler.

The optimum dose of bronchodilator treatment (β agonist or anticholinergic) in acute COPD is not known. Mestitz et al showed that terbutaline was equally effective given by metered dose inhaler or nebuliser and the dose response was still rising at 40 mg. However, doses of β agonist above 5–10 mg tend to be associated with unacceptable side effects such as tremor or palpitations. Gross and colleagues showed that the optimum response to ipratropium bromide occurred at 0.4–0.6 mg. A review of practice in Britain shows that salbutamol or terbutaline (5 mg), with or without ipratropium bromide (0.25–0.5 mg), is usually administered to patients with acute airflow obstruction. This would require 50 inhalations of salbutamol followed by 25 inhalations of ipratropium bromide via a metered dose inhaler. Most doctors mix salbutamol and ipratropium bromide respirator solutions in a single nebuliser chamber and administer it immediately. It has recently been suggested that the Turbohaler dry powder device may be used effectively by patients with severe airflow obstruction.
the airways and nebulised terbutaline or saline may help patients with bronchiectasis to ex-
pectorate. Whether this is also true in acute COPD is not known.

Does the addition of an anticholinergic agent to a high dose β agonist have any benefit in the treatment of acute exacerbations of COPD? Although combined treatment seems to be more effective in acute asthma,12 the same authors found that patients with acute ex-
acerbations of COPD did not seem to gain any extra benefit from combined treatment. Furthermore, a recent study of 70 patients admitted to hospital with acute COPD who were not already taking combination nebuliser treatment at home failed to show that the addition of nebulised anticholinergic treatment during their stay in hospital had a clear bene-

Evidence from clinical trials of bronchodilator treatment in COPD

Given the differences in particle size and any extra beneﬁt from combined treatment. 

Home nebuliser use for patients with COPD

This remains a controversial area and the ar-
genent inhalers, and other inhalation devices is this is no longer a valid reason for prescribing a home nebuliser except in a very few cases.9 The optimum duration of nebuliser treat-

ment is not known. Based on clinical practice a personal experience, it is suggested that nebulised terbutaline (2.5–5 mg) or terbutaline (5–10 mg) be given 4–6 hourly for 24–48 hours or until the patient is clinically stable. Ipratropium bromide (0.5 mg) should be added if the patient is poor response to β agonist therapy. The patient should be changed to a metered dose inhaler 24–48 hours before discharge to ensure that the patient is stable, to check the inhaler technique, and to reassure the patient that his or her condition is controlled by their usual med-

ication.
benefit from a high dose nebulised broncho- dilator than from lower dose metered dose inhaler treatment.

**PATIENT ASSESSMENT**

Details of home nebuliser assessment for patients with COPD are given in the guidelines on page S10. The key steps are:

1. An assessment by a respiratory specialist to confirm the diagnosis of COPD and to explore other treatment options. An assessment needs to be made also of a patient’s ability to use hand held inhalers.
3. A trial of treatment with an oral steroid, if not already done.
4. A trial of high dose treatment by hand held inhaler – for example, a dry powder device or metered dose inhaler and spacer with 1 mg terbutaline or 400 μg salbutamol and 160 μg ipratropium bromide four times daily.
5. A formal trial of a home nebuliser – for example, 2.5–5 mg salbutamol or 5–10 mg terbutaline four times daily or ipratropium bromide 0.25–0.5 mg four times daily or a combination of these treatments.
6. A careful assessment of the patient’s response to these treatments over at least two weeks each. Laboratory based single dose reversibility studies will not identify patients who should be given home nebuliser therapy and such trials cannot identify the best treatment options for individual patients.6,7
7. After an assessment process the clinician decide with the patient if the nebuliser treatment has produced subjective and objective benefit. The doctor and patient need to discuss whether the degree of benefit is sufficient to justify the high cost and inconvenience of home nebuliser therapy.

**SIDE EFFECTS AND OUTCOME**

Safety issues are important when patients are given high dose treatment at home. There has been considerable concern about the use of high dose β2 agonists in patients with asthma8 and the same concerns (arrhythmias, tachyphylaxis, failure to call help in an emergency) apply to patients with COPD. Patients with severe airflow obstruction taking high doses of treatment are more likely to die of their disease than patients with milder disease taking standard doses. This is likely to be a marker of disease severity rather than an effect of the drugs themselves. Studies of asthma deaths have found no evidence for direct toxicity of the bronchodilator drugs.8,10

Little is known about the long term prognosis of patients with COPD who use home nebulisers. The drugs might be toxic in high doses, especially in patients with coexistent cardiac disease due to an intrinsic cardiac effect or to indirect effects such as hypokalaemia. However, deaths from arrhythmias have not been widely reported among home nebuliser users. It is suggested that ECG monitoring is a sensible precaution when the first dose of nebulised bronchodilator is given to a patient with known ischaemic heart disease or cardiac arrhythmias. Perhaps the greatest danger is over reliance by patients on home nebulisers rather than the summoning of medical help in an emergency. The frequency with which this happens is not known. Other theoretical hazards include the development of tachyphylaxis during prolonged administration, although there is no evidence for this in clinical practice,11 and the risk (which largely applies to hospitalised patients with acute COPD) of giving prolonged nebulised treatment driven by pure oxygen to patients who have type II respiratory failure thus worsening carbon dioxide retention. Careful attention to limiting the duration of nebuliser use and the use of air driven nebulisers in selected patients should avoid this hazard, which in practice is rarely a significant problem.

The life expectancy of patients with severe COPD is mainly determined by the severity of their airflow obstruction.12 A recent study has shown that the five year survival of patients using nebulisers and metered dose inhalers was similar.13 These patients had similar FEV1 values on entry to the study (0.88 l) and the five year mortality was approximately 46%, most deaths being due to respiratory failure or lung cancer with the risk of death being directly related to the patient’s initial FEV1. These data provide some reassurance as they suggest that the excess mortality amongst nebuliser users in cross sectional studies is probably due to disease severity rather than the treatment itself.

If ipratropium bromide is used, patients with prostatism should use the smallest possible dose to reduce the risk of acute urinary retention must decide with the patient if the nebuliser treatment driven by pure oxygen to patients who have type II respiratory failure thus worsening carbon dioxide retention. Careful attention to limiting the duration of nebuliser use and the use of air driven nebulisers in selected patients should avoid this hazard, which in practice is rarely a significant problem.


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