Domiciliary nebulised bronchodilator therapy in chronic obstructive pulmonary disease

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Introduction

Regular nebulised bronchodilator therapy in the home is commonly prescribed for patients with chronic obstructive pulmonary disease (COPD). If this therapy is administered inappropriately it exposes patients to potential side effects and has considerable financial cost to the health service. In a recent large audit in Liverpool we found that many patients with mild to moderate disease have obtained nebuliser from a variety of different sources including hospitals, primary care physicians, relatives and even the small advertisements of local papers.¹ In this review the current rationale and recommendations for domiciliary nebulised bronchodilator therapy for patients with COPD are discussed.

In 1997, the British Thoracic Society published guidelines concerning the supply, use and maintenance of nebuliser-compressor systems for chronic therapy in the patient's home.² It was recommended that in the management of patients with COPD, such treatment should be reserved for only a minority in whom bronchodilator therapy, when effectively administered at a high dose from a hand-held inhaler device, fails to provide adequate symptomatic relief. These guidelines also state that nebuliser provision should be made only after a full assessment by either a respiratory physician or trained hospital specialist or general practitioner.

Low dose or high dose bronchodilator therapy for COPD

The majority of patients with COPD respond inadequately to conventional doses of bronchodilator via hand-held inhaler. Previous work in stable COPD has shown that high dose bronchodilator therapy produces significant improvement in peak pulmonary function values compared to standard doses. It has also been shown that the duration of bronchodilation resulting from high dose treatment is significantly more prolonged than that achieved by standard dose therapy.³ Although these differences do not always result in symptomatic benefit,⁴ there is evidence to suggest that a subgroup of COPD patients benefit significantly from high doses of bronchodilator drugs.⁵ High dose salbutamol is best defined as the dose that gives maximal bronchodilation. Dose response studies suggest this is approximately 80 mcg⁶, and such a dose is readily administered by hand-held inhaler, particularly when used with a spacer device. Similar observations have been made with antimuscarinic agents, with findings suggesting that ipratropium doses greater than 160 mcg (8 puffs of metered dose inhaler) produce no significant additional bronchodilation.⁵ By comparing equipotent

doses of drug, other workers have concluded that nebulised therapy produces no symptomatic nor bronchodilator advantage over efficiently administered hand-held inhalers.⁸ However, nebulised therapy usually involves 2.5 to 5 mg of salbutamol (i.e. three to six times the maximal bronchodilator dose). Supporting evidence for chronic administration of these large doses of bronchodilators is lacking.

Optimising patient treatment before a nebulised trial

The decision to prescribe nebulised therapy for home use for patients with COPD is often a difficult one. Physicians may simply commence treatment out of desperation to help a chronically symptomatic patient who is not responding to standard inhaler therapy. However, several aspects of patient care need to be addressed prior to commencing domiciliary nebulised treatment.

1. The patient should have a full assessment making sure that the diagnosis is properly established, and trials of other treatment such as corticosteroids should be considered.
2. It should be established that the patient can use their inhaler satisfactorily and is taking the prescribed dose of drugs. In nearly all cases an effective delivery system can be found.
3. It should be ensured that the patient has received adequate trial of high dose bronchodilator via a hand-held device (up to 800 mcg of salbutamol and 160 mcg of ipratropium bromide). Nebulised treatment provides little additional benefit for delivery for the same dose of bronchodilator drug.⁹

Undertaking a trial of nebulised bronchodilator therapy

If a patient is still symptomatic despite these therapeutic interventions it is reasonable to proceed to a formal trial of nebulised bronchodilator therapy. Current guideline² concerning patient assessment for domiciliary nebuliser treatment recommends twice daily recording of the peak expiratory flow (PEF) as well as monitoring the symptomatic response at home to various drug regimes for 2-week periods. The initial observation should be made during a period whilst taking high dose bronchodilator therapy via hand-held inhaler. Patients should then be educated in the use of the nebuliser, and should receive the first dose under medical supervision in case of tachyarrhythmias or other adverse reactions. Single measurement of the acute bronchodilator response to

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nebulised therapy is an unacceptable method of assessing patients for domiciliary treatment. This is because the acute response, in terms of both FEV₁ and symptom scores, correlates poorly with the longer-term PEF and symptom responses.¹⁰ Following this initial assessment, those patients with symptomatic improvement and PEF increase of >15% compared to values obtained on standard inhaled therapy should be considered for long term home treatment with nebulised bronchodilators (previous studies have shown high correlation between peak flow and symptom response among patients undergoing placebo-controlled nebuliser trials).¹⁰ Great care should be exercised before home therapy is initiated, at the physician's discretion, for those patients who derive symptomatic benefit from the nebuliser trial, but who do not achieve a 15% increase in peak flow measurements.

Once provided, it is recommended that patients use domiciliary nebulised bronchodilator therapy as required, up to four times a day. However, in order to avoid a delay should emergency treatment be necessary, patients should be advised to seek medical help if symptoms of dyspnoea do not improve following the use of their nebuliser.

Advantages and disadvantages of domiciliary nebulised therapy

It is clear that many patients with COPD derive benefit from domiciliary nebulised bronchodilators. O'Driscoll et al.¹ showed that about half of a group of patients with severe stable COPD who are symptomatic despite taking high dose inhalers achieve either subjective or objective improvement from home nebuliser therapy. This may, in some cases, be due to previous sub-maximal inhaled bronchodilator therapy, but other factors may also contribute; nebulised therapy may aid in sputum expectoration.² Psychological factors may influence patient's perceived symptomatic response to nebulised treatment; breathlessness may be reduced by the reflex in which a mist of cold damp air directed at the face results in subjective improvement of dyspnoea.³ There may be a placebo effect induced by "high tech" equipment at home.

Patients may request provision of a home nebuliser on the basis of a previous positive response to nebulised bronchodilator given for an acute exacerbation of airflow obstruction. Indeed, in our experience, the vast majority of patients with COPD using home nebulisers have previously received nebulised bronchodilators in hospital for treatment of an acute exacerbation. Jenkins et al.⁴ showed in a placebo controlled trial comparing equipotent bronchodilator given via inhaler and nebuliser to patients with stable COPD that no difference was apparent between the two methods of drug delivery in terms of symptomatic and PEF response, but all patients attribute symptomatic improvement to the nebuliser. Nevertheless, it appears that a proportion of COPD patients do improve symptomatically with domiciliary nebulised treatment.

Domiciliary nebulised therapy is expensive. In our practice, the most commonly prescribed drug regimen is salbutamol 5mg and ipratropium 500mcg four times a day. The drug costs alone are over £960 per person per year. This compares to less than £90 for standard doses of salbutamol and ipratropium administered by metered dose inhaler four times a day.⁵ In addition there are costs for maintenance and repairs of the compressor system.

It should be remembered when commencing nebulised therapy, that high dose bronchodilator treatment may cause side effects. High doses of β -2 agonist bronchodilators may provoke hypoxaemia and cardiac arrhythmias.^{16,17} Whilst large doses of anticholinergics may result in the development of urinary retention and glaucoma. Evidence supporting the development of airway β -receptor resistance as a consequence of long-term, high-dose β -agonist use is however, weak.^{18,19} Long-term nebulised β -agonists does not result in reduction of acute bronchodilator response to low-dose inhaled β -agonist. Furthermore there is no evidence of decrease with time of perceived symptomatic benefit from long-term nebulised bronchodilator,¹⁰ although high-dose therapy may result in a decrease in the duration, if not the peak, of the resultant bronchodilator response.⁷

Nebulised bronchodilator therapy at home in COPD patients has not been shown to improve survival or reduce the rate of decline in pulmonary function in the long-term.

Conclusion

Domiciliary nebulised therapy is a safe and effective method of symptom control in a small group of patients with severe COPD who have been adequately assessed for this form of treatment in keeping with recommended guidelines. The indiscriminate use of home nebulisers for patients with mild or moderate disease cannot be justified, may expose patients to complications of therapy and is not cost-effective. ■

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