THE PLACE OF TIOTROPIUM IN THE TREATMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Prepared by the Tayside Respiratory Formulary Sub-Group

Background

Chronic obstructive pulmonary disease (COPD) is a major burden on both primary and secondary care resources in Tayside. Smoking is the main aetiological factor behind COPD. Although the prevalence of smoking is likely to decrease in the future, the heritage of smoking that we inherit from the past few decades, particularly amongst young people, will ensure that the incidence of COPD continues to rise in Tayside for the next 10-20 years. In the past this unglamorous disease has been less successful than others at attracting resource, however, its profile has been raised by a number of national initiatives and, more locally, by the Dundee LHCC COPD programme. Furthermore, COPD is a quality marker within the new General Medical Services (GMS) contract.

Management of COPD

The bulk of COPD is managed in primary care. It is important that a firm diagnosis is made in each patient. Patients with COPD have irreversible airway obstruction, which is best demonstrated with spirometry. A diagnosis made just on clinical or radiological grounds is very unreliable. Spirometry will also classify the severity of COPD which, in turn, will influence the treatment that is offered to the patient.

There are a number of therapeutic interventions, both pharmacological and non-pharmacological, available for COPD. The most important of these for the individual patient is smoking cessation and there are an increasing number of programmes in Tayside offering this service. Pulmonary rehabilitation has also been shown to be effective at improving quality of life and exercise tolerance, and also at reducing burden on healthcare resource, in patients with moderate or severe COPD. A successful outpatient programme has run from the Chest Unit in Dundee for some years and more recently programmes have been set up in Perth and in Dundee primary care settings. There is currently no pulmonary rehabilitation facility in Angus, but there are proposals in the pipeline. Influenza and pneumococcal vaccination should be offered to all patients with COPD.

Pharmacological Treatment

The pharmacological treatment of COPD has evolved significantly in recent years. Prescribing patterns have varied greatly in the past, in part due to the lack of clear evidence-based guidance that was available. However, in recent years a number of randomised controlled trials have reported which have allowed the role of bronchodilators, particularly long-acting β2 agonists (LABA) and the newly available long-acting anti-muscarinic agent, tiotropium, to be better defined in COPD. LABA’s have been shown to produce sustained improvements in symptom scores and reduce exacerbation rates with consequent improvement in health status in patients with moderate or severe COPD. Likewise tiotropium, which has been approved by the Scottish Medicines Consortium for use in Scotland, has similar effects in moderate or severe COPD and has been shown to be more effective than shorter acting anti-muscarinics such as ipratropium. Both LABA’s and tiotropium should only be used in COPD if the diagnosis has been confirmed and the FEV₁ is less than 60% predicted. There is currently no evidence to demonstrate that LABA’s and tiotropium have additive clinical benefit in COPD and at present we cannot recommend co-prescription of these expensive drugs. They are different drug classes, working through different mechanisms, and it is possible that this advice will change in the future once trials report on their combined effects.
The role of inhaled steroids in COPD is less clear (refer to Tayside Prescriber Issue 83, June 2001). The available evidence suggests that they should be used if there is a clear asthmatic component (ie airway reversibility of >15%). There may also be long-term clinical benefits of inhaled steroids in patients with severe COPD (FEV₁ < 50% predicted) who also have frequent exacerbations.

The following guidelines on COPD management have been produced by the Tayside Respiratory Formulary Sub-Group, which includes medical, nursing and pharmacy representation from Angus, Dundee and Perth & Kinross LHCC’s and secondary care. These guidelines replace an earlier (pre-tiotropium) version included in the 1st Edition of the Tayside Area Prescribing Guide (TAPG). The updated guidelines will shortly be available on the Tayside Drug & Therapeutics Committee Website (www.show.scot.nhs.uk/thb/adtc) under ‘Formulary’ and ‘Guidelines’.

### Tayside Chronic Obstructive Pulmonary Disease (COPD) Guidelines

1. **Establish diagnosis**
   - Rule out other conditions
   - Spirometry essential for confirmation of diagnosis and assessing degree of airflow obstruction
   - To help rule out asthma, reversibility to short acting β₂ agonist should be performed
   - Chest X-ray at first presentation

2. **Address underlying cause**
   - eg smoking cessation

3. **Pharmacological treatment**
   - Bronchodilators are the mainstay of COPD therapy
   - Annual influenza vaccine
   - Consider pneumococcal vaccine
   - Long-term oxygen therapy (LTOT) (see section 3.6 of the TAPG)
   - The role of inhaled steroids in the treatment of COPD is contentious. If there is clear evidence of an asthmatic component, a **trial of moderate to high dose inhaled steroids** should be performed
   - Inhaled steroids **may** be of benefit to those patients with a FEV₁ <50% and who frequently exacerbate.

4. **Non-pharmacological treatment**
   - Pulmonary rehabilitation
   - Lifestyle advice

5. **Acute exacerbation**
   Referral for hospital assessment **should be considered** if any of the following:
   - Acute confusion
   - Severe breathlessness
   - Severe COPD
   - Increasing cyanosis
   - New or worsening peripheral oedema
   - Impaired level of consciousness
   - Already receiving LTOT
   - Rapid rate of onset
   - Uncertainty of diagnosis
Therapeutic Notes

**Bronchodilator therapy for COPD**

- Start therapy at step/dose most appropriate to severity of COPD (determined by spirometry and symptoms)
- Each step should be initiated on a 4 week trial basis and withdrawn if no benefit
- **Patient perceived benefit** should guide bronchodilator treatment rather than changes in spirometry

- **Short acting β₂ agonist**
- **Add regular ipratropium**
- **Replace ipratropium with *tiotropium or**
  - **Add long-action β₂ agonist**
- **Consider oral theophylline - may help expectoration**
- **Increase bronchodilators via MDI and spacer eg salbutamol 6 puffs**
- **Assessment carried out by appropriately trained person**
- **Salbutamol 2.5mg/2.5ml nebule four times daily**
- **Nebulised combination bronchodilator may be of further benefit**

* Tiotropium is a **potent** anticholinergic bronchodilator and should not be co-prescribed with any short-acting or nebulised anticholinergic.
* Tiotropium or long-acting β₂ agonists should **only** be used in patients with proven COPD and an FEV₁ of less than 60% predicted.
* There is currently no evidence for, or against, co-prescription of tiotropium and long-acting β₂ agonists. Although they produce bronchodilations through different mechanisms and may well have additive benefit when given together, co-prescription cannot be advocated until more evidence is available.

**Treatment of exacerbation at home**

**Antibiotics**
Recommended if: increased breathlessness and increased sputum purulence

**Bronchodilators**
Increase dose and frequency of existing short-acting β₂ agonist bronchodilator therapy. Nebuliser therapy can be given in severe exacerbation.

**Oral Corticosteroids**
May be useful in moderate or severe exacerbations.

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