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North of England evidence based guidelines development project: summary version of evidence based guideline for the primary care management of asthma in adults

North of England Asthma Guideline Development Group

This is the second of three articles on developing evidence based guidelines for the primary care management of asthma and angina in adults

The evidence on which these guidelines are based appears in full on the BMJ's world wide web page: http://www.bmj.com/bmj/

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Members of the guideline development and technical advisory groups are listed at the end of this report.

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The aim of this guideline is to provide recommendations (evidence based when possible) to guide primary health care professionals in their management of adult patients with asthma. It is a summary version of the full guideline,[1] to which reference should be made for clarification or further information. The development group assumes that health care professionals will use general medical knowledge and clinical judgment in applying the general principles and specific recommendations in this document to the management of individual patients. Recommendations may not be appropriate for use in all circumstances. Decisions to adopt any particular recommendation must be made by the practitioner in the light of available resources and circumstances presented by individual patients. Throughout this guideline categories of evidence (cited as I, II, and III) and the strength of recommendations (A, B, or C) are as described in the first article in the series.[2]

Scope of guideline

Aspects covered by the guideline are the use of peak flow measurement in diagnosis and management, drug treatment, non-drug treatment, and referral. All recommendations are for primary health care professionals and apply to adult patients attending general practice with asthma.

Aims of treatment

Comment—British Thoracic Society guidelines state the aims of treatment as patients having the least possible symptoms; the least possible need for relieving bronchodilators; the least possible limitation of activity; the least possible circadian variation in peak flow; the least possible adverse effects from medicine; and the best peak flow possible.[3] It is preferable to adjust treatment to cover exposure to day to day triggers such as exercise and cold air because avoidance imposes inappropriate restrictions on lifestyle. Specific comments about adjusting the dosages of drugs are made within the relevant sections on drug treatment.

Peak flow: diagnosis and management

RECOMMENDATIONS

- Peak flow variability can be used to help in the diagnosis of recurrent wheeze (B)
- The routine home use of peak flow meters for self management is not mandatory (A)
- Morning "dipping" should be regarded as a sign of transient poor control (B)
- Peak flow monitoring can be useful to assess patients and inform management (C).

Peak flow variability can be used to help in the diagnosis of recurrent wheeze (II).[4,5] Though monitoring peak flow can be useful to assess patients and inform management (III), the routine home use of peak flow meters does not alter patient outcomes (I).[6] Morning "dipping" of peak flow values reflects transient rather than long term poor control (II).[7] Additionally, in acute situations peak flow can be used to predict outcome (III).[8]

Drugs used in the treatment of asthma

Comment—All recommendations for treatment apply only in the absence of recognised contraindications, side effects, or interactions as documented in the *British National Formulary*.[9]

Compliance

RECOMMENDATION

- Compliance with treatment is important and should be checked regularly, especially if symptom control is poor or treatment is about to be increased (C).

Sequencing of treatment

Comment—There is little evidence to answer the important clinical questions of appropriate sequencing of treatment and the relative places of various agents in drug management. Drugs are therefore considered in the order of presentation in the *British National Formulary*.[9] A suggested sequencing is provided after consideration of the drugs.

Short acting β_2 agonists

RECOMMENDATIONS

- Short acting β_2 agonists are effective bronchodilators (A)
- They should be used on an as required basis to relieve symptoms (C)
- They should be used before exercise in patients who have exercise induced bronchospasm (A).

Though short acting β_2 agonists are effective as judged by an increase in peak expiratory flow (I),[10] there is conflicting evidence on the issue of as required versus regular dosage (I).[11,12] For patients who need four daily doses of a short acting β_2 agonist the two studies identified give contradictory findings. Salbutamol is effective for exercise induced bronchospasm and is more effective than sodium cromoglycate (I).[13]

Long acting inhaled β_2 agonists

Comment—We identified no evidence to suggest whether long acting β_2 agonists should be used before or after inhaled anti-inflammatory drugs. At the time of completion of the guideline the only prescribable long acting inhaled β_2 agonist was salmeterol.

RECOMMENDATIONS

- Most patients treated with salmeterol will achieve satisfactory control with 50 μg twice daily. If it is used in higher doses attention must be paid to inquiring about side effects (A)
- In patients using short acting β_2 agonists four times daily regular salmeterol should be added to treatment (A)
- The short acting β_2 agonist should be continued on an as required basis (C)
- Salmeterol should be considered if overnight relief is required (A).

Salmeterol produces appreciable bronchodilatation for 12 hours; there is little additional effect from dosages above 50 μg twice daily and side effects increase (I).[14-16] Used twice daily it is more effective than short acting inhaled β_2 agonists used four times daily (as a metered dose inhaler or powder) (I).[17-19] In one short term evaluation salmeterol was as safe as a short acting β_2 agonist (I), though this was a negative study without a power calculation.[20]

Comment—If the introduction of salmeterol is based on frequency of short acting β_2 agonist use there is benefit in using it in line with the recommendation above. We identified no evidence on the use of salmeterol at lower frequencies of short acting β_2 agonist use, nor any evidence in relation to frequency of inhaled anti-inflammatory use.

Inhaled anti-inflammatory agents

Steroids

RECOMMENDATIONS

- Patients requiring short acting β_2 agonists more than two or three doses a day should be treated with inhaled steroids (A)
- Inhaled steroids are effective on a twice daily basis (A)
- If symptoms are not controlled on twice daily dosing and there is concern about the total daily dose, then increasing the dosage frequency to four times daily but at the same total daily dose should be tried (A)
- If symptoms are not controlled with standard doses (up to a daily equivalent of 800 μg beclomethasone) higher doses of inhaled steroids should be used up to a daily equivalent of 2000 μg beclomethasone (A)
- A one to three month period of stability should be shown before stepwise reduction in inhaled steroids is undertaken, decreasing the dose by 25-50% at each step (C)
- As there is no good evidence of clinically important differences between differing inhaled steroids, patients should be treated with the cheapest inhaled steroid that they can use and which controls their symptoms (C).

Inhaled steroids are effective (I)[21-23] and can allow a reduction of oral steroid dosage in steroid dependent patients (I).[24-27] There are no clinically important differences in effectiveness between the various inhaled steroids that cannot be addressed by dosage adjustment (I).[28-34] The clinical relevance of differences in cortisol suppression between different agents is unclear (III).[29,31] In patients requiring short acting β_2 agonists more than two or three times a day adding an inhaled steroid improves peak flow and symptoms and reduces short acting β_2 agonist use (I).[23,35]

Comment—Though there may be benefit from introducing inhaled steroids at a lower level of use of β_2 agonists, as suggested by the British Thoracic Society guidelines, we did not identify any evidence for this. We identified no evidence on the use of inhaled steroids as first line treatment.

Inhaled steroids are slightly more effective when used four times daily than when used twice daily and are more effective when used twice daily than when used once daily; differences in lung function, however, are not large (I).[36] Of the five studies that examined the effectiveness of differing dosage frequencies of inhaled steroids, all were small and four were negative studies without a power calculation and therefore at risk of type II errors.[37-40] The group recognised the importance of compliance with treatment, though this was not formally studied; in most patients twice daily dosing is acceptable. Symptom control is better with high rather than low doses of inhaled steroids (I),[32,36] though surprisingly few studies were identified to support this widely held clinical view. We identified no direct evidence on when to decrease the dose of inhaled steroids. One study indirectly suggested that some patients using inhaled steroids may be receiving an unnecessarily high dose (III).[41]

Other inhaled anti-inflammatory agents

RECOMMENDATION

- Nedocromil or sodium cromoglycate may be useful in occasional patients as an adjunct to inhaled steroids or as an alternative in those patients who cannot tolerate or do not wish to take inhaled steroids. They should be considered as second line treatment to inhaled steroids. We identified no evidence to prefer nedocromil over sodium cromoglycate or vice versa (C).

Though nedocromil is more effective than placebo as a first line anti-inflammatory agent, its effect is not large and it has a questionable effect as a second line anti-inflammatory drug (I).[41-46] Sodium cromoglycate is more effective than placebo as a first line anti-inflammatory drug and is effective delivered in either a metered dose inhaler or a spinhaler (I).[47] There is no evidence to prefer nedocromil to sodium cromoglycate or vice versa (I).[48]

Drug delivery devices

RECOMMENDATIONS

- Health care professionals advising patients should use the cheapest drug delivery device that the patient can use and comply with effectively (C)
- Large volume spacer devices should be used with inhaled drugs when the aim is to increase their effectiveness without increasing the dose. Additionally, they should be used with high dose inhaled steroids to decrease oral candidiasis (A)
- In acute situations large volume spacer devices are an effective alternative to nebulisers for delivering high dose bronchodilators (A).

Comment—A range of drug delivery devices is available; given this range the evidence on the relative merits and the therapeutic place of differing inhaler devices is sparse.

Metered dose inhalers are as effective as powder devices (I),[34,47] and autohalers are no more effective than metered dose inhalers (I).[49] The use of spacer devices increases the effectiveness of inhaled drugs and decreases oral candidiasis in patients using inhaled steroids (I).[50] Additionally, spacer devices can be as effective as nebulisers in delivering drugs for acute asthma (I).[51]

Inhaler technique

RECOMMENDATIONS

- Health care professionals should ensure that patients can use their inhalers adequately (C)

• Inhaler technique should be rechecked whenever control is in doubt (C).

The only paper addressing inhaler technique evaluated an electronic meter to improve technique; it conferred no advantage (I).[52]

Oral bronchodilators

RECOMMENDATION

• Oral bronchodilators should be considered as second line treatment to inhaled bronchodilators (C).

Oral bronchodilators act more slowly than inhaled agents and are much less suitable for short term relief of symptoms (III). Oral theophylline is more effective than placebo (I)[53] and produces similar therapeutic effects to oral salbutamol (I).[54] When theophylline is added to oral salbutamol it produces a rise in peak expiratory flow, greatest in patients with the lowest initial peak expiratory flow and with higher doses of theophylline (I).[55]

Sustained release terbutaline is more effective than short acting oral salbutamol (I)[56] and equivalent to inhaled steroids in terms of controlling nocturnal symptoms (I).[57] Bambuterol is no better than milligram equivalent doses of controlled release terbutaline (I).[58-60]

Oral steroids

RECOMMENDATIONS

• Steroids should be used in exacerbations of asthma (A)

• They should be given by mouth, as intravenous administration offers no advantages (A)

• When used in short courses of up to two weeks the dose of oral steroids does not need to be tapered; oral steroids can be stopped from full dosage (C).

Steroid treatment provides important benefits to patients presenting with acute exacerbations of asthma; oral and intravenous dosing are equally effective (I).[61] When used in short courses oral steroids are safe; they produce very low rates of gastrointestinal bleeding. The greatest risk is in patients with a history of gastrointestinal bleeding or taking anticoagulants (III).[62]

Comment—The *British National Formulary* states: "Corticosteroid therapy is weakly linked with peptic ulceration; the use of soluble or enteric-coated preparations to reduce risk is speculative only."[9]

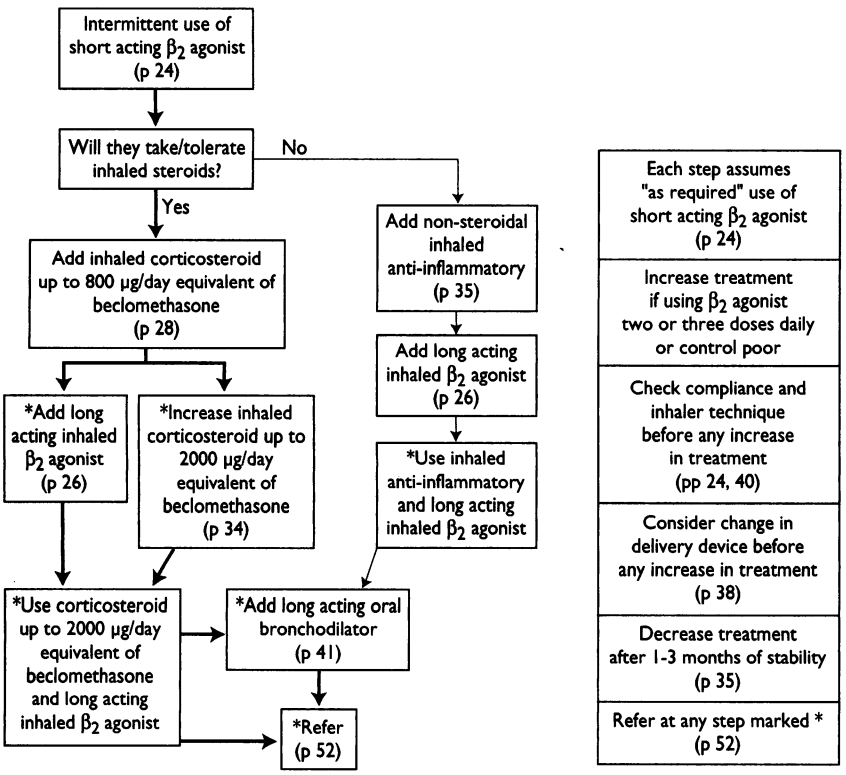

Fig 1—*Sequencing treatment algorithm (page numbers refer to main guideline document)*

Intravenous therapy in acute asthma

RECOMMENDATION

• Intravenous therapy should not be used in preference to inhaled β_2 agonists in the treatment of acute asthma (I),[63-65] and nebulised salbutamol is more effective than intravenous salbutamol in acute asthma (I).[66]

Drug sequencing

Chronic asthma: sequencing drugs

RECOMMENDATIONS

• The trigger to increasing treatment at all stages is if the short acting inhaled β_2 agonist is being used more than two or three times daily or symptom control is not good (British Thoracic Society guidelines define good control as minimal (ideally, no) chronic symptoms; minimal (that is, infrequent) exacerbations; minimal need for relieving bronchodilators; no limitations on activities) (C)

• Compliance should be checked before any treatment increase (C)

• A one to three month period of stability should be shown before stepwise reduction in treatment is undertaken (C).

Figure 1 shows a proposed sequencing of treatment.

Chronic asthma: sequencing drug delivery devices

RECOMMENDATIONS

• Patients should initially be treated with a metered dose inhaler (C)

• If they cannot comply with a metered dose inhaler, then a large volume spacer device should be added (C)

• If they cannot comply with a metered dose inhaler plus large volume spacer, then they should be treated with the cheapest powder or automatic aerosol inhaler that they can comply with (C)

• If they find a metered dose inhaler plus large volume spacer difficult to carry during the day because of its bulk, then they should be treated with the cheapest powder or automatic aerosol inhaler that they can comply with (C).

Uncontrolled asthma: sequencing drugs

RECOMMENDATION

Patients with uncontrolled asthma should be treated as follows:

• Prednisolone 30-40 mg daily should be given until the episode has resolved, symptoms are controlled, and lung function values have returned to previous best. Though seven days' treatment will often be sufficient, treatment may need to be continued for up to 21 days (C)

• Depending on the severity of the episode patients may need a short acting inhaled β_2 agonist delivered via a nebuliser or a large volume spacer device (C).

Comment—British Thoracic Society guidelines[3] suggest that the indications for rescue courses of steroids should include day by day worsening of symptoms and peak expiratory flow; fall in peak expiratory flow to below 60% of patient's best; sleep disturbance by asthma; persistence of morning symptoms till midday; diminishing response to inhaled bronchodilators; emergency use of nebulised or injected bronchodilators.

Non-drug treatment

Acupuncture and yoga

RECOMMENDATION

- Patients should not be treated solely with acupuncture or yoga (A).

Neither acupuncture nor yoga has been shown to be of therapeutic benefit in asthma (I).[67-69] In the one identified study of yoga bronchial reactivity decreased.[68]

Precipitants

Allergen avoidance

Comment—British Thoracic Society guidelines[3] suggest that allergens (such as house dust mite, domestic pets, and pollens) should be considered and avoided when relevant.

Smoking and smoking cessation

RECOMMENDATIONS

- The current smoking status of all patients should be known (C)
- Patients who smoke should be advised to stop (C)
- There is no one strategy that is effective for all patients (C)
- Advice and strategies should be tailored to individual circumstances (C)
- Patients should avoid passive smoking (C).

Nicotine patches can help patients stop smoking (I).[70 71]

Patient education

RECOMMENDATION

- Patients should be offered education about their condition and its management (C).

Patient education can improve knowledge and beneficially alter behaviour (I).[72-77] The study designs were such that it was not possible to draw out common successful strategies.

Referral

Comment—We could identify no evidence concerning the referral of patients with asthma, either from primary to secondary care or between health care professionals within primary care. These recommendations are based on British Thoracic Society guidelines.[3]

Referral to a chest physician

RECOMMENDATIONS

Referral to a respiratory physician is appropriate for:

- Patients in whom there is diagnostic doubt
- Patients with possible occupational asthma
- Patients who present a problem in management (C).

Comment—The guideline development group made additional points of clarification:

- Occupational asthma should be referred for confirmation of the diagnosis, management of sensitiser avoidance, and management of other workers in the workplace (C)
- Patients whom a general practitioner is considering for long term oral steroids or home use of a nebuliser should be referred to a respiratory physician for assessment (C)
- Patients who have recently been discharged from hospital should have their treatment reviewed; this does not need hospital review if primary health care professionals have the relevant skills and resources (C)
- Patient preference should be accommodated in the decision to refer (C)
- Primary health care professionals should be aware of the range of skills and facilities available within their practice and should refer within the practice when appropriate (C).

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