

Common questions about hay fever

SUMMARY

This *Bulletin* explores common questions about hay fever around management of symptoms, over-the-counter (OTC) products, advice for pregnant women, evidence for newer antihistamines, alternative therapies and the place of immunotherapy. It complements *MeReC Bulletins* Vol 6, No 4, and Vol 9, No 3, which looked at general treatment in more detail.

- Intranasal corticosteroids and oral antihistamines are the usual treatment options for hay fever. In addition, patients can take practical measures to reduce exposure to pollen.
- There is little evidence to confirm whether, in practice, third generation antihistamines (e.g. desloratadine or levocetirizine) confer any benefit over second generation ones; they should be reserved for patients who cannot tolerate or have not responded to other therapies.
- Allergen-specific immunotherapy can provide major symptom relief to severe hay fever sufferers. However, it has the potential to cause anaphylaxis and should be reserved for patients whose symptoms remain poorly controlled despite use of other therapies.
- Alternative therapies, such as butterbur or homoeopathy, may be beneficial to hay fever sufferers but data are limited and further studies are needed to establish their place in treatment.

Hay fever (seasonal allergic rhinitis) sufferers are allergic to airborne pollens and spores, which stimulate release of histamine and other allergic mediators, such as prostaglandins, from affected cells.¹ This can result in symptoms such as sneezing, rhinorrhoea (runny nose), nasal congestion, itching of the soft palate, nose and eyes, watering of the eyes, wheezing and shortness of breath. Although hay fever is often thought of as a minor ailment, sufferers can feel very unwell. Symptoms usually occur between March and September — tree pollen is released from March to May and affects 25% of sufferers; grass pollen, which affects 90% of sufferers, is released from May to late July; and fungal spores are released until September.²

How should symptoms be managed?

The choice of treatment for hay fever is a balance between symptoms and the patient's preference for oral or topical therapy. Intranasal corticosteroids and oral antihistamines are the usual options. In addition, patients can take practical measures to reduce exposure to pollen.³ Examples include keeping doors and windows shut and using cars with air conditioning systems that include a pollen filter.

Intranasal corticosteroids are the treatment of choice in patients with moderate to severe hay fever, as they can relieve all symptoms, including nasal congestion.⁴ Patients using

intranasal corticosteroids should be advised that these preparations must be used regularly to be effective and that maximum efficacy develops over several days or weeks.⁵ Ideally, corticosteroid nasal sprays should be started two weeks before patients are likely to become symptomatic.⁵

Oral antihistamines relieve ocular symptoms, rhinorrhoea, sneezing and nasal irritation but most have little effect on nasal congestion.⁶ They have a more rapid onset of action than intranasal corticosteroids and can be taken when required, although they are best taken regularly.^{2,3} All antihistamines are effective but response to a particular agent and the occurrence of adverse events can vary between individuals.⁵ First generation antihistamines (also known as sedating antihistamines), such as chlorphenamine, tend to cause sedation and antimuscarinic side effects, such as dry mouth. Second and third generation antihistamines (also known as non-sedating antihistamines) are less likely to cause sedation.^{2,5}

Intranasal and intraocular antihistamines (e.g. levocabastine or azelastine) have a more rapid onset of action than oral antihistamines (15 minutes vs. 1–3 hours). Intranasal antihistamines reduce nasal symptoms, such as itching and sneezing but not congestion — they are probably more effective than intranasal sodium cromoglicate but are less effective than intranasal corticosteroids. A number of preparations are available for relief of ocular hay fever



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Panel 1. Treatment options for hay fever⁵

Intermittent mild symptoms

Intermittent or regular oral antihistamines are a good first choice. Intranasal antihistamines have a faster onset of action.

Intermittent moderate to severe symptoms

Intermittent or regular oral or intranasal antihistamines. Intranasal corticosteroids or decongestants ease nasal congestion. Intranasal decongestants can be used short-term to relieve congestion and allow penetration of an intranasal corticosteroid.

Persistent moderate to severe symptoms

Intranasal corticosteroids are the first-choice treatment. Intranasal decongestants can be used short-term to relieve congestion and allow penetration of an intranasal corticosteroid. If symptoms remain uncontrolled, increase the corticosteroid dose or use a different one. If itching and sneezing are troublesome, an antihistamine can be used. If watery rhinorrhoea is the predominant symptom, try intranasal ipratropium. If symptoms continue to be poorly controlled, consider a short course of oral corticosteroids.

If eye symptoms predominate

Oral antihistamines can be taken intermittently or regularly. Intraocular antihistamines are an alternative and act more rapidly; they may be preferable for intermittent use. Intraocular sodium cromoglicate can also be used for prophylaxis of persistent eye symptoms. If this is ineffective, try nedocromil or lodoxamide.

NB: PRODIGY'S classification of allergic rhinitis is:

- Intermittent — symptoms occur less than four days a week or for less than four weeks
- Persistent — symptoms occur more than four days per week and for more than four weeks
- Mild — symptoms are not troublesome and normal activities, such as sleep, sport, leisure, work and school, are unaffected
- Moderate — symptoms are troublesome and one or more of the following occur: impairment of normal activities, such as sport, leisure, work and school; disturbed sleep.

Few of the drugs used for treatment of allergic rhinitis are licensed for use during pregnancy

symptoms.⁷ Patients should be warned that antihistamine eye drops can cause local irritation and blurring of vision.⁷ The approach to treatment shown in **Panel 1** can be helpful when considering options (see **Table 1** for the relative effects of agents on symptoms).

If maximal medication appears to be ineffective, the patient's compliance should be checked. In patients with severe symptoms or on special occasions (e.g. when sitting examinations) it may be worth considering a short course of oral corticosteroids.⁵ Oral corticosteroids are preferred to depot corticosteroids, as the dose of depot preparations cannot be tailored to the severity of symptoms. In addition, morning dosing with an oral corticosteroid may be less likely to cause adrenal suppression than continuous release from a depot injection.⁵ Referral to a specialist may be necessary in some patients.

What is available over the counter?

A wide range of OTC medication is available for managing allergic rhinitis symptoms, including representatives of most of the above

drug classes, except oral and depot corticosteroids.⁷ Oral and intranasal decongestants are generally recommended for short-term use only, due to the risk of rebound congestion on withdrawal.⁵ The use of sodium cromoglicate and decongestants for treatment of hay fever was covered in *MeReC Bulletin* (Vol 9, No 3). Community pharmacists can help most hay fever sufferers to manage their own treatment by providing OTC medication (see **Panel 1**) and advice on allergen avoidance. However, some patients may not respond to OTC therapy or may have conditions/symptoms that require referral to their GP.

What advice should be given to pregnant women?

Management of hay fever during pregnancy can include allergen avoidance, pharmacological treatment and immunotherapy. The risk of drug-induced malformations is highest during the first trimester and, if possible, drug treatment should be avoided during this period. Few of the medications used for treatment of allergic rhinitis are licensed for use during pregnancy.⁷ Data are limited and drug choice is guided by results from observational studies, consensus, anecdotal reports and common sense.

If allergen avoidance is ineffective and/or the patient is unable to tolerate their symptoms, topical treatment with intranasal beclomethasone and/or sodium cromoglicate (intranasal or intraocular) should be considered first line, as topical administration minimises systemic absorption. Data on intranasal corticosteroid use during pregnancy are limited but those for systemic corticosteroids used in pregnant women for other indications (e.g. asthma) suggest that risks are small. Oral corticosteroids have not been associated with an increased rate of malformations. However, high doses (over 50mg daily of oral prednisolone) used over long periods have been associated with fetal growth retardation in a small number of patients.^{9,10}

Use of oral decongestants during pregnancy is not generally recommended because of conflicting data, the risk of rebound congestion and a possible association with fetal toxicity.⁹ A small number of case reports have been published, which imply that pseudoephedrine may be associated with an increased risk of gastroschisis (congenital fissure of the abdominal wall). However, two observational studies involving 2,509 women who had been exposed to pseudoephedrine found no increased adverse outcomes compared with controls.

Allergen-specific immunotherapy (see later) can be continued carefully during pregnancy in patients who are already deriving benefit from it. However, the risk of anaphylaxis is higher in pregnant women, so immunotherapy

should not be started nor doses increased, unless there is a serious clinical need.^{9,10}

Do new antihistamines have any advantages over existing ones?

First generation antihistamines (e.g. chlorphenamine) have been used to manage hay fever for many years but can cause sedation. Second generation antihistamines generally cause less sedation, although it can occur in a small number of patients. However, some second generation antihistamines have been reported to cause potentially fatal cardiac adverse effects, notably terfenadine and astemizole. These effects include prolongation of the QT interval, which has the potential to lead to torsade de pointes, ventricular tachycardia, atrioventricular block and cardiac arrest.¹

Mizolastine (*Mizollen*) is a newer second generation antihistamine and a potent peripheral H₁ antagonist.^{11–13} Theoretically, mizolastine has the potential to prolong the QT interval in some patients and is therefore contraindicated in patients with significant cardiac disease, a history of symptomatic arrhythmias or those taking drugs known to prolong the QT interval.¹¹

Mizolastine seems to be as effective as other second generation antihistamines. In a RCT, 375 patients with seasonal allergic rhinoconjunctivitis were randomised to receive mizolastine 10mg, cetirizine 10mg or placebo daily for 28 days. The results showed that mizolastine and cetirizine were similarly effective and that both were more effective than placebo ($P \leq 0.01$).¹² In a double blind study of 428 patients with perennial allergic rhinitis randomised to mizolastine 10mg, loratadine 10mg or placebo daily for 28 days, a statistically significantly greater improvement in patient-rated nasal score was observed with mizolastine after two and four weeks compared with placebo ($P=0.001$ and $P=0.01$, respectively). A significantly greater improvement statistically was seen with mizolastine compared with loratadine at two weeks only ($P=0.031$).¹³

Levocetirizine (*Xyza*®), a third generation antihistamine, is the active enantiomer of cetirizine, a second generation antihistamine. Data from preclinical studies suggest that the therapeutic effects of cetirizine are mainly due to levocetirizine, which has twice the affinity for

H₁ receptors as cetirizine.¹⁴ To date, there are no studies that compare these drugs for treatment of hay fever. Levocetirizine does not cause any clinically relevant changes to the QT interval and is unlikely to produce adverse cardiac events.^{1,15}

Desloratadine (*Neoclarityn*®), a third generation antihistamine, is the principal metabolite of the second generation antihistamine loratadine.¹⁶ No studies that compare desloratadine and loratadine have been published. A four-week double-blind study involving 331 patients with seasonal allergic rhinitis showed that desloratadine significantly improved reflective nasal congestion scores (patient assessment of congestion for the previous 12 hours) compared with placebo.¹⁷ Limited experience to date, including several studies and post marketing adverse event reporting, has indicated that desloratadine does not cause adverse cardiac effects such as QT interval prolongation or arrhythmias.^{1,16}

There is little evidence to confirm whether, in practice, third generation antihistamines confer any benefit over those from the second generation. Large, well-designed comparative studies are needed to establish whether third generation antihistamines are more efficacious and have a lower incidence of side effects than first or second generation drugs. In the mean time, if an antihistamine is considered appropriate therapy, it would seem sensible to reserve third generation antihistamines for patients who cannot tolerate or have not responded to other therapies.

Is there any evidence for alternative therapies?

Several alternative remedies have been studied for treatment of allergic rhinitis. **Butterbur** (*Petasites hybridus*, butter dock, bog rhubarb) is a plant that is native to Europe, northern Africa and south west Asia. Its leaves and roots contain sesquiterpenes (petasines) which inhibit leukotriene production and may be associated with an anti-inflammatory action in allergic reactions.¹⁸

A standardised extract of butterbur has been compared with cetirizine in a two-week RCT involving 125 patients with moderately severe hay fever. Both groups showed similar

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Table 1. Effect of therapies on hay fever symptoms⁸

	Rhinorrhoea	Sneezing	Nasal itching	Congestion	Eye symptoms
Oral antihistamines	++	++	+++	+	++
Intranasal antihistamines	++	++	++	+	0
Intraocular antihistamines	0	0	0	0	+++
Intranasal corticosteroids	+++	+++	++	+++	++
Intranasal decongestants	0	0	0	++++	0
Intranasal cromoglicate	+	+	+	+	0
Intraocular cromoglicate	0	0	0	0	++

Adapted with permission from ARIA

0 = least effect, ++++ = greatest effect

Allergen-specific immunotherapy should only be undertaken by a clinician experienced in its use

improvements measured using SF-36, a non-specific symptom score. However, the study was small and did not include a placebo. In addition, use of a test that was more specific to rhinitis symptoms would have helped to define butterbur's place in therapy better. The incidence of adverse effects was similar in both groups, but the trial was too small to show a significant difference between the treatments.¹⁸

Grapeseed extract is a natural source of catechin monomers that, *in vitro*, have prevented histamine release from mast cells in rats. An eight-week pilot study randomised 54 patients to grapeseed extract or placebo. There were no significant differences between the groups in terms of quality-of-life scores, nasal symptom scores or weekly symptom severity scores.¹⁹

Many patients with hay fever try **homoeopathy**. Limited evidence from a RCT that used a homoeopath-prescribed preparation of the patient's principal allergen suggested that such preparations may be of some benefit.²⁰ However, patient numbers were small and larger controlled trials are needed to confirm this.²¹ A range of commercial preparations are available, including *allium cepa*, *nux vomica* and *pulsatilla*. However, there are no published data to support their use.²

What is the role of immunotherapy?

Allergen-specific immunotherapy is effective and can be of lasting benefit to patients with seasonal allergic rhinitis.²² It involves administering increasing doses of a specific allergen extract over months to years, to relieve symptoms associated with subsequent exposure to that allergen.⁴ Allergen-specific immunotherapy should only be undertaken by a clinician experienced in its use, as it is associated with a small risk of anaphylaxis, especially during induction or the upward dose titration phase.^{6,7} It should be reserved for patients who have poorly controlled symptoms and/or evidence of clinically relevant IgE-mediated disease, despite allergen avoidance and use of appropriate medication.⁶

The Committee on Safety of Medicines has advised that patients with hay fever and persistent asthma should not be treated with allergen-specific immunotherapy because they are at greater risk of developing severe adverse reactions than other patients.⁷

Conclusion

Several third generation antihistamines are now available for treatment of hay fever (e.g. desloratadine or levocetirizine) but there is not enough evidence at the moment to favour their use over second generation antihistamines,

such as loratadine and cetirizine. Use of third generation antihistamines should be reserved for patients that cannot tolerate or do not respond to other therapies. A wide range of medication is available OTC for the treatment of hay fever. Community pharmacists are ideally placed to advise on choice and appropriate use of hay fever medication, allergen avoidance and on when patients need to be referred to their GP. Alternative therapies, such as butterbur or homoeopathy, may provide some benefit, but data are limited and further studies are needed to establish their place in therapy.

For patients with severe hay fever, who have not responded to appropriate therapies and allergen avoidance, allergen-specific immunotherapy can provide major symptom relief. However, it should not be used in patients with asthma and has the potential to cause severe allergic reactions.

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