

Introduction

Rhinosinusitis affects one in six people (17,18). It has a major impact on the patient's quality of life (19) and also has significant economic consequences. A conservative estimate of the cost of decreased productivity caused by allergic rhinitis or its treatment in North America is four billion dollars (20).

Definition

The term "rhinitis" implies a pathological diagnosis but the diagnosis is made clinically on the basis of the presence of two or more of the following symptoms for more than one hour on most days: sneezing, itching, rhinorrhoea and / or nasal obstruction (47). The nasal lining is continuous with that of the sinuses and so most patients with these symptoms have "rhinosinusitis".

Classification

The International Rhinitis Management Working Group in their consensus report agreed three main aetiological groups: Allergic, Infective and another group of heterogeneous conditions. More than one aetiology may affect the individual patient.

Allergic

This may be seasonal or perennial depending on the allergen involved. Seasonal allergic rhinitis due to grass pollens presents in May in the United Kingdom. Tree pollen allergy usually occurs earlier and weeds and moulds cause symptoms in summer and autumn. House dust mite and cat dander are the commonest causes of perennial allergic rhinitis.

Infective

This can be acute or chronic if symptoms persist beyond eight to twelve weeks. Acute rhinosinusitis is usually viral but when inflammation of the nasal lining impedes sinus ventilation / drainage through the region of the middle meatus (the so called ostiomeatal complex) secondary bacterial infection may develop.

Other:

1. Non-allergic, non-infective rhinosinusitis.

This group includes patients previously described as having intrinsic rhinitis, idiopathic rhinitis and vasomotor rhinitis. NARES (non-allergic rhinitis with eosinophilia) is also recognised (3). Some of these patients show a heightened sensitivity to non specific triggers such as humidity, air temperature and irritants and may complain of watery rhinorrhoea rather than blockage.

2. Rhinosinusitis with nasal polyps.

Nasal polyps can occur with cystic fibrosis (6,7) , asthma (8) and as part of a syndrome of aspirin sensitivity (9), but most commonly occur alone. The cause is unknown and while the prevalence of allergy is not higher in patients with polyps, mast cell reactions and eosinophil activation with subsequent inflammation seem to be implicated and explain why corticosteroids are therapeutically effective.

3. Endocrine

Pregnancy, puberty, hypothyroidism and acromegally are all associated with rhinosinusitis.

4. Rhinitis Medicamentosa and Drug - induced rhinitis

This condition may result from dependency on nasal decongestants. Beta blockers, NSAIDs and the oral contraceptive are other drugs commonly implicated.

5. Occupational rhinosinusitis

A variety of workplace chemicals - grain, wood-dusts and platinum salts for example - are known to cause a rhinosinusitis.

6. Atrophic rhinosinusitis

This is characterised by progressive atrophy of the sinonasal mucosa with viscid mucus which dries to fetid crusts. Klebsiella may be implicated but it may also result from over-aggressive surgery with removal of excessive mucosa, Sjogren's syndrome, ageing and SLE.

7. Food

Food can produce rhinosinusitis by a number of mechanisms (4). Gustatory rhinorrhoea (5) may occur when eating spicy foods. Specific allergic hypersensitivity reactions occur to particular foods (or preservatives / colourants) Alcohol produces a physiological vasodilatation and nasal congestion but can also provoke symptoms due to hypersensitivity. True food allergy is over-diagnosed and never causes isolated nasal symptoms.

8. Structural factors

Normal mucociliary clearance will be impaired where there is mucosal - mucosal contact - as in deviation of the nasal septum and concha bullosa and will result in neuropeptide mediated inflammation. These mechanical factors are amenable to corrective surgery and are classified by some authors as a separate major diagnostic group.

Differential Diagnosis.

When symptoms are unilateral one should be suspicious of malignancy. Where there is watery rhinorrhoea one should consider a cerebrospinal fluid leak, especially if unilateral. Lower respiratory tract pathology such as Wegener's and sarcoidosis may also be associated with nasal and sinus manifestations.

History.

Factors elicited in the history will help in determining the main aetiology. The chest and allergy deserve special attention. As well as eliciting specific nasal symptoms and their chronology, a thorough general medical history should be taken.

Examination.

Examination should include assessment of the external appearance and the anterior nasal septum to exclude structural deformities causing obstruction. Further assessment of the intranasal cavity may reveal polyps. Intranasal examination has been considerably enhanced with the advent of rigid and flexible endoscopes. The colour of the turbinates and mucus provide little diagnostic information.

Investigations

Immunological

Skin Prick Tests

Immediate hypersensitivity mediated by IgE can be demonstrated by skin-prick tests. They are preferred to scratch or intradermal tests which are less reproducible and more dangerous. However, the findings need careful interpretation in light of the clinical history as both false negative and false positive results occur (10) and there is little correlation between weal or flare size and symptoms (11). The majority of patients with allergic rhinitis are sensitive to a relatively small range of aeroallergens. A positive skin-prick test provides supportive evidence for the clinical diagnosis and is reassuring where costly or time-consuming allergen avoidance measures are suggested. It also re-inforces patient understanding.

Serum Specific IgE

When there is no extract for skin-prick testing, or skin-prick testing is not possible because of skin disease or the patient is on antihistamines specific serum IgE measurements can be made. (Radioallergosorbent-RAST test)

Radiological

Plain Sinus Radiographs

Plain radiographs have a limited role in the management of rhinosinusitis because they have such poor specificity and sensitivity (12). A positive finding of a fluid level in acute sinusitis may be helpful.

CT scans

CT scans provide important anatomical information if surgery is contemplated and demonstrate the extent of disease. There are false positives (48) but a clear scan is useful in excluding chronic sinonasal disease.

Bacteriology

Guarded specimens obtained under direct endoscopic visualisation of the middle meatus correlate well with formal sinus aspirates, in contrast to blind nasal swabs.

Other Investigations

In the specialist and research setting further investigations may help to determine a complex aetiology and assess treatment outcome. These include assessments of ciliary function, olfaction, and the nasal airway.

Treatment (After International Rhinitis Management Working Group)

Seasonal Allergic Rhinosinusitis · Allergen avoidance

Some allergens eg pollen are ubiquitous and avoidance is not always possible. However measures can be taken to minimise exposure. In the case of house-dust mite sensitivity these would include synthetic bedding and mattress covers, removing soft furnishings and carpet from the bedroom, and regular vacuuming.

Mild disease or occasional symptoms

Rapid onset oral non-sedating antihistamines or topical antihistamines or cromoglycate drops are recommended when symptomatic.

Moderate disease

A recent meta analysis of sixteen randomised controlled trials comparing intranasal corticosteroids and H1 receptor antagonists in the treatment of allergic rhinitis(21) suggests that intranasal corticosteroids are superior to antihistamines in treating the nasal symptoms of allergic rhinitis and (22), as effective as antihistamines in treating the eye symptoms.

If above ineffective refer for:

-nasal examination

-allergy testing

-systemmic steroids or betnesol

-consideration of immunotherapy

Perennial Allergic Rhinosinusitis in Adults

Allergen avoidance

Topical nasal steroid if long term exposure

Oral non-sedating antihistamines (and possibly oral decongestant) in intermittent disease.

Perennial Allergic Rhinosinusitis in Children

Allergen avoidance

Topical nasal sodium cromoglycate spray

Oral non-sedating antihistamine

Topical nasal steroid if above ineffective or if long-term exposure

Perennial Non-Allergic Rhinosinusitis

With little watery discharge Avoidance of irritants and advice to stop smoking Topical nasal steroid sprays (if effective may be needed long-term)

If treatment ineffective after one month:

- consider betnesol drops for six weeks or short course of systemic steroids
- oral decongestants
- referral to specialist
- With copious watery discharge Avoidance of irritants and advice to stop smoking Topical nasal anticholinergic

Pharmacology Antihistamines

Antihistamines act as competitive antagonists at the histamine receptor. They are effective in reducing established symptoms of sneezing, itching and watery rhinorrhoea in particular. Cetirizine, loratidine, acrivastine and terfenadine suppress skin reactions for about four days after drug ingestion whereas astemizole has a much longer half-life and reduces skin prick reactions for up to eight weeks (23). Cetirizine is unique in that it is not metabolised in the liver but excreted in the urine.

Reports (24,25) have associated astemizole and terfenadine with serious cardiac arrhythmias. This is because in high doses the delayed rectifier potassium channels are blocked prolonging the QT interval (26). The drugs are metabolised in the liver by the cytochrome P450 system and should therefore not be used in hepatic failure or together with competitors for the P450 system (such as macrolide antibiotics and antifungals). Fexofenadine, the active metabolite of terfenadine is free of this arrhythmogenic effect.

Though controversial it is likely that antihistamines exert an anti-inflammatory effect beyond that produced solely by antagonism of the H1 receptor. Certainly the production of adhesion molecules (ICAM-1), and the release of interleukin- 8 (a neutrophil chemotactic and

activating factor) and granulocyte-macrophage colony stimulating factor from epithelial cells stimulated by activated eosinophils is reduced (27).

Comparative studies between oral antihistamines are difficult to evaluate. Full dose-response curves have not been performed in the same individuals to compare efficacy and side effects. However the greater cost of the non-sedating antihistamines is substantially offset by the lack of effect on performance.

Topical antihistamines such as azelastine and levocabastine are available and can be used for acute symptomatic relief and prophylaxis of allergic rhinitis without systemic side effects.

Corticosteroids

Corticosteroids penetrate the cell membrane and bind to hormone receptors in the cytoplasm. Within the nucleus the steroid/receptor complex binds to specific DNA sites which have a regulatory role in protein synthesis. This is manifest in a reduction in inflammatory cell infiltration and its consequences (29).

Corticosteroids may be given topically, taken orally or administered intravenously.

Topical corticosteroids are effective in reducing nasal blockage, itching, sneezing and rhinorrhoea in allergic and non-allergic non-infective rhinosinusitis (34). Their ability to reduce nasal blockage and efficacy in non-allergic rhinitis gives them an advantage over antihistamines. They are more effective in symptomatic control of allergic rhinitis than sodium cromoglycate (35), antihistamines (36) and decongestants (37).

Numerous comparative studies have been performed but there are no published studies that show one nasal steroid is more effective than any other (eg 53,54,55). Therefore, choice of agent depends on patient preference and cost.

Beclomethasone was introduced in 1973 and combined high topical efficacy with rapid hepatic metabolism (28). Subsequently a variety of topical nasal steroid sprays have become available. These are: budesonide (rhinocort), flunisolide (syntaris), fluticasone (flixonase), mometasone (nasonex) and triamcinolone (nasocort). With the exception of beclomethasone and flunisolide they are once-a-day preparations.

Environmental concerns have led to the elimination of CFC driven aerosols. Topical corticosteroids are therefore administered by mechanical pump sprays in aqueous or glycol solutions or as a dry powder. There has been some concern that benzalkonium chloride, a preservative used in intranasal corticosteroid sprays, has toxic effects on cultured nasal epithelium (48) but this effect has not been demonstrated in vivo (49).

Of greater concern is the extent of systemic absorption and the effects on growth in children. Although there are few studies into the effects of topical nasal steroids there have been numerous ones into the effects of inhaled and oral steroids on growth. A meta-analysis performed in 1994 (30) indicates that while oral steroids do indeed reduce final height, the use of inhaled beclomethasone dipropionate does not appear to be associated with diminished stature even at twice the normal dose. However in a randomised double blind crossover study of 19 schoolchildren with mild asthma, treated by inhaled steroids, compared with fluticasone, use of beclomethasone was associated with a statistically significant reduction in lower leg growth velocity (38). The Committee on Safety of medicines and the Medicines Control Agency have concluded (50) that “ clinically important systemic adverse effects occur at licensed doses “ but in mitigation state: “It is important to emphasise that inhaled ... corticosteroids provide proven, effective control of ... rhinitis ... and may in some patients remove the necessity for oral corticosteroid therapy. The recognition that systemic effects may occur, and that the lowest effective dose should be used, does not alter the favourable risk-benefit profile of these medicines”. Topical nasal steroids are not recommended under the age of four.

Short courses of oral steroid can be used, perhaps immediately prior to or following surgery, but only with caution. Contraindications to treatment with systemic steroids include diabetes mellitus, gastric ulceration, osteoporosis, severe hypertension and herpes keratitis or other severe infection. Betamethasone sodium phosphate drops are also very effective in symptomatic relief of allergic and non-allergic non-infectious rhinosinusitis. They are however capable of producing minor systemic steroid effects so their longterm use cannot be recommended. Two drops of betamethasone to each nostril twice daily has been estimated to be equivalent to 1.15mg prednisolone daily (31). Proper drop insertion technique is crucial. Radiological studies and clinical evidence support the “head down and forwards technique” (32,33).

Sodium Cromoglycate

Sodium cromoglycate was first synthesised in 1965 and noted to cause a novel inhibition of degranulation of rat peritoneal mast cells (39). This gave rise to the concept of mast cell “stabilisation”. Although this action has been demonstrated in in-vitro studies of human lung mast cells and mast cells recovered by bronchoalveolar lavage (40), this mechanism does not seem to apply in mast cells recovered from nasal scrapings in rhinitis (41). Instead the

effectiveness of the drug in this setting is attributed to its ability to influence granulocyte chemotaxis (42) and reduce endothelial adhesion molecule expression (43).

Sodium cromoglycate reduces nasal itching, sneezing, rhinorrhoea and blockage in allergic rhinitis. It has negligible side effects (burning sensation) but needs to be applied four times a day. It is primarily a prophylactic drug for use in children but is less effective than topical corticosteroids.

Anticholinergics

Cholinergic receptors are important in the production of nasal secretions but have no effect on nasal blockage, itching or sneezing (44). Ipratropium bromide is therefore useful in the treatment of patients with profuse rhinorrhoea but can cause local drying of the nasal mucosa which is minimised by allowing the patient to decide on the lowest effective dose (45).

Decongestants

The nasal administration of local vasoconstrictors is not usually recommended for more than 3-4 weeks because of the risk of rhinitis medicamentosa (51). However, used prior to other treatments for short periods they can be a useful adjunct to therapy.

Future Developments

As the mechanisms of rhinitis are elucidated and the roles of specific inflammatory mediators clarified new therapeutic strategies suggest themselves. For example leukotriene receptor antagonists may prove helpful for aspirin sensitive patients who produce excessive leukotrienes and exhibit increased sensitivity to them. Immunotherapy The efficacy of desensitisation is well documented in double blind controlled trials but can cause life-threatening reactions, especially in asthmatics. For this reason the practice has been significantly curtailed and in the UK asthmatics are specifically excluded from this treatment. Patients should only be desensitised by suitably trained physicians with adrenaline immediately available (46).

Specific immunotherapy is appropriate where pharmacotherapy inadequately controls the symptoms of allergic rhinitis or the side-effects are unacceptable or appropriate avoidance measures fail. There should be at least a six month history in perennial rhinitis or two season

history in allergic rhinitis and positive skin tests or serum specific IgE which correlate with the symptoms.

Surgery (52)

Surgery should be reserved for patients in whom medical treatment has failed.

When medical treatment has failed, numerous studies have found that surgery benefits at least 80% of patients. When surgery is indicated it should be directed at removing diseased mucosa (including nasal polyps) and mucosal contact areas. This will help to drain the sinuses and allow aeration, facilitate the recovery of cilia and allow access for topical nasal medication.

Whilst surgery provides good symptomatic relief continued medical treatment and further surgery are often required.

Endoscopic surgery has the advantage that no external incision is required

Surgical procedures on the internal and external nasal structures to correct mechanical obstruction of the airway results in improvement in subjective nasal symptoms as well as objective measurements.

Cost Comparison.

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