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Management of chronic rhinosinusitis

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Chronic rhinosinusitis (CRS) is a common medical condition presenting to the primary care physician. The 2012 update of the European Position Paper on Rhinosinusitis and Nasal Polyps (EP^{3}OS) reported that it may affect between 5% and 15% of the population in Europe and the United States, although high quality epidemiological data is scarce.[1] A multicentre questionnaire survey of adults in Europe estimated that one in ten participants had CRS but with notable geographic variation.[2] Prevalence estimates for nasal polyps are difficult to achieve given the need for nasal endoscopy for a reliable diagnosis—questionnaire data may overestimate the prevalence of nasal polyps.[3]

One American study analysing a multiemployer database from 1991 ranked sinusitis as the ninth most costly health condition.[4]

What is chronic rhinosinusitis?

Rhinosinusitis is the appropriate term used to describe the common concurrence of inflammation and infection within the nasal passages and paranasal sinuses.[5] The EP^{3}OS taskforce (a group of international experts who appraise and report on the available literature) developed a clinical definition of rhinosinusitis that is based on the Allergic Rhinitis and its Impact on Asthma (ARIA) group guidelines (box 1).[1] Chronic rhinosinusitis (CRS) is distinguished from acute rhinosinusitis (ARS) by the persistence of symptoms for at least 12 weeks, without resolution.[1]

Who gets chronic rhinosinusitis?

A national health interview survey in the United States and a Canadian prevalence study have both found that CRS without nasal polyps is more commonly found in women (an estimated 2:1 ratio) and that prevalence increases with age, before levelling off after the age of 60.[6 7] Epidemiological data for CRS with nasal polyps is complicated by the need for nasal endoscopy for accurate detection. Furthermore, silent or transient nasal polyps may go unrecognised or be missed, and one epidemiological survey carried out in France found that 32% of patients with symptomatic nasal polyposis had not sought medical advice.[8]

What causes chronic rhinosinusitis?

CRS can be broadly defined as either with nasal polyposis (CRSwNP) or without polyps (CRSsNP), generally based on the findings of nasal endoscopy. This investigation is performed in a specialist setting so it is not possible to make the definitive diagnosis in primary care. These separate disease entities are likely to have differing pathogeneses and certainly can be individually distinguished by their unique inflammatory characteristics, although both come under the umbrella term of chronic rhinosinusitis.[4]

Nasal polyposis is a multifactorial condition reflecting chronic inflammation and the infiltration of eosinophils and neutrophils within the upper airway.[9] In the context of chronic rhinosinusitis, nasal polyps constitute a source of direct physical obstruction within the airway.

Several hypotheses exist as to the underlying causes of the rhinosinusitis conditions. One hypothesis attributes CRS to an extreme host response to fungi,[10] but this may be too limited and a more complex, multifactorial aetiology is being described by ongoing research. The current consensus suggests that a deranged interaction between the host genetic and immunological factors, and environmental and infectious agents, leads to the chronic inflammation and remodelling processes within the upper airway.[3]

The precipitation of rhinosinusitis may arise following obstruction of the sinus ostium, particularly the maxillary sinus ostium beneath the middle turbinate, causing mucus retention and subsequent infection.[11] There are numerous potential predisposing factors. The prevalence of CRS is higher in smokers and the impact of smoking is exacerbated in allergic patients.[1 6] Dysfunctional cilia, such as in cystic fibrosis, lead to impaired clearance of the sinuses and a prevalence of nasal polyposis in up to 40% of those with cystic fibrosis.[12] The EP^{3}OS taskforce notes that CRS and allergy are commonly associated, and that impaired mucociliary clearance may be partly attributable to swelling of the nasal mucosa in allergic

Box 1 | EP^{3}OS guidelines definition of chronic rhinosinusitis

Rhinosinusitis (including nasal polyps) is defined as: Inflammation of the nose and the paranasal sinuses characterised by two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip):
- ± facial pain/pressure
- ± reduction or loss of smell for >12 weeks.

SUMMARY POINTS

Chronic rhinosinusitis (CRS) is a chronic inflammatory condition of the nasal passages and paranasal sinuses
CRS can occur with or without nasal polyps
The mainstay of treatment is topical corticosteroids
Facial pain is a poor diagnostic indicator of CRS
Where medical therapy does not resolve symptoms, patients require referral to an ear, nose, and throat specialist

SOURCES AND SELECTION CRITERIA

We searched Medline, the Cochrane Library, and PubMed using the search terms "chronic rhinosinusitis", "rhinosinusitis", "rhinitis", "sinusitis", "chronic disease", and "nasal polyps". We also referenced expert position papers such as the European Position Paper on Rhinosinusitis and Nasal Polyps.[1] When possible, we used level I evidence from systematic reviews or randomised controlled trials.

Box 2 | Features of CRS

Key clinical features
- Nasal blockage/obstruction
- Nasal congestion
- Anterior/posterior rhinorrhoea
- Facial pain/pressure
- Anosmia (total/partial)

Minor symptomatic features
- Ear pain/pressure
- Dizziness
- Halitosis
- Dental pain
- Cough
- Drowsiness/malaise
- Sleep disturbance
- Fever

Box 3 | Red flag symptoms
- Unilateral symptoms
- Blockage
- Bleeding/bloodstained discharge
- Cacosmia
- Proptosis
- Diplopia
- Epiphora
- Neurological symptoms

disease.[1] Indeed, two review studies have suggested that atopy may increase the risk of CRS.[13 14] However, despite the common co-occurrence, the epidemiological evidence for a direct causal link does not exist. A similar association is seen with asthma, and, in particular, aspirin induced asthma may accelerate the development of nasal polyps.[15] But again, the precise causal relationship remains obscure.

How do people present with chronic rhinosinusitis?

There are numerous similarities between the presentations of acute and chronic rhinosinusitis although CRS is a more heterogeneous condition and symptoms may be less severe. Symptomatology is the main impetus for most patients seeking advice, but a clinical diagnosis may need to be supplemented with objective clinical findings, from nasal endoscopy or computed tomography. An important distinction is between CRS and recurrent ARS—defined as between two and four episodes of ARS per year with complete resolution of symptoms between episodes.[16] The key clinical features of CRS identified by the EP^{3}OS taskforce include nasal blockage/congestion, anterior or posterior rhinorrhoea, facial pain/pressure, headache, and a reduction in the sense of smell.[1] Additional and more general symptoms include throat pain, cough, malaise, and fever. Minor symptoms such as ear pain, halitosis, or sleep disturbance may be more unique to CRS (box 2).[1 13] When taking a history it is important to ask about cigarette smoking, allergy, asthma, aspirin sensitivity, nasal trauma, or previous nasal surgery. See box 3 for red flag symptoms where urgent referral to an ENT specialist is indicated.

Chronic rhinosinusitis and facial pain

Many patients who report facial pain believe that it is "due to their sinuses," but it is rarely due to rhinosinusitis unless an underlying bacterial infection is unable to drain.[3] Indeed, prospective studies have noted that most patients with mucopurulent discharge from the paranasal sinuses do not report facial pain and that in patients with nasal polyps, facial pain or pressure is more likely to be coincidental and of neurological origin.[17 18] Facial pain alone, in the absence of other nasal symptoms, is therefore a poor indicator of CRS. Similarly, the majority of patients with headache do not have rhinosinusitis. Indeed according to the International Headache Society, CRS is not a validated cause of headache or facial pain except in the presence of acute exacerbations.[19] It is crucial therefore to clarify the diagnosis and the underlying cause of facial pain or pressure, or headache, before considering the role of surgery for CRS.

How is the diagnosis of chronic rhinosinusitis made?

Clinical

In most cases, diagnosis is made in primary care based on symptoms alone. However, one prospective cohort study[20] found that nasal endoscopy improved the quality of diagnosis and can be used to visualise features such as polyposis or discharge. An expert panel of national American societies considered endoscopically retrieved cultures for antibiotic selection to be associated with reduced morbidity and invasiveness.[21] However, nasal endoscopy will only be routinely available in secondary care.

The severity of the symptoms can be approximately judged using a subjective assessment instrument like the visual analogue scale (VAS) or the sino-nasal outcome test.[1] Patients are asked to quantify how troublesome their symptoms are on a 10point scale. For chronic rhinosinusitis, a statistically validated classification has been derived with a VAS score of 0-3 corresponding to a "mild" condition; >3-7 to "moderate"; and >7-10 to "severe".[22] EP^{3}OS recommends the visual analogue scale as a reproducible and easy to use clinical tool to assess and monitor patient symptoms before, during, and after treatment.[1]

Following a suspected diagnosis of chronic rhinosinusitis in a primary care setting, anterior rhinoscopy can be performed (using an otoscope with large speculum rather than with thudicums, which are not routinely used in this setting). Anterior rhinoscopy should form part of a routine clinical examination and may reveal signs of erythema and congestion of the nasal mucosa, discharge, or nasal polyposis, the latter being identifiable by their soft, mobile, and insensate features (fig 1). Allergy testing should be considered for patients who report allergic type symptoms in their history.[11]

Imaging

The Royal College of Radiologists' guidelines discourage the use of plain x rays of the sinuses for the diagnosis of sinusitis and one audit of facial x rays also found them to be diagnostically unsupportive.[23 24] Computed tomography is not recommended in primary care as a diagnostic tool,[1] since in this setting CRS is a clinical diagnosis. In addition, up to 20% of people without symptoms have

Fig 1 | Nasal polyps

been found to have sinus abnormalities.[25] Therefore, computed tomography is used to identify anatomical features and to corroborate a diagnosis, making it an obligatory preoperative tool when planning sinus surgery (fig 2).[1 26] In the presence of suspicious features, such as unilateral signs or symptoms, computed tomography may be involved in the initial diagnostic stages of suspected neoplasia. Features of mucoperiosteal disease observed on computed tomography can be quantified using validated systems such as the Lund-Mackay score.[1] A prospective study has found that the Lund-Mackay system correlates strongly with disease severity and outcome.[27] Magnetic resonance imaging also does not have a role in the primary investigation of CRS, although the EP^{3}OS panel notes that its improved soft tissue definition complements computed tomography in the investigation of suspected neoplasia.[1]

Fig 2 | Computed tomography scan of chronic rhinosinusitis

How is chronic rhinosinusitis managed?

See CRS primary care management algorithm web extra on bmj.com.

Intranasal corticosteroids

There is level 1 evidence (randomised controlled trials) to support the use of intranasal corticosteroids (sprays or drops) as the primary medical treatment for CRSwNP and CRSsNP.[1] Meta-analyses of level 1 evidence favour topical nasal steroids with no evidence from studies in the available literature to support one type of steroid over another.[1] The effect of corticosteroids may be mediated by a reduction in eosinophil activity in the mucosa.[28] Initial treatment should involve intranasal corticosteroids in conjunction with saline lavage (see below). If an underlying comorbidity such as nasal septal deviation or allergy is identified, these should be managed appropriately, through septal surgery, allergy testing, and treatment of allergies, for example.[11] The delivery of steroids to the affected area may be substantially limited with topical application, especially in CRS with mucosal oedema, and spray solutions may distribute little further than the nasal cavity.[29] The application of topical steroids to the nasal cavity is typically via nasal sprays or nasal drops. Evidence is lacking as to the superiority of one method over the other.[30 31] However, current evidence suggests that the penetration of irrigants may be improved following functional endoscopic sinus surgery (FESS).[32] Before such surgery, distribution to the sinuses is thought to be poor regardless of the mode of delivery.

Long term use of intranasal corticosteroids (over one year) is considered safe with no detrimental effect on microscopic structure of the nasal mucosa.[33 34]

Oral steroids

Level 1a evidence (meta-analysis of randomised controlled trials) exists to support the use of a short course of oral steroids in the treatment of severe CRSwNP (VAS >7-10).[1] There is no evidence for a specific dose regimen, but prednisolone was the most commonly used steroid in the available randomised controlled trials, and the dosage ranged from 25 mg to 50 mg daily, for durations ranging from two to twelve weeks.[1] Oral steroids can be used prior to the use of intranasal steroids, but for a chronic condition the role of systemic steroids is limited due to side effects outlined below.

Saline irrigation and topical decongestants

A Cochrane systematic review found nasal saline irrigations to be beneficial and well tolerated as the sole modality of treatment in CRS, although no distinction was made between CRSwNP and CRSsNP. The review concluded that although topical saline is not as effective as an intranasal steroid, evidence suggests that it is a useful adjunct.[35] Evidence exists to support the use of saline douches following sinus surgery.[1]

Short term use of decongestants may have a role in the treatment of acute rhinosinusitis, but there is no evidence to support their use for CRSwNP or CRSsNP.[1]

Antibiotics

The use of antibiotics for the treatment of CRS may be considered in secondary care. Level 1b evidence (two

ONGOING RESEARCH

With the pathogenesis of CRS largely unknown, the importance of bacterial biofilms has been an area of recent research interest. These are the morphological results of bacterial survival strategies, where bacteria form organised and protected colonies that can be more highly resistant to routine treatments.[45] Delineating their involvement in the development of CRS may further the understanding of the underlying immunological factors and disease characteristics.[46]

In the context of surgical interventions, the role of endoscopic balloon dilation of the sinus ostia remains insufficiently studied. A recent Cochrane review found only one relevant experimental trial of balloon dilation compared to functional endoscopic sinus surgery, which did not find any improvement in the intervention group.[47] Balloon sinuplasty may be considered a less invasive technique, but further research and more controlled trials are required to properly evaluate its value.

randomised controlled trials) exists for the use of long term (12 weeks) macrolide antibiotics in patients with CRSsNP who have failed to respond to intranasal steroids and saline irrigation.[1] Only one of these studies, however, demonstrated a significant benefit in favour of the macrolide group, particularly in patients with low IgE levels.[36] Limited level 3 evidence exists (non-experimental, descriptive studies) for the use of doxycycline, both short term (less than 4 weeks) and long term (12 weeks), in CRSwNP.[1] A review carried out by the EP^{3}OS taskforce did not identify any evidence supporting the use of topical antibiotics for CRS.

Side effects of treatment

Potential, common side effects of local corticosteroid use may include epistaxis and nasal irritation, although these are generally mild and well tolerated by most patients. One prospective, observational study found that 5% of patients using an intranasal steroid spray experienced epistaxis and that the side of bleeding was highly correlated with the handedness of the patient.[37] This can be minimised by directing the nasal spray with the contralateral hand towards the lateral wall of the nose, rather than the septum. In CRSwNP where corticosteroids may also be prescribed for the treatment of coexisting asthma, the potentially long term harms of steroid use should be balanced against the short term benefits.[1] The presence of extensive nasal polyps may demand the use of a short course of systemic corticosteroids, if not contraindicated, however this must be balanced against the risk of significant side effects (see primary care management algorithm web extra on bmj.com).

Duration of treatment

There is no evidence to indicate the optimal duration of topical steroid treatment in CRS. After initiating treatment for CRS in primary care, a review is recommended at four weeks.[1] If symptoms have improved, therapy can be continued. ENT specialists will continue treatment for up to three months before considering further treatment such as long term antibiotics or surgery.

When to refer

If treatment is initiated in primary care and no improvement has been achieved after four weeks of intranasal steroids and saline lavage, referral to an ear, nose, and throat specialist is recommended.[1]

Urgent referral may be required if the patient presents with red flag symptoms (box 3). Simple nasal polyps have a characteristic gelatinous grey appearance and are insensate on contact when probed (with a cotton bud, for example). Visible red, fleshy swellings, particularly if unilateral and associated with bleeding, should be considered suspicious and urgent referral is recommended.

The role of surgery

FESS, or functional endoscopic sinus surgery, is currently the principal form of surgery practised widely by ENT surgeons for chronic rhinosinusitis. These are endoscopic procedures on some or all sinus groups with the specific aim of restoring ventilation and mucociliary clearance within the sinuses.[38] By opening up sinus groups this type of surgery may also aid the delivery of nasal preparations into the nose and sinuses.[39] The EP^{3}OS taskforce reviewed several large prospective studies and concluded that level 2 and level 3 evidence supports functional endoscopic sinus surgery as safe, effective, and appropriate for CRSsNP and CRSwNP where medical interventions have failed.[1 40] Outcomes may be best for nasal obstruction and facial pain, rather than for post-nasal drip or hyposmia. However, high quality trials of this procedure are lacking and it may remain a topic of some controversy—a 2006 Cochrane review noted that some randomised controlled trials have found no significant benefit associated with functional endoscopic sinus surgery when compared with medical therapy.[41]

CRS and links to other conditions

The relationship between allergy, asthma, and CRS is a complex one that is not clearly understood, but these conditions commonly coexist and treatment of one can influence the other: for example, successful treatment of CRSwNP can improve asthma control.[7] Nasal polyposis is also found in a high proportion of patients with aspirin sensitivity.[42] When accompanied by asthma, this group of conditions is called Samter's triad.[43] One retrospective study of CRS patients undergoing functional endoscopic sinus surgery found that 5.9% of adults had Samter's triad.[43]

In such cases, aspirin exposure may exacerbate the symptoms of asthma and rhinosinusitis. Although the

EDUCATIONAL RESOURCES FOR PATIENTS

ENT UK (www.entuk.org)—An important source of information about ENT practice in the UK. It is maintained by the main professional association for ENT surgeons in the UK

Patient.co.uk (www.patient.co.uk)—Easily accessed resource for patient information in the UK. It provides easy to follow advice on sinusitis, including important information about techniques used when giving nasal drops

method has not been extensively studied, aspirin desensitisation and maintenance with soluble lysine-aspirin has been effective in some patients at reducing the risk of polyp recurrence and improving respiratory symptoms.[3 20] An audit study measured the response to the leukotriene antagonist montelukast in patients with nasal polyps associated with asthma, and found that it produced some benefit in terms of clinical symptoms measured using VAS.[44] Montelukast may also be used in some cases of rhinitis where standard therapy has been ineffective. But the overall evidence for its use in CRS remains insufficient and further research may be necessary.

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