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Chronic Rhinosinusitis in Children

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Abstract

Purpose of review: Pediatric chronic rhinosinusitis (CRS) is a common condition that is often misdiagnosed and can be challenging to treat. This review aims to 1) Review definitions, presentation, complications, and management of CRS in children. 2) Highlight the paucity of evidence in the management of pediatric CRS.

Recent findings: There are few studies supporting the usual recommended medical therapy for pediatric CRS (antibiotics, nasal saline irrigations, intranasal steroid). Adenoidectomy remains a mainstay of surgical treatment, but recent evidence demonstrates the utility of balloon sinuplasty and functional endoscopic sinus surgery (FESS) for patients who fail adenoidectomy alone.

Summary: Pediatric CRS is distinct from ARS and adult CRS. It is a common problem that is poorly studied, in part because of significant symptomatic overlap with related conditions. Recent evidence supports the use of surgical treatment in children who fail medical management. However, further outcome studies are needed to better evaluate the effectiveness of current medical and surgical management protocols.

Keywords

Chronic rhinosinusitis; nasal polyposis; pediatric; endoscopic sinus surgery; balloon sinuplasty

Introduction and Background

Chronic rhinosinusitis (CRS) is a syndrome characterized by persistent inflammation of the mucosa of the nose and paranasal sinuses. In children, this results in the symptoms of chronic nasal congestion, purulent rhinorrhea, facial pain and pressure, and cough. The etiology and pathogenesis of this inflammation are often unclear, though it is thought that

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Conflict of Interest

Lourdes Quintanilla-Dieck and Derek J. Lam declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent

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this represents an inappropriate or excessive immune response to an external stimulus inhaled through the nasal airway.

The exact prevalence of pediatric rhinosinusitis is unknown because only a small percentage of cases present to the physician's office. It is estimated that 6% to 13% of children will have had an episode of rhinosinusitis by 3 years of age[1]. The average child will have 6-8 upper respiratory infections per year during the first decade of life, and it is thought that 5%-10% of these will be complicated by rhinosinusitis[2]. This disease consumes a vast amount of health care resources; for example, in 1996 an estimated $1.8 billion was spent on treating rhinosinusitis in children under 12 years of age[3]. Quality-of-life studies have shown that CRS can have meaningful adverse effects on children and adults that potentially exceed other chronic illnesses such as chronic respiratory and arthritic disease[4-6]. A recent analysis of the National Ambulatory Medical Care Survey (NAMCS) database that includes ambulatory visits between 2005 and 2012 demonstrated that visits for pediatric CRS were significantly more prevalent than for acute rhinosinusitis (RR 3.4, 95%CI 2.7-4.1) and was similar in overall prevalence to allergic rhinitis (2.1% vs 2.6% respectively).[7] CRS in children can be difficult to accurately diagnose, given multiple possible contributing factors and varying symptoms that can be challenging to ascertain in children. Studies of pediatric CRS often focus on select populations of patients with upper respiratory complaints. Prevalence of CRS does appear to be age-related, being most common among 2-6 year olds gradually decreasing prevalence with increasing age.[7-9]

Definitions

Sinusitis signifies an inflammatory condition involving the paranasal sinuses that may or may not be associated with an infectious process. The term "rhinosinusitis" denotes the intimate anatomic and pathophysiologic relationship between the nose and paranasal sinuses. This term points to the observation that inflammation of the contiguous nasal mucosa and obstruction of the lateral wall of the nose regularly precedes development of sinusitis. As in adults, pediatric rhinosinusitis is typically categorized as either acute or chronic.[4,10] Acute rhinosinusitis (ARS) has a duration between 10 days and 12 weeks with possible symptom-free intervals if the problem is recurrent; and chronic rhinosinusitis (CRS) is defined as lasting longer than 12 weeks. A European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) published in 2012 offered a more specific definition of pediatric CRS based on at least two symptoms and one objective clinical sign.[10] This definition was later adapted for the Clinical Consensus Statement published in 2014 by the American Academy of Otolaryngology-Head and Neck Surgery which defined pediatric CRS as at least 90 continuous days of 2 or more symptoms of purulent rhinorrhea, nasal obstruction, facial pressure/pain, or cough *and* either endoscopic signs of mucosal edema, purulent drainage, or nasal polyposis, and/or CT scan imaging showing mucosal changes within the ostiomeatal complex and/or sinuses[4]

Pediatric CRS can be subclassified into CRS with or without nasal polyposis. In the Clinical Consensus Statement for pediatric CRS, there was a strong consensus that children who present with polyps represent a distinct patient subgroup compared to children who do not have polyps[4]. Patients with nasal polyposis are thought to constitute a different subtype of

CRS with differing pathophysiology and optimal management. Specifically, these children carry an increased risk of underlying conditions such as cystic fibrosis, allergic fungal sinusitis and antrochoanal polyps. An assessment for these conditions needs to be considered in their workup.

Anatomy of the sinuses in pediatrics

The paranasal sinuses are air-containing spaces aligned around the nasal cavities ventilated through narrow (1-3 mm) channels called ostia, which are their natural openings. These sinuses are lined by ciliated, pseudostratified, columnar epithelium containing cilia which serve to clear secretions and maintain a relatively sterile environment[3,11]. The sinus mucosa contains goblet cells for mucous production. Normal function of the sinuses depends on normal mucous secretion, normal ciliary function, and patency of the ostia, including the important common pathway of drainage and aeration known as the ostiomeatal complex (OMC). The OMC is formed within the middle meatus, where the frontal, maxillary and anterior ethmoid sinuses drain. The posterior ethmoid and sphenoid sinuses empty into the superior meatus and flow posteriorly.

The paired maxillary and ethmoid sinuses begin development in the 10th week of gestation and are fully formed at birth[2]. The sphenoid sinuses show evidence of pneumatization at approximately 9 months of age and are fully formed at 7 to 8 years of age, while the frontal sinuses usually appear between 7 and 8 years of age. The frontal sinuses generally reach adult size by puberty[2,11]. Given this pattern of development, sinus infections usually occur in the maxillary and/or ethmoid sinuses during childhood. Systemic diseases such as cystic fibrosis (CF) can affect the growth and shape of the paranasal sinus cavities such that the sinuses that develop after birth (frontal and sphenoid) can be significantly underdeveloped[11].

Pathophysiology of CRS in children

The path to developing a bacterial rhinosinusitis infection usually begins with a viral respiratory infection with concomitant mucosal inflammation. This results in obstruction of the sinus ostia with impaired aeration of the sinuses, decreased ciliary function, and stasis of secretions within the sinuses. These factors are believed to constitute the primary factors in the pathophysiology of sinus disease, which then lead to secondary infection by bacteria residing within the nose and nasopharynx[3,11]. It has been estimated that 0.5% to 13% of upper respiratory infections (URIs) in children progress into bacterial rhinosinusitis[3,4].

A multitude of factors exist that could lead to a predisposition for CRS. Anything that contributes to obstruction of the sinus ostia would constitute such a factor. Some examples include anatomic elements which can be intrinsic or extrinsic. Intrinsic factors include septal deviation, nasal polyps, and lateral wall anomalies such as concha bullosa, paradoxical middle turbinates and Haller cells[2]. Extrinsic factors consist of nasal foreign bodies including nasogastric and nasotracheal tubes. Other factors could exist that lead to a chronic inflammatory state and therefore cause inflamed sinonasal mucosa that then obstructs sinus flow; some examples include allergic rhinitis, allergic fungal sinusitis (a hypersensitivity reaction of the sinus mucosa to airborne fungal species in immunocompetent individuals),

gastroesophageal reflux, and tobacco smoke[2,11]. A recent systematic review noted particularly poor outcomes of surgery for CRS among children exposed to second-hand smoke.[12]

Some studies point to allergic rhinitis having an association with pediatric CRS, but others do not support this[4]. One large study looking at more than 4000 pediatric patients found that allergic rhinitis is the most common comorbidity, with 26.9% of patients carrying the diagnosis. Nearly 50% of children with refractory chronic rhinosinusitis have positive skin tests to environmental allergens[13]. Physical examination findings that are consistent with allergic rhinitis include pale, boggy turbinates, infraorbital darkening, and a transverse crease on the nasal dorsum[2]. An evaluation for underlying allergy may be warranted in the workup for patients with recurrent or chronic rhinosinusitis. In addition to allergens, environmental irritants such as air pollutants or tobacco smoke may play a role in chronic mucosal inflammation[11].

The role of GERD as a risk factor for rhinosinusitis is still debated. In the Clinical Consensus Statement published in 2014 for Pediatric CRS, no consensus was reached regarding this issue[4]. It is possible that GERD leads to direct inflammation of the sinonasal mucosa, resulting in ostial obstruction. Reflux extending into the nasopharynx has been demonstrated by pH probe[2]. Several studies in children indicate that medical treatment for gastroesophageal reflux disease (GERD) significantly improves rhinosinusitis symptoms[14].

Systemic diseases should also be considered in cases of pediatric CRS resistant to usual medical therapies. The most commonly identified immune defect in patients with recurrent or recalcitrant rhinosinusitis is a humoral deficiency, particularly IgA or IgG deficiency[2]. Testing for immune compromise may be useful, and these tests include quantitative immunoglobulin measurements, IgG subclass levels, functional antibody testing and ruling out Human Immunodeficiency Virus (HIV) infection[14]. It is important to remember that patients on immunosuppressive medications have a significant predisposition to rhinosinusitis.

Patients with CF typically have rhinosinusitis as a consequence of the dehydration of mucosal fluids and the sulfation of mucous glycoproteins, a combination leading to retention of viscous sinus secretions that predispose to bacterial superinfection. Pediatric patients with nasal polyposis especially at an early age, or nasal or sinus colonization with *Pseudomonas* species should be tested for CF. Testing can consist of either quantitative sweat chloride testing and/or genetic testing.

Another condition that should be ruled out in pediatric patients with recurrent ARS or CRS is ciliary dysfunction such as with primary ciliary dyskinesia.[15] The malfunction of the cilia within the sinus and nasal cavities in these patients results in decreased clearance of mucus and bacteria, increasing risk of infection. These patients usually have otitis media and pneumonia in addition to the CRS, and nearly half have *situs inversus* with or without dextrocardia. Diagnosis requires biopsies from the nasal mucosa and carina for electron microscopy examination of the ciliary structures or genetic testing[16].

Microbiology

Traditionally, normal sinuses were thought to be sterile and without a normal microbial population. However, some recent studies suggest otherwise. Abreu and colleagues describe a reduced diversity of sinus microbes in patients with CRS compared to healthy controls[17].

Viral upper respiratory tract infections frequently precede bacterial infections of the sinuses. The most common causal organisms of acute and subacute rhinosinusitis are *Streptococcus pneumoniae, Haemophilus inflenzae,* and *Moraxella catarrhalis*[14]. In contrast, the most common bacteria found in CRS are alpha hemolytic streptococci *and Staphylococcus aureus,* followed by *S. pneumoniae, H. influenza,* and *M. catarrhalis.*[18] Other common bacterial species include *Pseudomonas aeruginosa* and anaerobes[7]. *P. aeruginosa* and other aerobic gram-negative rods are more common in sinusitis of nosocomial origin or in immunocompromised individuals or those with CF[2].

The prevalence of penicillin-resistant organisms in rhinosinusitis can be significant. *S. pneumoniae* has geographic variation but is thought to have 15-50% rate of resistance to penicillin[1,14]. Both *H. influenzae* and *M. catarrhalis* can produce β–lactamase and are resistant to penicillin and its derivatives. The prevalence of macrolide-resistant *S. pneumoniae* is 10-40%.

Fungi are increasingly being recognized as an etiologic factor in CRS. The most commonly involved pathogens are *Bipolaris, Curvularia, Aspergillus,* and *Dreschlera* species.

Biofilms and bacterial exotoxins have been implicated in the pathogenesis of CRS. Biofilms consist of bacteria aggregating on surfaces within an external matrix of polysaccharides, nucleic acids, and proteins. Biofilms provide a protected environment for pathogens, and may be responsible for persistent or recurrent disease. In CRS, biofilm formation may decrease the efficacy of antibiotics as much as 100 fold, allowing bacteria to thrive in the nose and sinuses. Other studies have reported the presence of biofilms in adenoid tissue from patients with chronic infectious disease of the upper airways[11]. Exotoxins are released by bacteria and may trigger a symptomatic immune response.

Clinical Presentation

Other than the duration of symptoms, it is worthwhile distinguishing between acute rhinosinusitis (ARS) and CRS. Though there is overlap in the presenting symptoms of nasal congestion, discharge, facial pain and pressure, and cough, symptoms in CRS are typically lesser in intensity. ARS usually presents in three ways: a) initial viral upper respiratory infection (nasal congestion, rhinorrhea, cough) that remain persistent with worsening after 10 days; b) severe symptom onset (high fever of at least 38.5 degrees C for at least 3-4 days with purulent nasal discharge); or c) biphasic disease with symptoms worsening on the 6th or 7th day of illness after previous improvement[1].

Because the symptoms of pediatric CRS are more indolent and non-specific than an episode of ARS, it can be difficult to distinguish from recurrent viral upper respiratory infections, chronic allergic rhinitis, or chronic nasal congestion due to adenoid hypertrophy. Adenoid

hypertrophy and adenoiditis are a prominent contributor to the pathogenesis of CRS in young children and may not be possible to differentiate from CRS in this age group. As noted previously, the AAO-HNS Clinical Consensus Statement defined pediatric CRS as at least 90 continuous days of 2 or more symptoms of purulent rhinorrhea, nasal obstruction, facial pressure/pain, or cough. Chronic cough lasting more than 4 weeks in duration, especially if associated with rhinorrhea and nasal congestion, should prompt an evaluation for CRS. Unlike in adults, hyposmia and headache are less common in children, though there may be greater irritability and behavioral changes. In addition, these symptoms should be accompanied by at least one objective sign from a nasal endoscopic exam (mucosal edema, purulent drainage from one or more sinuses, nasal polyposis) or positive findings on a sinus CT scan or sinus plain radiographs (mucosal thickening, sinus opacification).[4]

Evaluation

History

In addition to the clinical presentation described above, a thorough history should include the number, severity, and time course of past infections, need for antibiotics and other medical therapies, response to these treatments, history of asthma and whether it is adequately treated, and any adverse reactions to NSAIDs.

Exam

A thorough head and neck examination should emphasize the nasal exam, in particular findings relevant to the clinical presentation described above (purulent rhinorrhea, mucosal edema, nasal polyps, etc). Signs associated with allergic rhinitis should also be noted including allergic shiners, Dennie’s lines, and the allergic salute. Suspicion of allergic sensitization as a contributing factor to CRS should prompt a referral for allergy testing.

Nasal Endoscopy

Flexible fiberoptic examination of the nasal passages allows a more magnified and thorough evaluation of mucosal edema and inflammation as well as visualization of the OMC. This technique can determine the presence of purulent discharge, nasal polyposis, adenoid hypertrophy and adenoiditis, post-nasal drainage, septal deviation, and turbinate hypertrophy. These findings are key to helping to establish a diagnosis of CRS.

Imaging

CT imaging is the preferred modality with higher resolution and better visualization of bony and soft tissue anatomy compared to plain films, but it does carry a slightly increased lifetime risk of developing a malignancy of the head and neck. It is worth noting that even children with no history of symptoms to suggest CRS have a higher rate of abnormality on CT imaging (up to 45%) than adults.[19] One study demonstrated an average Lund McKay score of 2.8 in an asymptomatic pediatric population.[20] In a recent survey study, most pediatric otolaryngologists typically perform adenoidectomy prior to CT imaging to evaluate the sinuses, and overall CT use has declined in the last decade in this group of providers.[6]

Complications of Chronic Rhinosinusitis

Complications of CRS with or without nasal polyps are relatively rare and less dramatic than complications of ARS such as subperiosteal abscess formation. They include bony erosion and expansion due to polyps or mucoceles, sclerosis due to chronic osteitis, and recurrent pulmonary exacerbations in the setting of asthma or cystic fibrosis.

Mucoceles are fluid-filled epithelial-lined sacs that are typically unilocular and slow-growing. They can eventually fill an entire sinus and cause expansion or erosion of the surrounding bone, particularly if an acute bacterial infection results in a pyocele. Mucoceles tend to be unilateral and occur most commonly in the fronto-ethmoid sinuses. The mass effect caused by a large fronto-ethmoid mucocele can cause orbital displacement and proptosis. Fortunately, such mucoceles are rare in children and generally respond well with endoscopic marsupialization with reported recurrence rates ranging from 0-13%[21,22].

Chronic nasal polyposis can similarly exert a mass effect with thinning of bone, most often affecting the ethmoid sinuses and lamina papyracea. A condition that can often predispose to nasal polyposis in children is allergic fungal sinusitis (AFS). AFS is a condition caused by a type I hypersensitivity to fungal pathogens, most commonly Bipolaris, Aspergillus, Alternaria, Curvularia, and Dreschslera species. leading to a chronic eosinophilic infiltrate and inflammation of the sinus mucosa. This can often result in polyposis and unilateral sinus opacification and expansion. [23]

The association between CRS and osteitis of the paranasal sinuses has been demonstrated in both animal models and in human histologic studies of patients with CRS. Chronic osteitis is thought to lead to increased bone turnover, neo-osteogenesis, and sclerotic bony changes. The severity of these changes has been shown to correlate with the extent of mucosal disease as assessed by the Lund-Mackay score.[24,25]

Management

Medical Therapy

The initial therapy in pediatric CRS is medical with surgery reserved for patients who do not respond to medical treatment. Although there is strong evidence supporting the use of antibiotics in the treatment of pediatric ARS,[26] to date there is no good evidence supporting the use of antibiotics for CRS in children. Nevertheless, medical therapy for CRS is extrapolated from guideline recommendations for treatment of pediatric ARS[27] and adult CRS, and begins with long term courses (usually 3-6 weeks) of oral antibiotics targeting the most common bacterial pathogens (Streptococcus pneumoniae, Moraxella catarrhalis, Hemophilus influenza, beta-hemolytic Streptococcus pyogenes). High dose amoxicillin (90mg/kg) is a typical first-line choice of antibiotic while amoxicillin-clavulanate or a 3rd or 4th generation cephalosporin can be used if amoxicillin alone fails or if a broader spectrum of antibiotic coverage is required to treat more atypical pathogens. Clindamycin or trimethoprim-sulfamethasoxazole may be used for patients with a penicillin allergy or where there is a history of infection with methicillin-resistant S. aureus (MRSA).

Nasal saline and intranasal corticosteroid are adjunct medical therapies for which there is a paucity of good evidence in children.[28] A recent Cochrane review of nasal saline included 3 trials conducted in children.[29] Though variable in tonicity and delivery technique, in general they demonstrated that saline was beneficial in the treatment of CRS. Intranasal corticosteroids reduce eosinophilic viability and activation and the secretion of chemotactic cytokines by nasal mucosa and epithelial cells. Multiple randomized trials have demonstrated the beneficial impact of intranasal corticosteroids in improving symptom scores in adults with CRS.[30] Studies in children are lacking in part due to concern for endogenous corticosteroid suppression and growth inhibition. Only one randomized placebo-controlled trial has been published in children ages 6-17 years with nasal polyposis, with a primary goal of investigating the safety of intranasal mometasone furoate. This study found no significant differences in urinary free cortisol between treatment and placebo groups indicating minimal systemic absorption. Secondary treatment efficacy endpoints were not tested for significant differences because this study was not powered or designed to specifically address the question of efficacy.[31] However, intranasal mometasone has been shown to be effective in reducing symptoms of allergic rhinitis in children.[32,33] Based on this limited data in children and the large body of evidence supporting the use of both nasal saline and intranasal corticosteroids in adults with CRS, it is reasonable to include both as part of a medical therapy regimen in children, in addition to antibiotics. Oral steroids, antihistamines, and anti-leukotrienes are less commonly prescribed adjunct medications.[6]

Surgical Treatment

As in adults, surgery in children with CRS is reserved for those who have failed maximal medical therapy. However, unlike adults, adenoidectomy alone may be an effective surgical technique for children with CRS. The adenoids are thought to act as a bacterial reservoir facilitating chronic infection of the sinuses. Several studies have demonstrated a correlation between the bacteria isolated from adenoid specimens and sinus cultures from patients with CRS, and a lack of correlation among those without CRS.[34,35] A meta-analysis of adenoidectomy alone in children with CRS found that 69% of children showed improved outcomes after adenoidectomy.[36] Risk factors for failure of adenoidectomy and subsequent need for salvage functional endoscopic sinus surgery (FESS) include age less than 7 years and a history of asthma.[37]

While adenoidectomy alone may be the preferred initial surgical intervention in most children, those with cystic fibrosis, AFS, or nasal polyposis may require a FESS in order to alleviate the more extensive disease associated with these conditions. Among children who fail adenoidectomy, FESS remains the most common form of surgical treatment. Hebert et al. reported a meta-analysis of 8 studies of FESS in children ranging in age from 11 months to 18 years and demonstrated an 88.7% success rate in reducing the symptoms of CRS with an average of 3.7 years of follow-up.[38] Depending on the age of the child, a limited approach that includes only maxillary antrostomy and anterior ethmoidectomy may be safer than a more complete FESS. This approach has been shown to be effective in improving symptoms associated with CRS.[39] FESS has been shown to be effective in improving overall quality of life in children with CRS with or without nasal polyposis.[40-42] Though favorable

outcomes with FESS have been reported between 71-100% of operated children, children with cystic fibrosis have a 50% recurrence rate and often require revision surgery.[41]

Other surgical techniques that have been described are maxillary sinus irrigation and balloon sinuplasty.[6] Both have been shown to yield slightly better outcomes than adenoidectomy alone.[43,44] Proposed as an alternative to FESS for refractory CRS, the addition of maxillary sinus irrigation to adenoidectomy is thought to help clear trapped mucous and can facilitate prolonged courses of culture-directed antibiotics. This protocol demonstrated 78-89% rate of complete resolution in several studies.[43,45,46] However, because maxillary sinus irrigation is performed by blindly passing a trocar through the inferior meatus into the maxillary sinus, complications such as epistaxis and pseudoproptosis following irrigation have been reported.[47] Endoscopic guided cultures of the middle meatus has been observed to have similar efficacy in identifying bacteria and directing antibiotic treatment.[47]

Balloon sinuplasty is another alternative to traditional FESS that has been increasingly utilized in recent years, with one recent multicenter study reporting that approximately 12% of all pediatric sinus surgery in a single year included balloon sinuplasty.[48] A survey of a national commercial insurance database reported a lower complication rate and lower rate of revision with balloon sinuplasty compared to traditional FESS.[49] Balloon sinuplasty has demonstrated significantly improved quality of life 6 months after surgery in both primary school aged children and teenagers,[50] and it has resulted in subjective improvement and improved Lund-Mackay CT scores in children ages 6-18 years up to one year after surgery.[51] While one might consider balloon sinuplasty or FESS in addition to or instead of adenoidectomy as an initial procedure, one recent analysis found that adenoidectomy alone remains the most cost-effective as a sole first procedure for pediatric CRS.[52]

Conclusions

Pediatric CRS is a prevalent problem resulting in significant morbidity. Despite this, CRS in children remains poorly studied, and most treatment recommendations are based on extrapolations from studies of ARS or adult CRS. Initial management should include antibiotics, nasal saline irrigations, and intranasal steroids even though evidence for these treatments are lacking. Adenoidectomy should be considered as the initial surgical intervention for those who fail medical management, and if this fails either balloon sinuplasty or FESS may be considered for persistent disease. Further study is needed to elucidate the optimal medical and surgical management for pediatric CRS.

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