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RHINOSINUSITIS (J MULLOL, SECTION EDITOR)

Clinical Guidelines on Chronic Rhinosinusitis in Children

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Abstract

Purpose of Review Pediatric chronic rhinosinusitis (CRS) is a prevalent problem that can elude diagnosis. In addition, given the burgeoning interest in pediatric sinonasal disease, treatment modalities are constantly evolving.

Recent Findings The diagnosis of pediatric CRS is primarily based on clinical history and signs supported by objective findings (i.e., nasal endoscopy and/or computed tomography (CT) imaging). Cultures are indicated in patients who have not responded to medical therapy or have significant comorbidities. Nasal saline irrigation, nasal saline spray, and oral antibiotics are currently recommended for initial medical management. In children with CRS who have failed medical therapy, a stepwise approach to surgical intervention can lead to significant improvements in quality of life.

Summary This review provides an overview of the current guidelines and recent literature regarding the diagnosis, microbiology, and treatment options of CRS in the pediatric population.

Keywords Chronic rhinosinusitis · Pediatric rhinosinusitis

Introduction

Pediatric chronic rhinosinusitis (CRS) accounts for 5.6 million outpatient visits per year in the USA, more than the number of visits for acute rhinosinusitis (ARS) and similar to the number of visits for allergic rhinitis [1••]. Concern has been raised about the over diagnosis of both ARS and CRS. Therefore, the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) and the American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF) developed guidelines and consensus statements, respectively, regarding clinical symptoms, time course, and severity of disease prior to initiating antibiotic and other therapies [2, 3••, 4, 5]. When correctly diagnosed, CRS can be ameliorated with medical therapy, and in recalcitrant cases, surgery and treatment significantly increases patients' quality of life [6–8]. Given new literature and advances in knowledge amongst the pediatric population, diagnosis and treatment options are constantly evolving. In this review, we present the current guidelines and recent literature regarding the diagnosis, microbiology, and treatment options of CRS in the pediatric population.

Diagnosis

CRS is defined as at least 3 months of two or more symptoms of purulent rhinorrhea, nasal obstruction, facial pressure/pain, or cough *and* either endoscopic evidence of mucosal edema, purulent drainage, or nasal polyps and/or CT scan showing ostiomeatal complex or sinus edema (Fig. 1) [3••, 5].

The cause of CRS in children has not been fully elucidated. While ARS is primarily due to infection, CRS represents a spectrum of disease with varying degrees of contribution from comorbid medical conditions, infection, and environmental triggers. The contributing factors vary by age, with adenoiditis a more important contributing factor in younger children and allergic rhinitis in older children [6]. Comorbid predisposing diagnoses also include cystic fibrosis, primary ciliary dyskinesia, asthma, and gastroesophageal reflux disease. Young children experience between 3 and 8 viral upper respiratory infections (URIs) per year [9]. Of URIs, it is estimated that

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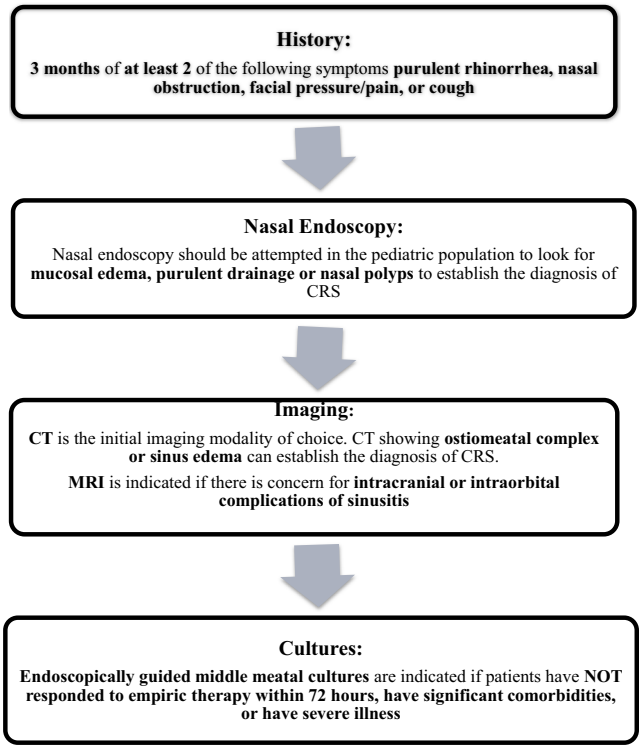

Fig. 1 Making a diagnosis of chronic rhinosinusitis. CRS is defined as at least 3 months of two or more symptoms of purulent rhinorrhea, nasal obstruction, facial pressure/pain, or cough *and* either endoscopic evidence of mucosal edema, purulent drainage, or nasal polyps and/or CT scan showing ostiomeatal complex or sinus edema. Cultures are only indicated if patients have not responded to empiric therapy within 72 h, have significant comorbidities, or have severe illness

0.5–5% are complicated by acute bacterial rhinosinusitis, while an unestablished percentage can progress to CRS [9]. Environmental contributions to CRS include smoke exposure [10], industrial pollution [11], and participation in daycare [12]. The multifactorial inflammation of the sinus mucosa leads to obstruction of the ostiomeatal complex, while edema leads to blockage of the sinus ostia, stasis of secretions, reduced oxygen tension, inhibition of ciliary function, and chronic bacterial infection [9].

Nasal Endoscopy

Nasal endoscopy provides direct visualization of the nasal cavity, which is ideal in diagnosis of CRS. In addition, there is no associated radiation exposure. Despite the benefits, many children are not able to tolerate the examination without sedation. Although nasal endoscopy may be challenging in the pediatric population, both the AAO-HNSF consensus statement and EPOS guidelines recommend attempting nasal endoscopy as an initial objective modality to aid in diagnosis of CRS [3••, 5].

Imaging

Computer tomography (CT) is the initial imaging modality of choice to evaluate for CRS per the EPOS guidelines [5]. CT is ideal, because it can aid in navigation during surgical procedures and it provides high sensitivity for mucosal inflammation [13]. Given the high sensitivity, there has been concern for potentially high false-positive rates as mucosal edema can occur in any child with a URI. Interestingly, a prospective study by Bhattacharya et al. demonstrated a CT sinus can provide a high sensitivity and specificity for pediatric patients with CRS [13]. The study compared CT sinuses and Lund-Mackay scores of pediatric patients with clinical evidence of CRS to patients who had CT facial imaging for non-sinus related illnesses. Using a Lund-Mackay score cut-off of five to define CRS, the sensitivity and specificity of CT imaging was 86% and 85%, respectively. This study shows the ability of CT imaging to differentiate CRS from other disease, including common viral URI. A second concern with use of CT imaging is radiation exposure. This is especially important amongst the pediatric population given the longer time period to potentially develop malignancy. A retrospective cohort study found that one head CT before the age of 10 years led to one excess case of brain tumor and one excess case of leukemia per 10,000 patients [14]. The study also found that 2–3 head CTs would triple the risk of brain tumors, while 5–10 CT brains would triple the risk of leukemia. Although CT scans are recommended to aid in diagnosis of CRS, the risks must be carefully weighed.

Magnetic resonance imaging (MRI) is indicated if there is concern for intracranial or intraorbital complications of sinusitis given superior soft tissue visualization based on the EPOS guidelines [5]. Plain radiographs are not recommended by the AAO-HNSF consensus statement or the EPOS guidelines, given the lack of correlation with CRS [3, 5].

Bacteriology/Culturing

Hsin et al. analyzed the maxillary aspirates of children with CRS and found the most common bacteria to be alpha-hemolytic *Streptococcus* (20.8%), *Haemophilus influenza* (19.5%), *Streptococcus pneumonia* (14.0%), coagulase-negative *Staphylococcus* (13.0%), *Staphylococcus aureus* (9.3%), and anaerobes (8.0%) [15]. Despite these estimates, it can be difficult to predict the bacteriology of patients with CRS based on unique exposure and previous history of antibiotic usage. Neither the AAO-HNSF consensus statement nor the EPOS guidelines recommend cultures at initial presentation [3••, 5]. Both guidelines recommend that cultures

should be obtained only when patients have not responded to empiric therapy within 72 h, have significant comorbidities, or have severe illness.

Pediatric patients may have difficulty tolerating office-based cultures. Maxillary sinus aspirations are considered to be the gold standard method of culturing; however, the invasiveness of the procedure and need for sedation limit the usefulness in the pediatric population. Blind paranasal swabs are not recommended given poor correlation with sinus aspirations [16]. Endoscopically guided middle meatal cultures have proven to be effective in providing microbiological data. The EPOS guidelines recommend the use of endoscopically guided middle meatal cultures in the pediatric population if it can be performed in clinic [5]. For patients who require sedation, the EPOS guidelines recommend performing maxillary sinus aspirations over endoscopically guided cultures, given nasal irrigations can be performed concomitantly providing additional therapeutic benefit.

Treatment

There are a variety of medical and therapeutic options proposed to alleviate CRS. Table 1 summarizes the evidence-based recommendations regarding the use of medications and surgery for CRS in the pediatric patients.

Nasal Saline Spray

Saline irrigations improve clearance of pathogens within the nasal passage and decrease inflammatory mediators [17]. Several studies have proven the effectiveness and tolerability of saline irrigations in the treatment of rhinosinusitis in the pediatric population [18, 19]. Hong et al. sought to analyze the relative compliance and effectiveness of saline irrigations in pediatric patients with CRS who had failed outpatient antibiotics [20]. They found 63.6% of children were compliant with nasal saline irrigations. Children between 6 and 8 years of age were the most compliant. While those over the age of 9

Table 1 Evidence-based recommendations regarding medical and surgical treatment of pediatric chronic rhinosinusitis (CRS)

Therapy	Recommendation	Level of evidence
Nasal saline spray	• First-line treatment option.	• Well supported in current literature.
Nasal steroid spray	• First-line treatment option.	• Although limited evidence in pediatric population, given relative effectiveness and limited risk demonstrated in adult population, nasal steroid stray is recommended in the pediatric population.
Antibiotic irrigation	• No consensus at this time. • May be most useful following endoscopic sinus surgery.	• Limited evidence analyzing risks and benefits at this time.
Oral antibiotics	• First-line treatment option. • Amoxicillin, amoxicillin/clavulanate, or cephalosporin are recommended as first line. • Clindamycin recommended for anaerobes. • For penicillin-allergic patients, dual therapy with third-generation cephalosporin and clindamycin or levofloxacin is recommended. • Duration of therapy: no consensus, however, 20 days is superior to 10 days.	• There is limited evidence in current literature regarding pediatric CRS specifically. These recommendations are mainly extrapolated from studies analyzing benefits seen in pediatric ARS.
Intravenous antibiotics	• No utility for routine pediatric CRS. • Indicated for intraorbital or intracranial complications of CRS.	• Limited evidence for routine pediatric CRS. • Utility is well supported when complications of CRS are present.
Adenoidectomy	• First-line surgical option if failed medical therapy.	• Well supported in current literature.
Balloon sinuplasty	• No consensus at this time.	• Although safety profile is well supported, limited evidence demonstrating benefit at this time.
Endoscopic sinus surgery	• First-line surgical option with or without adenoidectomy if failed medical therapy. • Indicated if patient has anatomic obstructing lesions, nasal polyps, or if patient has comorbidities such as cystic fibrosis, primary ciliary dyskinesia, or immunodeficiencies.	• Well supported in current literature.

and under the age of 6 years were less compliant. Patients who were compliant with saline irrigations had significantly greater improvements in symptoms and reduced need for surgery compared to patients who were not compliant. Given the relative effectiveness and limited risk of saline irrigations, both the AAO-HNSF clinical consensus statement and EPOS guidelines support the use of saline irrigation both as a sole modality and ancillary treatment in CRS.

Nasal Steroid Spray

CRS is defined by chronic inflammation of the paranasal sinuses. The use of nasal steroids is widespread given the belief that steroids can significantly reduce inflammation. A Cochrane review analyzing 18 randomized controlled studies comparing intranasal steroids to placebo or no intervention found significant improvement in symptoms with use of intranasal steroids [21••]. Of note, only 1 of the 18 studies in the Cochrane review included pediatric patients. Despite limited evidence focused on the pediatric population, both the AAO-HNSF consensus statement and EPOS guidelines recommend daily topical steroid spray as a first-line treatment for pediatric patients with CRS with or without nasal polyposis [3••, 5]. Given concerns for slowing of growth velocity in young children, a preparation with low systemic bioavailability, such as mometasone or fluticasone, should be chosen [22].

Antibiotic Irrigations

Given the proven benefits of nasal saline irrigations, some researchers hypothesize that intranasal antibiotic irrigations might provide the efficacy of antibiotics while avoiding the systemic side effects that can occur with oral or intravenous antibiotics [23, 24]. A study by Wei et al. compared the outcomes of children with CRS using daily saline irrigations versus low-dose gentamycin irrigations [23]. Both groups had improvement of quality of life scores and Lund-MacKay CT scores following treatment. Interestingly, there was no statistically significant difference between groups. One limitation of this study is that it does not analyze patients who have received sinus surgery. A minimum ostial diameter of approximately 3 mm may be required to successfully irrigate the paranasal sinuses [25]. A review of the current adult and pediatric evidence demonstrates that antibiotic nasal irrigations may be most useful when used following endoscopic sinus surgery. [24] However, given the limited evidence in the pediatric population, including medication dosing and risk of ototoxicity, it is difficult to provide conclusive recommendations for pediatric patients. Based on the limited available evidence to date, the AAO-HNSF did not reach consensus regarding the use of topical antibiotic irrigation for the pediatric population [3••].

Oral Antibiotics in Chronic Rhinosinusitis

The current literature supporting the use of oral antibiotics for pediatric CRS is also sparse. Otten et al. performed a double blinded, randomized study analyzing the utility of oral antibiotics in pediatric patients with CRS [26]. Children with purulent rhinosinusitis for 3 months underwent sinus aspiration and washout followed by randomization into treatment with cefaclor or placebo for 1 week. At the 6-week follow-up, there was no statistically significant difference in resolution of sinusitis clinically or on imaging between groups. However, given that patients underwent pre-treatment with sinus aspiration/washout and received a very short course of therapy, it is difficult to draw definitive conclusions regarding the benefits of oral antibiotics in pediatric CRS.

Considering the limited evidence, the choice of antibiotic is often based on treatment regimens for pediatric ARS. The EPOS guidelines recommend the use of amoxicillin initially [5]. Amoxicillin/clavulanate and cephalosporins are alternatives if there is concern for beta-lactamase producing bacteria. Clindamycin is indicated if anaerobes are suspected. The Infectious Disease Society of America (IDSA) guidelines recommend the use of amoxicillin/clavulanate over amoxicillin given concern for current high rates of beta-lactamase producing bacteria [27]. In patients with allergies to penicillin, dual therapy with a third-generation cephalosporin and clindamycin or levofloxacin may be considered. If flouroquinolones are used, it is important to weigh the risks of arthropathy with the patient and family [28].

The appropriate duration of antibiotic therapy is also uncertain given the lack of evidence in the literature. The AAO-HNSF consensus statement and EPOS guidelines both advocate for a longer duration of therapy [3••, 5]. However, the EPOS guidelines do not suggest a specific time frame, while AAO-HNSF reached consensus that treatment for 20 days was likely superior to 10 days of therapy.

Intravenous Antibiotics

The number of studies analyzing the benefits of intravenous (IV) antibiotics in the pediatric CRS population is sparse. In a retrospective study, children with CRS who had no improvement with oral antibiotics were treated with maxillary sinus aspiration with or without adenoidectomy followed by postoperative IV antibiotics [29]. Those who had no improvement underwent endoscopic sinus surgery. The study found that 89% of patients treated with maxillary aspiration with or without adenoidectomy and IV antibiotics had complete resolution of symptoms. However, 14% developed complications due to prolonged IV access including superficial thrombophlebitis, fevers, serums sickness, dislodged catheters, and pseudomembranous colitis. In a similar retrospective analysis, children with CRS who failed medical therapy were treated

with maxillary sinus aspiration, irrigation, adenoidectomy, and IV antibiotic therapy until resolution of symptoms [30]. After IV therapy, 100% patients had initial clinical improvement while 77% had continued resolution at 12 months follow-up. Although these studies do demonstrate clinical benefit, the utility of IV antibiotics alone is difficult to ascertain due to concurrent surgical interventions and lack of a control group. Given the current limitations in evidence, the EPOS guidelines do not support the use of IV antibiotics in routine pediatric CRS [5]. However, both the AAO-HNSF consensus statement and the EPOS guidelines support the use of IV antibiotics if there is concern for an intraorbital or intracranial complication of rhinosinusitis [3••, 5].

Surgery

In some cases, medical therapy is unable to adequately improve patients' symptoms and surgery may play a valuable role in their care. First-line surgical therapy for CRS is adenoid removal. In some cases, this may be combined with antral irrigation or balloon dilation of the maxillary sinuses. Endoscopic sinus surgery is reserved for treatment failures and those patients with nasal polyps [5].

Adenoidectomy Chronic adenoiditis can lead to CRS. This is supported by a study comparing the biofilms noted on adenoids following adenoidectomies for CRS and for obstructive sleep apnea [31]. In patients with CRS, 94.9% of the adenoid surface was covered with biofilms, while only 1.9% was noted in patients with obstructive sleep apnea. Adenoids are believed to harbor nasopharyngeal bacteria, which can be a nidus for chronic infection and inflammation in the paranasal sinuses [32••, 33]. This is supported by the fact that adenoidectomy alone has a success rate between 40 and 69% in improving symptoms of CRS [31–34]. Given the relative efficacy and low risks of adenoidectomy, the AAO-HNSF consensus statement and EPOS guidelines recommend adenoidectomy as first-line surgery for pediatric patients with CRS.

Balloon Sinuplasty The addition of balloon sinus dilation has been shown to be safe in children and to possibly increase the success rate of adenoidectomy [35•]. One non-randomized prospective trial compared the effectiveness of adenoidectomy with or without balloon sinuplasty in the pediatric patient with CRS who failed medical therapy [35•]. Sinus irrigation was performed at the time of balloon sinuplasty if indicated. At 1-year follow-up, 80% of patients in the balloon sinuplasty group demonstrated improvement, which was significantly greater than the 52% who underwent adenoidectomy alone. Given the concurrent procedures, it is difficult to discern the benefits of balloon sinuplasty alone from this study; however, the benefits of balloon sinuplasty as an ancillary procedure are evident.

In a more recent study, Soler et al. performed a prospective, multicenter, single arm study analyzing the outcomes of balloon sinuplasty alone versus balloon sinuplasty with concurrent procedures. No difference in symptom control was identified in children who underwent balloon sinuplasty versus children who underwent balloon sinuplasty with adenoidectomy, turbinate surgery, or ethmoidectomy. Multivariate regression found that improvements in Sinus and Nasal Quality of Life Survey (SN-5) scores were maintained despite controlling for numerous factors, including the performance of adjunctive procedures, suggesting that balloon dilation in and of itself contributes to efficacy. Of note, there was no control group and participants were not randomized to procedure type; therefore, causality could not be proven [36•]. None of the patients had significant complications demonstrating the safety of balloon sinuplasty.

Both the AAO-HNSF consensus statement and the EPOS guidelines acknowledge the safety profile of balloon sinuplasty [3, 5]. However, given the limited evidence, neither guideline recommended the use of balloon sinuplasty as a sole treatment modality.

Endoscopic Sinus Surgery In the absence of adenoiditis or after adenoid removal, patients with persistent symptoms despite medical management are candidates for potential endoscopic sinus surgery (ESS). A meta-analysis examining clinical outcomes of ESS in pediatric CRS reported significant improvement in symptoms (greater than 80%) with minimal complications (0.6%), demonstrating the safety and efficacy of ESS in the pediatric population. Ramadan et al. performed a prospective, non-randomized study to compare the efficacy of adenoidectomy to ESS [37]. Pediatric patients who failed medical therapy for 6 months were treated with either adenoidectomy or ESS. The study found greater improvement in symptoms amongst the ESS group (77%) over the adenoidectomy group (47%). Ramadan performed a second study determining the utility of ESS in relation to age [38]. Interestingly, patients over the age of 6 years had improved outcomes from ESS compared to those less than six. Initial concerns about possible adverse effects on facial growth have been allayed by animal studies and by a long-term follow-up study which showed no impact on qualitative or quantitative parameters of pediatric facial growth, as evaluated up to 10 years post-operatively [6, 39]. Based on the available evidence, the AAO-HNSF consensus statement and EPOS guidelines recommend ESS when symptoms of CRS are persistent despite maximal medical management with or without adenoidectomy [3, 5].

ESS is especially useful when anatomic obstructive lesions are noted or when patients have comorbidities. More specifically, symptomatic patients with:

- Anatomic variations leading to obstruction
- Nasal polyposis
- Cystic fibrosis
- Allergic fungal rhinosinusitis
- Primary ciliary dyskinesia
- Immunodeficiencies not responding to medical treatment
- Asthma secondary to refractory CRS not responding to systemic steroids
- Antrochoanal polyps
- Orbital or intracranial complications of rhinosinusitis

may require ESS for disease control, improve drainage, and to optimize penetration of topical medications. Although no guidelines or consensus exists regarding the appropriate extent of surgery, a limited approach in children is often advocated consisting of removal of any obvious obstruction, opening the maxillary sinus, and removing anterior ethmoid partitions [40].

Conclusion

The diagnosis of pediatric CRS is primarily based on clinical signs supported by objective findings on nasal endoscopy and/or CT imaging. Imaging should be reserved when surgical intervention is being considered, there is concern for complications, or atypical presentations. In children with CRS who have failed medical therapy, a stepwise approach to surgical intervention can lead to significant improvements in quality of life.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
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