

REVIEW ARTICLE

Management of acute rhinosinusitis

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Abstract

Acute rhinosinusitis (ARS) is one of the most common reasons for physician visits and for significant school absenteeism, although precise data on its prevalence and incidence are still lacking. RS is defined as acute if there are symptoms lasting < 12 wk with complete resolution. Superinfection by bacteria following a viral infection is the most important mechanism of ARS. Diagnosis of ARS should be made on clinical grounds alone. Typically, acute bacterial RS is self-limited and goes through spontaneous recovery within 4 wk. Recognizing the occurrence of bacterial superinfections of the sinuses during a common viral respiratory infection is fundamental to making the decision to start an appropriate antibiotic treatment. Topical treatments such as saline irrigation, nasal decongestants, steroids, antihistamines, and fungicides are all in widespread pediatric use, but analyzing the literature gives poor evidence of efficacy, except for topical steroids. RS is a multifactorial condition that poses a diagnostic and management challenge to infectivologist and ear-nose-throat specialists as well as to pediatricians.

Owing to anatomic, physiologic, and pathophysiologic continuity between the nasal cavity and paranasal sinus, rhinitis and sinusitis are usually associated or rhinitis precedes sinusitis (1). These aspects make the term 'rhinosinusitis' (RS) preferable to rhinitis or sinusitis alone (2, 3). Acute rhinosinusitis (ARS) is one of the most common reasons for physician visits and for significant school absenteeism, although precise data on its prevalence and incidence are still incomplete (4).

RS is defined acute if there are symptoms lasting < 12 wk with complete resolution (5). The paranasal sinuses are divided according to their location and routes of drainage into four spaces: the ethmoid, maxillary, frontal, and sphenoid sinuses.

Pathogenesis

Three factors are of paramount importance in ensuring the functionality of the nasal and paranasal spaces: the patency of the ostia, the function of the ciliary apparatus, and the quality of the secretions. A state of inflammation, which may be sustained by a heterogeneous group of disorders, affects the pseudostratified columnar ciliated epithelium, interspersed

with goblet cells that cover the surface of all the paranasal sinuses and the nasal cavity. Infectious diseases mostly affect young children, owing to their immunologic immaturity. On the contrary, inflammatory diseases (allergic or not) typically involve adults, teenagers, and school children. The *primum movens* in the pathogenesis of infectious RS is nasopharyngeal colonization. The pathogens may subsequently spread into the contiguous space causing epithelial disruption, mucosal edema, and excessive production of mucus (6).

Risk factors

Superinfection by bacteria following a viral infection is the most important mechanism of ARS. During the common cold, only 5–13% of viral infections are complicated by bacterial RS (7). Sinusitis, however, is commonly described in association with or after a common cold so the role of other risk factors should be taken into account: non-immunologic (i.e., diabetes and cystic fibrosis) and immunologic factors (atopy or any defect of immunity); environmental factors (climate, exposure to infectious agents or irritants, mold, indoor and outdoor air pollution, and tobacco smoke); allergy.

Clinical manifestations

The clinical appearance of RS may be various and may change over the years in the same person. The duration of symptoms and, above all, the severity of illness may characterize the disease expression as well. Typically, symptoms indicative of ARS are nasal blockage, congestion or stuffiness, nasal discharge or post-nasal drip (often mucopurulent), facial pain or pressure, headache, and reduction in or even loss of smell (1). Younger children may show non-specific symptoms such as irritability, poor appetite, throat clearing, and malodorous breath. Older children and adolescents may complain of more specific symptoms, such as headache, facial pain, and vomiting (5).

Wald suggested that ARS may appear in children with different presentations (8). The first consists of persistent symptoms and signs of an upper respiratory tract infection. The second presentation of ARS is with more severe symptoms, but it is less common than the first (9). A third is characterized by a cold that worsens after several days of improvement (with or without fever).

Diagnosis

The American College of Radiology has stated that the diagnosis of acute uncomplicated sinusitis should be based on clinical criteria. ARS could be diagnosed based on two major or one major and two minor symptoms (10, 11). According to the definition of the RS task force, major symptoms and signs include facial pain/pressure, facial congestion/fullness, nasal obstruction/blockage (continuous or intermittent), nasal discharge/purulence, hyposmia/anosmia, purulence on nasal examination, and fever. The minor symptoms and signs include headache, fever, halitosis, fatigue, dental pain, cough, and ear/pain/pressure/fullness (12).

Differential diagnosis

A number of similarities have been described between signs and symptoms of acute bacterial RS and those of prolonged viral upper respiratory tract infection. It can be difficult to distinguish repeated episodes of uncomplicated upper respiratory tract viral infections from the onset of acute bacterial RS with persistent symptoms. Uncomplicated viral upper respiratory infections generally last 5–7 days but may last longer (5, 11) with a progressive spontaneous improvement within 10 days. Persistent fever and cough, mucoid or purulent rhinorrhea, halitosis and facial pain should direct the diagnosis toward a bacterial infection.

Complications

ARS may easily become complicated because of the direct extension of the infective process to the orbits and endocranial structures as a result of contiguity or bloodborne disease. Complications are more frequent in children because of some distinctive anatomic characteristics: thin sinus walls, larger vascular granules, more porous bones, and unsoldered sutures (13, 14).

Preventive measures

Several approaches have been experimented to reduce the frequency of RS and, in general, of upper respiratory diseases, ranging from environmental measures to the use of standard or specific immunoglobulin immune modifiers and vaccinations (6).

Vaccination against influenza and pneumococcal infections is successful for children with upper respiratory diseases. In particular, a decreasing incidence of otitis media and acute bacterial RS has been observed thanks to the widespread use of conjugated pneumococcal vaccines (15). Influenza vaccination has also proven to be useful in preventing upper respiratory diseases especially in children younger than 2 yr of age (6). Finally, antibiotic prophylaxis has been proposed but not recommended for the prevention of RS (16).

Antibiotic treatment

Typically, acute bacterial RS is self-limited and goes through spontaneous recovery within 4 wk. The recovery rates depend on the causative organism: 15% for *Streptococcus pneumoniae*, 50% for *Haemophilus influenzae*, and 50–70% for *Moraxella catarrhalis* (8, 17). For this reason, the need for antibiotics in children with ARS has been discussed by several authors (18). There is consensus in the literature that ARS should be treated with antibiotic agents, in particular for those children with ARS defined as 'persistent' or 'severe' as previously described (3, 19). This will minimize the number of children with uncomplicated viral upper respiratory tract infections who are treated with antimicrobials, and it will promote the judicious use of antibiotics. Antibiotics are the primary and most appropriate form of medical treatment for acute bacterial RS. The rationale of antimicrobial therapy consists of rapid clinical cure, sterilization of the sinus secretions, prevention of orbital and intracranial complications, and the blockage of the vicious cycle leading to chronic sinus disease (20). Among the most frequently detected bacteria *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*, some of them can produce beta-lactamase, resulting in resistance to penicillin and its derivatives. The prevalence of penicillin-resistant *S. pneumoniae* has recently increased by 25–50%. Age <2 yr, attendance in child care, use of antibiotics within the past 3 months, and sinus aspirate culture showing the growth of an amoxicillin-resistant pathogen are factors increasing the risk for bacterial resistance (21). Amoxicillin is recommended as first-line therapy because of its general effectiveness, narrow spectrum of activity, safety, palatability, and low cost in cases of mild ARS. The standard dose of 50 mg/kg divided into three oral doses can be increased to 90 mg/kg/day in three doses in the presence of specific risk factors or proven resistance. The lower dose can be employed in children with non-severe sinusitis who are older than 2 yr of age, who are not in child care, and who have not received antimicrobial therapy in the previous 90 days. If children do not improve within 48–72 h and the diagnosis of ARS is confirmed, the antimicrobial agent should be changed. Furthermore, the majority of improvement in treated patients should occur during

the first 72–96 h of treatment (19). Against beta-lactamase-producing strains, the combination of amoxicillin/potassium clavulanate (80–90 mg/kg/day of amoxicillin component, with 6.4 mg/kg/day of clavulanate in three divided doses) can inhibit the beta-lactamase enzymes, even if adverse effects such as diarrhea may occur. Cephalosporins are commonly prescribed as a valid choice to treat ARS. First-generation agents (cephalexin and cefadroxil) have poor effectiveness against *H. influenzae* infection. Cefaclor (50 mg/Kg/day in two doses), an early second-generation cephalosporin, has poor coverage for all beta-lactamase-producing *M. catarrhalis* and some, but not all, *H. influenzae* strains. Other second-generation cephalosporins (cefuroxime axetil, 30 mg/kg/day and cefprozil, both in two doses as oral suspension) have positive activity against beta-lactamase-producing bacteria. Other third-generation cephalosporins cefixime, ceftibuten, cefpodoxime axetil (10 mg/kg once daily), and cefdinir (14 mg/kg/day in one or two doses) can be administered as oral suspension once or twice a day. One should, however, take into account that cefixime and ceftibuten are ineffective against penicillin-resistant strains and have poor activity against *S. pneumoniae*. Because of increased pneumococcal resistance, some antibiotics used in the past (trimethoprim–sulfamethoxazole and erythromycin–sulfisoxazole) should no longer be prescribed. Ceftriaxone (100 mg/kg/day in a single dose or in two doses) or ampicillin–sulbactam (100 mg/kg/day in three doses) or amoxicillin–clavulanic acid in three doses or cefotaxime (100 mg/kg/day in three doses) intravenously or intramuscularly can be used in children who do not tolerate oral antibiotics because of the occurrence of vomit as an adverse event or in patients not improving 24–48 h after a second course of antibiotic treatment (2, 22). Usually, 24 h after the initial response to intravenous or intramuscular therapy, it is possible to switch to an oral antibiotic to continue and complete the treatment. If the patient is allergic to amoxicillin, third- or second-generation cephalosporins can be recommended except in the case of type 1 hypersensitivity allergic reaction. In this case, clarithromycin (15 mg/kg/day in two divided doses) or azithromycin (10 mg/kg/day on day 1, then 5 mg/kg/day for 4 days as a single daily dose) can be used because they belong to a completely different class of antibiotics (2, 20). If an anaerobic pathogen is suspected as the cause of ARS, clindamycin or metronidazole can be added to a broad-spectrum drug (5). The optimal duration of therapy for patients with acute bacterial RS is not well defined, but treatment for 10–14 days seems to be adequate for mild acute forms, and 14–21 days seems to be appropriate for severe acute and subacute forms. There are empiric recommendations for 10, 14, 21, and 28 days of treatment.

Other treatment options

Oral corticosteroids can be added to treat ARS when the patient does not respond to initial therapy in the case of nasal polyposis or marked mucosal edema (2). Concerning antihistamines, a double-blind, placebo-controlled trial showed that in patients with allergic rhinitis developing ARS, the adjunct to antibiotics of the second-generation antihista-

mine loratadine achieved a significant improvement in sneezing and nasal obstruction (23). Antihistamines seem useful in the case of concomitant acute bacterial RS and allergic RS because they reduce the inflammatory component and favor a positive response to antibiotics.

Concerning mucolytics, only one clinical trial is available in non-atopic children or adults with acute bacterial RS (24). In current practice, mucolytic agents do not seem to be more effective than placebo. There are no studies on the efficacy of antileukotrienes in ARS (25). Also for antimycotics in fungal RS, there are no controlled trials (25). Instead, herbal preparations myrtol oil and *Andrographis paniculata* have been proven to be superior to placebo (26). Allergen-specific immunotherapy is highly effective in allergic rhinitis reducing the risk of complication including ARS (25).

Topical treatment

Various types of topical treatments are used, including antibiotics, corticosteroids, saline sprays at different osmotic pressures, nasal decongestants, and topical fungicides. However, there is still no clear evidence in the literature on the efficacy of topical therapy, and the guidelines of the American Academy of Pediatrics and those of the Italian Society of Pediatrics mention it only as an adjunct to conventional antibiotic therapy for rhinosinusitis (19, 27). Topical antibiotics could be used to maximize their effective concentration and reduce systemic effects, which may be significant as the doses would have to be 100–1000 times greater. In the study by Desroisiers et al. (28), the effect of moxifloxacin was assessed *in vitro* on biofilms from patients treated surgically for uncontrolled rhinosinusitis. The results showed that the MIC of moxifloxacin had no effect on biofilm growth; 1000-fold greater concentrations are needed to reduce the number of viable bacteria (by more than 99%) but the bacteria that remain viable are able to create a substrate for a re-infection. Mupirocin is a topical agent that produced good results both *in vitro* and *in vivo*, decreasing the subjective symptoms of patients with rhinosinusitis and the degree of mucosal inflammation (29).

Topical nasal corticosteroids may reduce nasal edema and improve ostial drainage and ventilation of the sinus. It has been assumed that corticosteroids may potentially cause a spread of infection in acute sinusitis; however, the concurrent administration of antibiotics rules out this possibility. One study found that intranasal flunisolide spray as an adjunct to oral antibiotic therapy for rhinosinusitis improved the outcome (30). Similar observations were reported for budesonide, the addition of which to antibiotics in childhood sinusitis was followed by a prompt reduction in nasal discharge and cough during ARS (31). Meltzer et al. evaluated the efficacy of mometasone furoate nasal spray vs. amoxicillin and placebo in patients with acute, uncomplicated RS. The authors concluded that in patients with acute, uncomplicated RS, mometasone furoate, 200 µg twice daily, significantly reduces symptoms compared with amoxicillin and placebo without predisposing factors or bacterial infection (32).

Nasal washes are widely used for the management of upper respiratory infections like rhinitis, ARS or CRS,

allergic and non-allergic rhinitis, non-specific nasal symptoms (retropharyngeal discharge) and for the post-operative treatment of surgical patients (33). However, a study comparing nasal wash vs. placebo in the treatment of CRS showed that washes were not more effective than the placebo option (reflexology) in mitigating symptoms or in curbing the use of drugs in the management of this disease (34). There are different devices and preparations for nasal washes such as sprays, rinses, irrigation with bulb syringes, isotonic and hypertonic solutions with additives, which may expand the variety of therapeutic options available and further compound choices. Several studies have suggested that hypertonic saline is better than isotonic saline for sinus irrigation. In a study by Shoseyov et al. (35), pediatric patients with RS were randomized to receive nasal wash with hypertonic (3.5%) or isotonic saline. Symptoms improved in both groups but patients using hypertonic saline also had cough reduction and better radiologic scores. Another study highlighted that mucociliary clearance increased with the use of hypertonic saline (36) but the finding was not statistically significant in children because only 11 of the 60 subjects in this study were between 12 and 19 yr of age. A study by Snidvongs et al. (37) compared the use of nasal spray vs. syringe irrigation of saline in 14 patients to measure which was better in reaching the paranasal sinuses of patients with RS with osteomeatal block. The patients had a CT scan to evaluate the quantity and location of the solution in the paranasal sinuses. The results showed that the two techniques worked in the same way but they managed to bring only a small amount of solution in the paranasal sinuses: 0.0009 ml with the spray and 0.001 ml with the irrigation. The study concluded that these methods are not effective in bringing saline into the paranasal sinuses of patients with RS. A Cochrane systematic review of 2010 on the use of saline solutions in the upper respiratory infections, including RS, concluded that because trials were too small and carried a high error risk, one cannot confidently state that there are potential benefits from nasal washes in the management of RS and upper respiratory infections (38). Overall, the use of nasal washes is not supported by controlled clinical trials. Topical decongestants are often used in the treatment of ARS or CRS as they may decrease nasal resistance and facilitate the opening of the osteomeatal complex. However, these agents seem to reduce the mucosal viscosity and nasal blood flow, and their use is surrounded by controversy (19). Michel et al. (39) compared the efficacy of saline vs. xylometazoline in 2- to 6-yr-old children for 14 consecutive days and observed a reduction in symptoms, but the study had no placebo control group. A study by Braun et al. (40) highlighted the efficacy of a proteolytic enzyme found in fresh pineapple, bromelain, as a nasal decongestant in the treatment of CRS compared to conven-

tional therapy in patients with no allergy to pineapple. There are no data to recommend the use of topical antihistamines that have a role in the management of allergic rhinitis, in ARS (41).

Surgery

There is general agreement on the opportunity of surgical management in some acute complications of ARS (42). Complications of maxillary and ethmoid sinusitis are quite frequent and may occur at any age, while frontal sinusitis usually does not concern small children. Sphenoid sinusitis is more rare but is associated with a high incidence of neurologic and ophthalmologic complications that may result in permanent disabilities (14, 43). Intracranial complications of ARS (frontal and sphenoid sinuses) are cavernous sinus thrombosis, meningitis, subdural empyema, epidural abscess, and brain abscess. Orbital complications include periorbital and orbital cellulites, subperiosteal abscess, and orbital abscess (42). A CT scan of paranasal sinuses, orbits, and brain is mandatory when such complications are suspected; magnetic resonance imaging is helpful in differentiating complications such as orbital cellulitis and subperiosteal abscess (44).

Conclusions

Thus far, several preventive measures for avoiding ARS have been experimented, but only vaccinations seem to be effective. Recognizing the occurrence of bacterial superinfections of the sinuses during a common viral respiratory infection is fundamental to making the decision to start an appropriate antibiotic treatment. The decision to prescribe an antibiotic should be well pondered in order to avoid a noxious rather than beneficial effect. Typically, the clinical appearance of acute bacterial RS should lead us to the right diagnosis. All cases of acute purulent rhinitis generally resolve spontaneously. Antibiotics should be required for persistent forms (symptoms lasting more than 10 days) or severe forms. A confirmation can be obtained by the prompt response (within 72 h) to antimicrobial therapy. When in the presence of complicated or not responding cases, auxiliary diagnostic tools (fiberoptic endoscopy, CT, MR) and sinus aspiration for culture can be used in order to make the right decision in the management of ARS. RS is a multifactorial condition that poses a diagnostic and management challenge to infectivologists and ear-nose-throat specialists as well as to pediatricians.

Conflict of interest

The authors declare no conflict of interest.

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