

Pediatric Sinusitis

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Acute sinusitis is one of the most common and serious childhood infections [1]. It has been demonstrated that children have upper respiratory tract infections 6-8 times per year of which 5-10% are associated with sinusitis [2-5]. While acute sinusitis is usually diagnosed in children aged between 4 to 7 years, it has been demonstrated that it specifically affects children between 1 and 5 [6]. Sinus infections most often develop secondary to upper respiratory tract infections or an underlying allergic disease [7]. For this reason, childhood sinusitis cases are among the most frequent and important problems of Family Medicine, Pediatrics and Otorhinolaryngology practices. Moreover, chronic sinusitis can develop when the underlying cause cannot be successfully treated with conventional treatment methods, and may seriously impair the children's quality of life. This may result in worsening of the underlying disease or unresponsiveness to the treatment [2,8,9]. A detailed understanding of the pathophysiology and microbiology and knowledge about medical and surgical principles are important for the treatment of childhood sinusitis [2].

ANATOMY

Paranasal sinuses are air spaces in the cranial bones that are connected to the nasal passage through the ostium. They are covered by ciliated epithelium that sweeps mucus to the ostium. In children, the most commonly infected sinuses are the maxillary and ethmoid sinuses that are present at birth. The sphenoid sinuses begin to develop during the third year of life while the frontal sinuses can be seen radiologically from the seventh year. Pneumatization of these sinuses is completed by 12-13 years of age. Sphenoid and frontal sinuses do not fully develop in 26% and 15% of the normal healthy population [10,11].

PATHOPHYSIOLOGY

The normal function of the sinuses requires normal ostium, proper mucociliary function and systemic and local immune response. When all these systems work well, the sinuses are generally sterile. Low-intensity bacterial contamination is transient [12]. Sinusitis often begins with inflammation and occlusion of the sinus ostium [2]. Impaired mucociliary clearance, blocked sinus drainage or anatomical structures near the sinuses that contain different potential microorganisms may play a role, individually or in combination, in the development of sinusitis [4]. This leads to accumulation of secretions and reduction of sinus ventilation. Oxygen absorption and negative pressure in the sinuses develop [2]. pH in the sinuses decreases. Purulent secretions contribute to reduced oxygenation in the sinuses [4]. Intranasal and nasopharyngeal contents (bacteria) leak into the sinus. The presence of viral infection facilitates bacterial proliferation by inhibiting the ciliary function [2]. Bacteria on the nasopharynx, adenoid tissue and tonsils may constitute a source of infection for adjacent sinuses. However, sinus drainage blockage and exposure to microorganisms are not the only causes of sinusitis. Persistent changes in the nasal epithelium may also cause clinical signs of sinusitis [4].

THE ROLE OF INFLAMMATION

In sinusitis cases, mucosal biopsy samples exhibited eosinophils, neutrophils, lymphocytes and intensive inflammation (due to exposure to irritant factors such as bacterial superantigens or cigarette smoke). Vasodilation associated with mediators, increased mucosal secretion, plasma extravasation, neurogenic inflammation and mast cell-nerve interactions can be seen. Inflammation leads to local changes that contribute to the development of infection [13]. Sinus mucosal samples of children aged between 1 and 8 years are predominated by lymphocytes while those of adults are predominated by eosinophils and neutrophils. Thickened basal membrane and submucosal gland hyperplasia and eosinophilic predominance seen in adults are not present in children. Early diagnosis and treatment of sinusitis can prevent long-term changes [14].

It is difficult to identify microorganisms that cause sinusitis. Empirically administered antibiotics may cause false results in nasopharyngeal samples. Moreover, bacteria that normally colonize in the flora may be falsely considered infectious agents. Unresponsiveness to treatment is generally explained by biofilm formation in the sinus mucosa [15,16].

Biofilms are colonies of microorganisms that live strongly adhered to surfaces such as respiratory mucosa in the polysaccharide matrix produced by the bacteria themselves. Bacterial gene expressions with different metabolic requirements may be present in the biofilms, and these adaptations make the biofilm bacteria resistant to antibiotics and immune factors. Adenoid, tonsillar and nasopharyngeal mucosae are biofilm reservoirs for the sinuses. Biofilms associated with sinusitis are generally polymicrobial, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *coagulase-negative staphylococci*, *Moraxella catarrhalis*, *Haemophilus influenzae*, anaerobes and even fungi [17,18].

Table 1: Preparatory Factors.

PREPARATORY FACTORS / COMORBIDITIES:	
1. Environmental Factors:	<p>Viral upper respiratory tract infections are the most common predisposing factor for bacterial sinusitis. It has been demonstrated that the prevalence of upper respiratory tract infections is increased in children in nursery period; thereby increasing the prevalence of sinusitis associated with these. Viral sinusitis leads to nasal congestion and abnormal mucosal activity. Bacteria or fungi increase the risk of secondary infections [11,19].</p> <p>The smoke of cigarette inhibits clearance and epithelial regeneration. Contaminant harmful inhalants such as ozone, chlorine or small particles can irritate the nose and sinuses [6,20].</p>
2. Allergic Rhinitis:	<p>While the prevalence of allergic rhinitis is 15-20% in the general population, children with sinusitis and their families have a history of allergic rhinitis at a rate of more than 80% [2,3]. Allergic inflammation affects the mucociliary activity of the sinuses thereby changing the sinonasal physiology. Moreover, late phase allergic inflammation can also contribute to the development of sinusitis. The role of allergy in the development of sinusitis is however still controversial. It is difficult to differentiate between these two conditions because of the similarity of their signs. Some studies show that sensitivity to allergens is the same in patients with sinusitis and in general pediatric population while others show that the prevalence of atopy is higher in patients with sinusitis compared to general population. Allergic inflammation response may be high (presence of IgE, IL-4) also in non-allergic sinusitis patients [10].</p> <p>It has been demonstrated that some patients may have allergic rhinitis without positive skin tests or elevated serum IgE levels (local allergic rhinitis) [21].</p> <p>While the prevalence of non-allergic rhinitis in healthy population is 5 to 10%, it is seen in 17 to 52% of patients with sinusitis [11].</p> <p>Allergic fungal sinusitis which is common especially in adolescents is a non-invasive form of chronic sinusitis [24]. This condition is the most common form of pediatric sinusitis. All children with allergic fungal sinusitis are atopic and almost all have nasal polyps. Allergic fungal sinusitis should be considered in children who have unilateral asymmetric nasal polyps, facial anomalies or proptosis [22].</p>
3. Asthma:	<p>Sinusitis resulting from increased inflammatory mucus and decreased nasobronchial reflex has been associated with asthma attacks. While 80% of children and adolescents with asthma have sinusitis, 40% of children with sinusitis have asthma. Asthma and sinusitis correlate with each other thereby increasing the severity of each other [2,3].</p>
4. Immunodeficiency:	<p>Immunodeficiency may contribute to the pathophysiology of sinusitis in children. One of the most common complications in children with common variable immunodeficiency is chronic sinusitis which is generally seen without polyps [23,24]. In pediatric patients who develop immunodeficiency secondary to chemotherapy, increased prevalence of sinusitis and invasive fungal sinusitis has been observed [8]. If a patient has recurrent pulmonary infections and otitis media in addition to chronic sinusitis or does not respond to usual sinusitis treatment, immunodeficiency should be considered [24].</p>
5. Gastrointestinal Conditions:	<p>Childhood sinusitis infection may be associated with gastroesophageal reflux [9]. Gastroesophageal reflux is a physiologic process that occurs during the first 3rd to 4th months of life and naturally expected to decrease after this period, but may continue in 20% of infants. Half of these children have been demonstrated to have pharyngeal reflux [25]. It has been demonstrated that 63% of patients with chronic sinusitis have gastroesophageal reflux and one thirds have nasopharyngeal reflux. In children, gastroesophageal reflux is difficult to diagnose since typical signs and complaints such as heartburn, regurgitation and postnasal burning are rare in this population. Less specific signs such as nausea and loss of appetite are observed. Reflux of gastric acid to pharynx and nasopharynx can cause impaired mucociliary clearance, inflammation of sinus ostium, and eventually sinusitis [26].</p>
6. Cystic Fibrosis:	<p>Cystic fibrosis causes recurrent respiratory track infections (associated with <i>P.aeruginosa</i> and <i>S.aureus</i>) including sinusitis. Nasal polyps are seen in 5-86% of children with cystic fibrosis. The prevalence of sinusitis is higher in carriers of cystic fibrosis compared to normal population [27].</p>

7. **Local Factors:** Primary ciliary dyskinesia is a rare genetic disease in which sinonasal cilia have abnormal morphology and function, and the number of cilia is reduced. This increases susceptibility to infection. Mucociliary dysfunction may also develop secondary to infection. Excessive use of topical decongestants also results in loss of ciliated epithelial cells. Rhinitis medicamentosa develops. The sinonasal mucosa cannot normalize immediately after discontinuation of vasoconstrictor agents [28].

The bacterial burden of the adenoid tissue is an additional risk factor, and the adenoid tissue is a bacterial reservoir for the paranasal sinuses [29].

Anatomical abnormalities that cause nasal congestion may lead to unilateral or bilateral sinusitis. Septal dislocation due to birth trauma, unilateral choanal atresia, nasal fractures, foreign bodies in the nose, septal deviation or concha bullosa (i.e pneumatization of the concha media) can cause nasal congestion. Dental infections can spread into sinuses thereby causing odontogenic sinusitis [12].

ETIOLOGY

The main bacterial pathogens in acute bacterial sinusitis are *Streptococcus pneumoniae* (30-40%), *Haemophilus influenzae* (20-30%), *Moraxella catarrhalis* (12-20%) and *Streptococcus pyogenes* (up to 3%). Anaerobic agents are more commonly seen in maxillary sinusitis associated with odontogenic infections. It has been demonstrated that the etiology IN orbital or intracranial complications are mainly *S.aureus*. Fungi are most commonly seen in children with immunodeficiency and/or diabetes [7].

CLASSIFICATION [30]

A. Etiologic classification By causes of infection

- a) Viral
- b) Viral-bacterial
- c) Bacterial
- d) Fungal

B. Classification by duration of disease

1. Acute
2. Subacute
3. Recurrent acute
4. Chronic

C. Classification by location

1. Maxillary
2. Frontal

3. Ethmoidal
4. Sphenoidal

D. Classification by localization of chronic infections

1. Nosocomial
2. Odontogenic

DESCRIPTIONS

Acute Sinusitis

Sinusitis with mild or severe symptoms lasting up to four weeks [30].

Recurrent Acute Sinusitis

A rare condition involving sinus infections each lasting shorter than 30 days separated by intervals of 10 days, that have occurred at least four times during the last year. Recurrent acute sinusitis should be differentiated from allergic rhinitis, chronic sinusitis or recurrent upper respiratory tract infections. Investigations for allergic rhinitis, immunodeficiency (IgA and IgG deficiency), cystic fibrosis, gastroesophageal reflux or immotile cilia syndrome should be assessed in children with recurrent acute sinusitis. Similarly, anatomical abnormalities that block one or more sinus openings, and anatomical defects such as septal deviation, nasal polyps and concha bullosa can also lead to recurrent acute sinusitis [31].

Sub acute Sinusitis

Sinus infections lasting up to 4-12 weeks [30].

Chronic Sinusitis

An infection that lasts at least 3 months and involves signs such as nasal congestion, nasal discharge, cough, halitosis and headache [30].

DIAGNOSIS

Diagnosis requires presence of two major or one major-two minor symptoms [30]

Major Symptoms

Facial pain, feeling of pressure and fullness

Nasal congestion

Nasal or postnasal purulent discharge

Hyposmia-anosmia

Fever (only for acute sinusitis)

Minor Symptoms

Headache

Cough

Halitosis

Fever

Fatigue

Dental pain

Ear pain, feeling of pressure and fullness

The diagnosis of acute sinusitis is more difficult in pediatric population than in adults for various reasons. Difficulty of communication with children makes it difficult to describe the presence and severity of signs. Studies have demonstrated that the prevalence of acute bacterial sinusitis that does not respond to medical therapy peaks between 3 and 6 years of age. This is caused by more intensive exposure of children to pathogens that may cause upper respiratory tract infections resulting from the time spent in the nursery. The immune system of children of this age group is not sufficiently developed to protect them from infections [32]. Since children are often prone to diseases such as upper respiratory tract infections and allergic rhinitis, it is difficult to tell when these diseases stop and sinusitis starts with similar signs [16].

Viral upper respiratory tract infections are accompanied by nasal symptoms and/or cough. Nasal discharge resembles clear water; however its texture may change as the disease continues (mucous, viscous). In such conditions, antimicrobial therapy is not needed for simple viral upper respiratory tract infections. Viral upper respiratory tract infections without complications are accompanied by fever, headache and myalgia during the early period of the disease. The condition improves within 24-48 hours. It covers a period of 5 to 7 days [9-12]. Respiratory symptoms become evident and severe between 3rd and 6th days. Signs and symptoms may last up to 9-10 days in some patients. Symptoms of sinusitis and viral upper respiratory tract infections are often similar. Long-term persistence of symptoms without improvement contributes to the diagnosis of sinusitis [33-35].

Table 2: Symptoms that suggest bacterial sinusitis in a child.

Symptoms that suggest bacterial sinusitis in a child presenting with acute upper respiratory infection [31]:	
1.	Persistent illness: Nasal discharge and/or cough during the day, or these two symptoms lasting longer than 10 days, or
2.	Worsening course: Newly onset or increasingly worsening nasal discharge, day-long cough, or fever that accompanies all these symptoms, or
3.	Serious onset: Body temperature above 39 degrees, followed by purulent nasal discharge lasting 3 days.

Inspection may reveal nasal discharge (viscous-inviscid, serous-mucoid or purulent), mouth breathing, cough, muffled voice and halitosis. Additionally, fatigue, headache and loss of appetite are evident. However, these symptoms are non-specific for acute sinusitis. Physical examination findings are not sufficient to differentiate between viral upper respiratory tract infections and acute bacterial sinusitis [31]. The percussion and translumination of the sinuses are not reliable in children. Nasal examination using an otoscope, headlamp, and nasal speculum or nasal endoscopy may be difficult in young children because of the requirement of cooperation; however if can be performed, this is appropriate for examination of the mucosal changes, polyps or anatomical barriers, and foreign bodies. Conchae may be swollen. The normal pink-orange color of the nasal mucosa with good hydration and slight brightness is not seen. Foul-smelling mucus is usually associated with a foreign body in the nose [11].

In children below two years of age, chronic sinusitis may not be considered since the paranasal sinuses are not fully developed. Symptoms depend relatively on the age. In this age group, irritability, getting tired easily, and less eating may be seen. Mucus cough followed by retching and vomiting may be experienced by young children. Sleeping in abnormal positions, restless sleeping, snoring or apnea may be seen. The main complaints of older children may be general malaise, worsening school performance and attention deficit. Fever and headache are less common in chronic sinusitis [7,11,12].

Cough is generally considered as a sign of asthma. However, in one-thirds of patients with nocturnal cough, the cause of the symptoms is sinusitis, not asthma. Chronic cough is an important sign of sinusitis in children. Because of “cough-variant asthma”, a diagnosis generally adopted by pediatricians, one may unintentionally steer away from the diagnosis of sinusitis [22,36,37].

CULTURE

Empirical therapy can be initiated after sinusitis is clinically diagnosed. Theoretically, identification of the relevant microorganisms through maxillary sinus puncture is the gold standard, however routine application is not possible since it is an invasive procedure [11].

IMAGING

Imaging methods were preferred to make or support the diagnosis of sinusitis in the past, however, today direct sinus x-ray is unnecessary and non-specific except for exceptional cases. This method may give many false positive or false negative results. Studies demonstrated that

abnormalities detected in direct x-rays of patients with acute viral upper respiratory tract infections without complications and of those with sinusitis (diffuse opacity, air - fluid level or mucosal swelling of at least 4 mm) are similar [38].

Computerized tomography is not necessary for routine diagnosis. It is only preferred before surgery. There are articles suggesting sinus tomography in cases of suspected chronic sinusitis which do not respond to three-week antibiotic therapy. In cases of orbital complications such as proptosis, impaired eye movements or vision loss, tomography should be performed immediately. Magnetic resonance imaging may be performed in children with focal or systemic neurological findings that suggest intracranial complications. Magnetic resonance imaging is also useful in differential diagnosis of inflammation and malignancy by differentiating between sinus secretions and mucosal thickening and in the detection of chronic fungal sinusitis [12,22].

IDENTIFICATION OF COMORBID CONDITIONS

Skin tests, nasal provocation tests, and pulmonary function tests may be performed in children with suspected allergy or asthma if deemed necessary by a Pediatric Allergist. If immunodeficiency is suspected, immunoglobulins and lymphocytes should be evaluated. pH monitoring should be performed if gastroesophageal reflux is considered. Sweat test should be performed for cystic fibrosis. Mucosal biopsy may be taken to diagnose mucociliary dyskinesia [22,25,39]

MEDICAL THERAPY

Sinusitis should be considered rather than acute viral upper respiratory tract infection, and antibiotic therapy should be recommended if body temperature is rapidly increasing and/or above 39°C and purulent nasal discharge lasting longer than three days is present. Similarly, antibiotic therapy is recommended if symptoms do not improve or persist or worsen after the third day [40,41].

The American Academy of Pediatrics states that some children with persistent sinusitis symptoms may overcome the disease through their immune systems and that the risk of suppurative complications is low in such patients. Therefore they recommend short term follow-up in selected patients or antibiotic therapy. Persistent acute bacterial sinusitis can affect the quality of life of patients mildly (cough-nasal discharge) or seriously (sleep disturbance, school failure). Decision of follow-up or antibiotherapy is evaluated based on the severity of the symptoms, how they affect the quality of life of the patient, recent history of antibiotic use, current experience relating to acute sinusitis, the cost and availability of the antibiotic, the concerns of the parents about the possible side effects, or development of complications [31].

Antibiotic therapy is recommended if the patient [31]:

- Received antibiotic therapy within the last four weeks but have concurrent bacterial infection (pneumonia, suppurative lymphadenitis, group A beta-hemolytic streptococcal pharyngitis or acute otitis media),

- has complications or suspected complications,
- has asthma, cystic fibrosis, immunodeficiency or a history of sinus surgery,
- has an anatomical abnormality in the upper respiratory tract.

Amoxicillin-clavulanic acid should be preferred for the first-line treatment. It is recommended because of its efficacy, safety, affordability, pleasant flavor and narrow microbiological spectrum. 45mg/kg/day as two doses is recommended in children with acute bacterial sinusitis who are followed-up without complications and who have not received antibiotics for the last 4 weeks while 80-90 mg/kg/day as two doses (max 2 g/day) is recommended in populations with high resistance to pneumococci [42,43].

Treatment with high dose (80-90 mg/kg/day) is recommended in sinusitis patients aged < 2 years who present with moderate or severe clinical symptoms. Parenteral single dose 50 mg/kg ceftriaxone may be administered to patients who vomit or cannot tolerate oral therapy. Ceftriaxone is an agent which has been demonstrated to be effective against the identified microorganisms in acute bacterial sinusitis in 95-100% of the cases. If improvement is observed within 24 hours after administration of ceftriaxone, treatment may be continued with an oral antibiotic. An additional dose of ceftriaxone may be administered before switching to oral antibiotic in symptomatic children whose fever persists despite the treatment [44-46].

Studies have demonstrated that the risk of allergic reactions that may develop with the use of 2nd or 3rd generation cephalosporins in patients who are allergic to penicillin or amoxicillin is almost the same as in those who are non-allergic to these agents. Therefore cefdinir, cefuroxime and cefpodoxime can be safely used in patients with allergies of non-type 1 hypersensitivity reaction [47-48].

S. pneumoniae and *H. influenzae* are sensitive to cefdinir, cefuroxime and cefpodoxime at rates of 60-75% and 85-100%, respectively. Cefixime and clindamycin (or linezolid) combination may be preferred to be attentive to the resistance of *S. pneumoniae* and *H. influenzae* in children of < 2 years of age with moderate/severe bacterial sinusitis who have serious allergic reaction to penicillin. Linezolid is an antibiotic that is highly sensitive even against penicillin-resistant *S. pneumoniae* but poorly effective against *H. influenzae* and *M. catarrhalis*. No oral preparation of linezolid is available in our country. In areas with high resistance to penicillin, it has been demonstrated that using TMP-SMX and azithromycin is not useful since pneumococci strains are resistant to these agents [44-46].

Quinolone antibiotics are sensitive to both *S. pneumoniae* and *H. influenzae*; however routine use in children of < 16 years of age because of the possibility of toxicity [45,49].

No optimal duration of antibiotic therapy has been specified; however it is stated that the duration of therapy will vary between 10 and 28 days. Another recommendation is to continue the antibiotic therapy for 7 days after resolution of the signs and symptoms [50].

The microorganisms causing recurrent acute bacterial sinusitis are not different from those causing acute bacterial sinusitis. Antibiotherapy preferences are not different. It should always be remembered that antibiotherapy given for acute sinusitis attacks at short intervals may cause emergence of resistant bacteria species. Prophylactic antibiotic therapy may be considered during months during which respiratory tract diseases are commonly seen and in the presence of possible predisposing factors, however, routine administration is not recommended [31].

Antibiotic use is required in chronic sinusitis. There are many different views about short- and long-term use, but no determinative studies have been conducted relating to this issue. The antibiotic preferences are similar to those in acute sinusitis [31].

Table 3: Antibiotics and Doses Used for Treatment of Sinusitis in Children [51].

Antibiotics and Doses Used for Treatment of Sinusitis in Children	
Antibiotic	Dose
Amoxicillin-Clavulanic Acid	90-6.4 mg/kg in two doses
Cefprozil	30 mg/kg/day in two doses
Cefuroxime-axetil	30 mg/kg/day in two doses
Cefdinir	14 mg/kg/day in two doses
Cefpodoxime	10 mg/kg/ day in a single dose
Cefditoren pivoxil	8-12 mg/kg/day
Azithromycin	10 mg/kg at the first day, 5mg/kg/day for four days
Clarithromycin	15 mg/kg/day in two doses
Clindamycin	30-40 mg/kg/day in two doses

Table 4: Linezolid is poorly effective against H influenzae and M catarrhalis [31].

INDICATION	DAILY DOSE
Initial treatment	Amoxicillin-clavulanate 90mg/kg/day PO 2 doses (This dose should be preferred especially in countries with high resistance of S. Pneumoniae such as Turkey.)
In children who vomit or cannot tolerate oral therapy	Ceftriaxone 50 mg/kg/day IV 2 doses
Allergy to beta-lactam	
• Type 1 Hypersensitivity	Cefdinir 14mg/kg /day 2 doses or Cefuroxime 30mg/kg/day 2 doses or Cefpodoxime 10mg/kg/day single dos
• Non-Type 1 Hypersensitivity	Cefdinir14mg/kg /day 2 doses or Cefuroxime 30mg/kg/day 2 doses or Cefpodoxime 10mg/kg/day single dose
In children of < 2 years of age with moderate/severe sinusitis who have Type 1 Hypersensitivity to penicillin	Clindamycin 30-40 mg/kg/day PO (or linezolid*) + cefixime 8 mg/kg/day PO combination
Other therapies that may be an alternative in cases of allergy to penicillin	TMP-SMX or Azithromycin
*Linezolid is poorly effective against H influenzae and M catarrhalis.	

Table 5: Indication and Daily Dose [52].

INDICATION	DAILY DOSE
Initial empirical treatment	Amoxicillin-clavulanate 90mg/kg/day PO BID
<ul style="list-style-type: none"> • Allergy to beta-lactam • Type 1 Hypersensitivity • Non-Type 1 Hypersensitivity 	Levofloxacin 10–20 mg/kg/day PO every 12-24 hours?????
	Clindamycin 30-40 mg/kg/day PO + Cefixime 8 mg/kg/day PO or Cefpodoxime 10 mg/kg/day PO
If there is a risk of resistance to antibiotics, the initial treatment is not successful	Amoxicillin-clavulanate 90mg/kg/gün PO BID
	Clindamycin 30-40 mg/kg/day PO + Cefixime 8 mg/kg/day PO or Cefpodoxime 10 mg/kg/day PO
	Levofloxacin 10-20 mg/kg/day PO every 12-24 hours
In cases of severe infection requiring hospitalization	Ampicillin/sulbactam 200-400 mg/kg/day IV 4 doses
	Ceftriaxone 50 mg/kg/day IV 2 doses
	Cefotaxime 100-200 mg/kg/day IV 4 doses
	Levofloxacin 10-20 mg/kg/day IV 1 or 2 doses

Table 6: Antibiotherapy in Sinusitis [30].

Antibiotherapy in Sinusitis			
Type	Organism	Drugs	Others
Acute	S.pneumoniae H.influenzae M.catarrhalis	Amoxicillin-Clavulanic Acid 90/kg/day	Second Generation Cephalosporins Macrolides if the patient is allergic to penicillin
Subacute	S.pneumoniae resistance B-lactamase-positive H.influenzae or M.catarrhalis	Amoxicillin-Clavulanic Acid 90/kg/day	Second Generation Cephalosporins Macrolides if the patient is allergic to penicillin
Chronic	Resistant organisms, polymicrobial infection agents, Pseudomonas species and anaerobes	Amoxicillin-Clavulanate, second generation cephalosporins, third generation cephalosporins (Cefdinir), macrolides may be preferred as second-line therapy.	S.pneumoniae highly resistant to clindamycin may be given for 2-3 weeks. Treatment against the causative organism after performing a culture, and identification of the underlying predisposing factors
Recurrent Acute	Resistant and polymicrobial infection	After the initial treatment Prophylaxis at the 3 rd -4 th weeks	Culture
Suppurative Complications	Gram-negative and S.Aureus are the most common causative organisms	Cefuroxime, Ceftriaxone, aminoglycosides	Surgical treatment if the patient does not respond within 24-48 hours

If the initial signs or symptoms do not improve or worsen within 72 hours from the first presentation of the patient, or new signs or symptoms appear, treatment should be reconsidered. The 3-day period is an optimal period that is determined based on many clinical studies and is sufficient to see the response to the treatment. During this period, the physician should reconsider and if necessary reinstitute the treatment. If the patient's condition is poor, this may indicate a complication or requirement of a parenteral treatment [31].

Irrigation with saline solution: Nasal irrigation or lavage with saline solution removes infectious agents and inflammatory mediators by facilitating removal of nasal debris, facilitates drainage by reducing edema, liquefies the secretions, and may provide relief by showing a slight vasoconstrictor effect on the nasal blood flow. Isotonic or hypertonic sprays/drops may be preferred [11,53].

Nasal decongestants, mucolytics, antihistamines: There are insufficient data on the use of these drugs in patients with acute bacterial sinusitis. Antihistamines may be used in patients who have topical allergic symptoms. Antihistamines should not be used for the treatment of bacterial sinusitis in the absence of allergy because they thicken and dry the secretions [54]. Oral mucolytics such as guaifenesin may be utilized in the treatment of chronic sinusitis [36].

Leukotriene antagonists: These drugs do not have proven efficacy in the treatment of sinusitis [11,22].

Nasal steroid sprays: Intranasal steroids, that are also used in acute sinusitis, are known to reduce edema with their anti-inflammatory properties, and speed up the improvement process by facilitating drainage. However, the response by age is still unclear. Budesonide, flunisolide, fluticasone propionate and mometasone furoate are not superior over one another when used at the same doses. Mometasone furoate is the only intranasal corticosteroid approved for patients older than 2 years of age. It has no long-term effect on growth or the pituitary axis. Fluticasone propionate may be used in children above 4 years of age [16].

Oral corticosteroids: They are safe and effective for severe chronic sinusitis signs. However, repeated or long-term use increases the risk of side effects. If polyp disease is an important factor, systemic steroids can reduce large, obstructive polyps, thereby facilitating the administration of topical steroid sprays. They may be used before surgery to reduce the polyp size and to minimize blood loss [55].

With respect to the medical therapy of patients with chronic sinusitis, identification of the underlying factors is very important for the treatment. The patient should not be exposed to cigarette smoke. Antihistamines seem useful in patients with underlying allergic rhinitis. However, more serious cases may require allergy tests, avoidance of allergens and immunotherapy [36,54-56].

H2 receptor antagonists or proton pump inhibitors are generally sufficient to control the underlying reflux disease [57].

S.pneumoniae and H.influenzae vaccines are preventive measures for acute sinusitis and chronic sinusitis. S.pneumoniae vaccine has been demonstrated to reduce the frequency of severe infections, but the number of outpatient sinusitis cases have not decreased. Food supplements containing vitamin A, omega-3 fatty acids and selenium may be potential therapeutic aids, but the results are based on a single pilot research [58].

Intravenous antibiotic therapy draws interest to avoid surgical treatment in patients resistant to medical therapy [59]. Don et al. used a protocol that involved selective use of parenteral antibiotics instead of sinus surgery. They took cultures of sinus aspirates. They gave intravenous antibiotic therapy for 1-4 weeks. Symptoms requiring functional endoscopic sinus surgery improved in 89% of the patients. It was noted that young age and shorter duration of symptoms are better determinants of prognosis in terms of response to the treatment. The authors think that intravenous antibiotic use may be useful as an alternative to sinus surgery in such patients [60].

SURGICAL TREATMENT

Surgery is rarely needed and should be considered as the last resort in children [12]. The first step to remove the biofilm reservoir in chronic sinusitis is surgical adenoidectomy. Functional endoscopic sinus surgery (**FESS**) may be applied to enlarge natural ostium and to correct anatomical deformities that predispose to chronic sinusitis. FESS may be used in cases of unsuccessful medical therapy, cystic fibrosis, unsuccessful adenoidectomy, ciliary dyskinesia, patients with immunodeficiency and allergic fungal sinusitis. There are concerns that FESS may inhibit midfacial growth [24].

Children who do not respond to broad-spectrum antibiotics and other treatments for 3-6 weeks should be referred to otorhinolaryngologists for surgery. The first-line surgical management is adenoidectomy i.e to remove the adenoid tissue which is a bacterial reservoir for the sinuses. Concurrent middle meatal culture from the affected sinuses by irrigation or maxillary sinus aspiration may be performed at the discretion of the surgeon [2]. Many studies have demonstrated the efficacy of adenoidectomy in the treatment of sinonasal symptoms in children including chronic sinusitis, chronic adenoiditis, chronic otitis media with effusion and nasopharyngeal airway obstruction [61-67]. Children whose symptoms persist after adenoidectomy should be referred for assessment of the status of the immune system, allergy tests and sinus tomography [62,63].

The importance of adenoidectomy in the treatment of chronic sinusitis was underlined by Ungkanont. 37 children with chronic sinusitis, most of whom had upper respiratory tract obstruction and accompanying symptoms, were prospectively examined. A statistically significant reduction in the acute sinusitis and obstructive symptoms were found at the end of the first year after the adenoidectomy. The authors concluded that adenoidectomy is an effective option before endoscopic sinus surgery in pediatric patients with chronic sinusitis, especially in those with obstructive symptoms [66].

The role of adenoidectomy in nasopharyngeal obstruction was evaluated by Cassano et al., and it was shown that most of the complaints of nasal obstruction, sinusitis, otitis and obstructive sleep apnea improve after adenoidectomy [67].

The role of endoscopic sinus surgery is increasingly evolving in pediatric patient population. It is a safe and effective technique with a complication rate of less than 1% in the treatment of sinusitis [68]. Although the effect of sinus surgery on midfacial growth is an important concern, Bothwell et al. demonstrated that sinus surgery does not affect inhibit midfacial growth as a result of a 10-year objective follow-up [69].

However, specific indications of endoscopic sinus surgery are still controversial. The evaluation conducted by Lieu et al. demonstrated that children who meet the Stage III (those who have headache, use daily drugs other than antibiotics, or have two or more diseases (e.g. asthma, allergy or immunodeficiency) accompanied by chronic sinusitis, but do not have daytime cough) and Stage 2 (those who have nocturnal cough and halitosis except for Stage 3 patients and Stage 4 patients who have persistent daytime cough) criteria may be good candidates for endoscopic sinus surgery. This study underlined that adenoidectomy should be performed before endoscopic sinus surgery and that the benefit of endoscopic sinus surgery is higher in patients with chronic sinusitis in whom medical therapy has been unsuccessful [5].

Clary suggested that children who do not respond to medical therapy and adenoidectomy, whose tomography findings and medical history meet the chronic sinusitis criteria, and whose immune function tests are normal are candidates for endoscopic sinus surgery [61]. On the other hand, Slavin suggested that in children with chronic sinusitis who are resistant to medical therapy, the condition should be accompanied by structural anatomical anomalies such as nasal polyps, septal deviation, bone spurs and osteomeatal unit obstruction for surgical indication [54].

In pediatric patients, one of the most common indications of endoscopic sinus surgery is orbital and/or intracranial complications.

SINUSITIS COMPLICATIONS AND THEIR TREATMENT

Complications are rarely seen in sinusitis patients. These are orbital and/or intracranial complications. Serious such as visual impairment, neurological deficit or death may be encountered in patients who have such complications. Since the signs resemble those of sinusitis the diagnosis of complications may be delayed [22,70,71].

Orbital complications are seen especially in infants and young children while intracranial complications are most commonly seen in older children [32]. Although all paranasal sinuses are close to the orbita, ethmoid sinus infections play a key role in the development of complications in infants and young children. In such cases, viewing all sinuses and the orbita by performing CT at the coronal and axial sections. Consultation with ophthalmology should be obtained for eye and vision examination. Parenteral antibiotic therapy and/or surgical treatment should be evaluated on case by case basis [72].

Intracranial complications of sinusitis may develop mostly in older children during both acute and subacute exacerbations of chronic sinusitis. Infections are most commonly seen in the frontal

and ethmoid sinuses. The most common intracranial complications are subdural abscess (56%), epidural abscess (44%), cerebral abscess (19%) and meningitis (19%). Meningeal inflammation and increased intracranial pressure may lead to head-neck pain, lethargy, fever, neck stiffness, vomiting, altered state of consciousness, convulsion and coma [32].

Magnetic resonance imaging is essential for intracranial complications. Consultation with neurology is required to identify the pathogen and to confirm the severity of the infection [6,12,22].

Parenteral use of high-dose broad-spectrum antibiotics that pass the blood-brain barrier and surgical drainage of the affected sinuses by endoscopic sinus surgery constitute the reference point of the treatment [32].

Infection spreading to bone walls from the sinuses may cause osteomyelitis. Patients feel swelling in the affected area and pain in the affected bone. Frontal sinus osteomyelitis is more common and dangerous than its maxillary variant. It may lead to Pott's Puffy tumor that causes severe ache and pain symptoms. Pott's Puffy tumor may be associated with subdural empyema, cerebral abscess, cortical vein thrombosis and epidural abscess. Multidisciplinary approach and surgical treatment is recommended [73].

CONCLUSION

Childhood sinusitis is a common condition that may be confused with other upper respiratory tract infections. Amoxicillin-clavulanic acid is the first-line therapy, and 2nd and 3rd generation cephalosporins may be preferred in the treatment. Establishment and follow-up of the prevalence of resistance of Pneumococci in the population is a guide in the determination of the treatment options. While good response can be achieved with appropriate antibiotic therapies, the relevant specialists should be consulted if no response could be achieved or for some special cases [36].

1. When evaluation of underlying allergic or immunologic diseases is required, if no response is achieved despite treatment with an appropriate dose and duration,
2. If the disease recurs so frequently that this affects the quality of life and performance of the child,
3. If there are findings suggesting opportunistic infections and sinusitis complications,
4. If the condition is accompanied by other factors such as gastroesophageal reflux .

If no response can be achieved with medical therapy in patients with chronic sinusitis, adenoidectomy is recommended as the first-line surgical treatment. It is promising that intravenous antibiotic therapy is an alternative to a potential endoscopic sinus surgery in young children. Endoscopic sinus surgery is a safe and effective treatment method when the other treatment methods prove to be unsuccessful, but more studies are needed. Although there is no clear consensus on the timing of endoscopic sinus surgery for patients with chronic sinusitis, the indications for endoscopic sinus surgery include cases in which the disease persists despite

medical therapy, adenoidectomy, and systemic antibiotic use following culture, anatomical anomalies blocking normal passage, polyps that do not respond to medical therapies, presence of orbital and intracranial complications, and improvement of quality of life and antibiotic efficacy in patients with cystic fibrosis [2].

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