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Acute Sinusitis
Guide to Selection of Antibacterial Therapy

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Contents

Abstract

Primary care doctors should be cautious in the diagnosis and treatment of sinusitis as acute bacterial sinusitis is currently over-diagnosed and over-treated in primary care practice. The clinical diagnosis of acute bacterial sinusitis is difficult in primary care practice; however, a history of purulent rhinorrhoea, purulent secretions in the nasal cavity on examination, tooth pain, worsening of symptoms following initial improvement, lack of effect of decongestants and an elevated erythrocyte sedimentation rate are supportive evidence of bacterial infection. Patients with symptoms for <7 days are not as likely to have bacterial infection.

Acute sinusitis is over-treated in primary care practice for several reasons. Firstly, most cases of acute sinusitis are caused by viral infections and resolve without antibacterial treatment. Secondly, in clinical trials of antibacterial treatment, only about one-half of patients diagnosed with acute bacterial sinusitis by experienced primary care physicians have bacterial infection. Thirdly, antibacteri-

al treatment of acute sinusitis is indicated only in patients with severe symptoms of sinusitis or in patients with moderate symptoms of >7 days duration. Symptomatic treatment is sufficient in patients with mild symptoms. Three recent meta-analyses have concluded that newer and broad-spectrum antibacterials are not significantly more effective than narrow-spectrum agents, such as amoxicillin or phenoxymethylpenicillin (penicillin V). However, because of the rapid increase in antibacterial resistance of *Streptococcus pneumoniae* and *Haemophilus influenzae*, treatment must take into account current recommendations for treating infections caused by these organisms. Fourthly, sinus imaging studies are not recommended in routine diagnosis but may be helpful in selected cases. Finally, other than pain medication, there is little evidence that use of adjunctive treatments, such as decongestants, is effective in symptom relief. However, a recent study in patients with recurrent sinusitis demonstrated that patients who received fluticasone propionate in addition to antibacterials had a higher rate of clinical success than did patients receiving placebo and antibacterials.

1. Epidemiology of Acute Sinusitis

Studies from European general practice give estimates of the frequency of sinusitis. The incidence of sinusitis-like illness severe enough to prompt a visit to the doctor is between 1.6 and 3.5 episodes per 100 adults per year in Western developed countries.[1,2] Studies from several countries give estimates of the frequency of sinusitis based on diagnosis in general practice (primary care). In Larvik, Norway, which has 31 000 adult inhabitants, 1138 cases of acute sinusitis were diagnosed in primary care offices during a 1-year period, an incidence of approximately 3.5 per 100 adults per year.[1] Seven percent of the patients had two episodes and 0.5% had three or more episodes during the 12-month recording period. There was significant seasonal variation with the highest frequency in the winter months and lowest in summer/autumn.[1] In a Swedish general practice study, sinusitis was the diagnosis in 2% of patients seeking medical care.[3] In studies in British and Dutch general practice where the diagnoses were based on clinical examination only, an incidence of 21–25 episodes of acute sinusitis per 1000 patient visits per year was found.[2] The study by van Duijn et al.[2] from The Netherlands demonstrated a frequency of confirmed sinusitis of 1.6 per 100 adults per year, 9% of whom had recurrent episodes.

We know little about people with sinus infections who do not seek medical care. From community-based studies in the US, it has been estimated that adults have two to three common colds each year and that 0.5–2% of those with a common cold develop acute bacterial sinusitis.[4-6] In a telephone survey in Canada, over a 2-week period, only 15% of people with acute respiratory infection symptoms sought medical care.[7] Based on the estimate by Gwaltney[6], 1000–2000 cases of acute sinusitis per year would be expected in the Larvik, Norway study, and 1138 episodes were diagnosed.[1] Treatment studies have demonstrated that acute sinusitis is a self-limiting disease in many cases, since one-half of the patients receiving placebo recover after 10–14 days.[8-10] Therefore, many patients with sinus infections may not seek medical care.

1.1 Gender Differences in Acute Sinusitis

Acute sinusitis is diagnosed more often in women than in men,[1,2] and this difference is not entirely because of differences in healthcare-seeking behaviour. In a large Norwegian study which included 250 000 patients in primary care, the proportion of women diagnosed with acute sinusitis was 68% compared with 58% for other acute respiratory illnesses.[11] Thus, women are diagnosed as having acute sinusitis more often than men, which cannot be explained by different care-seeking behaviour.

We see two reasonable explanations for a higher incidence in women than in men. First, because of childcare duties, women aged 20–39 years are exposed more often to upper respiratory tract infections than men. Secondly, menstruating women have an increased mucosal thickening because of estrogen exposure and this may lead to a greater likelihood of ostial obstruction and subsequent sinus infection.[1]

2. Pathogenesis, Aetiology and Definitions

Sinusitis means inflammation of the mucosa of the paranasal sinuses, irrespective of the cause. Because sinusitis is invariably accompanied by inflammation of the contiguous nasal mucosa, rhinosinusitis has become the preferred name. Most cases of rhinosinusitis involve more than one of the paranasal sinuses, most commonly the maxillary and ethmoid sinuses. A distinction is usually made between acute sinusitis lasting <30 days, subacute sinusitis lasting from 1–3 months and chronic sinusitis lasting >3 months.[12] The term rhinosinusitis has been introduced to show the close relationship between infections in the nose and sinuses. In this article we use acute sinusitis as the main term.

2.1 Predisposing Factors

In primary care settings the most common predisposing factor for acute sinusitis is upper respiratory infection, such as the common cold and influenza.[6,13] Allergic rhinitis is assumed to be a predisposing factor, but research data are conflicting.[6] Upper respiratory infections and allergic rhinitis can lead to mucosal oedema, ostial narrowing, increased secretion and decreased mucociliary activity. Anatomic malformations, polyps, septal deviation, foreign bodies and tumours may cause ostial obstruction leading to sinusitis.[14] In 5–10% of patients, sinusitis is caused by upper tooth infections that spread directly to the maxillary sinus.[6]

2.2 Pathogenesis

Our knowledge of the pathogenesis of acute sinusitis is based on studies of the maxillary sinus. It is presumed that the same mechanisms cause sinusitis in the other paranasal sinuses. The primary common cold causes mucosal thickening and secretion, resulting in obstruction of the ostium. Obstruction of the narrow sinus passages is crucial in the pathogenesis of sinusitis.[6]

2.2.1 Serous (Viral) Sinusitis

Viral infections cause mucosal thickening that may narrow or close the ostium. The closing of the ostium leads to a change in the sinus environment. The concentration of oxygen decreases and the carbon dioxide concentration increases, while the normal drainage through the ostium is obstructed.[15] This leads to the formation of a serous secretion in the sinus. This condition is called serous sinusitis and may give modest symptoms of facial pressure. The prognosis is good and with symptomatic treatment alone the chance of spontaneous cure is substantial.[16]

Maxillary sinus radiographs of young adults with typical viral upper respiratory tract infections showed mucosal abnormalities in 39% of cases on the seventh day of illness,[17] and computed tomographic (CT) scans were abnormal in 87% of similar cases.[18] These studies show that some degree of sinus mucosal inflammation is very common in viral upper respiratory tract infections

2.2.2 Purulent (Bacterial) Sinusitis

Acute bacterial sinusitis is usually a secondary infection resulting from sinus ostia obstruction and/or impaired mucus clearance mechanisms caused by an acute viral upper respiratory tract infection.[6] A healthy sinus is sterile. A prerequisite for development of a bacterial sinusitis is presence of bacteria in the sinuses. Nose-blowing may create pressure differentials that cause depositions of bacteria-containing nasal secretions into the sinus.[6] If bacteria enter via the ostium, and serous secretion and good growth conditions are present, rapid growth of bacteria will result.[6] The body responds with an inflammatory reaction, and polymorphonuclear (PMN) leucocytes are mobilised, resulting in pus formation.

The development of purulent secretions indicates that the defence system of the body has been

mobilised. The PMN leucocytes phagocytose and kill the bacteria. In this phase the pus is mucopurulent. The finding of mucopurulent pus is, in fact, of good prognostic value as it indicates that the immune system is mobilised.[19] This is the usual situation in acute mucopurulent sinusitis, as it appears in general practice.

Occasionally the inflammatory system of the body does not limit bacterial growth. The process progresses and the pus becomes thinner and more fluid-like, homogenous and sometimes foul smelling. This finding indicates that the immune system is not capable of killing the bacteria. If such findings occur, there is greater risk of irreversible damage to the sinus mucosa.[20,21] In this category of patients there is also a risk of serious sinus complications. The best way to cure these patients seems to be sinus puncture and lavage, combined with antibacterial treatment. These cases are rare in primary care practice.

2.3 Microbiology

As discussed in the previous section, acute bacterial rhinosinusitis is usually a secondary infection resulting from sinus ostia obstruction and/or impaired mucus clearance mechanisms caused by an acute viral upper respiratory tract infection.[6] The gold standard for diagnosis of bacterial rhinosinusitis is sinus puncture with aspiration of purulent secretions yielding growth of at least 10^4 organisms per mL of a likely respiratory pathogen on culture.[6] However, sinus puncture is an invasive procedure and seldom performed in primary care.

Figure 1 shows the aetiological agents of acute maxillary sinusitis.[6] The most common bacterial pathogens are *Streptococcus pneumoniae* and

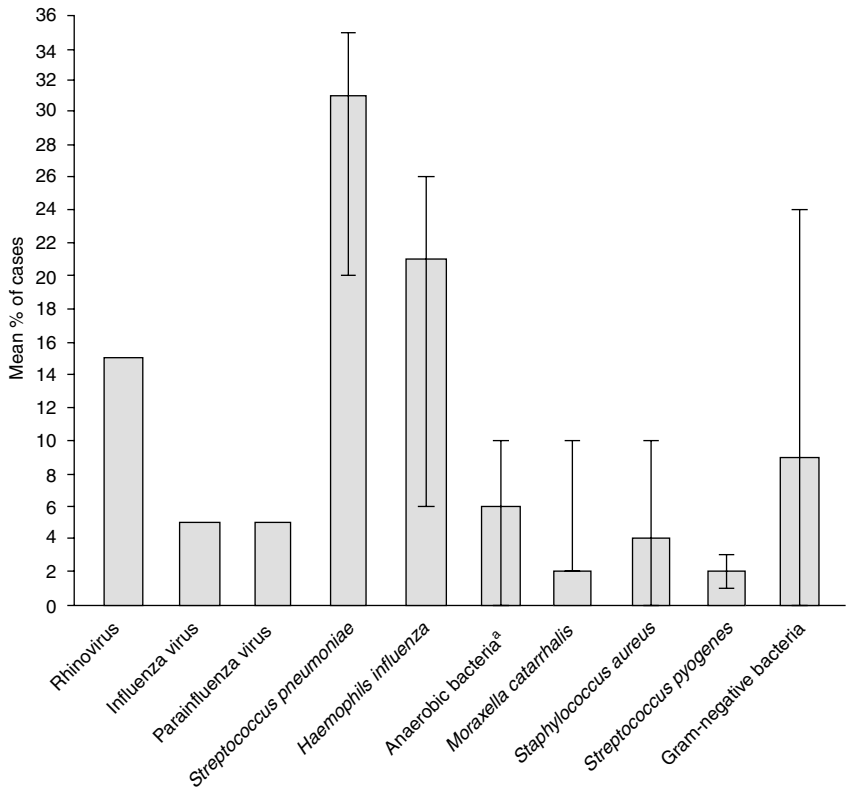

Fig. 1. Viral and bacterial aetiology of acute maxillary sinusitis based on sinus puncture in adults.[6] Lines indicate range. **a** = for example, *Bacteroides*, *Peptostreptococcus* or *Fusobacterium* spp.

Table I. Sensitivity and specificity of tests for sinusitis in adults (reproduced from Lindbaek & Hjortdahl,[26] with permission)

Test	Sensitivity (%)	Specificity (%)	Reference
Radiograph (air-fluid level or total opacity)	0.73 (95% CI 0.60, 0.83)	0.80 (95% CI 0.71, 0.87)	27
Radiograph (air-fluid/total opacity or mucosal thickening)	0.90 (95% CI 0.68, 0.97)	0.61 (95% CI 0.20, 0.91)	27
Ultrasonography	0.76 (range 0.44–0.92)	0.84 (range 0.52–0.91)	12
CT (air-fluid/total opacity or mucosal thickening)	Unknown	0.61 (range 0.58–0.84)	12
CT (air-fluid/total opacity)	Unknown	Unknown (PPV 0.90)	JG Hansen, Denmark, personal communication

CT = computed tomography; **PPV** = positive predictive value.

Haemophilus influenzae. The next most likely organism is *Moraxella catarrhalis,* of which there is a reasonably high prevalence, and many produce β-lactamase. Some anaerobes have been found as aetiological agents, most of them being β-lactamase-producing. In patients who fail to respond to penicillin therapy, an over-representation of *Haemophilus* spp. and staphylococci resistant to phenoxymethylpenicillin (penicillin V) has been found.[22]

2.4 Sinuses Involved in Acute Infections

A study by Lindbaek et al.[23] showed the results of CT findings in patients with clinically diagnosed acute sinusitis. Of 201 patients, 49 (24%) had normal CT (group 1), 25 (13%) had moderate mucosal changes with no total opacification or signs of fluid in any sinuses (group 2), and 127 (63%) had extensive changes with total opacification or signs of fluid in one or more sinuses (group 3). Of the 127 patients in group 3, 84 patients (42%) had fluid level and/or total opacification of the maxillary sinus, and 43 patients (21%) had fluid level and/or total opacification of ethmoid, sphenoid or frontal sinuses. This demonstrates that one-third of all patients with CT-confirmed purulent sinusitis were mainly affected in the small sinuses, primarily in the ethmoid sinuses.

3. Diagnosis of Acute Purulent Sinusitis

The best diagnostic standard for bacterial sinusitis is sinus puncture and aspiration of purulent secretions that grow $\geq 10^4$ organisms per mL. The clinical diagnosis of sinusitis in primary care practice is difficult because of the lack of specific clinical features that distinguish it from nonbacterial upper respiratory tract infections. Primary care doctors over-diagnose acute bacterial sinusitis. Relying on overall clinical impression, primary care doctors classifying patients as highly likely to have bacterial sinusitis are correct in approximately 40–50% of cases.[7,18,24,25] Plain radiographs are not generally indicated because of their low positive predictive value and CT scans, although more accurate, are of limited value because of their expense and limited availability. When mucosal thickening is included as a sign of acute sinusitis, both CT and plain radiograph have a low specificity (table I).

3.1 Clinical Findings that Predict Acute Purulent Sinusitis

Four studies from primary care practice provide useful information on symptoms, signs and blood tests that help discriminate purulent sinusitis from viral upper respiratory infections[2,24,25,28] (table II[26]). Purulent rhinorrhoea as a symptom was associated with purulent sinusitis in three of the studies while purulent secretion in the nasal cavity was associated in two of the studies. Tooth pain was associated with purulent infection in two studies. Other findings were less consistent predictors of purulent sinusitis. A biphasic history with worsening following initial improvement and lack of effect of decongestants were associated in one study each and were not investigated in the others. An erythrocyte sedimentation rate (ESR) >10 mm/h for men and >20 mm/h for women was associated in the two studies in which it was investigated, while C-reactive protein (CRP) >10 mg/L was associated in one,

Table II. Symptoms, signs and blood tests independently associated with a confirmed diagnosis of acute sinusitis in four studies from general practice[a] (reproduced from Lindbaek & Hjortdahl,[26] with permission)

	Reference standard (no. of patients)				
	puncture (n = 174)[25]	CT sinus (n = 201)[24]	radiograph (n = 247)[28]	ultrasound (n = 441)[2]	total
Symptoms[a]					
Purulent rhinorrhoea	–	1.5 (78%)	1.5 (59%)	1.9 (47%)	3+ 1–
Pain in teeth	–	–	2.5 (11%)	2.1 (26%)	2+ 2–
Beginning with common cold	–	–	–	1.4 (78%)	1+ 3–
Unilateral maxillary pain	–	–	–	1.8 (27%)	1+ 3–
Two phases in history	0	2.1 (59%)	0	0	1+
Lack of response to nasal decongestant	0	0	2.1 (28%)	0	1+
Signs[a]					
Purulent secretion in nasal cavity	–	5.5 (42%)	2.1 (34%)	–	2+ 2–
Pain on bending forward	–	–	–	1.6 (52%)	1+ 3–
Transillumination of sinus	0	0	1.6 (56%)	0	1+
Blood tests[a]					
ESR >10 mm/h (men) and >20 mm/h (women)	2.9 (39%)	1.7 (61%)	0	0	2+
CRP >10 mg/L	1.8 (57%)	–	0	0	1+ 1–
Predictive values					
Positive (numbers of factors)	0.68 (2 of 2)	0.86 (3 of 4)	0.80 (4 of 5)	Not stated	
Negative (numbers of factors)	0.74 (2 of 2)	0.53 (3 of 4)	0.66 (4 of 5)	Not stated	

a Numbers represent association given by Likelihood Ratio (frequency in trial).

0 = not investigated; **CRP** = C-reactive protein; **CT** = computed tomographic; **ESR =** erythrocyte sedimentation rate; **+** indicates association; **–** indicates no association.

but not in the other study in which it was investigated. However, all of these studies are limited by the use of imperfect diagnostic standards. None used the best criterion for diagnosing bacterial sinusitis: aspiration of purulent secretions that grow $\geq 10^4$ organisms per mL of a likely respiratory pathogen on culture. No single sign or symptom had strong diagnostic value in any study.

3.1.1 Evaluation of Clinical Predictors in the Four Good Quality Primary Care Studies

Hansen et al.[25] used the best reference standard in their study. They studied 174 patients with acute sinusitis referred from general practitioners (GPs) in Denmark and used maxillary sinus aspiration of purulent or mucopurulent fluid as the diagnostic criterion. Of these patients, 53% had pus or mucopurulent fluid on sinus aspiration and two-thirds of this group had positive bacterial cultures. In the bivariate analysis, unilateral maxillary pain, maxillary toothache, unilateral tenderness of the maxillary sinus and mucopurulent nasal discharge were statistically more likely in patients with positive sinus aspirates, but the magnitude of association was small (odds ratios ranging from 1.9 to 2.5). These findings were common in patients with and without bacterial infection. The results of the study did not change when analysed by culture results. When a logistic regression was performed, only elevated ESR and/or CRP were independently associated with bacterial infection; none of the clinical findings were.

Lindbaek et al.[24] used air-fluid level or complete sinus opacification on CT sinus radiography as the diagnostic standard, which has an approximately 90% positive predictive value for purulent or mucopurulent secretions on sinus aspiration (JG Hansen, personal communication). They found worsening of upper respiratory tract infection symptoms after initial improvement, purulent rhinorrhoea and purulent

secretions in the nasal cavities to be the best independent clinical predictors of acute sinusitis. Elevated ESR was also associated.

Williams and Simel[28] identified five independent predictors of acute purulent sinusitis radiographically diagnosed on plain films in a study of men with suspected sinusitis in a Veterans Administration outpatient clinic: history of coloured nasal discharge, purulent nasal secretions on examination, poor response to decongestants, maxillary toothache and abnormal transillumination. Preceding upper respiratory tract infection, purulent rhinorrhoea, facial pain on bending forward, unilateral maxillary pain and tooth pain were significantly associated with positive ultrasonography in a Dutch study of 400 primary care patients with 441 episodes of suspected sinusitis.[2] Studies that rely on plain sinus radiography or ultrasonography as the diagnostic standard must be interpreted cautiously because these images overestimate the presence of bacterial infection by as much as 50%, giving a large opportunity for misclassification bias.[29]

Furthermore, a number of clinical signs and symptoms that have been presented in clinical guidelines, have not been demonstrated to be of value in primary care-based studies. Three of these (preceding upper respiratory tract infection, facial pain on bending forward and unilateral maxillary pain) were not confirmed in three of the four studies discussed in this section. In addition, the following factors have been suggested: bilateral pain over maxillary sinus, pain over frontal sinuses, headache, allergy, malaise, cough, anosmia and cacosmia, nasal congestion, fever >38°C, tenderness over maxillary and frontal sinuses, purulent pharyngeal discharge and oedema over maxillary sinuses. Although many of these factors may be frequent in patients with acute sinusitis, they are not good predictors in the clinical setting in general practice, because these symptoms are equally common with viral upper respiratory tract infections. A prior diagnosis of sinusitis is also not a predictor of bacterial sinusitis.[25]

3.2 The Importance of Duration of Symptoms

Because acute bacterial sinusitis usually develops as a complication of viral upper respiratory tract infections, experts have proposed that duration of illness of <7 days be used as a negative diagnostic criterion. In clinical trials of diagnosis and treatment of sinusitis, duration of illness alone did not reliably distinguish prolonged viral infection from bacterial sinusitis.[30] Two studies by Lindbaek et al.[16,24] provide useful information regarding the predictive value of duration of illness. Of the 440 patients in these two studies combined, 202 of 254 (80%) of patients with CT-confirmed sinusitis were symptomatic for >7 days, while 131 of 186 (70%) of the patients without CT-confirmed sinusitis were symptomatic for >7 days. The difference is statistically significant ($p = 0.03$), but has not been analysed in a multivariate logistic regression (unpublished data). In these studies, the sensitivity and specificity of duration of symptoms >7 days as a diagnostic test for purulent sinusitis are 80 and 30%, respectively. The positive predictive value is 60% and the negative predictive value is 51%. In other words, of patients in general practice presenting with sinusitis symptoms of >7 days duration, about 60% will have purulent sinusitis and 40% will have prolonged viral respiratory infections. On the other hand, of patients presenting with sinusitis symptoms of ≤7 days duration, 50% will have purulent sinusitis and 50% will have viral upper respiratory tract infections. Therefore, duration of symptoms is a poor predictor of acute purulent sinusitis.

3.3 Use of Radiography and Ultrasound in the Diagnosis of Acute Bacterial Sinusitis

Table I[29] shows the sensitivity and specificity of the reference standards compared with sinus puncture as gold standard. Radiographs have been used in a number of studies, and as demonstrated in the table, there is a major difference if only patients with fluid levels or total opacification are included, compared with including these patients in addition to those with mucosal thickening >5mm. When using fluid or opacity as criteria for bacterial sinusitis, the sensitivity and specificity of radiographs is 73 and

80%, respectively. Twenty percent would receive a false-positive diagnosis of bacterial sinusitis using these criteria. For ultrasonography, the test characteristics vary considerably from study to study. The specificity is low (84%), giving a high proportion of false-positives. A recent study demonstrated both low sensitivity and specificity of ultrasonography compared with sinus puncture when GPs performed the procedure.[31]

Sinus CT appears to have a high specificity when using fluid level and total opacification as the criteria of acute sinusitis. This assertion is based on the finding of a high positive predictive value of 90% from the study by Hansen et al.[25] on CT compared with puncture of the sinus. CT also has an advantage of giving good evaluation of the small sinuses, such as frontal, sphenoidal and, in particular, ethmoid sinuses, all of which can be frequently affected.[23]

3.4 Differential Diagnosis

A serious common cold is the condition most often confused with acute bacterial sinusitis.[18] A number of pain conditions such as atypical migraine, tension headache, trigeminal neuralgia and dysfunction of the mandibular joint are also common among the differential diagnoses.[22] These are all conditions associated with facial pain which may recur. Many of these conditions have been misinterpreted as sinusitis. Recurrent episodes of facial pain with few signs of infection (purulent nasal secretion) should be ruled out before starting antibacterial treatment. A negative radiograph or ultrasonography will exclude sinusitis in these patients. A combination of a pain condition and a common cold can be difficult to distinguish from a bacterial sinusitis.

4. Treatment of Acute Sinusitis

4.1 Symptomatic Treatment

Patients presenting with <7 days of mild-to-moderate symptoms consistent with acute sinusitis should be given symptomatic treatment only. Many of these cases of sinusitis will be caused by viruses, as bacterial sinusitis usually takes a least 7 days to develop.[32] Regardless of the duration of illness, patients with no purulent nasal secretions probably do not require antibacterials unless they have significant facial pain.

Although there is no evidence that they shorten the duration of illness, symptomatic treatments may be offered to all patients. These include decongestants and non-prescription pain relievers. Nasal irrigation with salt water has also been suggested, especially by ear-nose-throat (ENT) specialists.[33]

The results of eight randomised trials of various symptomatic treatments of rhinosinusitis symptoms in adults have been inconclusive.[34-41] Topically or orally administered α-adrenergic agents (decongestants), proteolytic enzymes, mucolytic agents, antihistamines and corticosteroids have been used. Theoretically, agents that encourage drainage of sinus secretions may be of value. Topical and oral decongestants may ameliorate some of the nasal symptoms and promote mucus clearance. Decongestants reduce the mucosal oedema of the ostia, thus potentially improving the drainage from the sinuses. Studies have shown that oral decongestants improve the function of the sinus ostium and reduce the nasal airway resistance, but a significant clinical effect on acute sinusitis has not been documented.[42] However, in a placebo-controlled trial a combination of an oral decongestant and analgesic was effective in relieving symptoms from the sinuses.[43] Well designed placebo-controlled trials of these ancillary treatments are needed to determine their effectiveness in treating acute rhinosinusitis. They can be offered to patients with mild symptoms as an alternative to an antibacterial. Pain control is always important, as over 50% of patients with acute bacterial rhinosinusitis report facial pain.[24,25]

4.2 Antibacterial Treatment

Symptomatic treatment and reassurance is the preferred initial management strategy for patients with mild symptoms. Antibacterial therapy should be reserved for patients with moderately severe symptoms meeting the criteria for the clinical diagnosis of acute bacterial rhinosinusitis (symptoms >7 days, including maxillary facial/tooth pain and purulent nasal secretions) and for those with severe rhi-

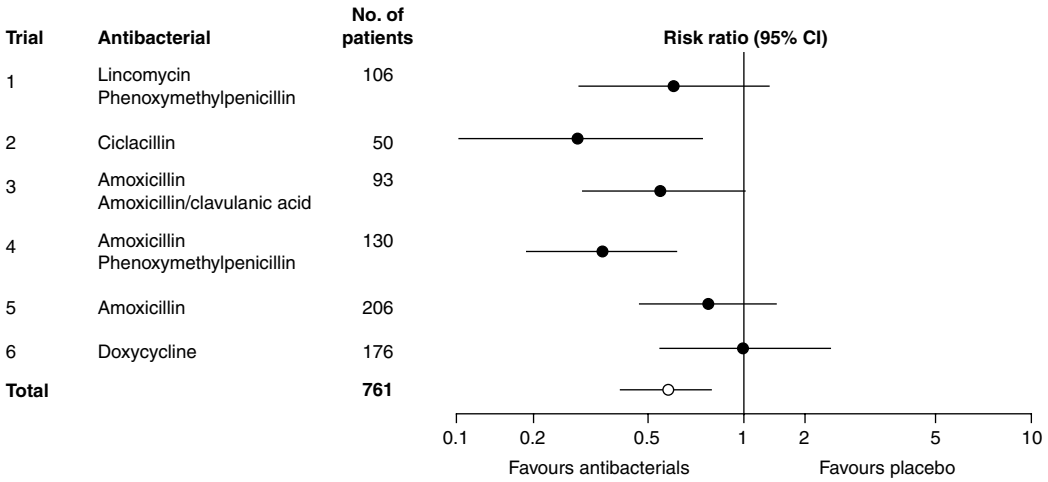

Fig. 2. Random effects model of risk ratios (95% CIs) of clinical failure associated with antibacterial treatment of acute sinusitis compared with placebo (reproduced from de Ferranti et al.,[48] with permission from the BMJ Publishing Group). **1** = Axelsson et al.[44]; **2** = Ganança and Trabulsi[45]; **3** = Wald et al.[49] (study conducted in children); **4** = Lindbaek et al.[8]; **5** = Van Buchem et al.[9]; **6** = Stalman et al.[10]

nosinusitis symptoms regardless of the duration of illness. Initial treatment should be with the most narrow-spectrum agent that is active against the likely pathogens, *S. pneumoniae* and *H. influenzae.*

Randomised, double-blind, placebo-controlled trials of antibacterial treatment of acute bacterial rhinosinusitis using pre- and post-treatment culture of sinus aspirates have not been performed. This would represent a gold standard for assessing antibacterial therapy, and without such studies the evidence base is weak. However, non-randomised treatment trials have shown appropriate antibacterials to be highly effective in eradicating or substantially reducing bacterial growth in the sinuses.[6] Antibacterial treatment is effective from a bacteriological standpoint. Is it effective from a clinical standpoint?

Five randomised, double-blind clinical trials with good methodology have compared antibacterial with placebo treatment of acute rhinosinusitis in adults.[8-10,44,45] Three recent meta-analyses (one under the auspices of the Cochrane Collaboration,[46] another under contract from the Agency for Health Care Policy and Research[47] and the third in the *British Medical Journal*[48] [figure 2]) have recently been published. All three conclude that, although antibacterials are statistically more effective than placebo in reducing or eliminating symptoms at 10 and 14 days, the effect size (degree of benefit) is relatively small, and the majority of placebo-treated patients improve without antibacterial therapy.

The specific findings of each of these five trials have been well summarised by Williams et al.[46] One used clinical clues for inclusion,[10] three used plain radiographs for diagnosis of sinusitis[9,44,45] and one[8] used CT criteria. When considered in aggregate, 47% of the antibacterial-treated patients and 32% of the placebo-treated patients were considered cured at 10–14 days' follow up, while 81% of antibacterial-treated patients and 66% of placebo recipients were responders (with clinical findings of either cure or improvement).[46] This is an absolute benefit of 15%, giving a number-needed-to-treat of seven.

However, the two most recent placebo-controlled trials of acute rhinosinusitis in primary care failed to find a significant clinical effect of antibacterial treatment. Stalman et al.[10] studied the effectiveness of doxycycline compared with placebo in general practice patients with symptoms of bacterial rhinosinusitis. The inclusion criteria were based on the guidelines set by the Dutch College of General Practitioners: three main symptoms (complaints after a common cold or influenza, purulent nasal

discharge, pain in the maxillary sinuses on bending forward); or two main symptoms and one other symptom (predominately unilateral maxillary pain, toothache or pain when chewing). There was no significant difference in time to resolution of facial pain and return to normal activities between doxycycline and placebo recipients. Using radiographs for the diagnostic standard, Van Buchem et al.[9] found no significant advantage of a 7-day course of amoxicillin over placebo at 14 days. Symptoms were substantially improved or resolved in 83% of patients receiving amoxicillin and 77% of patients receiving placebo.

The one modern placebo-controlled trial in a primary care population showing a positive treatment effect for amoxicillin or phenoxymethylpenicillin used CT scanning for diagnosis and eligibility for the study.[8] Only patients with an air-fluid level or complete opacification of a sinus were eligible for inclusion. At day 10 of treatment, 56% of patients treated with placebo, 82% of those treated with phenoxymethylpenicillin and 89% of those treated with amoxicillin were substantially better. The median duration of disease until recovery was 9 days in the amoxicillin group, 11 days in the phenoxymethylpenicillin group and 17 days in the placebo group (figure 3).

The reason these clinical trials as a whole show antibacterial treatment of sinusitis to be less efficacious than one might predict from the bacteriological studies can be explained by the 'Pollyanna' phenomenon.[50] That is, because the clinical and radiological diagnosis of acute bacterial rhinosinusitis is inaccurate, the measured treatment effect of antibacterials for the entire treatment group is diluted by the cases that do not truly have bacterial infection. The radiograph studies used total opacity, fluid level or a mucosal thickening over 5mm as inclusion criteria, which has a low sensitivity of 0.63, giving a high proportion of false-positive radiographs. Thus, the treatment trial using a more specific diagnostic standard, a positive CT scan,[8] showed a significant benefit for antibacterials while the trials using the less specific diagnostic standards, clinical[10] and plain radiograph diagnosis,[9] did not. Another possible explanation for the differences in results between these studies could be that the studies by Van Buchem et al.[9] and Stalman et al.[10] included topical vasoconstrictors and steam inhalations as a required part of treatment, while Lindbaek et al.[8] allowed but did not require this therapy. However, the authors feel this explanation is unlikely, since patients in the latter trial were provided with decongestants and most patients appeared to have used them.

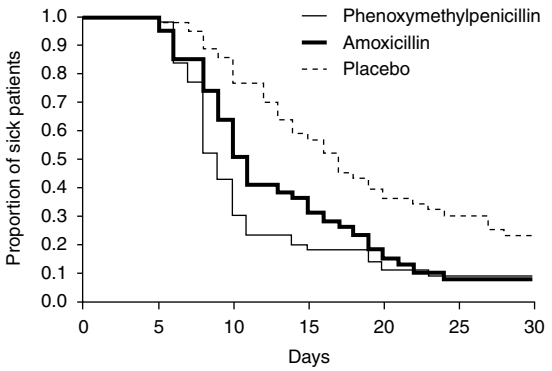

Fig. 3. Kaplan-Meier plot of proportion of 127 patients in three treatment groups with computed tomography-confirmed sinusitis by days from start of antibacterial treatment (reproduced from Lindbaek et al.,[8] with permission from the BMJ Publishing Group).

A recent study from Denmark, which was not included in the meta-analyses, included 133 patients from general practice with clinically suspected acute sinusitis based on maxillary pain and an elevated ESR and/or CRP.[51] The patients were given phenoxymethylpenicillin or placebo. Hansen et al.[51] found that, after 7 days, 75% of phenoxymethylpenicillin recipients were cured (defined as an absence of pain in the sinuses) versus 51% in the placebo group, which was significantly higher, and that sinus pain was significantly more improved in the treatment group. The patients with most pain had the greatest benefit from antibacterial treatment. In their previous study, Hansen et al.[25] demonstrated that elevated ESR/CRP is a good predictor for bacterial sinusitis with purulent secretion on puncture.

Taking into consideration the 40–50% prevalence of purulent rhinosinusitis in patients diagnosed by signs and symptoms, and the modest effectiveness of antibacterial treatment, a cost-effective-

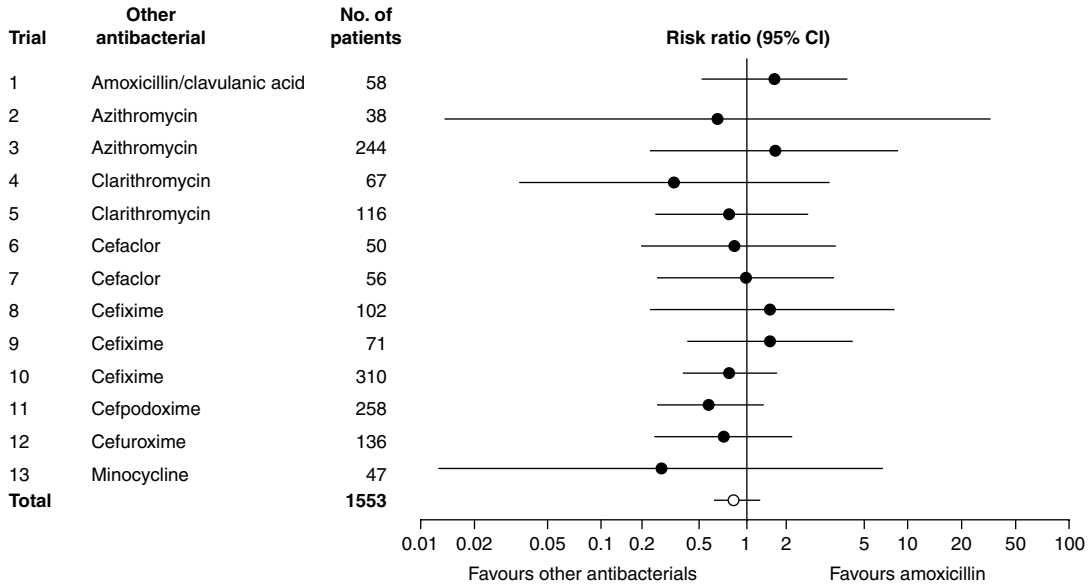

Fig. 4. Random effects model of risk ratios (95% CIs) of clinical failure associated with treatment of acute sinusitis with more expensive antibacterials compared with amoxicillin (reproduced from de Ferranti et al.,[48] with permission from the BMJ Publishing Group). **1** = Wald et al.[49]; **2** = Casiano[54]; **3** = Felstead et al.[55]; **4** = Karma et al.[56]; **5** = Calhoun and Hokanson[57]; **6** = Wald et al.[58] (study conducted in children); **7** = Huck et al.[59]; **8** = Edelstein et al.[60]; **9** = Matthews et al.[61]; **10** = Rimmer et al.[62]; **11** = Von Sydow et al.[63]; **12** = Brodie et al.[64]; **13** = Matucci et al.[65]

ness model sponsored by the Agency for Healthcare Research and Quality favoured antibacterial treatment for patients with moderate to severe symptoms and symptomatic treatment for those with mild symptoms.[52] In a cost-effectiveness analysis de Bock et al.[53] found that postponing antibacterials for 1 week in patients presenting with a clinical diagnosis of acute sinusitis is the most cost-effective strategy.

Three recent meta-analyses have concluded that newer and broad-spectrum antibacterials are not significantly more effective than narrow-spectrum agents[29,46,47] (figure 4). However, because of the rapid increase in antibacterial resistance of *S. pneumoniae* and *H. influenzae*, treatment must take into account current recommendations for treating infections caused by these organisms.

Most clinical trials of new antibacterials compare the drugs with other newer drugs rather than with the inexpensive older drugs that were examined.[46] There is societal value in decreasing the unnecessary use of newer, broad-spectrum antibacterials to reduce the cost of care and, possibly, the rate of development of resistant microorganisms in the community.[46]

Some studies have compared short- and long-course treatment for acute sinusitis. In one of them, Williams et al.[66] found no significant differences between 3 and 10 days of treatment. However, a weakness in this study was the use of plain radiographic findings as inclusion criteria and, again, there is the possibility of the 'Pollyanna' phenomenon.[66]

Another important issue is the adverse effects of the antibacterials. In all of the placebo-controlled trials the adverse effects were significantly and considerably more frequent in the antibacterial recipients than the placebo recipients.[8-10] In a situation where there is a modest effect of antibacterial treatment, this may be an argument for a shared decision with the patient concerning the start of antibacterial treatment. It is likely that some patients would rather tolerate a few extra days of sinus complaints than

take antibacterials and have a substantial chance of getting unpleasant adverse effects.

Questions have arisen regarding whether corticsteroid treatment of sinusitis would be rational. In three studies,[41,67,68] topical corticosteroids were given in addition to antibacterial treatment.[33] Inclusion of corticosteroids was found to be useful in only one of these studies.[41] A recent study in patients with recurrent sinusitis demonstrated that patients who received fluticasone propionate in addition to antibacterials had a higher rate of clinical success than patients receiving placebo and antibacterials.[69]

4.3 Sinus Puncture

The indication for sinus puncture and irrigation of the sinuses is sinus empyema, when there is no natural drainage from the affected sinus and antibacterial treatment has produced no clinical progress. In this situation there is danger of serious complications. In these patients, antibacterials possibly have low penetration and the mucosal concentration may not reach bactericidal levels, even with high dosages. Thus, puncture should be performed as often as every second day until improvement.[22] Some specially trained GPs perform puncture themselves, but most of these patients should be referred to ENT specialists for further treatment and follow up.

However, the need for puncture in the treatment of acute bacterial sinusitis seems to be rare. In two of the studies where the need for puncture was reported, only 1–2% of the patients needed puncture for resolution of symptoms.[1,9] Both of these studies were in patients with confirmed sinusitis.

4.4 Complications

What is the danger of withholding antibacterial treatment for bacterial rhinosinusitis? Serious complications of sinusitis such as meningitis, brain abscess and periorbital cellulitis are rare, and good data regarding the frequency of these events in treated compared with untreated patients are not available.[27] An estimated 1 of 95 000 hospital discharges in the US is for brain abscess, and the proportion of these admissions caused by acute sinusitis is unknown.[27] No serious complications have been reported in sinusitis treatment trials. Nonetheless, some patients with acute bacterial sinusitis present with dramatic symptoms of severe unilateral maxillary pain, swelling and fever. These patients must be treated promptly with an appropriate antibacterial and may require surgical referral for sinus drainage.

Complications of sinusitis can be serious, including brain abscess, orbital cellulitis, subdural empyema and meningitis; however, we found no mention of such complications among more than 2700 patients in 27 trials. Large referral hospitals rarely report such complications.[46] To our knowledge, there are no data to suggest that the use of newer, more expensive antibacterials would reduce the rate of these rare complications. Nevertheless, it should be emphasised that our data apply to patients with uncomplicated, community-acquired, acute sinusitis. Patients with complicated sinusitis and those severely ill with sinusitis or with important underlying diseases might merit initial treatment with drugs other than amoxicillin or a folate inhibitor.[46]

Among the studies on diagnosis and treatment that have been performed in general practice, only one case of a serious complication was reported – a case of meningitis secondary to a bacterial sinusitis.[1] The 60-year-old woman, who initially received oral antibacterial treatment for 3 days, was hospitalised and recovered from her meningitis after intravenous antibacterial therapy without any sequelae.[1] This may indicate that oral antibacterials do not prevent such serious complications.

Another important complication is the development of chronic sinusitis from inadequately treated acute sinusitis. The frequency of this happening is not known. Van Buchem et al.[9] found that after 1 year, 5 of 488 patients with suspected sinusitis had developed chronic complaints. In their population study, Lindbaek et al.[1] found that 5 of 386 patients with acute sinusitis developed chronic complaints. From these two studies one may conclude that 1–2% of patients with acute sinusitis may develop chronic sinusitis.

4.5 Recurrent Sinusitis

Patients with recurrent sinusitis constitute 7–9% of all patients with acute sinusitis.[1,2] These patients could have an underlying physiological or anatomic abnormality. Most common is allergic rhinitis that may respond well to various treatments, and first choice should be topical corticosteroids. Effective treatment for allergic rhinitis decreases mucosal oedema and may give improvement of associated sinusitis because of improved sinus drainage.[12] If allergic rhinitis is not present, other predisposing factors should be considered. Sinusitis can be a manifestation of immune compromise or an underlying anatomic abnormality. Nasal polyps may be present or there may be abnormalities in the ostiomeatal complex, giving reduced drainage of the sinuses. Patients with more than three episodes of acute sinusitis per year should be evaluated by a specialist for further investigation and possible functional endoscopic sinus surgery.

5. Conclusions

The clinical diagnosis of acute bacterial sinusitis is difficult in primary care practice. A history of purulent rhinorrhoea, purulent secretions in the nasal cavity on examination, tooth pain, worsening of symptoms following initial improvement, lack of effect of decongestants and an elevated ESR are supportive evidence of bacterial infection. Patients with symptoms for <7 days are not as likely to have bacterial infection.

Acute sinusitis is overtreated in primary care practice. First, most cases of acute sinusitis are caused by viral infections and resolve without antibacterial treatment. Secondly, in clinical trials of antibacterial treatment only about half of patients diagnosed with acute bacterial sinusitis by experienced primary care physicians have bacterial infection. Thirdly, antibacterial treatment of acute sinusitis is indicated only in patients with severe symptoms of sinusitis or in patients with moderate symptoms of duration greater than 7 days. Symptomatic treatment is sufficient in patients with mild symptoms.

Further studies are needed to single out clinical features that distinguish acute purulent sinusitis from serous sinusitis. Furthermore, studies are needed to assess which patients with acute purulent sinusitis benefit most from antibacterial treatment.

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