# Is it justified to delay initiation of antibiotic treatment in patients who have had acute sinusitis for less than ten days?

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#### INTRODUCTION

Acute rhinosinusitis, often referred to as sinusitis, is a condition where inflammation of the mucosal passage and paranasal sinuses lasts less than 12 weeks. The estimated prevalence of acute sinusitis is 6-15%. Historically, patients diagnosed with acute sinusitis were prescribed antibiotics, but at present the National Institute for Health and Care Excellence (NICE) do not recommend antibiotic prescriptions for patients who have symptoms for less than ten days. Should the patient's symptoms persist beyond ten days, then NICE recommends considering antibiotics. This critical review will explore current evidence to determine whether it is justified to delay initiation of antibiotic treatment in patients who have had acute sinusitis for less than ten days.

#### **BACKGROUND**

Acute sinusitis is more common in adults because sinuses are absent at birth. As children's teeth erupt and they go through puberty their nasal mucosa rapidly expands and sinuses develop. Patients with sinusitis present with sudden onset nasal obstruction; purulent discharge; facial pain over sinuses and change in a sense of smell. To be diagnosed with acute sinusitis, patients must have two or more of these clinical features. Other associated signs and symptoms seen in sinusitis include headaches, halitosis, dental pain and aural fullness.<sup>1</sup>

Following a clinical diagnosis of acute sinusitis, further investigation is not routinely warranted. A computed tomography (CT) scan is only required when there are complications – but this is rare. Complications include orbital cellulitis, preseptal cellulitis, brain abscess, osteomyelitis, meningitis and Pott's puffy tumour. Patients with symptoms for less than ten days are symptomatically managed. Analgesia and warm face packs are recommended to relieve pain, nasal decongestants or nasal irrigation with warm saline for nasal obstruction and adequate fluid intake and rest recommended. Only when symptoms worsen, persist beyond this or patients are at high risk (immunosuppressed) will antibiotics be considered.

NICE guidelines<sup>3</sup> can be understood according to the course and nature of acute sinusitis infections. Acute viral sinusitis is more common than acute bacterial sinusitis.<sup>2</sup> Patients experience symptoms for less than ten days, but the viral infection is usually self-resolving. When symptoms persist beyond ten days, bacterial aetiology should be suspected as acute bacterial sinusitis tends to follow a viral infection.<sup>2</sup> Therefore, antibiotic use should be beneficial when symptoms persist beyond ten days – as a bacterial infection is more likely.

#### CURRENT GUIDELINES

NICE guidelines on antimicrobial prescribing for acute sinusitis<sup>3</sup>

- 1.1.1 Patients who have had symptoms of acute sinusitis for less than ten days should not initially be offered antibiotics.
- 1.1.2 Patients should be advised about the duration of acute sinusitis; why antibiotics are not needed; the best way to manage symptoms and when they should seek medical help.
- 1.1.8 Only when patients are systemically unwell; present with features of a serious illness or have a high risk of complications is immediate antibiotic prescription required.

#### **AIMS**

This critical review evaluated whether it is justified to delay initiation of antibiotic treatment in patients with acute sinusitis for less than ten days, by taking three factors into consideration. First, the efficacy of antibiotic use in acute sinusitis was reviewed; secondly, evidence on the associated risks of antibiotic use in acute sinusitis was reviewed and finally, the financial implications of antibiotic use was compared to symptomatic treatment.

#### DISCUSSION

## Efficacy of antibiotic treatment of acute sinusitis compared to symptomatic treatment

Studies<sup>4,5,6</sup> measured the efficacy of antibiotic use in patients with acute sinusitis according to the rate of clinical failure, this was described as failure of symptoms to resolve or patients requiring an additional course of antibiotics. A systematic review of 15 randomised control trials (RCTS) with a total of 3057 participants, compared the effect of antibiotic use to a placebo or no treatment, in people with rhinosinusitis like symptoms or confirmed sinusitis.4 The review found antibiotic use decreased the occurrence of clinical failure.4 In the antibiotic group, five fewer participants per 100 experienced clinical failure, compared to the placebo group which received nasal spray.4 Blin et al's prospective cohort study also found that antibiotic treatment reduced the risk of treatment failure by 3.3. fold.<sup>5</sup> 5460 patients with acute sinusitis were followed up and evaluated at ten days and two months. Treatment failure was determined by whether patients required an additional course of antibiotics; 96.2% of the antibiotic group did not experience treatment failure, compared to 88.7% of the placebo group. 5 In addition to this, Benninger et al also found that use of antibiotics to treat acute bacterial rhinosinusitis reduced the incidence of clinical failure by 50%.6

## Is it justified to delay initiation of antibiotic treatment in patients who have had acute sinusitis for less than ten days? Moyosore Olukoga

Studies also determined the efficacy of antibiotic use in patients with acute sinusitis by evaluating how quickly treatment reduced the duration of symptoms. <sup>4,5,9</sup> Lemiengre *et al's* 2018<sup>4</sup> systematic review found that antibiotics shortened cure time in an additional 5-11 people per 100. Blin *et al's* 2010<sup>5</sup> prospective cohort study required patients to keep a diary during the first ten days to record their symptoms, need for consultation or further investigation. From these diary entries, it was found that the antibiotic group experienced symptoms for a shorter duration.<sup>5</sup> Another study found that patients using antibiotics reported a better quality of life earlier in the study than those using a placebo.<sup>9</sup>

study than those using a placebo. A few studies 1,8,9 did not find a difference between the efficacy of antibiotics and symptomatic treatment. A review of 31 RCTs found that a placebo was just as effective as antibiotics were. Stalmen et al found there wasn't a significant difference in patients treated with doxycycline or patients given a placebo. In the doxycycline group, over 50% of patients experienced resolution of facial pain by day four and resumption of normal daily activities by day five. The same was observed in the placebo group on day five and day six respectively. Furthermore, even though patients reported improved quality of life earlier in the Garbutt et al study; the number of days missed from work was the same in both the antibiotic and placebo group.

Although studies have highlighted the effectiveness of antibiotic treatment, the effect size measured is often small as demonstrated by Lindbaek's review. <sup>10</sup> In addition to this, the number needed to treat (NNT) for an additional beneficial patient outcome is relatively large. The NNT measured in some of the studies ranged from 13 to 19. <sup>4,5,11</sup> Is it worth treating these many patients with antibiotics to benefit one patient?

Some studies<sup>5,6,8,10</sup> selected patients based on clinical features associated with bacterial sinusitis. These included a history of nasal surgery; purulent unilateral or bilateral rhinorrhoea; pus observed in the nasal cavity on examination; poor oro-dental conditions and raised CRP. However, some of these participants also underwent investigation with bacterial cultures and sinus imaging. This meant patients were more likely to have a bacterial infection and therefore this may have contributed to the observed efficacy measured with antibiotic use. In clinical practice, these investigations are not routinely used, and these clinical features can also present in acute viral sinusitis. This casts uncertainty on the use of antibiotics to treat acute sinusitis presenting in everyday clinical practice. Further research into clinical features which clearly distinguish viral from bacterial sinusitis, may help clinicians to know when to commence antibiotic treatment for sinusitis.

Overall, antibiotics are superior to symptomatic treatment, but a few studies illustrate that antibiotic use makes no difference. A similar conclusion was reached by Burgstaller *et al*,<sup>12</sup> following a systematic review of six RCTs. Some studies found that at day three of treatment, patients in the antibiotic group had a greater rate of improvement, compared to those in the placebo group. Whereas other studies found that antibiotic use had no positive effect.<sup>12</sup>

#### Risk of antibiotic use in acute sinusitis

On an individual level, antibiotic use is associated with adverse effects such as skin rashes, diarrhoea, abdominal pain, nausea and vomiting. Lemiengre et al,4 found an increased number of side effects experienced in the antibiotic group compared to the placebo, this may override the efficacy of antibiotics demonstrated in the shorter cure time of acute sinusitis. Stalman<sup>8</sup> reported that 17% of participants in the doxycycline treatment group experienced adverse effects. Furthermore, in this study some participants discontinued their medication due to side effects; twelve patients in the doxycycline group discontinued medication and eight patients in the placebo group.8 One study demonstrated that placebos were as efficacious as antibiotics but also had a lower side effect profile compared to the antibiotics which recorded a 40% incidence of minor side effects.7

The adverse effects patients experienced when being treated with antibiotics for acute sinusitis, influences whether to use antibiotics over supportive measures. Some patients may be unhappy to experience this in order to relieve their acute sinusitis; whilst other patients may just want their symptoms resolved as quickly as possible. As sinusitis is typically a self-limiting disorder and symptomatic management is also effective with the additional benefit of a low side effect profile – is it right to expose patients to antibiotics given the adverse effects?

At a population and international level, unnecessary antibiotic use contributes to antibiotic resistance developing. Huang and Hung<sup>13</sup> collected samples of discharge from the middle meatus of patients diagnosed with acute sinusitis for culture and antibiotic sensitivity. The incidence of MRSA isolates was 2.7%.<sup>13</sup> In 2004, Huang<sup>14</sup> also analysed bacterial resistance in patients with acute rhinosinusitis over three years. Samples collected from patients found 81.4% of S. pneumoniae were resistant to penicillin; 69.2% of H. influenzae resistant to ampicillin and 88.9% of M. catarrhalis resistant to ampicillin.<sup>14</sup> Brook *et al*<sup>15</sup> conducted a microbiological evaluation on the sinus secretions of patients with acute maxillary sinusitis. They discovered an increase in the frequency of MRSA isolated from these patients. From 2001 to 2003, 30% of S. aureus isolates were MRSA, this increased to 69% between 2004-2006.<sup>15</sup>

Antibiotic resistance is a worldwide issue which requires good antimicrobial stewardship to tackle it. Existing evidence highlights there is an increase in resistance which can be directly attributed to antibiotic use in acute sinusitis. However, further research is required, especially in the UK. Acute sinusitis with a viral aetiology tends to be more common and is difficult to distinguish from a bacterial infection. If antibiotics are routinely prescribed in acute sinusitis, there is a risk that a proportion of patients will unnecessarily be exposed to antibiotics and this can contribute to the development of antibiotic resistance.

The benefits of antibiotic use need to be weighed against side effects and antibiotic resistance. Considering that acute sinusitis is a self-resolving illness without antibiotics and complications are rare, it is difficult to justify antibiotic use especially given the associated risks.

## Is it justified to delay initiation of antibiotic treatment in patients who have had acute sinusitis for less than ten days? Moyosore Olukoga

#### Financial cost of antibiotic use

Resources within the NHS are limited therefore recommended treatments should be cost-effective. de Bock *et al* reviewed the cost of different treatment options used to manage acute sinusitis in healthy adults. There was a "wait and see" treatment option, where patients use analgesia to control symptoms and returned in one week if there was no improvement in symptoms. There was a selective prescribing option; patients were prescribed antibiotics if they had a maxillary toothache, transillumination, purulent discharge or were considered to require antibiotics based on the clinician's overall clinical impression. Some patients were immediately prescribed antibiotics to manage acute sinusitis. The cost per clinically cured patient was measured for each treatment approach as illustrated in Table 1.

**Table 1:** Summarising the observed cure rate for each treatment approach and cost for each treatment approach. At the time 3 Dutch Florin (DFL) was equivalent to 1 Great British Pound.<sup>16</sup>

	Cure rate after one week	Cost per cured patient in Dutch Florin	Cost in GBP
Wait and see	91.5%	44.15	14.72
Selective prescription of antibiotics	93.2%	53.12	17.70
Immediate prescription of antibiotics	94.5%	71.6	23.87

Immediate antibiotic use was associated with a higher cure rate than the wait and see approach, however both approaches achieved a cure rate of over 90%. <sup>16</sup> Furthermore, the wait and see approach had the lowest cost per cured patient, financially supporting existing guidelines to initially withhold antibiotic treatment in acute sinusitis. <sup>16</sup>

However, a meta-analysis found selective antibiotic to be the most cost-effective treatment.<sup>6</sup> To be prescribed antibiotics, patients had to have at least three of the following – unilateral or bilateral purulent rhinorrhoea, localised pain or pus observed in the nasal cavity. The cost per symptom free treatment day for these patients was \$3.76.<sup>6</sup> The cost per symptom free treatment day was \$3.95 with symptomatic treatment and \$5.30 when all patients were treated empirically with antibiotics.<sup>6</sup>

It can be concluded from these studies that symptomatic treatment and selectively treating patients with antibiotics is the most cost-effective approach. However, further studies are required, especially in the United Kingdom.

#### CONCLUSION

This critical review found antibiotics to be an efficacious treatment option for acute sinusitis compared to symptomatic treatment. Evidence demonstrated that antibiotic use relieved symptoms, reduced the occurrence of clinical failure and shortened the duration of sinusitis

symptoms. Given these findings, it would be expected that antibiotics would be used earlier in the management of acute sinusitis. However, the NICE guidelines and other international guidelines recommend symptomatic treatment first, then consider initiating antibiotics should symptoms persist beyond ten days.

Some of the studies reviewed used bacterial cultures and sinus imaging, identifying and including patients who were more likely to have acute bacterial sinusitis and therefore more likely to demonstrate the efficacy of antibiotics. In clinical practice, acute sinusitis is a clinical diagnosis, viral infection tends to be more common and it is challenging to clinically distinguish between acute viral and bacterial sinusitis. Therefore, it can be concluded that antibiotics are effective in acute bacterial sinusitis – as would be expected – rather than acute sinusitis in general.

Antibiotic use in acute sinusitis is associated with adverse effects. The evidence reviewed consistently reported skin rashes, diarrhoea, nausea and vomiting in the antibiotic groups. Furthermore, antibiotic use in acute sinusitis has been associated with emergence and an increase in antibiotic resistance. 13,14 Although further research into acute sinusitis and antibiotic resistance is required, clinicians must practice antimicrobial stewardship to reduce the spread of antibiotic resistance. Finally, the effectiveness of antibiotics cannot be considered in isolation, due to financial constraints and limited resources of the NHS. Overall, the studies demonstrated that empirical antibiotics use in acute sinusitis were not cost effective. This is reinforced by the small effect size seen with antibiotics; symptomatic treatment being more cost-effective and the potential future costs of managing resistant acute sinusitis.

#### Concluding guideline

Antibiotic use has demonstrated greater efficacy than symptomatic measures in the management of acute sinusitis. However, symptomatic measures can also be efficacious; adverse events are experienced with antibiotic use; there is a risk of antibiotic resistance and antibiotics are not as cost-effective as supportive measures.

As the drawbacks of antibiotic use outweigh the benefits of antibiotic use – there should be no change in the existing guideline about when to commence antibiotic treatment in acute sinusitis.

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## Is it justified to delay initiation of antibiotic treatment in patients who have had acute sinusitis for less than ten days? Moyosore Olukoga

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### **Obituary for Mr Richard Yelverton Wilson**

Gavin Wilson, Peter Duffy

Richard Wilson, Consultant Urological Surgeon passed away peacefully at St Mary's Hospice, Ulverston on Monday January 11th 2021.

Dick, as he was affectionately known to colleagues and friends, worked extensively around Cumbria and Lancashire throughout his career with the University Hospitals of Morecambe Bay NHS Trust (UHMBT). He was appointed in 1977 and managed over 30 years of front-line service, ultimately specialising in urological surgery.

Born in mid-December 1943 to a non-medical family, Dick grew up in Kalgoorlie, Western Australia, the son of a gold mining engineer and himself serving as a fitter's mate in the mines, before studying medicine at the University of Western Australia, graduating in 1966. Dick also served as the Doctor for the Australian Special Air Service selection course, completing (to their surprise) their brutal training regime and, as a result being made an Honorary Mess Member of the Australian SAS. Finishing his surgical training in London, Dick met his wife-to-be, Geraldine, at the Withington Hospital, Manchester and shortly settled into life in South Cumbria.

Initially, whilst working as a general surgeon in London, Dick was famous for simultaneously operating on a young couple who had been the victims of a road traffic accident, carrying out a splenectomy on one and a thoracotomy on the other in adjacent theatres. Both survived. In later life Dick switched to urological surgery,

uniting the previously separate Morecambe Bay urology departments. He introduced two-consultant radical cystectomies to Furness General Hospital and the Royal Lancaster Infirmary and was rewarded, shortly before his retirement, with UHMBT being lauded in a regional audit as having the shortest stay, shortest operating time and least blood loss of any of the units in the North-West.

Dick was clearly losing his long battle with cancer over his last 12 months, but managed to visit his beloved Australia in 2019, determined to meet up for one last time with his family and old medical school contemporaries. Cheerful, uncomplaining and outgoing to the end, he passed away peacefully with his family present on the night of the 11th January 2021. Richard is succeeded by his children Fiona, Gavin and Murray, and grandchildren Callum and Luke, Poppy, Scarlett and Noah, Zara and James.

Richard Yelverton Wilson. FRCS. MD. 1943-2021.