C-reactive protein measurement in general practice may lead to lower antibiotic prescribing for sinusitis

Lars Bjerrum, Bente Gahrn-Hansen and Anders P Munck

SUMMARY

Background: *Symptoms of bacterial sinusitis overlap with viral sinusitis, and it is difficult to distinguish between the two conditions based only on a clinical examination. Uncertain diagnosis results in the significant overuse of antibiotics, which is considered to be one of the most important reasons for development of bacterial resistance to antibiotics. A raised C-reactive protein (CRP) level is an indicator of bacterial infection and the CRP rapid test has been shown to be useful for the diagnosis of bacterial sinusitis in general practice.*

Aims: *To examine whether general practitioners (GPs) who use the CRP rapid test in their practice have a lower antibiotic prescribing rate for sinusitis than GPs who do not use the test.*

Design of study: *Observational design.*

Setting: *General practice in Denmark.*

Method: *A group of GPs registered all contacts (*n *= 17 792) with patients who had respiratory tract infections during a 3-week period between 1 November 2001 and 31 January 2002. GPs who used a CRP rapid test were compared with GPs who did not, and the treatment of their patients (*n *= 1444) with suspected sinusitis was compared.*

Results: *A CRP rapid test was used by 77% (*n *= 281) of the GPs. In the group of GPs using a CRP rapid test, the rate of antibiotic prescribing was 59% (95% confidence interval [CI] = 56 to 62) compared with 78% (95% CI = 73 to 82) in the group of GPs who did not use a CRP test. Performing a CRP rapid test was the factor that exerted the greatest influence on whether the patients were prescribed antibiotics, and the level of CRP had a strong influence on the prescribing rate.*

Conclusion: *The CRP rapid test has a substantial influence on the treatment of sinusitis, and implementing the test in general practice may lead to a reduction in antibiotic prescribing to patients with sinusitis.*

Keywords: *antibiotics; C-reactive protein; general practice; sinusitis.*

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Introduction

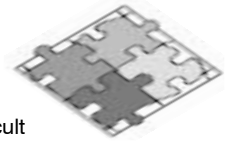
ACUTE sinusitis is an inflammation of the paranasal sinuses lasting for up to 4 weeks, and is caused by either bacterial (purulent sinusitis) or viral (serous sinusitis) infection.[1] Acute sinusitis is a frequently occurring problem in general practice, and it is challenging for the general practitioner (GP) to diagnose. The 'gold standard' to assess the aetiology is a sinus puncture followed by aspiration and bacterial culture. However, this invasive procedure is of limited practical value and it is seldom used in primary care. Other tests, such as plain radiography, A-mode ultrasonography, computed tomography, and magnetic resonance imaging, which are of value in diagnoses, are not available in general practice. The clinical symptoms of purulent and serous sinusitis are often identical, making it difficult to distinguish between the two conditions. If the diagnosis is based on clinical examination alone, the rate of false-positive results is high, and patients are consequently prescribed unnecessary antibiotics.[2]

Markedly raised concentration of C-reactive protein (CRP), an acute phase protein produced in response to circulating cytokines from inflammatory foci, is an indicator of bacterial infection. Increased levels of CRP can be detected 6–12 hours after the onset of a bacterial infection by means of a rapid test. Studies have shown that measurement of CRP is useful for the diagnosis of bacterial sinusitis in general practice.[1,3-5] With regard to the impact of CRP measurement on the prescribing of antibiotics in patients with respiratory tract infections (RTIs), there are, however, conflicting results.[6,7] The aim of this study was to examine whether GPs who use a CRP test have a lower antibiotic prescribing rate for sinusitis compared to GPs who do not use a CRP test.

Method

A group of Danish GPs (*n* = 367) participated in a prospective registration of patients with RTIs during a 3-week period (15 working days) between 1 November 2001 and 31 January 2002. Data were registered according to the Audit Project Odense (APO) method described by Munck *et al*.[8] The APO method for prospective self-registration uses a simple registration chart to record selected issues of medical care (for example, reason for encounter, diagnostic procedures, and treatment), carried out by those personally engaged in the activity concerned. In our study, for each contact the GP recorded the age and sex of the patient, the date and type of contact (surgery consultation or home visit), the suspected focus of infection, the assessment of the microbiological cause and the anticipated cause of infection, and the treatment given.

HOW THIS FITS IN



What do we know?

Symptoms of bacterial sinusitis overlap with viral sinusitis, and it is difficult to distinguish between the two conditions based on a clinical examination. Uncertain diagnosis may result in the overuse of antibiotics and so contribute to the development of bacterial resistance to antibiotics. Raised C-reactive protein (CRP) level is an indicator of bacterial infection, and the CRP rapid test has been shown to be useful for the diagnosis of bacterial sinusitis in general practice.

What does this paper add?

Implementing the CRP rapid test in general practice may lead to a reduction in antibiotic prescribing to patients with sinusitis.

If the GP used a CRP rapid test, the result was recorded in corresponding to the following CRP concentrations: 0–9, 10–25, 26–49, 50–99, and >100 mg/l. Antibiotics were classified according to the anatomical therapeutic chemical classification code defined by the World Health Organisation,[9] and prescriptions were divided into the following groups: narrow-spectrum penicillins (J01CE), broad-spectrum penicillins (J01CA), penicillin plus β-lactamase inhibitor (J01CR), macrolides (J01F), tetracyclines (J01A9), cephalosporins (J01DA) and quinolones (J01M).

For each practice the following characteristics were registered: GP's age and sex, number of years working in practice, type of practice (group or single-handed), number of doctors working together, number of patients listed, access to CRP rapid tests, and self-assessment of workload in practice.

We compared GPs who used CRP rapid tests with GPs who did not, and examined the two groups, focusing on the antibiotic prescribing rate for patients with acute sinusitis, acute tonsillitis, and acute otitis. In Denmark, CRP tests are not used to assess the aetiology of tonsillitis and otitis. Both infections are common RTIs in general practice, and antibiotic prescribing for tonsillitis and otitis were used as CRP-independent indicators for antibiotic prescribing in practice.

Data were analysed by univariate and multivariate analyses. There was no cluster effect by practice as only one GP participated from each practice. The effect of possible confounders related to characteristics of patients, GPs, and practices were considered by logistic regression. Confidence intervals (CIs) were calculated at the 95% level, and were adjusted for the clustering effect caused by groups of patients listed with the same practice. Data were analysed by the statistical program STATA, version 8.0.

Results

Over 3 weeks, 17 792 patients suffering from upper respiratory infections were registered, and for 1444 (8%) the suspected infection foci were the paranasal sinuses. A CRP rapid test was performed by 77% (n = 281) of the GPs. The antibiotic prescribing rate for patients with acute sinusitis in the group of GPs who used rapid CRP testing was 59% (95% CI = 56 to 62) compared with 78% (95% CI = 73 to 82) in the group of GPs who did not use CRP rapid testing (Table 1).

Table 1. Comparison between practices that use the C-reactive protein rapid test and practices that do not.

	Practices using CRP rapid tests (n = 281)	Practices not using CRP rapid tests (n = 86)
Antibiotic prescribing rate for upper RTIs (% [95% CI])		
Acute sinusitis	59 (56 to 62)	78 (73 to 82)
Acute tonsillitis	42 (40 to 44)	46 (42 to 50)
Acute otitis	48 (45 to 50)	48 (43 to 53)
RTI patient characteristics		
Median (IQR) age of patients with RTIs in years	26 (4–47)	27 (4–48)
Median (IQR) age of patients with sinusitis in years	40 (31–53)	41 (31–54)
Percentage (95% CI) of female patients with RTIs	56 (55 to 57)	59 (57 to 60)
Percentage (95% CI) of female patients with sinusitis	68 (65 to 71)	72 (67 to 76)
Median (IQR) of patients with RTIs per GP	47 (34–58)	47 (35–70)
Practice characteristics		
Percentage (95% CI) of GPs in group practices	64 (58 to 70)	57 (48 to 68)
Median (IQR) of patients listed per practice	2150 (1600–3900)	1875 (1610–3050)
Median (IQR) age of GPs (years)	49 (45–54)	52 (46–56)
Percentage (95% CI) of female GPs	36 (25 to 47)	38 (32 to 45)
Percentage (95% CI) of GPs with high workload[a]	50 (44 to 56)	55 (44 to 66)

[a]Self-assessed. CRP = C-reactive protein; IQR = interquartile range; RTI = respiratory tract infection.

Table 2. Results of logistic regression relating access to CRP and practice characteristics to prescription of antibiotics.

Characteristic	Odds ratio	95% CI
Access to CRP testing (yes/no)	0.43	0.33 to 0.58
Type of practice (single-handed/group)	1·41	1.12 to 1.77

CRP = C-reactive protein.

The antibiotic prescribing rate for patients with tonsillitis and otitis did not differ significantly between the two groups of GPs. There were no significant differences in age and sex between patients in the two groups and the number of contacts per practice was almost the same. GPs who used a CRP rapid test were more frequently organised in group practices compared with GPs who did not use a test.

A logistic regression adjusted for patient sex, age, number of listed patients and workload in practice showed that the chance of being treated with antibiotics for sinusitis was significantly lower (odds ratio [OR] = 0.43), if consulting a

GP using a CRP rapid test compared with a GP who did not use a test (Table 2). Independent of using a CRP rapid test, we found that GPs in single-handed practices treated more patients with antibiotics compared with GPs in group practices (OR = 1.41). Performing a CRP rapid test was the factor exerting the greatest influence on whether the patients were prescribed antibiotics, and the value of CRP had a strong influence on the rate of prescribing (Figure 1). In both groups of practices the preferred antibiotic drug for the treatment of sinusitis was penicillin V, followed by macrolides and broad-spectrum penicillin.

Discussion

An important reason for performing the CRP rapid test is to avoid prescribing antibiotics to patients with non-bacterial sinusitis. We found that twice as many patients with sinusitis avoided antibiotic treatment when consulting a GP who used the CRP rapid test compared with a GP who did not use the CRP rapid test. The two groups of practices were similar concerning the GPs' age and sex, and the characteristics of the patients seen. However, GPs who used the CRP rapid test were more often organised into group practices.

The CRP rapid test was the factor that exerted the greatest influence on whether a patient with acute sinusitis was prescribed antibiotics. In practices using it, the result of the test had a strong influence on the rate of prescribing. About half of patients tested had a CRP level <10 mg/l and less than one-quarter of these were treated with antibiotics. In contrast, more than 80% of patients with CRP >25 mg/l were treated with antibiotics. In accordance with Scandinavian convention, penicillin V was the preferred antibiotic for the majority of patients treated, and there was no difference in the pattern of antibiotics prescribed in the two groups. It has been documented that penicillin V is effective in the treatment of patients with maxillary sinusitis, but only patients with pronounced pain benefit from the treatment.[10] Newer, broad-spectrum antibiotics are no better at relieving symptoms or improving cure rates than 'first-line' agents, such as penicillin V.[11]

Some limitations must be considered before a conclusion can be made. First, practices using CRP measurement may *a priori* have had a lower prescription rate of antibiotics, and the difference found might be due to different attitudes to antibiotic prescribing for RTI, irrespective of the access to CRP tests. To explore this question we examined the two groups focusing on antibiotic prescribing rates for tonsillitis and otitis; no significant difference was found. Thus, it is not very likely that the difference in antibiotic prescribing for patients with sinusitis was due to different attitudes concerning antibiotic prescribing. Second, the diagnostic procedure and the decision to prescribe are intricately linked in general practice and the GP may have decided whether or not to prescribe an antibiotic at the same time, or even before, he or she classified the patient to a specific diagnosis. After having taken the decision to prescribe, the GP may then have adjusted the diagnosis to fit the decision about treatment.[12,13] The diagnosis of bacterial sinusitis may, therefore, have been used in order to justify a prescription for antibiotics. The lack of clinical criteria for sinusitis and the reliance on poor predictors of bacterial infection may have

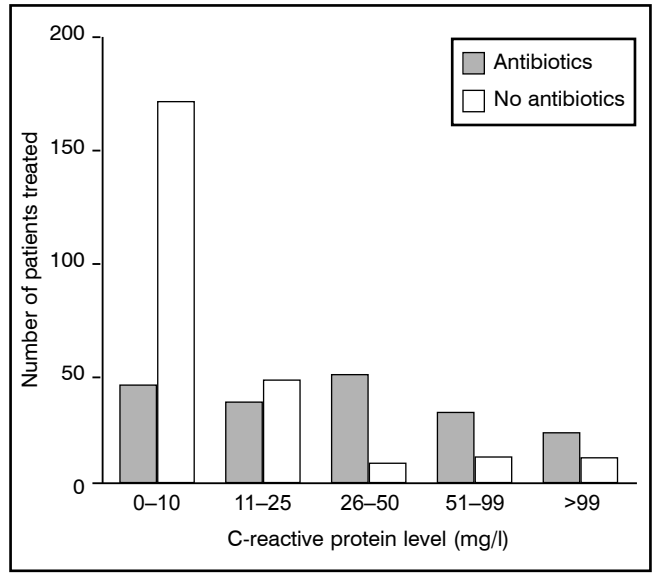


Figure 1. Relation between level of C-reactive protein, number of patients treated with sinusitis and antibiotic treatment.

strengthened this misclassification bias among patients from the group of doctors not performing CRP rapid tests. However, the fact that all respiratory tract infections had to be registered gave no special attention to sinusitis.

Audit registration has been performed in Denmark for many years and the majority of Danish GPs have been involved in audit registration at least once. Our sample of GPs was relative large (n = 367) comprising more than 10% of all Danish GPs. The GPs included in our study participated on a voluntary basis, and their prescribing habits may not represent the average for Danish GPs. Studies have shown that GPs participating in audits may be more interested in practice research and quality development than GPs in general. Furthermore, they are willing to use a substantial part of their working hours on registration without getting any payment.

In terms of reliability of the APO method, experience from other audit projects has shown that prescription data based on the APO method are in good agreement with prescription data obtained from other data sources.[14,15] There is no reason to suspect that a potential selection bias concerning participation in audit should have a different influence on the two groups of practices. The two groups were compared and adjusted for a number of possible confounders related to practice and patient population. There may, however, be confounders not accounted for in our study.

In a study focusing on patients with symptoms of sinusitis, Hansen *et al* found that a raised CRP level or sedimentation rate in combination with a pain score was useful to identify patients who benefited from treatment.[10] However, Diederichsen *et al* found that the CRP rapid test had no impact on the use of antibiotics in general practice.[7] Their study included all patients with RTI, and a possible influence of the CRP rapid test on the subgroup of patients with sinusitis may have been overlooked because the number of patients was very small. Dahler-Eriksen examined the effect of implementation of a near-patient CRP test in general practice and found no major changes in GPs' antibiotic prescribing

rate.[16] Similarly, Melbye found that access to the CRP rapid test had no significant effect on antibiotic prescription to patients with lower respiratory infections in general practice.[17] Unmasking a potential effect of the CRP rapid test on the overall use of antibiotics depends on the setting and the type of infection examined. In the studies mentioned above there may have been an effect of the CRP rapid test on the individual use of antibiotics, but the overall use of antibiotics could be unaffected because of a decrease in use of antibiotics in patients with low CRP levels and an increase in antibiotic use in patients with high CRP levels.

This study indicates that implementing the CRP rapid test in general practice may lead to a reduction in antibiotic prescribing for patients with sinusitis. However, based on this observational design we cannot conclude that the use of CRP tests was the only reason for lower prescribing. Other factors may be involved, and the association found may not be based on a causal relationship. Further studies are needed to investigate patient outcomes due to the reduction in antibiotic prescribing and to analyse the cost-effectiveness of implementing CRP rapid tests for sinusitis in general practice.

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