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What is This?
No Evidence for Distinguishing Bacterial from Viral Acute Rhinosinusitis Using Symptom Duration and Purulent Rhinorrhea: A Systematic Review of the Evidence Base

Medard F. M. van den Broek, MD1,2*, Corien Gudden, MD1,2*, Wouter P. Kluijfhout, MD1,2*, Manon C. Stam-Slob, MD1,2*, Mark C. J. Aarts, MD, PhD1, Nina M. Kaper, MD1, and Geert J. M. G. van der Heijden, PhD1,2,3

No sponsorships or competing interests have been disclosed for this article.

Abstract

Objective. To evaluate the diagnostic value of symptom duration and purulent rhinorrhea in adults suspected of having acute bacterial rhinosinusitis.

Data Sources. PubMed, EMBASE, and the Cochrane Library.

Review Methods. We performed a comprehensive systematic search on March 28, 2013. We included studies on the diagnostic value of duration of symptoms and purulent rhinorrhea in patients suspected of having acute bacterial rhinosinusitis. We assessed study design of included articles for directness of evidence and risk of bias. We extracted prevalence and positive and negative predictive values.

Results. Of 4173 unique publications, we included 1 study with high directness of evidence and moderate risk of bias. The prior probability of bacterial rhinosinusitis was 0.29 (95% confidence interval [CI], 0.24-0.35); we could not extract posterior probabilities. Odds ratios (95% CI) from univariate analysis were 1.03 (0.78-1.36) for duration of symptoms and 2.69 (1.39-5.18) for colored discharge on the floor of the nasal cavity.

Conclusion and Recommendation. We included 1 study with moderate risk of bias, reporting data in such a manner that we could not assess the value of symptom duration and purulent rhinorrhea in adults suspected of having acute bacterial rhinosinusitis. Recommendations to distinguish between a viral and a bacterial source based on purulent rhinorrhea are not supported by evidence, and the decision to prescribe antibiotic treatment should not depend on its presence. Based on judgment driven by theory and subsidiary evidence of a greater likelihood of bacterial rhinosinusitis after 10 days, antibiotic therapy may seem a reasonable empirical option.

Keywords

acute rhinosinusitis, acute viral rhinosinusitis, acute bacterial rhinosinusitis, diagnosis, purulent rhinorrhea, nasal discharge, symptom duration, evidence-based medicine

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Clinical Scenario

A 58-year-old woman visits your ear, nose, and throat (ENT) outpatient clinic with complaints of purulent rhinorrhea, nasal obstruction, loss of smell, and facial pressure for 2 weeks. On physical examination, you find right maxillary sinus tenderness and purulent rhinorrhea. You wonder whether the duration of her symptoms and the presence of purulent rhinorrhea indicate that the origin of her acute episode of rhinosinusitis is bacterial. If so, these symptoms could help you to accurately prescribe antibiotics to this patient.

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Background

Acute rhinosinusitis (ARS) is defined as symptomatic inflammation of the sinuses and nasal cavity with a symptom duration of 12 weeks or less. The incidence of ARS is high, and it is estimated to occur 2 to 5 times per year in an average adult.¹ The diagnosis is responsible for major direct health care costs and has a huge socioeconomic impact by decreased productivity and quality of life.²,³ Viral rhinosinusitis can promote growth of bacterial pathogens by obstructing sinus drainage. About 0.5% to 2.0% of viral infections are complicated by acute bacterial rhinosinusitis (ABRS).⁴ Accurate differentiation between a viral and bacterial source of ARS can help to avoid unnecessary prescription of antibiotics. The current reference test to distinguish between bacterial and viral rhinosinusitis is a culture from either sinus puncture or antral aspirate obtained by nasal endoscopy.³ However, this is an invasive diagnostic test with a waiting time for culture results, so feasibility is low in daily practice. Current clinical practice guidelines recommend that the presence of a bacterial infection is more likely with a duration of symptoms of 10 days.¹,³,⁵,⁶ Purulent nasal discharge is one of the cardinal symptoms of ABRS, although alone it cannot differentiate between a viral or a bacterial pathogen.³

Searching for Evidence

We evaluated the evidence base on the diagnostic value of symptom duration (>10 days) and purulent rhinorrhea at physical examination in adults suspected of having ABRS.

Retrieving Studies

Assisted by our clinical librarian, we conducted a comprehensive search in PubMed, EMBASE, and the Cochrane library on March 28, 2013. The full search syntax with combined relevant search terms and synonyms is displayed in Appendix 1 (available at otojournal.org). Two authors (W.P.K. and M.C.S.-S.) independently screened for title and abstract, selecting studies that assessed the aforementioned symptoms in patients with ARS. For this they used predefined selection criteria (Figure 1). They removed duplicate publications and excluded studies concerning patients with aberrant anatomy, studies in immunocompromised patients, animal or laboratory studies, nondiagnostic studies, systematic reviews, and case reports. For final selection, 4 authors (M.F.M.B., C.G., W.P.K., and M.C.S.-S.) independently screened full texts of eligible titles in depth and with more detail. They completed article retrieval by cross-reference checking in Scopus and Web of Science for selected articles, while citations of retrieved reviews, meta-analyses, and guidelines on rhinosinusitis were screened for omitted studies. A similar procedure was followed to check for eligibility of articles that were thereby retrieved. Any initial disagreements on eligibility and selection of articles were resolved by discussion, and their inclusion is based on a full consensus.

Assessing Studies

On the basis of predefined criteria, 4 independent reviewers (M.F.M.B., C.G., W.P.K., and M.C.S.-S.) assessed the design of studies reported in the included articles on directness of evidence (DoE) and risk of bias (RoB). Disagreements were solved by discussion. When item information for the study assessment was not reported in the study, it was labeled as insufficient. When an item was reported, we judged it as either satisfied or not satisfied. Assessment of the DoE involved evaluation of study design characteristics for appropriateness of (1) patients (ie, adults suspected of having ABRS), (2) index test(s) (ie, duration of symptoms or purulent rhinorrhea at physical examination), and (3) outcome (ie, bacterial rhinosinusitis confirmed by culture). Studies were classified as high DoE if they satisfied all aspects of our 3-part question, moderate DoE if they satisfied 2, and or low DoE if they satisfied only 1.

Assessment of the RoB involved evaluation of the study design characteristics for (1) selection bias (ie, inclusion of an inception cohort), (2) the use of an adequate reference standard, (3) completeness of reported data, (4) information bias (ie, mutual blinding of the assessment of index and reference test(s), and standardization of (5) index test(s) and (6) outcome (reference test). Studies were classified as low RoB if they satisfied criteria 1 and 2, plus all other study design features, and moderate RoB if they satisfied criteria 1 and 2 but failed on 1 or 2 of the other 4 features; the remaining was classified as high RoB. We aimed to include studies for data extraction with a high and moderate DoE and low and moderate RoB.
Extraction and Analysis of Study Data
For the included articles, 2 authors (C.G. and M.F.M.B.) independently extracted data. We aimed to extract and recalculate the reported true and false positive and negative results for the index test(s). From this, we (re)calculated the prior probability (or prevalence) and the predictive values for a positive (or PPV) and a negative (or NPV) index test, with accompanying 95% confidence intervals (CIs). By comparing prior probabilities with the PPVs and NPVs for duration of symptoms and purulent rhinorrhea, we evaluated whether these clinical signs were of added value for ruling in or out a bacterial source of ARS. We excluded studies from our analysis if there were no such data reported, while we present the findings as originally reported if the necessary data could not be (re)calculated.

Results
Retrieving Studies
Our initial search yielded 4871 records. After removing duplicates, 4173 unique publications remained for title and abstract screening (Figure 1). Of these, 53 were identified as potentially eligible for study assessment during screening of title and abstract, and their full texts were retrieved. On the basis of full-text evaluation, we included 6 articles for study assessment.7-12 Cross-reference checking revealed 1 eligible article that was not listed in the searched databases or in the additional searched databases (CINAHL and Clinical Evidence).13

Assessing Studies
The assessment of studies showed that 3 studies7,8,13 had a high DoE; the remaining articles with moderate or low DoE were excluded9-12 (Table 1). We excluded 2 articles8,13 due to a high risk of bias; therefore, 1 article remained for data extraction and analysis.7

Table 1. Study Assessment.

<table>
<thead>
<tr>
<th>Study Characteristics</th>
<th>Adequate Reference</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inception Cohort</td>
<td>Reference Test</td>
</tr>
<tr>
<td></td>
<td>Test 1</td>
<td>Test 2</td>
</tr>
<tr>
<td>Lacroix et al, 20027</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hansen et al, 20098</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>van Buchem et al, 199513</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hansen et al, 19959</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Young et al, 200310</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Berg et al, 198811</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Berg et al, 198812</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Directness of Evidence
Patients Included patients >18 years with acute rhinosinusitis
Index test 1 Duration of symptoms >10 days
Index test 2 Purulent rhinorrhea at physical examination
Outcome Confirmation of the presence of a bacterial source for rhinosinusitis

Risk of Bias
Inception cohort Included patients suspected of having bacterial rhinosinusitis. Outcome is not known at time of inclusion.

Adequate reference standard Culture from either sinus puncture or endoscopically obtained antral aspirate
Complete data Adequate reporting of all included patients
Blinding for reference test The assessors of cultures were blinded for clinical symptoms
Index test standardization Protocolled, uniform assessment/measurement
Reference test standardization Protocolled, uniform assessment/measurement

Abbreviations: DoE, directness of evidence; H, high; L, low; M, moderate; RoB, risk of bias; ✓, satisfied; ○, not satisfied; ☐, insufficient information/unclear.
probability of 0.29). The true and false positive and negative results for the index tests, however, could not be extracted. The first author was contacted to obtain the necessary information but could not provide the requested data. Colored discharge on the floor of the nasal cavity was significantly associated (odds ratio [OR], 2.69; 95% CI, 1.39-5.18), while duration of symptoms (>10 days) was not significantly associated with ABRS (OR, 1.03; 95% CI, 0.78-1.36). Lacroix et al did not include colored discharge in their multivariate analysis (Table 2).

Comment

With our comprehensive search on the diagnostic value of duration of symptoms and purulent rhinorrhea in adults suspected of having ABRS, we identified 1 study with a high DoE and a moderate RoB.7 The study reported odds ratios, indicating an association between colored discharge on the floor of the nasal cavity found at physical examination and ABRS, while they did not find an association between duration of symptoms and ABRS. Some aspects need further consideration.

First, data on the value of duration of symptoms and purulent rhinorrhea in either ruling in or out ABRS were not provided and, therefore, this study fails to answer our research question. Second, despite our broad and comprehensive search, we retrieved 1 omitted publication through cross-reference checking.13 We missed this study because it was not present in the searched databases. However, we believe that, because of extensive cross-reference checking in Scopus and Web of Science for selected articles and citation screening of retrieved reviews, meta-analyses, and guidelines, it is unlikely that we have missed other potentially relevant studies. Third, Lacroix et al7 used a nasopharyngeal aspirate as a reference standard instead of a sinus aspirate, which is considered the optimal reference standard available.3 Fourth, Lacroix et al7 excluded patients receiving antibiotics and patients with an overall impression that antibiotics were required. As a consequence, the study population did not include the clinically ill patient with fever, thereby possibly underestimating the diagnostic value of signs and symptoms. Fifth, in the absence of direct evidence, we have to consider indirect evidence from studies that were not designed to answer our research question. We base our theory on studies that assess the natural course of viral rhinosinusitis and randomized controlled trials on antibiotics in ARS.

Symptoms of viral rhinosinusitis peak at 2 to 3 days and then decrease, although they may persist up to 14 days.14 After 10 days, the probability of a bacterial rhinosinusitis is 60%.15 In children, a symptom duration of 10 days or more, without improvement, is also associated with bacterial rhinosinusitis.16 In adults, a systematic review on antibiotics in acute rhinosinusitis did not show enhanced benefit from treatment for patients with a symptom duration of 6 days or more.17

Randomized controlled trials have shown that antibiotics can shorten duration in ARS.17,18 Many trials use persistent symptoms of approximately 7 days as an inclusion criterion,18 suggesting a higher prevalence of bacterial rhinosinusitis in these patients. On the contrary, trials investigating the effect of antibiotics in upper respiratory tract infections or purulent rhinitis with symptoms less than 10 days show no benefit of antibiotics.19

Based on these subsidiary sources of evidence, one could argue that a prolonged duration of symptoms may be associated with bacterial rhinosinusitis.

Finally, Lacroix et al7 present data from univariate analysis, so we draw individual conclusions for both symptoms, although it should be noticed that this could lead to spurious results. In addition, conclusions in clinical practice are seldom based on one sign or symptom. We therefore advise caution in decision making after separating the 2 symptoms.

Conclusion and Recommendation

We included 1 study with moderate risk of bias, reporting data in such a manner that it was not possible to assess the value of duration of symptoms and purulent rhinorrhea in adults suspected of having ABRS. Recommendations to distinguish between viral and bacterial source based on purulent rhinorrhea are not supported by evidence. Moreover, the decision to prescribe antibiotic treatment should not depend on the presence of purulent rhinorrhea. Based on judgment driven by theory and subsidiary evidence of a greater likelihood of bacterial rhinosinusitis after 10 days, antibiotic therapy may seem a reasonable empirical option.

Translating Evidence into Practice

We informed the patient presenting to our clinic with complaints suggestive of acute bacterial rhinosinusitis that since her symptoms had persisted for 2 weeks, she might benefit

<table>
<thead>
<tr>
<th>Study Characteristics</th>
<th>No. of Patients</th>
<th>Prior Probability (95% CI)</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lacroix et al7</td>
<td>265</td>
<td>0.29 (0.24-0.35)</td>
<td>1.03 (0.78-1.36)</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
<td>2.69 (1.39-5.18)</td>
</tr>
<tr>
<td>Purulent rhinorrhea at physical examinationb</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

*aUnivariate analysis.

*bColored discharge at floor of nasal cavity.
from antibiotics. We therefore prescribed her antibiotics on an empirical basis.

Acknowledgments

We gratefully thank Bianca Kramer, Medical Information Specialist at the Library of the Utrecht University and Clinical Librarian at the University Medical Center Utrecht, for her assistance and advice in searching and retrieval of studies and J. D. van Amstel, E. M. Mominkhof, and C. H. van Werkhoven for their contribution to the pilot version of the study.

Author Contributions

Medard F. M. van den Broek, Corien Gudden, Wouter P. Kluijfhout, Manon C. Stam-Slob, construction of the search strategy, retrieval of articles, selection of relevant articles, assessment of study quality, extraction of study data, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; Mark C. J. Aarts, formulating clinical question, selection of relevant articles, assessment of study quality, extraction of study data, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; Nina M. Kaper, formulating clinical question, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; Geert J. M. G. van der Heijden, design of study, analysis and interpretation of data, revision of the manuscript, final approval of the version to be published, supervision of study.

Disclosures

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Supplemental Material

Additional supporting information may be found at http://oto.sagepub.com/content/by/supplemental-data

References