

Rapid diagnosis of bacterial sinusitis in patients using a simple test of nasal secretions

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ABSTRACT

Upper respiratory symptoms and sinusitis constitute a major reason for patient visits to their physician. The diagnosis of sinusitis is often made based on history and physical exam, but the accuracy of such diagnosis is questioned. Sinus films or CT scans are expensive. Obtaining pus from the middle meatus is impractical. We studied whether analysis of four easily measured substances (protein, pH, leukocyte esterase and nitrite) in nasal secretions could predict the presence or absence of bacterial sinusitis, as diagnosed by history combined with sinus x ray or CT. We enrolled 217 consecutive patients, aged 4–61 years, with clinically suspected bacterial sinusitis (duration of symptoms, 7–26 days), who had radiographic studies. All had their nasal secretions assayed using a simple rapid test. A clinical scoring system was developed to allow for a simple interpretation of test results of four assays in a single clinical score. All 52 patients with scores of 0 or 1 were CT or x-ray negative for bacterial sinusitis. All 144 with scores of ≥ 4 were imaging study positive. Of the 21 patients (10%) with scores of 2 or 3, 14 were imaging study negative and 7 were positive. We concluded that combining these four separate assays on nasal secretion into one number, it is possible to rule in or rule out bacterial sinusitis in 90% of patients. This inexpensive, simple test can decrease the cost and help increase the accuracy of the diagnosis, thus improving the care of patients with bacterial sinusitis.

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Key words: Bacterial sinusitis, chemical assay, clinical scores, CT, diagnosis, leukocyte esterase, nasal secretion, pH, protein, rapid

In the United States, sinusitis affects an estimated 31 million people and accounts for ~16 million doctor visits/year.^{1–7} It is considered the most common respiratory disorder, with a high morbidity and recurrence rate. The disease is usually preceded by a viral upper respiratory infection followed by bacterial infection.^{3,8,9} If untreated, the acute phase can become chronic in 4 weeks and can linger for months. The illness can severely impact the patient's quality of life. A few patients may develop severe intracranial complications if they are poorly managed. Because of the high prevalence of sinusitis, the annual cost for medical management can be very high. In 2005, it was estimated that the direct medical cost of sinusitis in this country amounted for more than 3 billion dollars per year.⁸ This was in part because of the use of costly

imaging studies such as sinus x rays or CT scans of sinus cavities. Those studies are currently recommended and are deemed necessary^{1–16} because the symptoms of other respiratory illnesses such as allergic rhinitis or viral rhinitis can be identical to or overlap with those of sinusitis.

Adding to the high cost of sinusitis management is the cost of treatment. Once the diagnosis is established, the length of antibiotic therapy may reach 3–6 weeks to eradicate the organism(s). Partial treatment invites recurrence or complications. More expensive β -lactam antibiotics may be needed to treat the resistant organisms.^{3,8,9,16}

Almost all sinusitis patients have copious nasal discharge.^{17–20} A few studies reported in the past tried to correlate nasal cytology with sinus x-ray findings²¹ or measurement of cytokines,²² but neither one has been applied to the clinical setting. We postulated that if other chemical findings from nasal mucus could be easily determined, and the results correlated with radiological findings, then not only would medical expenses be significantly lowered, but patients would be spared expense, time, and unnecessary exposure to radiation. The procedure would also help reduce the risk of patients being undertreated because costly imaging studies were avoided, or overtreated when antibiotics are prescribed for nonbacterial causes of rhinorrhea.

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METHODS

Patient Selection

Two hundred twenty-six consecutive patients attending the university hospital Allergy Clinic with clinically suspected acute sinusitis (duration of symptoms, 7–21 days, and one at 26 days) were studied. All of the patients presented with prolonged cold symptoms included headache, fatigue, copious or increased amount of nasal discharge, irritation of eyes, cough, postnasal drip, and nasal congestion. Radiological evaluation was available for 217 patients (12 patients had CT scans and 205 patients had three view sinus films). Sixty-six patients were negative and 151 patients were positive for sinusitis. A total of 151 patients showed positive radiological findings of sinusitis that included the presence of one or more of the following: mucosal thickening (> 4 mm in thickness), air-fluid level, and/or increased opacity or retention cyst. Five patients were already treated with amoxicillin for < 7 days and the remaining patients were not on antibiotic treatment at the time of the study. Eighty-nine patients ranged from 4 to 9 years, 101 patients ranged from 10 to 19 years, 20 patients ranged from 20–39 years, 6 patients ranged from 40 to 59 years, and one patient was > 60 years old. This study was approved by the Institutional Review Board of the University (#336-1996).

Collection of Nasal Secretion and Analysis using Urine Dipstick

After informed consent was obtained, patients were asked to blow their noses forcefully into a 12×12 in. piece of Saran Wrap (Dow Chemical, Midland, MI.) Test strips to measure protein, pH, leukocyte esterase, and nitrite were obtained from either the Bayer Corp. (Pittsburgh, PA) or Boeringer Mannheim (now Roche Corp., Burlington, MA) and were smeared evenly with the nasal discharge. These strips were left at room temperature, and color changes were read by two individuals following manufacturer directions. All tests were read at 1 minute after sample application, except for leukocyte esterase, which was read at 2 minutes. The readers were blinded to each other's results and to the radiographic findings. The agreement of reading between individuals was 99%. On the rare occasions when the readers differed, the sum of readings of leukocyte esterase, nitrite, protein, and pH were averaged. Scores were assigned accordingly to the following four pads and the scores of the four pads were added to give the total clinical scores:

Scoring System for Four Pads

Protein

below 2+ = 0; 2+ = 1; 3+ = 2; 4+ = 3

pH

below 7.5 = 0; 7.5 = 1; 8.0 = 2; 8.5 = 3

Leukocyte esterase

below 1+ = 0; 1+ = 2; $\geq 2+$ = 3

Nitrite:

no color = 0; light pink = 1; dark pink = 2

RESULTS

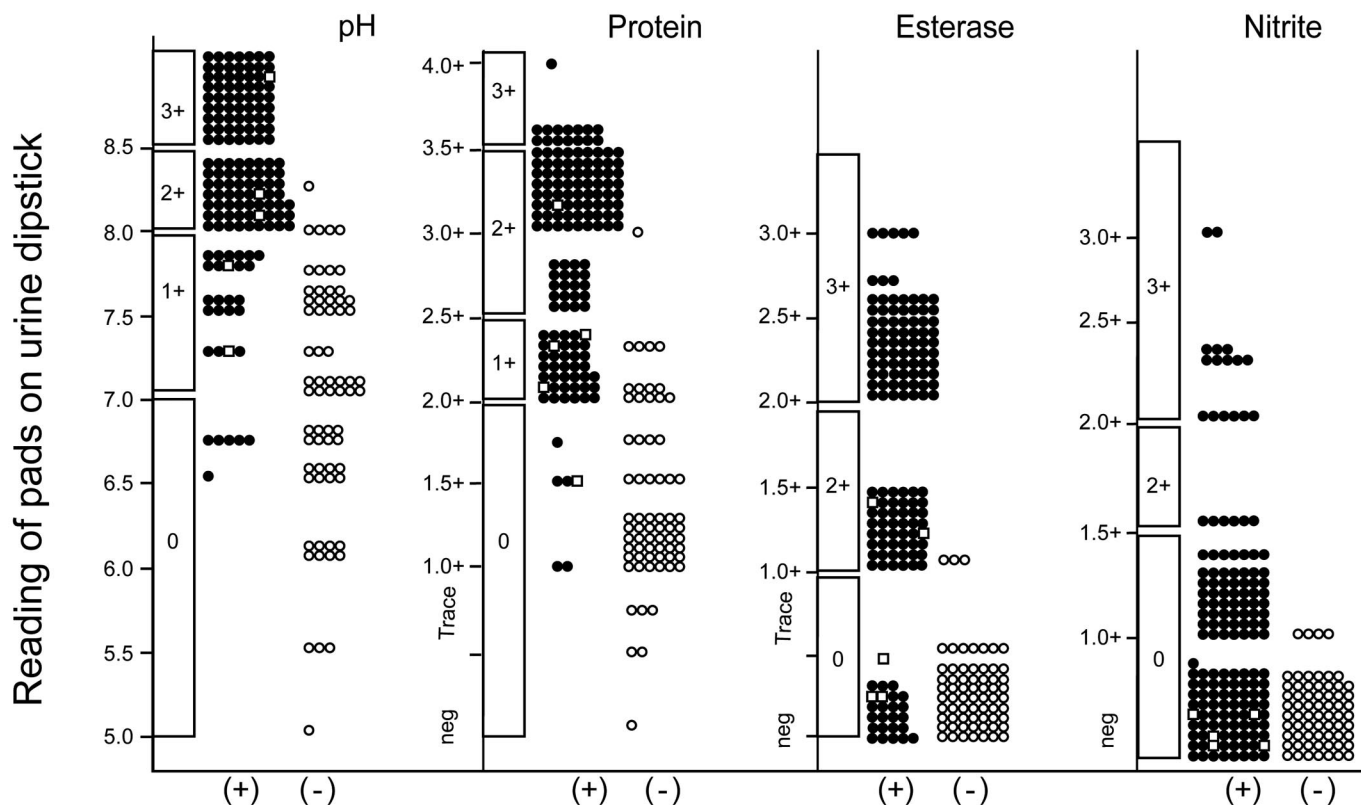
Figure 1 shows the data for the 217 patients who had both radiographic evaluation and assay of nasal secretions. Imaging studies refer to whether they were evaluated three view sinus films or CT and whether a diagnosis of sinusitis was made as positive (+) or negative (–). Protein, pH, leukocyte esterase, and nitrite test results were obtained by reading the reagent test pads. A negative sign (–) means the assay was performed but revealed no presence of either leukocyte esterase or nitrite. The clinical score is obtained using the formula provided in the Methods section.

Figure 2 shows that all 52 patients with clinical scores of 0 or 1 were CT or x-ray negative for bacterial sinusitis, and all 144 patients with clinical scores of ≥ 4 were imaging study positive. Of the 21 patients (10%) with scores of 2 or 3, 14 were x-ray negative and 7 were positive. The results show that 90% of cases had a positive correlation of clinical scores and results of imaging studies

DISCUSSION

Our experience indicates that using a rapid test using four combined test results on nasal secretions and using a unique clinical scoring system for the test results can discriminate between the presence or absence of bacterial sinusitis. Furthermore, adding other tests, such as ketones or glucose did not significantly improve the ability of the rapid test to rule in or rule out the presence of a bacterial infection. Individual tests alone were not capable of yielding the required sensitivity and specificity. For example, a pH of 8.5 is always associated with sinusitis, but a pH of 6.5, 7, 7.5, and 8 are all found in both sinusitis-negative and -positive patients. Protein readings of 3+ are, with one exception, always associated with sinusitis, but readings of 1+ or 2+ are found in both sinusitis-negative and -positive patients. When leukocyte esterase is present, with one exception, it is associated with sinusitis, but nearly 10% of patients with sinusitis have no detectable leukocyte esterase.

We speculate that the high pH may result from bacterial urease producing ammonia. If this is true, a high pH would suggest that the sinusitis might be caused by



Positive or negative finding of imaging study on sinuses

Figure 1. Illustration of the distribution of reading from each of four pads, pH, protein, leukocyte esterase, and nitrite from test strips using nasal discharge from individuals referred for evaluation of sinusitis. The groups were divided into (+) or (-), indicating positive or negative findings of imaging study on the sinuses. The dark circles indicate individuals with positive findings and open circles indicate negative findings for sinus infection. The open squares indicate individuals who had received a partial treatment of antibiotics for sinus infection.

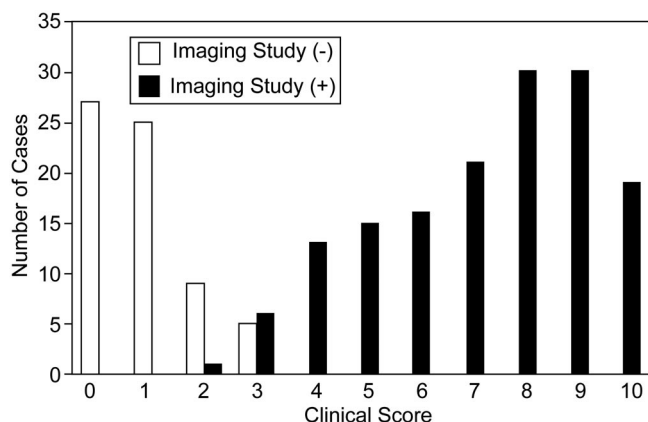


Figure 2. Illustration of the distribution of clinical scores, the sum of readings of four test pads from individuals referred for evaluation of sinus infection. The open bars indicate the imaging study was negative, and the closed bars indicate positive findings for sinus infection.

Streptococcus pneumoniae because they are the most common bacteria that cause sinusitis and have urease. Additional research will be required to determine

whether pH or other markers can be used to help identify specific bacterial pathogens.

High protein concentrations could be caused by leakage from damaged epithelium, exudate, and/or lysis of bacteria and white blood cells. Leukocyte esterase is almost certainly caused by lysis of white blood cells in the purulent material draining from the sinus.

Irrespective of the causes of the measured variables, the use of a four-component rapid test to analyze nasal secretions can be a useful tool to aid in the diagnosis of bacterial sinusitis. Compared with examination of nasal discharge cytology²¹ or measurement of cytokines,²² which are not readily available, this assay could be performed in the doctors office or hospital bedside with ease.

Currently, there is no diagnostic test available to satisfy the diagnosis of bacterial sinusitis that would not involve the positive bacterial culture and the presence of corresponding tissue changes in the sinus cavity. Clinical information and imaging studies remain as the mainstay of managing sinusitis by many clinicians. A recent study even indicated that the history alone may not be enough

to identify patients with sinusitis.²³ Thus, expensive imaging studies remains a viable option in identifying sinus infection. The new test system is very inexpensive when compared with imaging studies. It should prove to be useful in cutting cost and improving patient care and/or assisting in the diagnosis of bacterial sinusitis when imaging studies are not available. The ability to quickly and inexpensively rule out bacterial sinusitis should hopefully also reduce the misuse of antibiotic therapy.

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REFERENCES

1. Wald ER. Acute and chronic sinusitis: Diagnosis and management. *Pediatr Rev* 7:150–157, 1985.
2. Goldenhersh MJ, and Rachelefsky GS. Sinusitis: Early recognition, aggressive treatment. *Contemp Pediatr* 6:22–42, 1989.
3. Wald ER. Sinusitis in children. *N Engl J Med* 326:319–323, 1992.
4. Druce HM, and Slavin RG. Sinusitis: A critical need for further study. *J Allergy Clin Immunol* 88:675–678, 1991.
5. Lau J, Zucker D, Engles EA, et al. Diagnosis and treatment of acute bacterial rhinosinusitis. Evidence report/technology assessment no. 9, Agency for Health Care Policy and Research, publication no. 99-E016, 10–11, 1999.
6. , Brook I. Current issue in the management of acute bacterial sinusitis in children. *Int J Pediatr Otolaryngol* 1:1653–1661, 2007.
7. Mahoney MC, and Rosenfeld RM. Clinical diagnosis and evaluation of sinusitis in adults. *Am Fam Physician* 76:1620–1624, 2007.
8. Marple BF, Brunton S, and Ferguson BJ. Acute bacterial rhinosinusitis: A review of U.S. treatment guidelines. *Otolaryngol Head Neck Surg* 135:341–348, 2005.
9. Revai K, Dobbs LA, Nair S, et al. Incidence of acute otitis media and sinusitis complicating upper respiratory infection: The effect of age. *Pediatrics* 119:e1408–e1412, 2007.
10. Yeda D, and Yoto Y. The 10 day mark as a practical diagnostic approach for acute paranasal sinusitis in children. *Pediatr Inf Dis J* 15:576–579, 1996.
11. Arruda LK, Mimica IM, and Sole D. Abnormal maxillary sinus radiographs in children. Do they represent bacterial infection? *Pediatrics* 85:553–558, 1990.
12. Honer C, and Yogev R. or pediatric cold A persistent sinusitis. *J Respir Dis* 12:259–274, 1991.
13. Garcia DP, Corbeth ML, Eberly SM, et al. Radiographic imaging studies in pediatric chronic sinusitis. *J Allergy Clin Immunol* 94:523–530, 1994.
14. Rosenfeld RM, Andes D, Bhattacharyya N, et al. Clinical practice guideline: Adult sinusitis. *Otolaryngol Head Neck Surg* 137(suppl 3):S1–S31, 2007.
15. Brook I. Current issue in the management of acute bacterial sinusitis in children. *Infect Dis Clin North Am* 21:42–48, 2007.
16. Anzai Y, Jarrik JG, Sullivan SD, et al. The cost-effectiveness of the management of acute sinusitis. *Am J Rhinol* 21:444–451, 2007.
17. Gill FF, and Neiburger JB. The role of nasal cytology in the diagnosis of chronic sinusitis. *Am J Rhinol* 3:13–15, 1989.
18. Jeney EVM, Raphael GD, Meredith SD, et al. Abnormal nasal glandular secretion in recurrent sinusitis. *J Allergy Clin Immunol* 86:10–18, 1990.
19. Suzuki H, Takahashi Y, Wataya H, et al. Mechanism of neutrophil recruitment induced by IL-8 in chronic sinusitis. *J Allergy Clin Immunol* 98:659–670, 1996.
20. Ferguson BJ, and Bensimhon BA. What is causing your patient's rhinosinusitis? *J Respir Dis* 18:321–334, 1997.
21. Wilson NW, Talowayski AA, and Hamburger RN. A comparison of nasal cytology with sinus X-rays for the diagnosis of sinusitis. *Am J Rhinol* 2:55–59, 1988.
22. Hamilos DL, Leung DYM, Wood R, et al. Evidence for distinct cytokine expression in allergic versus nonallergic chronic sinusitis. *J Allergy Clin Immunol* 96:537–544, 1995.
23. Young J, Sutter AD, Meresnshtein D, et al. Antibiotics for adults with clinically diagnosed acute rhinosinusitis: A meta-analysis of individual patient data. *Lancet* 371:908–914, 2008. □

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