Effect of a Rapid Diagnostic Method on Prescribing Patterns and Ordering of Throat Cultures for Streptococcal Pharyngitis

Bev Lorraine True, PharmD, Barry L. Carter, PharmD, Charles E. Driscoll, MD, and J. Daniel House, PhD
Iowa City, Iowa

The sensitivity and specificity of a rapid identification test for group A β-hemolytic streptococcus and its impact on prescribing antibiotics and ordering throat cultures were evaluated in a primary care office setting. The calculated sensitivity, specificity, positive predictive value, and negative predictive value were 82 percent, 92 percent, 76 percent, and 94 percent, respectively. Throat cultures were ordered for 98 percent of patients with acute pharyngitis regardless of the method of testing available. After use of the rapid identification test within the office, a reduction was observed in physician prescribing of antibiotics before the throat culture results were known. Physicians were more likely to initiate antibiotics immediately when rapid test results for streptococcal infection were positive and provide patient education regarding symptomatic treatment when the results were negative. The rapid identification test is an acceptable alternative to the standard culture technique in the family practice office. The rapid test was apparently responsible for the observed reduction in antibiotic prescribing and should reduce unnecessary cost and antibiotic exposure in the ambulatory setting.

Pharyngitis is generally of viral origin[1]; however, because the symptoms of viral pharyngitis are similar to those of group A β-hemolytic streptococcal infection, the diagnosis cannot be established accurately based upon the patient's symptoms or the physician's clinical impression.[2,3] Throat cultures on blood agar plates have been the standard method used to identify bacterial pharyngitis. Routine use of such throat cultures, if handled appropriately, can reduce unnecessary antibiotic prescribing for viral pharyngitis.[4]

The primary disadvantage of the blood agar culture is the 24- to 48-hour period required to identify the organism. The impact of this delay has been that physicians frequently begin antibiotic treatment without throat culture confirmation of the diagnosis.[5] This approach to therapy renders the blood agar throat culture a less than optimal laboratory test. As a result of excessive prescribing and inefficient utilization of laboratory tests, patient costs and adverse drug reactions are increased.

With the recent availability of rapid identification tests for group A β-hemolytic streptococcus, it has become possible to diagnose bacterial pharyngitis accurately within 10 to 15 minutes during a patient's visit.[6-11] This study was performed to (1) evaluate the antibiotic prescribing patterns of primary care physicians before and after utilization of a rapid identification test for group A β-hemolytic streptococcus, and (2) determine the sensitivity and specificity of the Culturette Brand 10-Minute Group A Strep ID test in three representative primary care office settings.

METHODS

During the period from January 1985 to May 1985 all patients over 3 years of age who presented to The University of Iowa Family Practice Model Office with clinical findings suggestive of pharyngitis and who had

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From the Department of Family Practice, College of Medicine, and the College of Pharmacy, The University of Iowa, Iowa City, Iowa. Requests for reprints should be addressed to Dr. Barry L. Carter, College of Pharmacy, University of Iowa, Iowa City, IA 52242.

a throat culture ordered were approached for inclusion in the study. After written informed consent was obtained, duplicate throat cultures were taken from those patients who agreed to participate in the study. (No patients who had a throat culture ordered refused to participate.)

Two pharyngeal swabs were simultaneously obtained, one using a dacron-tipped swab (Culturette II, Marion Scientific, Kansas City, Missouri) and another using a dry sterile applicator (Falcon Dry Throat Culture Tube with Sterile Applicator, Cockeysville, Maryland). Immediately after vigorous swabbing of the tonsillar surfaces (or fossae) and posterior pharyngeal wall, the dry sterile applicator was plated onto 5 percent sheep blood agar and streaked. It was then incubated in 5 percent carbon dioxide at 35°C for 18 to 24 hours, examined for the presence of β-hemolytic streptococci, and subcultured using bacitracin disks to differentiate group A from non-group A β-hemolytic streptococci. Similarly, the dacron-tipped swab was immediately placed in a microtube provided with the Culturette Brand 10-Minute Group A Strep ID test with extraction reagents 1 and 2. The identification test was then performed according to the manufacturer's instructions.

The traditional culture method was performed and interpreted by one laboratory technician, and the rapid test was performed by one of three investigators. This method was chosen to (1) represent a "typical" primary care office where this function might be shared, and (2) minimize the disruption of office laboratory work flow, which could occur as a result of the study requirement for duplicate cultures.

PRESCRIBING PATTERNS AFTER RAPID TEST AVAILABILITY

Results from the rapid identification test were available to the physician approximately 10 to 15 minutes after ordered. Physicians were not aware that the primary intent of the study was to evaluate physician prescribing patterns; they simply were informed that a rapid identification method for group A streptococcal infection was being compared with the standard culture method currently used in the office laboratory. The prescribers at the Family Practice Model Office during the study period included 24 residents (eight at each of the three levels of training) and ten faculty physicians.

The charts and laboratory results were examined from all patients who received a throat culture during the study period and from the same period one year previously (January 1984 to May 1984). In addition, data were collected from both periods for all patients who received a diagnosis of pharyngitis but who did not receive a throat culture. The following data were extracted from all of the above patient records: patient's age, sex, level of physician training, secondary infections or other conditions, throat culture results, antibiotic prescribing pattern, specific antibiotic prescribed, and duration of treatment.

Data from the study periods were evaluated to determine whether the ordering of throat cultures and prescribing patterns differed significantly after the availability of the rapid group A streptococcal identification method.

SENSITIVITY AND SPECIFICITY OF THE RAPID TEST

In addition to evaluating the effect the rapid diagnostic test had on the patterns of prescribing and throat culture ordering, the throat culture results were analyzed to determine the sensitivity and specificity of the Culturette Brand 10-Minute Group A Strep ID test when used in a typical primary care office setting. To increase the number of agar culture-rapid test pairs available for analysis of sensitivity and specificity, two community-based family practice offices were used for data collection.

Statistical analysis using the chi-square test was performed to evaluate the effect of the Culturette Brand 10-Minute Group A ID test on physician prescribing patterns. Statistical significance was assumed for P values less than .05.

RESULTS

During the control period, year 1 (January 1984 to May 1984), and experimental period, year 2 (January 1985 to May 1985), there were 263 and 283 cases of acute pharyngitis observed, respectively. For 98 to 99 percent of the cases, a throat culture (either agar culture, rapid identification test, or both) was obtained (258 of 263 control, and 280 of 283 experimental). Of the patients who had throat cultures taken during the two study periods, there was no significant difference between the control and experimental periods in the number of male (94 and 87, respectively) and female (164 and 193, respectively) patients or positive (46 and 54, respectively) and negative (212 and 211, respectively) agar culture results. (During year 2 there were 15 cases in which only the rapid identification test was performed and all 15 tests were negative). In both study periods, approximately one fifth of all throat cultures obtained were positive.

There was no significant difference observed in age distribution between years 1 and 2 when the patients were grouped by age 16 years or younger (83 and 106, respectively) and older than 16 years (175 and 174, respectively). There was, however, a significant difference observed in both year 1 ($P = .030$) and year 2 ($P = .019$) in the frequency of positive and negative agar culture results for patients aged less than 16 years compared with those aged over 16 years. For both study periods, approximately one fourth to one third of

the younger patients, while only one sixth of the older patients, had a positive throat culture. This finding would be expected, as streptococcal pharyngitis is more frequently found in younger age groups.[12]

During year 1 and year 2 there were 16 and 13 patients, respectively, who had secondary infections or other conditions in addition to acute pharyngitis. The distribution of these cases (otitis media, pneumonia or bronchitis, sinusitis, patient took own supply of antibiotic before physician visit, heart murmur, peritonsillar abscess) was similar for both year 1 and year 2. These cases were excluded from the data analysis of prescribing patterns.

The four prescribing patterns observed in this study were (1) symptomatic treatment, no antibiotics prescribed, (2) antibiotics prescribed before either culture result or rapid identification test result known, (3) antibiotics prescribed after either culture result or rapid identification test result known, and (4) antibiotic prescription given to patient with instructions to fill only if culture result is positive.

Of the patients who received a throat culture, prescribing data were missing for six individuals in year 1 and two individuals in year 2. During the control and experimental periods, symptomatic treatment was prescribed for 58 and 63 percent of patients, respectively, who received a throat culture.

During year 1, 27 percent of the patients received an antibiotic before culture results were available; however, during year 2, only 9 percent of patients received an antibiotic prescription before either culture results or rapid test results were known. In contrast, the percentage of patients who were given an antibiotic prescription after either culture or rapid test results were known increased from 10 percent during year 1 to 26 percent during year 2. During the control and experimental periods there were 6 and 2 percent, respectively, of cases who received an antibiotic prescription with instruction to fill it only if culture results were positive. The change observed in the frequency of the four prescribing patterns between years 1 and 2 was statistically significant ($P < .001$). No significant difference was observed between control and experimental periods in the number of male or female patients who received a particular prescribing pattern. Thus, after the use of the rapid identification test, fewer patients received antibiotics before laboratory results were available, and fewer patients with negative results were exposed to antibiotics.

For individuals whose agar throat culture results were negative, there were fewer antibiotic prescriptions given prior to culture results (either agar throat culture or rapid test) when compared with year 2, when the rapid test became available ($P < .001$). For individuals whose agar throat culture results were positive, antibiotics were prescribed sooner when the rapid test was available (year 2). This finding is in contrast with year 1, when antibiotic prescriptions were delayed in some patients who had positive cultures while the physician waited for the agar throat culture results. The difference was significant between year 1 and year 2 for this prescribing pattern in this subgroup of patients (agar culture positive), $P = .02$.

After exclusion of the secondary diagnoses, the choice of antibiotic did not differ significantly between study periods. Penicillin was prescribed most frequently (71 to 80 percent of the time), followed by erythromycin (13 to 21 percent) and amoxicillin (5 to 7 percent). The majority of prescriptions (94 percent) were written for a duration of ten days, which did not differ significantly between years 1 and 2.

To determine the sensitivity and specificity of a rapid streptococcal diagnostic test in a primary care office setting, an evaluation of the Culturette Brand 10-Minute Group A Strep ID kit was performed. There were a total of 58 true-positive and 199 true-negative rapid identification tests, and 18 false-positive and 13 false-negative rapid identification tests. The calculated sensitivity, specificity, positive predictive value, and negative predictive value for the model office alone and in combination with the two other community-based primary care offices were 81 and 82 percent, 91 and 92 percent, 72 and 76 percent, and 94 and 94 percent, respectively. These values are within the ranges reported by other investigators.[6-11]

DISCUSSION

In this study, antibiotic prescribing patterns for acute pharyngitis by primary care physicians were changed when a rapid identification test for group A β-hemolytic streptococcus was utilized. The observed reduction in antibiotic prescribing for negative throat cultures is an improvement in the management of streptococcol pharyngitis. In addition, the Culturette Brand 10-Minute Group A Strep ID test appears to be a reasonable alternative to the standard streptococcal blood agar culture method employed in a "typical" primary care office setting.

Approximately ten rapid detection kits for group A β-hemolytic streptococcus are currently available. There are few published evaluations of these tests, and most of the evaluations have utilized laboratory technicians or medical professionals to perform the test. The figures reported here for sensitivity, specificity, positive predictive value, and negative predictive value (81 to 82 percent, 91 to 92 percent, 72 to 76 percent, and 94 percent, respectively) are within the range reported in the literature for these tests; however, they are at the lower end of that range.[6-11] The lower sensitivity and specificity values observed in this study are probably due to several factors related primarily to study design and setting.

Other published values are the result of studies designed specifically to establish the efficacy of the rapid test, and therefore have been performed in controlled laboratory environments usually with one highly

trained individual to perform and interpret the test and with utilization of batching to reduce variability. On the other hand, this study was designed primarily to evaluate prescribing patterns in the real-life office setting. The variabilities imposed by a primary care office include staffing changes, more than one individual to perform and interpret the test, proficiency of the individual(s) carrying out the test, and the desire to provide rapid turnaround time amidst patient-laboratory workflow, which results in minimal batching of tests.

Although interrater reliability in test performance and interpretation was not specifically evaluated, there did not appear to be an unequal distribution in the frequency of false-positive and false-negative rapid test results among the three individuals. The use of three persons to perform and interpret the rapid test, however, as well as other factors, probably contributes to the lower sensitivity and specificity values observed in this study when compared with previous reports.

There are several limitations to the assumption that 5 percent sheep blood agar and bacitracin disks should be the standard with which the rapid test was compared. Because the streptococcal strains were neither serogrouped nor semiquantitated, the accuracy of the standard is compromised. In addition, positive agar cultures were not serologically confirmed in this study to determine whether an individual was experiencing a streptococcal infection or was simply a streptococcal carrier. However, because the rapid test detects only the presence of streptococci and is unable to differentiate carrier patients from disease patients, the agar culture, as it was performed in this study, is the optimal comparison test. The results of this study are therefore limited to the type of standard employed, which is one of the most commonly used in the majority of private primary care office settings.

The standard blood agar culture and bacitracin disk technique utilized in the primary care office setting is associated with 10 to 20 percent false-positive and 20 to 40 percent false-negative results[13]; therefore, it also is associated with considerable variability in accuracy when used in this setting. The standard culture technique has been shown to cross-react with some nongroup A streptococci,[7] while the rapid identification test has not. Because of these reasons, the rapid identification test is an acceptable alternative to the blood agar culture technique when used in the primary practice setting.

EVALUATION OF PHYSICIAN PRESCRIBING PATTERNS

The almost routine use of antimicrobial medication for respiratory tract infections, of which 60 percent are probably viral in origin, raises the question of efficacy and economy of such a practice.[14] Because of the inherent delay associated with the blood agar throat culture, antibiotics are frequently prescribed excessively for acute pharyngitis.[5] One approach is to treat all patients suspected of having bacterial pharyngitis without performing a throat culture. It has been estimated, however, that the treat-all strategy would result in 448 excess serious and 210 excess mild allergic reactions while preventing only 11 cases of acute rheumatic fever within a sample of 100,000 patients with acute pharyngitis.[15] Widespread antibiotic prescribing, without confirmation of a bacterial cause, results in unnecessary patient expense for the majority of patients who have viral pharyngitis.

Probably the least appropriate management of a sore throat occurs when a physician orders a throat culture and initiates antibiotics immediately. In this situation the laboratory test does not serve a diagnostic function, as the decision to prescribe an antibiotic had already been made. Thus, a patient will be charged for an office visit, culture, and prescription for a condition that may not be bacterial. Holmberg and Faich[5] found that one half of the physicians they surveyed in Rhode Island cultured throat samples from all patients with sore throats, and that 44 percent of surveyed physicians did not get culture results back in time to influence therapy. These data indicate that many physicians frequently manage acute pharyngitis less than optimally.

There are several other treatment approaches that can be considered to be inappropriate, including partial antibiotic prescriptions with refill options and written prescriptions offered to patients to be filled after the culture results become available. Although these approaches to treatment sound reasonable, experience indicates that patients given a five-day course of antibiotics with a refill authorization generally will not continue treatment for the recommended ten days necessary for streptococcal pharyngitis. Whether reluctance to complete a full course of therapy is a result of the patient's improved symptomatology, the additional expense of the refill, or other factors has not been determined. Similarly, patients given a written prescription and instructions not to fill it unless they are informed of a positive culture will often disregard the advice, obtain the antibiotic, and take the medication at least until they obtain the culture results. Thus, both of these approaches to therapy tend to result in either insufficient duration of treatment or unnecessary cost and exposure to antibiotics.

With the recent availability of several serologic methods that use either coagglutination or latex agglutination for the rapid identification of group A β-hemolytic streptococcus, it has become possible to diagnose bacterial pharyngitis accurately within 10 to 15 minutes.[6-11] Data obtained in this study indicate that when culture results are available during a patient's visit, the physician is more likely to wait for the culture result before prescribing an antibiotic. Because 98 to 99 percent of patients seen for pharyngitis during the two study periods had a throat culture ordered, there was no change observed in the treat-all strategy; it

simply was not common practice in the office. However, by decreasing the use of antibiotics before culture results were known, patient cost and inappropriate drug exposure were reduced. In addition, because the results from the rapid identification method were available during a patient's office visit, physicians and other health professionals no longer needed to spend time contacting those patients with positive culture results as they did previously with the standard throat culture method.

Another potential advantage of early identification and treatment of streptococcal pharyngitis is that antibiotics might alter the clinical course of streptococcal pharyngitis. It has been suggested that antibiotics initiated after standard culture results are available, which is at least 24 to 48 hours after onset of illness if the patient was prompt in requesting a throat culture, do little to alter the clinical course of the disease. On the other hand, a small but well-designed double-blind placebo-controlled investigation has recently demonstrated rapid antibiotic initiation does significantly improve patient symptoms, decrease the duration of fever, and decrease the time interval to achieve a negative throat culture.[16] Thus, not only does the rapid identification test have the potential to minimize antibiotic exposure and expense, but it facilitates early initiation of antibiotic treatment to those patients in whom it is justified. Beginning antibiotics immediately could possibly result in quicker resolution of illness and infectivity and an opportunity to return more quickly to school, day care, or work.

With rapid test results, physicians were more likely to initiate antibiotics immediately when the culture results were positive and provide patient education for symptomatic treatment when the culture results were negative. In one ambulatory patient sample of 40 patients with sore throat, less than one half of the patients expected to receive an antibiotic for their complaint, and the majority of patients were satisfied with their care regardless of whether a prescription was provided.[17] Thus, it appears that instructions for the management of a viral sore throat provided in an empathetic manner is acceptable to the patient when compared with the alternative of providing an antibiotic to satisfy and justify a patient's office visit.

This study has demonstrated that excessive antibiotic prescribing is reduced after the rapid identification test for streptococcal infection was routinely used in the office laboratory. In contrast, the most typical consequence of technologic advances in testing is the marketing of extremely expensive diagnostic tests that may not add to the physician's clinical judgment, may not alter the course of therapy, and frequently lack established efficacy and safety.[18] Because the clinical diagnosis of acute group A β-hemolytic streptococcal pharyngitis is often unreliable, routine throat cultures are considered part of the standard of care. Because the results of agar cultures are not immediately available, they often have a minimal impact on therapy, except to increase expense.

This study demonstrates that the rapid diagnostic test for group A β-hemolytic streptococcus, when used in a primary care office, can provide results while a patient is still in the office, can change the physician's course of action, results in a reduction in excessive antibiotic prescribing, and thus can reduce unnecessary cost and antibiotic exposure.

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