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Comparison of Clinical Findings and Rapid Streptococcal Antigen Detection Test in the Diagnosis of Group A Streptococcal (GAS) Pharyngitis

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Abstract

Background: Group A β-hemolytic Streptococcal (GAS) pharyngitis is a common illness in children. Diagnosis and proper treatment of group A streptococcal sore throat is important particularly to prevent non-superlative sequel. Clinical findings continue to be used in differentiating streptococcal infection from viral sore throat.

Objectives: The aim of this study was to evaluate the accuracy of clinical findings and rapid test in comparison with culture in the diagnosis of group A Streptococcal (GAS) pharyngitis.

Patients and Methods: Ninety-four children between 3 to 16 years, who were referred to the pediatric clinic of Rasoul-e-Akram hospital with clinical findings of fever or sore throat were evaluated from October 2006 to May 2007. Clinical findings were recorded and swabs were taken for group A streptococcal cultures and streptococcal rapid antigen detection test. Analysis of statistical significance was performed using the chi-square method. The accuracy of clinical findings and rapid test was compared with the culture method as the gold standard, and sensitivity, specificity, positive predictive values, negative predictive value, positive likelihood ratio (LR^+) and negative likelihood ratio (LR^-) were calculated.

Results: The culture was positive in 38 (40.4%) of the 94 evaluated children. The mean age of children was 8 ± 3.7 years. The presence of petechiae, exudate and Lymphadenopathy (LAP) was more likely in children with positive streptococcus culture and rapid test (P value < 0.05). Lymphadenopathy was known to feature the most sensitivity (100%), specificity (76.8%), and positive predictive value (74.5%), negative predictive value (100%) and positive likelihood ratio (LR) (4.3) among clinical findings. The results of rapid test showed sensitivity of 89.4%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 93.3% in comparison with culture as the gold standard. In general, the accuracy of rapid test was found higher than subjective clinical findings ($P = 0.001$).

Conclusions: Although LAP had good performance in early diagnosis of GAS, a combination of clinical findings, including tonsillar exudates, petechiae with results of rapid antigen test or culture is necessary for clinician judgment. Throat culture is the gold standard test for detecting group A Streptococcal infection, but rapid test is a good replacement for culture.

Keywords: Clinical, Rapid, Culture, Streptococcal, Pharyngitis

1. Background

Acute Pharyngitis (AP) is one of the most common diseases in pediatric practice. Although the majority of APs is of a viral origin, group A β-Hemolytic Streptococcus (GABHS) is the most common bacterial etiology (1-4). Therefore, early diagnosis of this infection followed by appropriate antimicrobial treatment, is extremely relevant to the prevention of rheumatic fever and superlative complication (5).

Group A streptococcus (Streptococcus pyogenes) is responsible for 5 to 15% of cases of pharyngitis in adults and 20 to 30% of cases in children (6).

Common symptoms include sore throat, pain on swelling, fever and the presence of white exudates on swollen tonsils (6).

Throat culture remains the gold standard for the diagnosis of streptococcal pharyngitis. The sensitivity and specificity of throat culture for group A β-hemolytic streptococci is 90% - 95% and 99% under ideal conditions (7, 8).

Rapid tests for detection of group A streptococci (GAS) have been dominantly used during the last decade (9). They can be performed in office settings, and results can be available in 10 minutes after obtaining a throat swab (9,10). This test has a reported specificity of more than 95% but a sensitivity between 80% - 90% or even lower (76% - 87%) in

some previous studies (1, 7).

According to the American academy of pediatrics and American heart association, a positive rapid antigen detection test may be considered as definitive evidence for treatment of streptococcal pharyngitis (4). A confirmatory throat culture should be followed by a negative rapid antigen detection test when the diagnosis of group A β-hemolytic streptococcal infection is strongly suspected (7, 10).

Clinical prediction rules take into account key elements of a patient's history and physical examination and allow physicians the probability of group A β-hemolytic streptococcal pharyngitis (7).

2. Objectives

The objective of this study was to compare the accuracy of clinical findings and rapid antigen detection test in comparison with culture for diagnosis of streptococcal pharyngitis between 3 to 16 years old patients with pharyngitis, which were admitted to pediatric center of Rasoul-e-Akram hospital from October 2006 to May 2007.

3. Patients and Methods

The current study was a prospective, observational study undertaken at the pediatric clinic of Rasoul-e-Akram hospital between 2006 and 2007. Ninety-four children aged between 3 to 16 years old, which had evidence of a painful throat or inflammation of throat or tonsils on physical examination were enrolled.

Demographic and clinical data including fever, painful throat, palpable lymphadenopathy, painful lymphadenopathy, hyperemia and exudates from the palatine tonsils were recorded by the physicians and then a throat swab was used immediately for rapid test using a commercial kit (screenitalia, Italia), and blood agar culture and plates were incubated for 24 hours at 35°C under aerobic conditions.

Streptococcus pyogenes was identified in positive cultures by means of testing for sensitivity to Bacitracin.

3.1. Statistical Analysis

The accuracy of clinical diagnosis and rapid test was compared with the culture method as the gold standard and sensitivity, specificity, positive predictive values and negative predictive value, positive likelihood ratio (LR^+) and negative likelihood ratio (LR^-) were calculated. Moreover, analysis of statistical significance was performed using the chi-square method with a cut off of $P < 0.05$.

4. Results

Ninety-four children were included in the study consisting of 43 (45.7%) female patients and 51 (54.3%) male patients. The mean age of children was 8 ± 3.7 years. The results of culture were positive for GAS in 38 (40.4%) patients and negative in 56 (59.6%) patients whereas the results of rapid test showed 34 (36.17%) patients as positive and 60 (63.83%) as negative. There were no statistical differences between gender and positive culture results in this study ($P > 0.05$).

The frequency of clinical findings among 94 children was as follows, high temperature in 78.7%, LAP in 86%, petechiae in 51%, exudates in 58.5%, abdominal pain in 54.3%, vomiting in 53.2%, stomatitis in 1.1%, cough in 5.3%, rhinorrhea in 4.3% and LAP in 86.17%.

The frequency of clinical findings, lymphadenopathy (LAP), petechiae, exudates, abdominal pain, vomiting by culture and rapid tests are summarized in Table 1. As indicated, the clinical findings of LAP, petechiae, exudates, abdominal pain and vomiting were more frequent among the children with positive culture and rapid streptococcal antigen detection test than negative groups. There was a statistical significance among the mentioned clinical findings in the two groups of positive and negative culture and rapid test (P value < 0.05).

The results of sensitivity, specificity, positive and negative predictive value and likelihood ratio (LR) were calculated for clinical findings like petechiae, exudates and LAP, and rapid streptococcal antigen detection test in comparison with culture as the gold standard. The results are summarized in Table 2. As indicated, LAP had the most sensitivity (100%), specificity (76.8%), and positive predictive value (74.5%) and negative predictive value (100%) among clinical findings.

Positive likelihood ratio (PLR) for LAP was 4.3, which was more than PLR for petechiae (1.89) and exudates (1.42) in this study (Table 2).

The results of rapid test indicated sensitivity of 89.4%, specificity of 100%, positive predictive value of 100% and negative predictive value of 93.3%, in comparison with culture as the gold standard (Table 2).

5. Discussion

Throat culture has been used as the preferred diagnostic method and gold standard for the diagnosis of Group A Streptococcal Pharyngitis (1). More recently, however, the American college of physicians recommended selective diagnosis and therapy based on clinical findings and also suggested the adoption of rapid diagnostic tests to replace the standard throat culture (11, 12).

Table 1. Frequency of Clinical Findings Regarding Positive and Negative Diagnostic Methods in 3-16 Years Old Patients With Pharyngitis[a,b]

Methods	Culture Positive	Culture Negative	P Value	Rapid Test Positive	Rapid Test Negative	P Value
Clinical findings	38 (40.4)	56 (59.6)	-	34 (36.17)	60 (63.83)	-
High Temperature	32 (84.2)	42 (75)	N S	29 (85.3)	45 (75)	NS
LAP	38 (100)	43 (76.8)	0.001	34 (100)	47 (78.3)	0.003
Petechiae	27 (71.1)	21 (37.5)	0.001	25 (73.5)	23 (38.3)	0.001
Exudates	27 (71.1)	28 (50)	0.04	27 (79.4)	28 (46.7)	0.002
Abdominal Pain	30 (78.9)	21 (37.5)	0.001	27 (79.4)	28 (46.7)	0.001
Vomiting	28 (73.7)	22 (39.3)	0.001	25 (73.5)	25 (41.7)	0.003
Stomatitis	1 (2.6)	0	NS	1 (2.9)	0	NS
Cough	1 (2.6)	4 (7.1)	NS	1 (2.9)	4 (6.7)	NS
Rhinorrhea	2 (5.3)	2 (3.6)	NS	1 (2.9)	3 (5)	NS

[a] P value < 0.05 is significant.
[b] Values are expressed as No. (%).

Table 2. Comparison of Clinical Findings and Rapid Test With Culture in Diagnosing Group A Streptococcal (GAS) Pharyngitis

	True Positive	True Negative	False Positive	False Negative	Sensitivity[a]	Specificity[a]	PPV[a]	NPV[a]	PLR	NLR
Clinical findings										
Petechiae	27	35	21	11	71.1	62.5	56.3	76.1	1.89	0.46
Exudates	27	28	28	11	71.1	50	49.1	71.8	1.42	0.58
LAP	38	43	13	0	100	76.8	74.5	100	4.3	0
Diagnostic test										
Rapid test	34	56	0	4	89.4	100	100	93.3	Infinity	0.1

[a] Values are expressed as %.

In this study, children aged between 3 to 16 years old with a history of complaint with infectious sore throat and clinical findings compatible with group A Streptococcal Pharyngitis were evaluated and clinical findings and results of rapid streptococcal antigen detection test were compared with culture.

An analysis of the signs and symptoms that are predominant with group A streptococcal sore throat showed statistically significant differences for petechiae, exudate and LAP (P value < 0.05) among positive groups, confirmed by culture and rapid test, and negative groups in this study.

In this study, sensitivity, specificity, positive and negative predictive value and LR in rapid test were more than clinical diagnostic findings and finally LAP had the most sensitivity (100%), specificity (76.8%), positive predictive value (74.5%) and negative predictive value (100%) among clinical findings.

Several studies have already attempted to establish a relationship between the signs and symptoms of infectious sore throat and the presence of streptococcal pharyngitis. However, even for similar samples, the predominant signs and symptoms vary from various studies. Nandi et al. in India found significant associations between enlarged tonsils, pain in the throat, pharyngeal erythema and tender cervical lymphadenopathy and the presence of streptococcal pharyngitis. Combinations of various symptoms and signs gave sensitivity of 86 to 89% and specificity of 83 to 89% (13).

Dos Santos and Berezin have reported that symptoms like petechiae, exudate and painful glands were more frequent among the subset of children with positive cultures, with statistical significance (P < 0.001), this is similar to our study. Clinical findings like petechiae, exudate and painful glands had low sensitivity of 32%, 50% and 36% and good specificity of 89%, 64% and 85%, respectively (14).

Steinhoff et al. found low sensitivity and high specificity for exudate (31% and 80.8%) and tender nodes (33.6% and 82.2%), and temperature greater than 38°C (37.4%, 66%) for the diagnosis of GAS. In contrast, a large node had a high sensitivity (81.3%) and low specificity (45.1%) in comparison with culture. Finally Steinhoff et al. suggested a guideline that includes the features of enlarged anterior cervical nodes and pharyngeal exudates features with high sensitivity and good specificity for the diagnosis of GAS

(15).

The sensitivity and specificity of LAP in our study were 100% and 74.5%, respectively, which were more than the sensitivity and specificity of exudate (71.1%, 50%) and petechiae (71.1%, 62.5%).

In a study conducted by Rimoin et al. (16), there was a statistically significant difference in the frequency of signs: cervical lymphadenopathy, exudate, fever, absence of cough with GAS pharyngitis in various four countries, however, cervical lymphadenopathy was the only sign that was consistently and statistically associated with positive GAS culture at all different sites (17). This finding is consistent with our study.

In the present study, positive predictive value of petechiae, exudate and LAP were 56.3%, 49.1% and 74.5% and negative predictive value of the mentioned clinical findings were 76.1%, 71.8% and 100%, respectively, which means the results of our study is consistent with Dos Santos and Berezin's study with low positive predictive value for petechiae, exudate and painful glands of 49%, 31% and 43%, and high negative predictive value of 80%, 80% and 80% for the mentioned clinical findings (14).

The highest positive predictive value of 74.5% and negative predictive value of 100% were seen in patients who had LAP.

Positive Likelihood Ratio (PLR) for LAP in this study was 4.16, which was more than PLR for petechiae (1.89) and exudates (1.42). This denotes the result of PLR for LAP as one of the important clinical findings that shows the ability of LAP for pre-diagnosis of diseases in people who had GAS diseases. As the clinical positive likelihood of GAS increased, there were stepwise increases in sensitivity of clinical findings (from 71% to 100%).

Dos Santos and Berezin reported that the sensitivity, specificity, PPV and NPV of the rapid test was more than the medical opinion of a physician. The sensitivity, specificity, PPV and NPV of the rapid test in comparison with culture in the present study were 89.4%, 100%, 100% and 93.3%, respectively, that was more than the clinical findings, thus our results are similar with Dos Santos and Berezin findings with sensitivity, specificity, PPV and NPV of rapid tests being 96.7%, 94.4%, 84.8% and 98.9%, respectively (14).

The sensitivity of the rapid antigen test for GAS is not a fixed value but varies with the spectrum of disease (17).

Edmonson reported high sensitivity of 94% for the rapid test in comparison with culture in patients < 15 years old, who had tonsillar exudate and no cough and low sensitivity of 73% in patients clinically unlikely to have GAS (18).

In a study conducted by Forward et al. sensitivity, specificity, PPV and NPV of the rapid test in comparison with culture in diagnosing streptococcal pharyngitis were 71.9%, 94.3%, 76.9%, and 92.7% (19).

According to guidelines for the diagnosis and management of group A Streptococcal pharyngitis, swabbing the throat and testing for GAS pharyngitis by rapid antigen detection test or culture should be performed because the clinical features alone do not reliably discriminate between GAS and viral pharyngitis (20).

The results of a study showed that the rapid test is helpful for rapid diagnosis of GABHS pharyngitis. Although diagnosis of GABHS pharyngitis based on only clinical findings is misleading in the majority of cases in this study, there was good correlation between petechiae in the pharynx of patients and positive rapid test ($P < 0.004$) (21). Results of our study also showed statistically significant differences between petechiae and positive rapid test as well ($P < 0.001$).

In a study conducted in Brazil, Croatia, Egypt, and Latvia among children aged between 2 - 12 years old, sensitivity of rapid antigen detection test in comparison with culture in diagnosing streptococcal pharyngitis ranged from 72.4% to 91.8% while specificity ranged from 85.7% to 96.4%. The positive predictive value ranged from 67.9% to 88.6% and negative predictive value ranged from 88.1% to 95.7% (16).

In general, our findings showed that the rapid test with sensitivity and specificity of 89.4% and 100% had good performance in diagnosing GAS and LAP with sensitivity and specificity of 100% and 76.8%, and helps clinician with pre-diagnosis of GAS.

5.1. Conclusions

No single element of medical history or physical examination is sufficient to accurately diagnose streptococcal pharyngitis. However, LAP had good performance in precision of GAS, a combination of clinical findings including tonsillar exudates, petechiae and the absence of cough, and is helpful in predicting an increased probability of the disease. These findings should be coupled with additional clinical factors such as the patient's age, the results of rapid antigen testing or culture for clinician judgment.

Footnote

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