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소아청소년과 의원을 방문한 급성 인두염환자에서 신속항원검사 SD Bioline Strep A의 평가

김선주

경상대학교 의과대학 진단검사의학교실, 건강과학원

The Evaluation of SD Bioline Strep A Rapid Antigen Test in Acute Pharyngitis in Pediatric Clinics

Sunjoo Kim, M.D.

Department of Laboratory Medicine, Institute of Health Sciences, Gyeongsang National University School of Medicine, Jinju, Korea

Background : Acute pharyngitis is a very common respiratory tract infection. Rapid antigen tests (RATs) that detect group A streptococci (GAS) have an advantage over conventional throat culture in determining the cause of acute pharyngitis quickly. The efficiency of RAT should be good enough to be used in the laboratory or in the clinics.

Methods : From October 2008 through February 2009, throat swabs were taken from 293 children with acute pharyngitis and conveyed to the Gyeongsang National University Hospital in a transport medium. Two swabs from each patient were inoculated onto a blood agar plate, then returned to the transport medium and stored at -20℃ for several months. After the samples were thawed at room temperature, the SD Bioline Strep A RAT (SD, Korea) was performed.

Results : The sensitivity, specificity, positive predictive value, and negative predictive value of SD Bioline Strep A compared with throat culture were 95.9% (95% confidence interval [CI]: 93.6-98.2%), 91.8% (95% CI: 88.5-95.1%), 95.9% (95% CI: 93.6-98.2%), and 91.8% (95% CI: 88.5-95.1%), respectively.

Conclusions : The SD Bioline Strep A RAT kit can be useful as an alternative to throat cultures in the clinics for rapid diagnosis of GAS pharyngitis and for an early decision on the use of antibiotics. *(Korean J Lab Med 2009;29:320-3)*

Key Words : *Streptococcus, Rapid antigen test, Pharyngitis*

INTRODUCTION

Acute respiratory infections comprise almost half of human diseases. Most upper respiratory tract infections are caused by viruses, which commonly give rise to rhinorrhea, coughing, sneezing, and mild cervical lymphadenopathy. Group A streptococci (GAS) is a common cause of pharyngitis, especially in elementary school children, the disease being characterized by more severe cervical lymphadenopathy, high fever, and tonsillar exudate [1, 2]. Factors such as the winter season, acute onset, headache, and abdominal pain support the diagnosis of GAS pharyngitis [1-3]. How-

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Corresponding author : Sunjoo Kim, M.D.
Department of Laboratory Medicine, Gyeongsang National University School of Medicine, 90 Chilam-dong, Jinju 660-702, Korea
Tel : +82-55-750-8239, Fax : +82-55-762-2696
E-mail : sjkim8239@hanmail.net

ever, it is difficult to differentiate GAS pharyngitis from viral pharyngitis solely on the basis of clinical manifestations.

Most children with acute pharyngitis visit pediatric clinics, where the disease is diagnosed and treated on the basis of experience and clinical features. Antibiotics are commonly prescribed without identifying the etiologic agent. However, antibiotics should be given only for bacterial pharyngitis [2] to avoid resistance problems as well as higher medical costs; therefore, accurate diagnosis is essential. Although throat culture is the gold standard to confirm GAS pharyngitis, it requires equipment and tools rarely available in a pediatric clinic.

The recently developed rapid antigen test (RAT) using immunochromatography [4] is fast and easy to perform, does not require any special equipment, and gives objective results. In developed countries, RATs have been used for several decades; however, the RATs have a lower sensitivity compared with bacterial culture [5]. We evaluated the performance of the SD Bioline Strep A RAT (SD, Yongin, Korea) for the diagnosis of acute pharyngitis in pediatric clinics.

MATERIALS AND METHODS

Four pediatric clinics and six pediatricians participated in this study from October 2008 through February 2009. Two hundred ninety-three children (boys 162, girls 131) were included. The parents or guardians were given an explanation of the test and agreed to the study.

When the physicians suspected bacterial pharyngitis on the basis of the symptoms or signs, they took two swabs from both tonsils, put them into a transport medium (Asan Pharm, Seoul, Korea), and stored them in a refrigerator in the clinic. The samples were moved to the microbiology laboratory at Gyeongsang National University Hospital every other day and were inoculated onto blood agar plates (BAP). A bacitracin disk (0.04 U) was placed on the site of primary inoculation [6], and the BAP was kept in a 35℃ incubator in room air overnight. The small colonies producing beta-hemolysis and being inhibited by bacitracin disk were subjected to the latex agglutination test using Seroiden Strepto Kit (Eiken, Tokyo, Japan) to confirm the identification. The swabs were returned to the transport medium and stored at −20℃ for several months. Once they were thawed at room temperature, the SD Bioline Strep A RAT was performed according to the manufacturer's manual, and the findings were compared with the culture results.

All strips showed a color change for the control. Color changes in both the test and the control were interpreted as positive for GAS, whereas a color change only in the control was regarded as negative. A weak color change was regarded as positive.

Table 1. Comparison of SD Bioline Strep A Rapid Ag Test with throat culture

Throat culture	SD Bioline Strep A		
	Positive	Negative	Total
GAS positive	187	8	195
GAS negative	8	90	98
Total	195	98	293

Abbreviation: GAS, group A streptococci.

RESULTS

Of 293 samples, 195 were positive for both throat culture and RAT (Table 1). The sensitivity, specificity, positive predictive value, and negative predictive value of the SD Bioline Strep A were 95.9% (95% confidence interval [CI]: 93.6-98.2%), 91.8% (95% CI: 88.5-95.1%), 95.9% (95% CI: 93.6-98.2%), and 91.8% (95% CI: 88.5-95.1%), respectively (Fig. 1). Nine samples gave a weak color change with SD Bioline Strep A RAT.

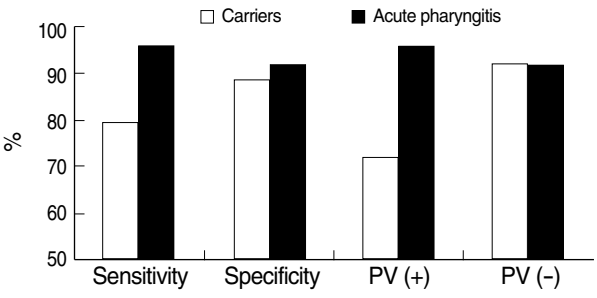

Fig. 1. Comparison of performance of SD Bioline Strep A between carriers and patients with acute pharyngitis. PV (+), positive predicitve value; PV (-), negative predictive value.

DISCUSSION

Bacterial pharyngitis is a concern especially in school children. That caused by GAS may lead to serious complications, such as para-tonsillar abscess, scarlet fever, rheumatic fever, and post-streptococcal glomerulonephritis [1, 2]. To avoid the complications of GAS pharyngitis and the spread of the bacteria, antibiotics may be used. However, such use must be highly selective, because misuse or overuse causes antibiotic resistance and higher medical costs. For example, in 2002, the rate of resistance of GAS to erythromycin and clindamycin was 51% and 36%, respectively, in Jinju, Korea [7].

To confirm GAS pharyngitis, throat culture is widely accepted as the gold standard. However, this method requires microbiological knowledge and experience, and it would not be easy to set up the necessary facilities in a small clinic. The most significant drawback, however, is the turnaround time; it takes one to two days to get the result, requiring the patient to visit the clinic again. It therefore is common to prescribe a few days of antibiotics until the results are available.

The recently developed RAT is useful in confirming GAS pharyngitis in clinics, as it does not require any special facilities, is easy to perform, and yields results within 10-15 min. The American Academy of Pediatrics recommends the RAT as a screening test for bacterial pharyngitis, with backup culture for patients with a negative RAT result [3].

Generally, RAT has a lower sensitivity (60-90%) compared with culture [5, 6]. A larger inoculum might be needed to get a positive result in RAT. In one experiment, for example, RAT gave a positive result only with an inoculum of 10^5/mL or more. Rarely, GAS produces alpha-rather than beta-hemolysis [8], so it is possible to get an erroneous result. Also, the *Streptococcus milleri* group that expresses the group A carbohydrate can produce false-positive results [8, 9]. The beta-hemolytic colonies of *S. milleri* group, group C, or group G streptococci can be inhibited by bacitracin [4]. A latex agglutination test to confirm GAS is recommended to reduce false-negative results. A final concern is that when the laboratory technicians do not have enough experience to spread culture samples correctly with a loop, beta-hemolytic colonies can be masked with abundant normal throat flora [6]. We need to find out more about the causes of discrepancy in results between RAT and bacterial culture.

The performance of the SD Bioline Strep A RAT for school children who carry GAS without symptoms or signs was reported in 2007 [10]. It is widely accepted that the carriers have fewer colonies than the patients with acute pharyngitis [1, 2]. The sensitivities were 79.3% for the carriers and 79.3% for acute pharyngitis group (χ^2 test, $P<0.05$) (Table 1). Positive predictive values showed a significant difference between the two groups (72.2% vs. 95.9%; χ^2 test, $P<0.05$). The RAT for the schoolchildren was performed directly at the classroom, whereas RAT for the patients was carried out later after storage of the swabs in the freezer in a transport medium. Nevertheless, vague or weak color change in the test strip was rare. Bacterial culture and identification was done by the same method in the two studies. As the culture-negative samples had been collected in the middle of the study, the positive samples outnumbered the negative ones. Different throat swab techniques or selection bias at each clinic might have affected the results.

The swabs stored in the transport medium seem to be adequate for the RAT. Therefore, if the test cannot be carried out on the site, it is recommended that the sample be put in a transport medium to prevent its drying out. The medium itself does not seem to affect the RAT result.

Use of the RAT should be restricted only when bacterial pharyngitis is highly suspected; otherwise, low sensitivity and unnecessary backup culture could occur [11]. Centor and colleagues [1] suggested four criteria for GAS pharyngitis: fever, anterior cervical lymphadenopathy, tonsillar rubor and exudate, and absence of cough. Education in the techniques or procedures of either throat culture or RAT is needed for successful performance [6, 12]. To know the microbiological or epidemiological characteristics of GAS in the region, bacterial culture is mandatory.

In conclusion, SD Bioline Strep A RAT showed excellent performance compared with bacterial culture in acute pharyngitis. The results of this study showed a significant im-

provement compared with the previous one, which was executed for carriers among school children. As false-positive or false-negative results were rare, the SD Bioline Strep A RAT can be used as an alternative to bacterial culture, especially in the pediatric clinic setting. The cost of antibiotics will surpass that of RAT, encouraging its use and possibly reducing a serious antibiotic resistance if empirical antibiotic is not routinely given.

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