The Efficacy and Safety of Rapid Antigen Detection Test in Adults: A Retrospective Study

Erişkinlerde Hızlı Antijen Testinin Etkinliği ve Güvenirliği: Retrospektif Bir Çalışma

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ABSTRACT

Aim: Acute respiratory infections are one of the diseases in which antibiotics are inappropriately used. Our study aim was to define the efficacy and safety of the rapid antigen detection test in decreasing the inappropriate use of antibiotics in adults.

Methods: This was a retrospective study on patients over 15 years of age who came to our clinic because of sore throat from September 2016 to 2017. Data on culture, rapid antigen detection test results, and the prescribed drugs were recorded from their files and were expressed as frequencies. Statistical analyses were performed by the Chi-square test and Student's t-test, with $p < 0.05$ accepted as statistically significant.

Results: Among a total of 2426 patients, the rapid antigen detection test and culture results had a perfect fit ($\kappa=0.911$) and had no statistically significant differences ($p=0.125$). Using culture as the standard, the rapid antigen detection test had a sensitivity of 86.4%, specificity of 99.9%, positive predictive value of 97.4%, negative predictive value of 99.2%, and correct awareness rate of 99.1%.

Conclusion: The use of rapid antigen detection test in cases with pharyngitis could make antibiotic prescription safe and appropriate.

Keywords: respiratory tract infections, antibiotics, antibacterial drug resistance

ÖZET

Amaç: Akut solunum yolu enfeksiyonları, antibiyotiklerin uygunsuz şekilde kullanıldığı hastalıklardan biridir. Çalışmamızın amacı, yetişkinlerde uygun olmayan antibiyotik kullanımını azaltmada hızlı antijen saptama testinin etkinliğini ve güvenilirliğini araştırmaktır.

Yöntem: Bu çalışma Eylül 2016- 2017 tarihleri arasında kliniğimize boğaz ağrısı nedeniyle gelen 15 yaş üstü hastaların retrospektif olarak tarandığı bir çalışmadır. Kültür, hızlı antijen tespit testi sonuçları ve reçete edilen ilaçlarla ilgili veriler dosyalarından kaydedildi. Gerekli olan istatistiksel analizler yapıldı (Ki-kare testi ve Student's t-testi). $p<0,05$ istatistiksel olarak anlamlı kabul edildi.

Bulgular: Toplam 2426 hasta arasında hızlı antijen tespit testi ve kültür sonuçları mükemmel uyum sağlamış ($\kappa=0,911$) ve istatistiksel olarak anlamlı fark ($p=0,125$) göstermedi. Hızlı antijen tespit testinin duyarlılığı %86,4, özgüllüğü %99,9, pozitif prediktif değeri %97,4, negatif prediktif değeri %99,2 ve doğru farkındalık oranı %99,1 idi.

Sonuç: Boğaz ağrısı ile gelen olgularda hızlı antijen tespit testinin kullanımı ve sonuca göre antibiyotik reçetelemesi uygunsuz antibiyotik kullanımını azaltacaktır.

Anahtar kelimeler: solunum yolu enfeksiyonları, antibiyotikler, antibakteriyel ilaç direnci

Introduction

Anti-microbial resistance (AMR) is the ability of microorganisms, such as bacteria, viruses and some parasites to stop an antimicrobial, such as antibiotics, anti-virals and anti-malarials from working against them. As a result, standard treatments become ineffective and infections can persist and spread to others (1). Inappropriate antibiotic use is one of the reasons for developing AMR.

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Acute respiratory infection (ARIs), which is most commonly caused by viruses, is one of the diagnoses for which antibiotics are inappropriately used (2). For example, pharyngitis is mostly caused by viruses and only 5% to 10% are caused by Group A beta-hemolytic streptococcus (GAS). Majority of ARIs are treated at primary care centers (3). According to the Centers for Disease Control and Prevention treatment guidelines for ARI, patients who meet two or more Centor criteria (e.g., fever, tonsillar exudates, tender cervical lymphadenopathy and absence of cough) should undergo a rapid antigen detection test (RADT). Antibiotic treatment is not recommended for patients with negative RADT results (4). In our daily practice, false-negative or false-positive test results can sometimes occur.

Our study aim was to define the efficacy and safety of RADT in adults.

Methods

Patients more than 15 years old who came to our clinic from September 2016 to 2017 for sore throat were included in this retrospective study. According to our clinical procedures, only the patients who fulfilled two or more Centor criteria were simultaneously cultured and tested by RADT. Data on culture, RADT results and the prescribed drugs were recorded by scanning the files retrospectively. A total of 2426 patients with sore throat came to our polyclinics between September 2016 and 2017 (Fig. 1); 1242 (51.2%) were men and the mean age was 34.40 ± 15.6 years (range, 15–92 years).

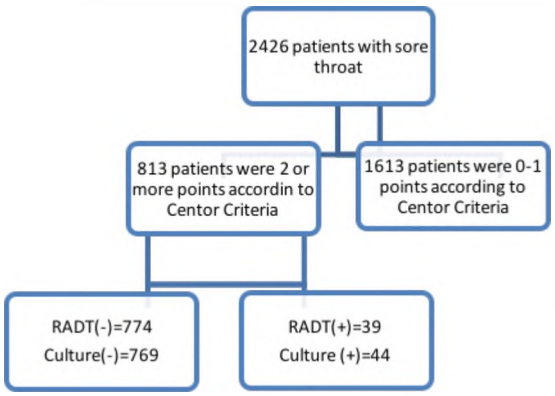

Figure 1. Study design

The socio-demographic features of the study group are shown in Table 1. According to the Centor criteria, 71.8% (n=1613) of the patients scored 0, 1 and were treated as viral infection, whereas 28.2% (n=813) underwent simultaneous culture and RADT. Of the 2426 patients, only 1.6% (n=39) were RADT-positive and 1.81% (n=44) were culture-positive.

The study was approved by the ethics committee of Sisli Hamidiye Etfal Training and Research Hospital on 3th October 2017 (Number:1700).

Table 1. Sociodemographic features of patients and associations between RADT and Culture

	n	%	RAD		p	Culture		p
			+ n (%)	- n (%)		+ n (%)	– n (%)	
Age groups								
15–19	119	14.6	5 (%4)	116 (% 96)		5 (%4)	114 (% 96)	
20–34	514	63.2	15 (%3)	499 (%97)	<0.001	16 (%3)	498 (%97)	<0.001
35–49	139	17.1	15 (%11)	124 (%89)		16 (%12)	123 (%88)	
50–64	41	5.0	6 (%15)	35 (%85)		7 (%17)	34 (%83)	
Gender								
Men	601	73.9	20 (%3)	581 (%97)	0.001	22 (%4)	579 (% 96)	<0.001
Women	212	26.1	19 (%9)	193 (%91)		22 (%10)	190 (%90)	

Measures

Centor criteria: The Centor criteria were developed to trace patients with streptococcal tonsillitis and comprise fever, tonsillar exudate, tender cervical nodes and absence of cough (5). Patients who score 0–1 points are diagnosed to have viral pharyngitis, whereas those who score 2 or more points are recommended to undergo RADT to determine the need for drug therapy.

Rapid Antigen Detection Test: Rapid antigen testing to detect GAS infection provides important information for decision-making on antibiotic use for patients with acute pharyngitis. The Infectious Diseases Society of America guidelines on streptococcal pharyngitis recommended using a rapid test in patients with a modest probability of GAS infection (6). Antibiotics are prescribed to those with a positive rapid test and withheld in those with negative rapid test.

Culture: Throat swab samples were submitted to our laboratory for culture. Samples were seeded on a blood agar plate and incubated at 37 °C in a 5% CO_2 atmosphere for 48 hours. Culture growth of any number of beta-haemolytic colonies was considered positive for group A beta-haemolytic streptococcus (GABHS).

Statistical analyses were performed using SPSS software version 20 (IBM SPSS, Chicago, IL, USA). Aside from the socio-demographic features, such as age and gender, results of RADT and culture and treatments were recorded. Frequencies were calculated. Chi-square and Student's t-tests were used and $p < 0.05$ was accepted as statistically significant.

Results

Among the 813 patients who underwent simultaneous culture and RADT, the mean age was 27.8 ± 10 years (range, 15–63 years). The associations of the socio-demographic features of the patients with the RADT and culture results are shown in Table 1. Female gender and the age group 35–49 years were significantly associated with RADT and culture positivity ($p<0.001$).

As shown in Table 2, there was a perfect fit between the rapid test and the culture results ($\kappa=0.911$). There was no statistically significant difference between the rapid test and the culture results ($p=0.125$). Using culture as the standard, the RADT had a sensitivity of 86.4%, specificity of 99.9%, positive predictive value of 97.4%, negative predictive value of 99.2%, and correct awareness rate of 99.1%.

Table 2. The relation between Culture and RADT

			Culture		
			Negative	Positive	Total
RADT	Negative	n	768	6	774
		%	99.2	0.8	100
	Positive	n	1	38	39
		%	2.6	97.4	100
	Total	n	769	44	813
		%	94.5	5.5	100

A total of 9.3% (n=76) of patients were prescribed antibiotics according to the RADT and culture results (Table 3). Of these, 6.6% (n=51) were prescribed antibiotics, most commonly amoxicillin/clavulanate, despite RADT negativity, and 35.9% (n=14) were not prescribed antibiotics despite RADT positivity. Similarly, 6.5% (n=50) were prescribed antibiotics, most commonly amoxicillin/clavulanate, despite culture negativity and 40.9% (n=18) were not prescribed antibiotics despite culture positivity. There were 6.5% (n=50) patients who were prescribed antibiotics despite negative RADT and culture results (i.e., inappropriate antibiotic use). The most commonly prescribed antibiotics were trimethoprim/sulfamethoxazole at 45.5% (n=20) for culture-positive cases and penicillin at 48.7% (n=19) for RADT-positive cases.

Discussion

About 80% of cases with sore throat are diagnosed in the primary care setting (7); and most of them are caused by viruses. In adults, GABHS infection accounts for approximately 5% to 15% (8); in this study, GABHS infection was detected 1.85%. In general, antibiotics are overprescribed for pharyngitis, which is commonly caused by viruses. In Turkey, according to the Prescription Information System,

Table 3. The prescribed antibiotics according to RADT results and culture

Antibiotic	RADT				p	Culture				p
	Negative		Positive			Negative		Positive		
	n	%	n	%		n	%	n	%	
None	723	93.4	14	35.9	<0.001	719	93.5	18	40.9	<0.001
Amoxicillin/ Clavulanate	28	3.6	6	15.4		28	3.7	6	13.6	
Trimethoprim-sulfamethoxazole	18	2.4	0	0.0		1	0.1	20	45.5	
Penicillin	2	0.3	19	48.7		1	0.1	0	0.0	
Macrolides	1	0.1	0	0.0		18	2.4	0	0.0	
Cephalosporin	1	0.1	0	0.0		1	0.1	0	0.0	
Amoxicillin	1	0.1	0	0.0		1	0.1	0	0.0	

55.51% of patients are prescribed antibiotics for pharyngitis. Similarly, in Europe, most antibiotics continue to be prescribed in the primary care setting and mainly for patients with ARIs (9). Even among experienced physicians, not more than 75% of the cases can be accurately diagnosed as streptococcal pharyngitis based on clinical findings alone (10). Therefore, both clinical criteria and diagnostic tests should be used.

Throat culture has a sensitivity of 90% to 95% in diagnosing GABHS infections, whereas lateral flow RADT has a wide variability in sensitivity (59% to 96%) (6). Optical immunoassays are 86% sensitive for diagnoses and molecular RADT models are even more sensitive (89% to 96%) in children (11). In our study, there was a perfect fit between the rapid test and the culture results ($\kappa = 0.911$). There was no statistically significant difference between the rapid test and culture results ($p = 0.125$). The sensitivity of the rapid test, using culture as the gold standard, was 86.4% in our study. In some studies, the high specificity (>95%) of RADT decreases the probability of obtaining false-positive results (12–14). The good diagnostic performance of RADT in this study implied that the prescription of antibiotics for RADT-positive cases were appropriate. These results were consistent with the results of a clinical trial, which found that the use of the RADT in primary care offices was associated with a significant reduction in the prescription of antibiotics among adults with a clinical diagnosis of acute pharyngitis (15). However, some cases with negative RADT may have positive culture results. In this situation, there was a question about this may cause or increase complications. One study showed that there were no differences among cases that were given immediate, delayed and no antibiotics for several symptoms and complications (16). Therefore, waiting for the culture result does not increase complications; moreover, antimicrobial therapy should be prescribed only for proven cases of GAS pharyngitis because of the generally increasing rate of resistance to antibiotics (17).

Patients with acute GAS pharyngitis should be treated with an appropriate antibiotic at an appropriate dose for a duration (usually 10 days) that is likely to eradicate the organism from the pharynx. The choice of antibiotic should be based on a narrow spectrum of activity, infrequent adverse reactions and modest cost (18). According to a Cochrane study, the first drug of choice remains to be penicillin (19), probably because β-lactam antibiotic resistance has not been reported (20). In our study, the trend for the most commonly prescribed antibiotics according to RADT and culture results implied that there remains inappropriate antibiotic use. The rate of inappropriate antibiotic use for pharyngitis in primary care was reported to be 14.7% in Iceland, 5.7% in Denmark (21) and 6.5% in our study. This may be because our clinic was in a training and research hospital, where educations are held about daily practice and the Centor criteria are applied using a computer program.

There remains considerable misuse of antibiotics. The reasons for prescribing inappropriate antibiotics for sore throat could be uncertainty about the microbial

etiology, influence of patient demand and other non-clinical factors (21). According to a study, limited time, poor doctor-patient communication and diagnostic uncertainty were major causes of inappropriate antibiotic use in ARIs (22). We suggest the use of the Centor criteria and RADT for diagnosis, an application to policlinic computer program that remember the Centor criteria and test and educations post graduate and in university training programs about antibiotic resistance and inappropriate antibiotic.

Inappropriate antibiotic prescription is not solely because of doctors, but also of patient knowledge on antibiotics and ARIs. In a study, the main reason of patients for expecting antibiotic prescriptions was the belief that antibiotics are effective for the common cold or influenza and that antibiotics can shorten the duration and prevent deterioration of their illness (23). Educational programs must be held in order to break these incorrect perceptions.

Conclusion

The rapid test had a perfect fit with the culture results, with sensitivity of 86.4%, specificity of 99.9%, positive predictive value of 97.4%, negative predictive value of 99.2%, and correct awareness rate of 99.1%. The use of computer applications and training the physicians about the Centor criteria and RADT for pharyngitis could reduce the rate of antibiotic prescription. Informing patients by media about inappropriate antibiotic use may reduce AMR.

Conflict of Interest

No conflict of interest was declared by the authors.

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