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The Importance of Rapid Antigen Testing for Group A Streptococcal Tonsillopharyngitis: A Single Center Experience

Grup A Streptokok Tonsillofarenjitinde Strep A Hızlı Antijen Testinin Önemi: Tek Merkez Deneyimi

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Abstract

Objective: Acute tonsillopharyngitis is one of the most common cause of admission to the pediatric emergency departments. Most of the acute tonsillopharyngitis is due to viral causes and 20-30% is bacterial origin. Bacterial agents are most commonly group A beta-hemolytic streptococcus (GAS). Diagnosis of GAS tonsillopharyngitis is accelerated by the use of rapid antigen detection test (RADT) as well as the gold standard is throat culture. We planned our study to share our clinical experience in GAS tonsillopharyngitis and to discuss the benefits of RADT in the context of the literature.

Material and Methods: We retrospectively reviewed the patients between the ages of 1 month and 18 years who were diagnosed acute tonsillopharyngitis between November 2014 and April 2018 in our hospital. Patients' ages, genders, RADT and throat culture results and also received treatments were recorded.

Results: In our pediatric emergency department, during 46 month period RADTs and throat cultures were taken from 22.445 patients which considered bacterial tonsillopharyngitis. 24.9% (n: 5591) of the sample were GAS positive. The mean age of the patients was 8.3 ± 3.22 years and 44.4% (n: 2487) were girls. RADT was positive in 98.5% (n: 5511) of patients infected with GAS and 1.4% (n: 80) of RADT was negative but throat culture was positive and antibiotherapy was applied. In 1.4% (n: 316) of the patients who underwent throat swabs, throat culture was negative while RADT was positive. In this group of patients, RADT was considered to be false positive.

Öz

Giriş: Çocuk acil polikliniklerine en sık başvuru nedenleri arasında akut tonsillofarenjit yer almaktadır. Akut tonsillofarenjitlerin çoğu viral nedenlere bağlı olup %20-30'u bakteriyel kaynaklıdır. Bakteriyel etkenler arasında ise en sık A grubu beta-hemolitik streptokok (GAS)'lara rastlanır. GAS tonsillofarenjiti tanısında altın standart boğaz kültürü olmakla birlikte hızlı antijen testi (HAT) kullanımı sayesinde tanı koyabilme süreci hızlanmaktadır. Çalışmamızı GAS tonsillofarenjitinde klinik deneyimlerimizi paylaşmak ve HAT'ın sağladığı faydaları literatür eşliğinde tartışma amacıyla planladık.

Gereç ve Yöntemler: Hastanemizde Kasım 2014-Nisan 2018 tarihleri arasında akut tonsillofarenjit tanısı alan 1 ay-18 yaş arasındaki hastalar retrospektif olarak incelendi. Hastaların yaşları, cinsiyetleri, HAT ve boğaz kültür sonuçları ile aldıkları tedaviler kaydedildi.

Bulgular: Çocuk acil polikliniğimizde 46 ay boyunca 22.445 hastadan bakteriyel tonsillofarenjit düşünülerek HAT ve boğaz kültürü alındı. Örnek alınanların %24.9 (n: 5591)'u GAS pozitifti. Hastaların yaş ortalaması 8.3 ± 3.22 yıldı ve %44.4 (n: 2487)'ü kızdı. GAS ile enfekte hastaların %98.5 (n: 5511)'inde HAT pozitif, %1.4 (n: 80)'ünde HAT negatif fakat boğaz kültürü pozitif olarak sonuçlanıp antibiyoterapi uygulandı. Boğaz sürüntüsü alınan hastaların %1.4 (n: 316)'ünde ise HAT pozitif iken boğaz kültürü negatifti. Bu grup hastalarda ise HAT'ın yanlış pozitif sonuçlandığı kabul edildi.

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Conclusion: Application of antibiotherapy to unproven acute tonsillopharyngitis cases with bacterial etiology increases antibiotic resistance. The clinic should be supported by diagnostic laboratory methods in patients who are compatible with bacterial tonsillopharyngitis to prevent the misuse of unnecessary antibiotics. The widespread use of RADTs with higher sensitivity and specificity rates, which produce faster results than throat cultures, will greatly contribute to the rational use of antibiotics.

Keywords: Group A streptococcus, rapid antigen detection test, tonsillitis

Sonuç: Bakteriyel etkene bağlı olduğu kanıtlanmamış akut tonsillofarenjit olgularında antibiyoterapi uygulanması antibiyotik direncini artırmaktadır. Gereksiz antibiyotik kullanımını önleyebilmek için kliniği bakteriyel tonsillofarenjit ile uyumlu olan hastalarda tanı laboratuvar yöntemleri ile desteklenmelidir. Boğaz kültürüne göre daha çabuk sonuç veren, yüksek duyarlılık ve özgüllük oranlarına sahip HAT'ların yaygınlaşması akılcı antibiyotik kullanımına büyük katkı sağlayacaktır.

Anahtar Terimler: Grup A streptokok, hızlı antijen testi, tonsillit

Introduction

Acute tonsillopharyngitis is one of the most common causes seen in pediatric emergency polyclinics. Most of the acute tonsillopharyngitis is due to viral causes and 20-30% is bacterial. Prescription of antibiotics according to clinical findings without the support of the bacterial tonsillopharyngitis by the laboratory causes inappropriate use of antibiotics and increased antibiotic resistance in society. Among bacterial agents, group A beta hemolytic streptococci (GAS) is the most common agent (1-3).

More than 10 clinical scoring systems have been developed to detect GAS pharyngitis; however, even for the patients with all features of these scoring, streptococcal pharyngitis is only found in 35-50% (4,5). GAS is the gold standard throat culture in the diagnosis of tonsillopharyngitis. However, considering the time taken to result in throat culture, the use of Strep A rapid antigen test (RADT) with high sensitivity and specificity provides advantages in terms of rapid diagnosis. It will be possible to apply early diagnosis and treatment in GAS tonsillopharyngitis especially with the extension of RADTs starting from the first level health institutions (6,7).

We planned this study to share our clinical experience in GAS tonsillopharyngitis and to discuss the benefits of RAT in the light of literature.

Materials and Methods

We have started to use RAT in the diagnosis of bacterial tonsillopharyngitis since November, 2014 upon the suggestion of the Antibiotic Control Committee in our clinic SBU Sisli Hamidiye Etfal Training and Research Hospital. Between November 2014 and April 2018, the patients between the ages of 1 month and 18 years with sore throat, fever, hyperemia or exudate in tonsils, headache, nausea, vomiting, abdominal pain, petechial rashes in the soft palate, whose throat culture and RADT were sampled, were examined retrospectively. The information of age and gender and the results of the RADT and throat culture of the patients were recorded according to the patient files. If the patient with findings consistent with tonsillopharyngitis below 3 years of age have a brother diagnosed with GAS tonsillopharyngitis at home, if the patient regularly goes to nursery school or has risk factors such as GAS tonsillopharyngitis in the nursery school, as suggested by the United States Disease Protection and Control Center (CDC), the throat culture of the patient was sampled (1). Patients were divided into four groups according to their age in order to examine the age distribution of GAS tonsillopharyngitis. The first group consisted of patients aged between 1 and 3 years, the second group was 3-5 years, the third group was 5-15 years and the fourth group consisted of 15-18 years. To determine the seasonal distribution of GAS infection, the admission times of the patients who were positive for RADT or throat culture were evaluated. The distribution of RADT and throat culture results was examined by years.

Double culture bars were used in order to obtain RADT and throat culture in a single time and to detect the sensitivity of RADT. Throat swabs were taken from both tonsil and posterior pharyngeal walls as recommended in the guidelines (1). For the detection of GAS antigen from throat swab samples during the study period, QuickVue + Strep A Test (Quidel Corporation, USA) based on lateral-flow immunoassay at different periods, Mascia Brunelli Strep A Card (Mascia Brunelli Spa, Italy), Bionexia Strep-A Plus (BioMérieux, France) or BD Veritor™ System (USA) LINES were used. The sensitivity, specificity, negative predictive values (NPV) and positive predictive values (PPD) of RADTs were examined. Simultaneously, sheep blood agar culturing for throat culture was performed in the Clinical Microbiology Laboratory. The culture plates were evaluated after 24-48 hours incubation for the beta hemolytic colony.

Single dose of benzatin penicillin G, one of the antibiotics recommended by the guidelines as a first choice for patients who had positive results of RAT, was administered 600.000 units to patients below 27 kg and 1.200.000 units to patients over 27 kg in the way of intramuscular (IM). For this purpose, IM benzathine penicillin receiving was maintained in our hospital pharmacy. In cases where the family does not accept parenteral antibiotherapy, oral penicillin V (250 mg in children, two or three doses; four doses of 250 mg in adolescents or 500 mg as two doses, 10 days) or oral amoxicillin 50 mg/kg/day (10 days,

max. 1000 mg/day) was started; and oral azithromycin (12 mg/kg/day, max. 500 mg, 5 days) or oral clarithromycin (15 mg/kg/day, 2 doses, 10 days) was started in the patients whose family declared penicillin allergy presence. Prescriptions of patients who received oral antibiotics could not be evaluated because the e-prescription system was not used in emergency services. Parenteral treatment application data were not available before April 2016 due to changes in the data processing system. Therefore, parenteral treatment application rates between April 2016 and April 2018 were examined.

Patients with negative results of RADT were called for polyclinic control after 48 hours and their throat culture results were evaluated. Antibiotics were administered to those with positive throat culture. The relatives of the patients who expressed that they could not come to the hospital were directed to the family health centers to which they were connected, in order to arrange their treatment.

Physicians working in our emergency polyclinics were trained regularly by our hospital's Antibiotic Control Committee to ensure the initiation of antibiotics in GAS tonsillopharyngitis, which was confirmed only by RADT or throat culture in the diagnosis of acute tonsillopharyngitis. Our clinical experience with the use of tests was discussed at our regular emergency service meetings every morning.

Ethics committee approval was obtained from the Ethics Committee of the Faculty of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital (Resolution No: 1041).

Results

124.9% of the 22.445 patients between the ages of 1 month and 18 years, who consulted to our emergency service from the date of November, 2014 in which the RADT was started to be applied in our hospital to the date of April, 2018, whose throat swab was sampled was diagnosed with GAS tonsillopharyngitis based on the (n: 5591) RADT and/or throat culture. The mean age of the patients was 8.3 ± 3.22 years and 44.4% (n: 2487) were female. 84.8% (n: 4742) of patients diagnosed with GAS tonsillopharyngitis was between the ages of 5 and 15 years, 9.5% (n: 535) was between 3-5 years, 3.1% (n: 178) was between 15-18 years and 2.4% (n: 136) was between 1 month-3 years. Distribution by age groups is shown in Figure 1. When the application times were examined seasonally, 35.9% (n: 2010) was in spring, 28.4% (n: 1590) was in winter, 24% (n: 1344) was in autumn and 11.5% (n: 647) was in summer. The distribution of RADT and throat culture results by years is shown in Table 1.

GAS tonsillopharyngitis was determined by RADT in 98.5% (n: 5511) of the patients and their treatments were regulated. In 1.4% (n: 80) of the patients with negative RADT, the throat culture was positive. RADTs of these patients were evaluated as false negative and their treatments were arranged according to the culture results. In 1.4% (n: 316) of the patients whose throat swab was sampled, the RADT was positive while the throat culture was negative. In this group of patients, RADT was considered to be false positive.

The sensitivity, specificity, NPD and PPD of different rapid antigen tests used at different periods during four years in the Clinical Microbiology Laboratory of our hospital are shown in Table 2. The test with the highest sensitivity was the BD Veritor System (98%) and the tests with the highest specificity were Mascia Brunelli Spa and Bionexia Strep A (100%).

Between April 2016 and April 2018, 30.8% of patients (n: 1457) took IM benzatin penicillin. No side effects were observed in any of the patients.

Discussion

GAS tonsillopharyngitis often presents with fever, sore throat, difficulty in swallowing, tenderness in the anterior cervical lymph nodes, growth in tonsils with pharyngeal erythema and/or exudates in children aged 5-15 years. This case may be accompanied by abdominal pain, headache, nausea and vomiting in children (7-9). GAS tonsillopharyngitis is frequently seen in winter and early spring months. In our study, we found that GAS tonsillopharyngitis is most frequently observed in the 5-15 age range (84.8%) and in spring months (35.9%) in accordance

Table 1. Between November 2014 and April 2018, RADT and throat culture rates obtained from patients with possible GAS tonsillopharyngitis in our Pediatric Emergency Clinic

Date	Number of RADT and throat cultures	Patients with < positive RADT (%)	Patients with positive throat culture (%)
November 2014-November 2015	4903	860 (17.5)	756 (15.4)
November 2015-November 2016	6604	1392 (21)	1299 (19.6)
November 2016-November 2017	7703	2672 (34.6)	2611 (33.8)
November 2017-April 2018	3235	903 (27.9)	925 (28.5)
Total	22445	5827 (25.9)	5591 (24.9)

RADT: Rapid antigen testing.

Table 2. Properties of rapid antigen tests used in our Clinical Microbiology Laboratory

	QuickVue + Strep A	Mascia Brunelli S.p.a	Bionexia Strep A	BD Veritor System
Sensitivity %	89	75	84	98
Specificity %	99	100	100	99
PPD %	94	100	100	97
NPD %	98	95	98	99
PPD: Positive predictive value, NPD: Negative predictive value.				

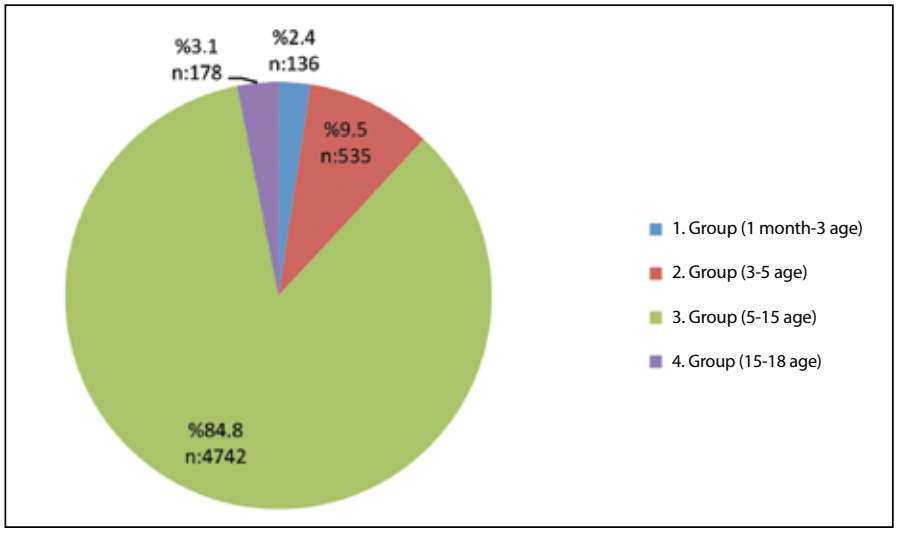


Figure 1. Age distribution of patients with GAS tonsillopharyngitis.

with the literature. When the RADT and throat culture results of the patients diagnosed as GAS tonsillopharyngitis were examined according to years, positive RADT and throat culture results has doubled in the last two years. Although there is no change in the practice or laboratory methods in our hospital, it is thought that we have more cases of bacterial tonsillopharyngitis as a result of the increase in the number of patients who applied to our emergency polyclinics due to the placement of our hospital.

The American Society of Infectious Diseases and the American Academy of Pediatrics recommend that diagnostic tests of GAS tonsillopharyngitis be performed only in patients with risk factors, as the classical findings of streptococcal pharyngitis will not be seen and rheumatic fever is uncommon below the age of three (1,10). In these patients streptococcal pharyngitis is characterized by a table called streptococcosis. Streptococcosis is characterized as a streptococcal infection-induced insidious picture which may last for weeks and is a fulminant in the children bleow the three years of age, which was defined first as "streptococcal fever" in the 1940s. In this age group streptococcal upper respiratory tract infections may be accompanied with mild fever, purulent rhinitis, common cervical lymphadenopathy and otitis media (11,12). In accordance with the recommendations of the CDC, throat swab was only taken if the patient among symptomatic patient group below the age of 3 had a brother with GAS tonsillopharyngitis only at home, if the patient regularly went to the nursery school or if there was epidemic GAS in the nursery school. In our study, we found that GAS tonsillopharyngitis was detected less in our patients below three years of age in compliance with the literature (n: 136, 2.4%).

The diagnosis of GAS tonsillopharyngitis and the initiation of antibiotherapy in the early period is beneficial in preventing the transmission of the disease to others who close contact with the patient and in shortening the period of the patient's complaints (13). The diagnosis of GAS infection should be supported by laboratory in patients whose symptoms and findings support bacterial tonsillopharyngitis. Although throat culture is the standard method in the microbiological diagnosis of GAS tonsillopharyngitis, 24-48 hours are needed for the result. The prolongation of the process may lead to delay in treatment or unnecessary use of antibiotics with the possibility that patients

will not consult for control on time. DATTs which can detect GAS tonsillopharyngitis without waiting for culture result have been used since 1980s (4,14,15). With the fastest antigen tests used today, results can be obtained in a short time such as 5-10 minutes (16). Therefore, we have received RADT and throat culture from 22.445 patients whose clinical findings are compatible with bacterial tonsillopharyngitis in our hospital. We found that the 24.9% (n: 5591) of the patients whose throat swabs were analysed had GAS infection. We identified this diagnosis with a high rate of 98.5% with the help of the RADT applied in the first appliance of the patient. Thus, we did not waste time in the diagnosis of GAS tonsillopharyngitis with a simple test in polyclinic conditions and we could start treatment in a short time via RADT with the high sensitivity rates.

The sensitivity of RADTs used in the diagnosis of GAS tonsillopharyngitis is 65.6-96.4%; and their specificity varies between 68.7-99.3% (17). The sensitivity of the RADTs used in our hospital at different times ranged between 75-98% and their specificity ranged from 99-100%. The false negativity rate is closely related to the RADT sensitivity used. We also evaluated the false negativity rates of RADTs used in our hospital. The RADS was negative in 1.4% of the patients diagnosed with GAS tonsillopharyngitis while the throat culture was positive. For this reason, we also aimed to minimize the false negative RADT rate by verifying the RADTs we received with throat culture.

False positivity in rapid antigen testing may be due to the *Streptococcus milleri* group, GAS nutrient variants, nonbeta-hemolytic variants or cross-reaction with non-live GAS bacteria (18,19). However, most of the false positive GAS results (76%) found in the studies were positive with polymerase chain reaction and showed that false positivity could be caused by bacterial inhibition especially caused by Staphylococcus aurous and RADT specificity was close to 100% (20). In our study, it was observed that the false positivity rate of RADTs used was very low (1.4%), and treatment was started upon the decision with the microbiology laboratory.

Treatment of streptococcal tonsillopharyngitis is important for the prevention of non-suppurative (ARA, glomerulonephritis) and supportive complications (peritonsillar abscess, cervical lymphadenitis, mastoiditis and other invasive infections) of Group A beta hemolytic streptococci (21). Among the complications of GAS tonsillopharyngitis in developing countries, ARA and rheumatic heart diseases affect approximately 20 million people and in the first five decades, they are the leading cause of death due to cardiovascular causes (9,22). The incidence of ARA in our country was 21/100.000 between 2000 and 2009. According to the Jones Criteria revised in 2015 in terms of ARA and rheumatic heart disease, Turkey is classified as mid and high-risk group (23,24). Therefore, it is important to detect and treat GAS tonsillopharyngitis in patients whose clinical findings are compatible with bacterial tonsillopharyngitis, to prevent possible complications and to decrease the incidence of ARA, which continues to be a public health problem in our country. Although the RADts developed in recent years have high sensitivity and specificity rates, the result should be verified with throat culture in order not to miss the patients with GAS infection due to false negative RADT results in intermediate and high-risk populations. The double bars that enable the RADT and throat culture to be taken at the same time are both advantageous in terms of patient comfort and also enable the validation of the RADT performed during the patient's application and the study of the throat culture as a back-up test when the result is negative. We also took the RADT with the throat culture and evaluated the sensitivities of the RADTs we used and increased the rate of diagnosing GAS tonsillopharyngitis.

The antibiotic therapy initiated for eradication of the organism in GAS tonsillopharyngitis should be administered during the recommended time period in the guidelines. Non-suppurtive complications cannot be prevented especially in these applications. Although the guidelines suggest penicillin group antibiotics as the first choice in GAS tonsillopharyngitis, it has been shown that penicillin use rates decreased to 61% today (25,26). Penicillin-resistant GAS has not yet been found. Therefore, penicillin is the first choice antibiotic group in GAS tonsillopharyngitis for patients with no known allergy due to its narrow spectrum of action, low cost and low side effect profile. Controlled studies show that IM depot penicillin is the most effective antimicrobial treatment in preventing the first attack of ARA (1,27). A single dose of IM benzathine penicillin is preferred in the treatment of the patients who are thought not to complete 10-day treatment with oral penicillin group antibiotics (eg, living in crowded environments and with low socioeconomic status). In our clinic, we applied IM benzathine penicillin safely to 30.8% (n: 1457) of the patients and we did not observe any side effects. Since we can easily obtain IM benzahtine penicillin from our hospital pharmacy, we have been able to treat both patients early and prevent possible problems such as the patient's failure to find the drug or not coming back for treatment.

The limitations of our study were the fact that the analyzes were performed in a single center, and in the first years of the study, the rates of treatment in which IM benzathine penicillin was applied could not be reached due to the change in the automation system and the e-prescribing system was not used in the emergency services and the prescriptions of the patients who were given oral antibiotics could not be evaluated.

Conclusion

In cases of acute tonsillopharyngitis which are not proven to be a bacterial agent, antibiotherapy increases the antibiotic resistance. In order to prevent unnecessary use of antibiotics,

the diagnosis should be supported with diagnostic laboratory methods in patients whose clinical findings are compatible with bacterial tonsillopharyngitis. The spread of RADTs with high sensitivity and specificity rates, which provides more rapid results than throat culture, will contribute greatly to rational antibiotic use.

Ethics Committe Approval: Ethics committee approval was obtained from the Ethics Committee of the Faculty of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital (Resolution No: 1041).
Informed Consent: Written informed consent was not obtained due to the retrospective nature of this study.
Peer-review: Externally peer-reviewed.
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Conflict of Interest: The authors have not reported a conflict of interest.
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References

1. *Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, et al. Clinical practice guideline for the diagnosis and management of group a streptococcal pharyngitis: 2012 Update by the Infectious Diseases Society of America. Clin Infect Dis 2012;55:e86-102.*
2. *Brennan-Krohn T, Ozonoff A, Sandora TJ. Adherence to guidelines for testing and treatment of children with pharyngitis: a retrospective study. BMC Pediatr 2018;18:43-50.*
3. *Gözüküçük R, Göçmen İ, Nas Y, Yılmazer F, Ünüvar E. Streptokoksik tonsillofarenjit tanısında strep-a hızlı testinin etkinliği. Çocuk Dergisi 2011;11:157-9.*
4. *Cohen JF, Cohen R, Bidet P, Elbez A, Levy C, Bossuyt PM, et al. Efficiency of a clinical prediction model for selective rapid testing in children with pharyngitis: A prospective, multicenter study. PLoS One 2017;12: e0172871.*
5. *McIsaac WJ, Kellner JD, Aufricht P, Vanjaka A, Low DE. Empirical validation of guidelines for the management of pharyngitis in children and adults. JAMA 2004;291:1587-95.*
6. *Lean WL, Arnup S, Danchin M, Steer AC. Rapid diagnostic tests for group A streptococcal pharyngitis: a meta-analysis. Pediatrics 2014;134:771-81.*
7. *Hersh AL, Jackson MA, Hicks LA; the Committee on Infectious Diseases. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. Pediatrics 2013;132:1146-54.*
8. *Çoban B, Kaplan H, Topal B, Ülkü N. The sensitivity and the specifity of rapid antigen test in group a streptococcal tonsillopharyngitis. J Pediatr Inf 2013;7:143-6.*
9. *Gerber MA, Baltimore RS, Eaton CB, Gewitz M, Rowley AH, Shulman ST, et al. Prevention of rheumatic fever and diagnosis and treatment of acute streptococcal pharyngitis. Circulation 2009;119:1541-51.*
10. *Larry K, Pickering LK, Baker CJ, Kimberlin DW, Long SS. Red Book. 2012 Report of the Committee on Infectious Diseases. Elk Grove Village, IL: American Academy of Pediatrics, 2012.*
11. *Dalgıç N. Streptokokkoz; kimde, ne zaman, nasıl sağaltım? 10. Ulusal Çocuk Enfeksiyon Hastalıkları Kongresi, 5-9 Nisan 2017. Antalya, Türkiye: Kongre Kitabı, 56. Sunum, s.187.*
12. *Akalın F. Acute rheumatic fever new presentations, new opinions. J Pediatr Sci 2010;6:9-19.*
13. *İşli F, Aksoy M, Alkan A, Kara A. Aile hekimliğinde akut tonsillofarenjit tanısında antimikrobiyal ajan tercihi kılavuzlar mı, kişisel tercihler mi? J Pediatr Inf 2017;11:15-18.*
14. *Sayğılı N, Bulut E, Deniz R, Dalgıç N, Aktaş E. Boğaz sürüntü örneklerinde A grubu beta-hemolitik streptokokların belirlenmesinde Bionexia Strep A Plus hızlı antijen testinin kullanımı. Türk Mikrobiyol Cem Derg 2017;47:138-45.*
15. *Vaz LE, Kleinman KP, Raebel MA, Nordin JD, Lakoma MD, Dutta-Linn MM, et al. Recent trends in outpatient antibiotic use in children. Pediatrics 2014;133:375-85.*
16. *Cohen JF, Bertille N, Cohen R, Chalumeau M. Rapid antigen detection test for group A streptococcus in children with pharyngitis. Cochrane Database Syst Rev 2016;7:1-391.*
17. *Ruiz-Aragón J, Rodríguez López R, Molina Linde JM. Evaluation of rapid methods for detecting Streptococcuspyogenes. Systematic review and meta-analysis. An Pediatr (Barc) 2010;72:391-402.*
18. *Rubin LG, Kahn RA, Vellozzi EM, Isenberg HD. False positive detection of group A Streptococcus antigen resulting from cross-reacting Streptococcus intermedius (Streptococcus milleri group). Pediatr Infect Dis J 1996;15:715-7.*
19. *Johnson DR, Kaplan EL. False-positive rapid antigen detection test results: reduced specificity in the absence of group A Streptococci in the upper respiratory tract. J Infect Dis 2001;183:1135-7.*
20. *Cohen JF, Cohen R, Bidet P, Levy C, Deberdt P, d'Humières C, et al. Rapid-antigen detection tests for group a streptococcal pharyngitis: revisiting false-positive results using polymerase chain reaction testing. J Pediatr 2013;162:1282-4.*
21. *Cohen JF, Cohen R, Levy C, Thollot F, Benani M, Bidet P, et al. Selective testing strategies for diagnosing group A streptococcal infection in children with pharyngitis: a systematic review and prospective multicentre external validation study. CMAJ 2015;187:23-32.*
22. *Gewitz MH, Baltimore RS, Tani LY, Sable CA, Shulman ST, Carapetis J, et al. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of doppler echocardiography a scientific statement from the American Heart Association. Circulation 2015;131:1806-18.*
23. *Orün UA, Ceylan O, Bilici M, Karademir S, Ocal B, Senocak F, et al. Acute rheumatic fever in the Central Anatolia Region of Turkey: a 30-year experience in a single center. Eur J Pediatr 2012;171:361-8.*
24. *Eroğlu AG. Akut romatizmal ateş tanısında güncelleme: 2015 Jones ölçütleri. Turk Pediatri Ars 2016;51:1-7.*
25. *Norton LE, Lee BR, Harte L, Mann K, Newland JG, Grimes RA, et al. Improving guideline-based streptococcal pharyngitis testing: a quality ımprovement ınitiative. Pediatrics 2018;142:1-9.*
26. *Dooling KL, Shapiro DJ, Beneden CV, Hersh AL, Hicks LA. Overprescribing and inappropriate antibiotic selection for children with pharyngitis in the United States, 1997-2010. JAMA Pediatrics 2014;168:1073-4.*
27. *Yıldız İ, Ünüvar E. Çocuklarda streptokoksik tonsillofarenjit. ANKEM Derg 2012;26:100-3.*