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Antibiotic prescription before and after rapid antigen detection test (RADT) for beta-hemolytic streptococci

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ABSTRACT

Objectives: Acute pharyngo-tonsillitis is one of the diseases that pediatricians and general practitioners most frequently experienced and only a small percentage of patients (20%-30% of pediatric patients, even less in adults) are actually suffering from pharyngo-tonsillitis by group A beta-hemolytic *Streptococcus* (GABHS). Also three quarters of pharyngitis patients have been treated with inappropriate antibiotics even these patients have viral infections. The aim of this study was to assess the effectiveness of the rapid antigen detection test (RADT) on the percentage of antibiotic prescriptions amongst patients with sore throat at a primary health care center in rural area.

Methods: Retrospective Cohort Study was designed to compare antibiotic prescription in patients with sore throats in two groups, one with the use of RADT and other with the clinical desicions of physicians. The x^2 test was used between two nominal variables to assess the impact of RADT on antibiotic prescription. For comparison of more than two independent variables, the ANOVA test was used and to identify the differences between groups, the Post-Hoc test was processed.

Results: Of the 580 patients, the avarage age of the study population was 25.8 years old while the median age was 21 years (min.=3, max.=65). There was a significant difference between two groups who had tested with RADT or not in terms of antibiotic prescription ($p < 0.001$). There was a significant difference between 3-14 years of age and 15-44 years of age ($p = 0.001$) as well as 3-14 years of age and 45-65 years of age ($p = 0.009$), however there was no significant difference between 15-44 and 45-65 years of age ($p = 1.00$).

Conclusions: Using the RADT is truly effective in reducing the percentage of antibiotic prescriptions in our setting. We believe that, the tools like RADTs which are quickly results and easy to use are really useful in practising (particularly in rural area).

Keywords: Rapid antigen detection test, *Streptococcus*, sore throat, antibiotic prescription

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Acute pharyngo-tonsillitis is one of the diseases that pediatricians and general practitioners most frequently encounter (15 million visits per year in the US alone), only a small percentage of patients (20%-30% of pediatric patients, even less in adults) are actually have pharyngo-tonsillitis by group A beta-hemolytic *Streptococcus* (GABHS) [1]. These are rare in children under 3 years of age, peak with the highest incidence between the ages of 3-15, and very rare in people over 50. With the exception of other rare

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bacterial infections of pharynx (caused by *Corynybacterium diphtheriae and Neisseria ghonorrhoeae*), antibiotic therapy is unnecessary for acute pharyngo-tonsillitis caused by other organisms than GABHS even more so because most cases are caused by viruses (in particular adenovirus, influenza and parainfluenza viruses). It is extremely important to make the diagnosis accurately to avoid unnecessary and potentially harmful antibiotic prescriptions [2, 3].

Inappropriate antibiotic prescriptions for treatment of pharyngitis have contributed to the emergence of resistant strains of oropharyngeal human flora and it causes increased morbidity, mortality and healthcare costs [4]. Approximately three quarters of pharyngitis patients have recieved inappropriate antibiotic prescriptions by antibiotics for viral infections [5, 6].

The aim of this study was to assess effectiveness of the rapid antigen detection test (RADT) on percentage of antibiotic prescriptions amongst patients with sore throat at a primary health care center in rural area.

METHODS

Study Setting

The study was conducted in a rural area -Yildizeli Family Health Center in Sivas (Turkey)- which has 6 family physicians. Informed permission were obtained from patients by clinic physicians. Retrospective Cohort Study was designed to compare antibiotic presicription in patients with sore throats in two groups, one with use of RADT and other with clinical desicions of physicians.

Participants

All patients between the ages of 3 and 65 years old with sore throat were asked to participate in the study between February and June 2017. Patients over 18 years old were given an informed permission and under 18 years old, informative sheet of study was given to their parents. For control group, all patients with sore throat between 3 and 65 years of age between February and June 2016 were selected. Ages are grouped as 3-14, 15-44 and 45-65 years of age.

Inclusion Criteria

- Males and females aged 3 to 65 years old.
- At least one symptom of acute pharyngitis (fever, sore throat, tonsillar exudates, tender servical nodes, absence of cough).

Exclusion Criteria

- Patients who did not consent to participate.
- Patients younger than 3 years and over 65 years old.
- Immunsuppressed condition such as neoplasm, AIDS (acquired immunodeficiency syndrome), reception of chemotherapy, radiotherapy, coticosteroids and immunsuppressive therapy (1 patients with recently received chemotherapy).
- Rheumatic hearth disease, hearth valve disease (4 patients with rheumatic hearth disease).
- Toncillectomy (12 patients).
- Patients who received antibiotics in previous two weeks (26 patients).

Samples

Samples were taken by family physicians who have trained previously to perform the correcttechnique (a throat swab was collected using a sterile swab from posterior pharynx, tonsils and/orinflamed areas). Samples were processed using the TOYO in vitro diagnostic test for GABHS (Türklab, Izmir, Turkey). According the manufacturer's instruction, this test has a 99% specificity and 97.3% sensitivity.

Statistical Analysis

Statistical analyses were performed using SPSS 22 for Windows. x2 test was used between twonominal variables to assess the impact of RADT on antibiotic prescription. For comparison of morethan two independent variables, the ANOVA test was used and to identify the differences betweengroups, the Post-Hoc test was processed. The statistical distrubutions of age and gender were specifiedin numbers and percentage values. P values of 0.05 or less were considered statistically significant.

RESULTS

Five hundreds and eighty patients participated in our study. The patients' demographics were shown in Table 1. In total, positive test results were obtained in

Table 1. Patient demographics

Variables	Data
Males, n(%)	307 (52.9%)
Females, n (%)	273 (47.1%)
Age (years)	25.8 ± 18.06
Median Age (min.- max.)	21 (3-65)
Assessed with RADT, n (%)	271 (46.7%)
Assessed with clinical decision, n (%)	309 (53.2%)
Total number of patients in the study, n (%)	580 (100%)

Data are shown as mean ± standard deviation or number (%). min = minimum, max = maximum, RADT = rapid antigen detection test

75 (27.7%) of the 271 patients who were tested with RATD and they were treated with antibiotics. One hundred and seventy-six (57%) of 309 patients who were not tested with RADT were treated with antibiotics according to clinical evaluation. There was a significant difference between two groups who had tested with RADT or not in terms of antibiotic prescription ($p < 0.001$). No statistically significant difference of antibiotic prescription was found by comparing patients by gender ($p = 0.184$). The patients were grouped as 3-14, 15-44 and 45-65 years of age and we compared them between each other with antibiotic prescription. There was a significant difference between 3-14 years of age and 15-44 years of age ($p = 0.001$) as well as 3-14 years of age and 45-65years of age ($p = 0.009$), however there was no significant difference between 15-44 and 45-65 years ofage ($p = 1.00$).

Table 2. Antibiotic preference

Prefered antibiotic prescriptions	Data
Penicillin, n (%)	215 (85.6%)
-Amoxicillin clavulanate	201 (80.0%)
-Penicillin-G	7 (2.7%)
-Amoxicilin	7 (2.7%)
Cephalosporins, n (%)	31 (12.3%)
-1. generation	7 (2.7%)
-2. generation	20 (7.9%)
-3. generation	4 (1.6%)
Macrolide, n (%)	4 (1.6%)
Tetracycline, n (%)	1 (0.3%)

Data are shown as number (%).

Antibiotics were prescribed to 251 patients. Among these prescriptions, penicillin was the most frequently preferred class (85.6%). Within this class, majority of prescriptions were amoxicillin clavulanate (80.0%), penicillin-G and amoxicillin were also prescribed (2.7% and 2.7% repectively). Twelve point three percent (12.3%) of the prescriptions were cephalosporins, with the first generation cephalosporins account for 2.7%, second-generation cephalosporins acount for 7.9% and third-generation cephalosporins account for 1.6%. Macrolides (1.6%) and tetracyclines (0.4%) were the less prefered groups of antibiotics (Table 2).

DISCUSSION

Most phayngo-tonsillitis cases are viral and with nasal congestion, low grade fever, cough, dysphonia, headache and myalgia. The process of bacterial pharyngo-tonsillitis is acute onset of high fever with chills, severe odynophagia and dysphagia but no cough. None of signs and symptoms are specific to acute pharyngitis caused by GABHS, so that the clinical criteria are of poorly use.

Various studies reported that, GABHS is the most common bacterial cause of acute pharyngitis and responsible for 5%-15% of sore throat visits in adults and 20%-30% in children [7].

Diagnosis

The culture is the gold standard for diagnosis but requires 18-24 hours of incubation at 37°C, causing a delay in identification of GABHS [8]. The time period for reading culture is its main limitations about using sistematically. Thus, to improve the diagnostic criteria, several scoring systems have been developed to predict, on a clinical basis, whether patients have bacterial or viral pharyngitis. Among many devised clinical scores, the Centor criteria has reliable predictors of GABHS pharyngitis. They include evaluating patients for tonsillar exudates, tender anterior servical lymphadenopathy or lymphadenitis, absence of cough and fever (oral temperature higher than 38.3 C; 101 F) [9]. More recently, the Centor score was modified by incorporating patient's age, which allows the physician to classify patient in low-

, moderate-, or high-risk groups [10]. On the other hand, Mistik *et al*. [12] have developed a scoring system (called Mistik Score) to diagnose viral sore throats. Within the last two decades, RADT) have become commercially available for the detection of *Streptococcus*. pyogenes using throat swabs. These tests offer an advantage of diagnosing streptococcal pharyngitis within a few minutes [12]. Although their specificity is more than 95%, sensitivity of test vary, which ranges from 65% to 95%. Several guidelines have been published on diagnosis and treatment of streptococcal pharyngitis, however not all are in agreement. The American College of Phsyician's (ACP) guideline endorsed by Center for Disease Control (CDC), American Academy of Family Phsyicians and the American Society of Internal Medicine recommends that patient with low Centor scores of "0" or "1" (low risk for streptococcal pharyngitis) do not require any testing or antibiotic prescription. For patients with Centor scores "2" and "3", guidelines suggest using a RADT and prescribing antibiotics to patients with positive tests. Empirical antibiotic treatment is recommended for patients with Centor score of "4" [13, 14].

Treatment

Patient with acute GABHS pharyngitis should be treated with an appropriate antibiotic at an appropriate dose for a duration likely to eradicate the organism from pharnx (usually 10 days). Based on their limited spectrums of activity, infrequency of adverse reactions and small costs penicillin or amoxicillin is recommended drug of choice for those non-allergic to these agents. Treatment of GABHS pharyngitis in penicillin allergic individuals should include a first generation cephalosporin for 10 days, clindamycin or clarithromycin for 10 days or azithromycin for 5 days [15].

The overconsumption of antibiotics for sore throat is main problem that is showed by several studies. In Athens, Maltezou *et al*. [12] stated that, diagnosis of streptococcal pharyngitis using clinical criteria only led to high rates of antibiotic prescription among children managed empirically (72.2%) [12]. In Pakistan, Palla *et al*. [16] stated that, antibiotics for suspected pharyngitis were prescribed to 98.5% of all patients included in the study. In Poland, Nitsch-Osuch *et al*. [17] stated that, the antibiotic therapy was ordered for 58% patients with influenza. Like these studies, our study showed, 57% of all patients with sore throat were treated with antibiotics according to clinical evaluation. These empirically managements may be the result of physicians' concerns about complications and their defensive approaches because of increasing malpractice lawsuits [18].

In our population, antibiotic prescription was reduced by 48.5% using the RADT compared with empirical management of patients. Similarly, in Greece Maltezou *et al*. [12] reported, the reduction is 61% with using RADT and McIsaac *et al*. [19] reported a 45% reduction in antibiotic prescription in adults using a RADT compared with empirical treatment.

In this study, when comparing antibiotic prescribing rates with age groups, there was a statistically significant difference between 3-14 years of age and 15-44 years of age ($p = 0.001$) and between 3-14 years of age and 45-65 years of age ($p = 0.009$). Prescribing more antibiotics to 3-14 years of age groups may be caused by; 1) the prevalance of GABHS is higher in this age group, 2) the family pressure for prescribing antibiotics, 3) the physicians' concerns and defensive approach to this group of age. The most commonly prefered antibiotics were penicillin and amoxicillin followed by cephalosporins and macrolides in our study setting. Our treatment choices are compatible with clinical guidelines [4, 15].

CONCLUSION

There are many conducted study in literature relevant with how to reduce inappropriate antibiotic prescriptions. It reveals that, throat swab is gold standart for diagnose GABHS; but not all physicians possess this opportunity while practising (particularly in rural area). In this situation, streptococcal pharyngitis is diagnosed with physicians' clinical experiment and/or clinical scoring systems like Centor. On the other hand, a lot of studies performed about RADT's sensitivity, specificity, positive and negative predictive values and it's insufficient sensitivity values (ranges from 65%- 5%).

In our study, we aimed not to calculate RADT's sensitivity, specificity, PPV or NPV while we aimed to evaluate RADT's impact on antibiotic prescriptions

and our study revealed that, using the RADT is truly effective in reducing the percentage of antibiotic prescriptions in our setting. We believe that, the tools like RADTs which are quickly results and easy to use are really useful in practising (particularly in rural area).

Author Contributions

Study Design: BD; Statistical Analysis: BD, SÖ; Data Interpretation: BD, SÖ; Data Collection: BD, SE; Manuscript Preparation: BD, SE; Literature Search: BD, SE; Funds Collection: BD.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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