Research Article

Assessment of acute tonsillitis using fiber-optic system

Seyit Mehmet Ceylan[1], Tuba Denkçeken[2], Cihan Atak[2], Merve Erdoğan[3], Hadiye Demirbakan[3]

[1]Department of Otorhinolaryngology, Fatih Sultan Mehmet Training and Research Hospital, İstanbul, Turkey, [2]Department of Biophysics, SANKO University School of Medicine, Gaziantep, Turkey, [3]Department of Medical Microbiology, SANKO University School of Medicine, Gaziantep, Turkey

Correspondence to: Tuba Denkçeken, E-mail: tdenkceken@sanko.edu.tr

Received: January 03, 2021; **Accepted:** January 21, 2021

ABSTRACT

Background: Diagnostic procedures for acute tonsillitis etiology consist of clinical evaluation, rapid diagnostic tests, and bacterial culture, blood tests do not have differential diagnostic value. It is important to determine that whether acute tonsillitis is due to a viral etiology such as rhinovirus, coronavirus, parainfluenza viruses, and herpesvirus or a bacterial factor such as A group beta-hemolytic streptococcus (GABHS) by real-time and non-invasive methods. **Objectives:** Our aim was to differentiate viral or bacterial acute tonsillitis from healthy controls with the elastic scattering spectroscopy. **Materials and Methods:** Spectral data were obtained from a total of five positive culture and rapid antigen test (RAT) bacterial etiology GABHS, 12 negative culture and RAT (viral etiology), and 20 non-tonsillitis people as the healthy control group. All data were obtained in the visible wavelength range. Measurements were compared with the culture and RAT results. Multivariate statistical analyses were performed through principal components analysis (PCA) and linear discriminant analysis (LDA), and performance was computed with the receiver operating characteristic curve. **Results:** The differentiation based on the discriminant score provided a sensitivity of 80% and specificity of 91.7% in differentiating negative culture and RAT from positive with an accuracy of 88.2%, sensitivity of 16.7%, and specificity of 90% in discriminating negative culture and positive RAT from non-tonsillitis with an accuracy of 62.5% and sensitivity of 100% and specificity of 85% in discriminating positive RAT from non-tonsillitis with an accuracy of 88%. **Conclusion:** We showed that scattering spectroscopy could discriminate tonsillitis with GABHS, viral tonsillitis, and healthy tonsils with high sensitivity using PCA and LDA. It can be concluded that the optical spectroscopy method has the potential for use in the fast determination of whether the patient's tonsillitis viral or a bacterial etiology with 80% sensitivity during the examination in real time.

KEY WORDS: Acute Tonsillitis; Spectroscopy; Culture; Rapid Antigen Test; Principal Component Analysis

INTRODUCTION

As our world goes through the pandemic process, it has been once again seen how important the detection of viral and bacterial infections. There are many methods for differentiating viruses and bacteria such as polymerase chain reaction, rapid antigen tests (RATs), and bacteria culture tests. These tests are very strong and have a high margin of accuracy. Of course, these tests have some advantages and disadvantages. Some are expensive and some requires a long time. As we consider upper respiratory infections, they can be due to viral etiology such as rhinovirus, corona virus, parainfluenza viruses, and herpesvirus or a bacterial factor such as A group beta-hemolytic streptococcus (GABHS). These two different causes of infections require different treatment. In general, antibiotic treatment is not necessary for the viral etiologic infections. Since this distinction has not been well considered, unnecessary use of antibiotics has increased worldwide.[1] Many hospitals use RAT to detect this distinction. Positive RAT means that this infection is bacterial and negative RAT means that it is viral. In addition, it is recommended that hospitals have systems to monitor the

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Website: http://www.ijmsph.com	Quick Response code
DOI: 10.5455/ijmsph.2020.01003202121012021	

use of antibiotics in various departments and ensure that they are used only when indicated.[2]

In the light of all this information, we tried to determine whether acute tonsillitis is due to a viral etiology or a bacterial factor with an optical method. Spectroscopic techniques allow a non-invasive option to define the status of the tissue. These methods are sensitive to the tissues' functional, morphological, and biochemical properties. Furthermore, these techniques present an objective method for determining the status of tissues and do not need user experience as they give quantitative outcomes. Optical fibers, placed in touch with the patient tonsil, deliver and detect light. The majority portion of the light is scattered from the cell nucleus, which is the most significant scatterer. Moreover, the difference between the cell membrane and cytoplasm refractive index causes scattering of light. Our research aim is that the acute tonsillitis with viral etiology has different morphological structure than the acute tonsillitis with bacterial factor. The scattered light from the cell saved as spectra, which depends on the wavelength. Acquired spectroscopic data do not need interpretation by an expert. Spectrum presents otorhinolaryngologist decision support by the quantitative and objective results.

Aim and Objectives

Our purpose was to demonstrate whether elastic scattering spectroscopy method has a determinant value for the differential diagnosis of acute tonsillitis in real time. The diagnostic algorithms can discriminate between positive RAT (GABHS), negative RAT (viral etiology), and non-tonsillitis by multivariate statistical analysis. The acquired spectra were evaluated in combination with linear discriminant analysis (LDA) and principal components analysis (PCA) to build an aide biomedical equipment for decision support during the otorhinolaryngologist examination.

MATERIALS AND METHODS

The clinical study was conducted at SANKO University Otorhinolaryngology Head and Neck Surgery Department with the approval of the SANKO University Ethics Committee (2019/01-03). Written informed consent was acquired from all patients with tonsillitis and healthy controls. Seventeen patients and 20 healthy controls were selected for the study, and the spectral data were implemented on total 37 subjects with the collaboration of the otorhinolaryngology head and neck surgery department. According to RAT results, we classified positive RAT group (GABHS) (total $n = 5$), negative RAT group (viral etiology) (total $n = 12$), and 20 non-tonsillitis healthy control group. We gathered eight spectra per each of them by placing the optical fiber tip to their tonsil. Then, the swabs taken from the patient group were sent to the microbiology laboratory and RAT results were obtained. Spectra were corrected in the 450 nm–750 nm wavelength regions. Our spectral results were compared with culture and RAT results to designate correlation.

The light scattering method comprises two adjacent fiber cables (each of 100 µm core diameter, 125 µm clad diameter, and 0.22 numerical aperture), a spectrometer (USB2000 Spectrometer, Ocean Optics), a halogen tungsten light source (HL-2000, Ocean Optics), and a laptop to save the spectra [Figure 1]. Fiber cables were used for delivering and receiving of light from the patient's tonsil.

The HK-2000 light source was connected to a fiber end and the USB2000 spectrometer to another end. The fiber delivered light to the patient's tonsil, and the other fiber received backscattered light to gain the spectra. Each spectrum was normalized, and three spectra were acquired for calibration. Calibration process was achieved according to the literature.[3-6] Multivariate statistical analysis was performed as stated in the literature[3,5-7] through PCA and LDA.[8,9] We utilized R-Studio program for PCA, LDA, and receiver operating characteristic (ROC) curve.[10]

RESULTS

In our study, we compared our spectral data with the culture and RAT results. The spectral pattern related to the light scattering from the nucleus and cell organelles is utilized as a diagnostic parameter. A total of 17 patients with acute tonsillitis and 20 non-tonsillitis control were involved in the study and total 296 spectra (40 spectra from positive RAT, 96 spectra negative RAT and 160 spectra from non-tonsillitis control) were analyzed. Figure 2 shows the corrected spectra of the system for positive acute tonsillitis, negative acute tonsillitis, and control groups. Multivariate statistical analysis, that is, PCA and LDA, was applied to differentiate the spectral patterns.

Initially, spectra were centered and scaled before statistical comparison. Second, PCA was performed for the

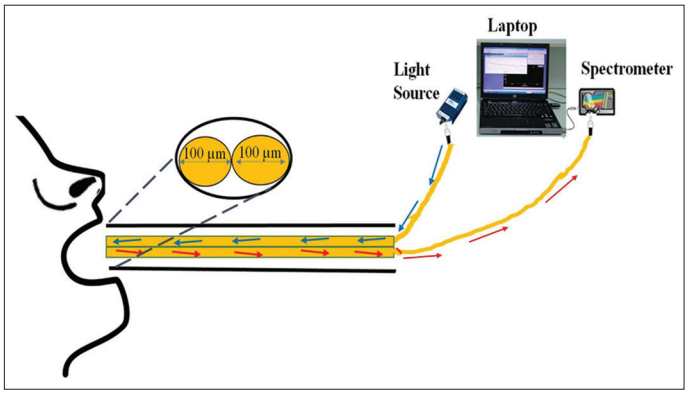

Figure 1: Light scattering spectroscopy system

differentiation of patient's tonsil. PCA was achieved to find significant variances (principal component [PC1]: 41.4%, PC2: 33.4%, PC3: 9%, PC4: 2%, PC5: 1%, PC6: 1%, and PC7-37). After that, Kruskal–Wallis H-test on all PC scores comparing positive culture and RAT, negative culture and RAT and non-tonsillitis control groups showed that there was two most diagnostically significant ($P < 0.05$) PC (PC5 and PC12) for discriminating these three groups. The vital PC5 and PC12 components were used as LDA input variables. The cross validation was performed by leave_one_out technique to prevent over-fitting.[11] The areas under the ROC curve (AUC) and its 95% confidence interval were computed. AUC, sensitivity, and specificity values were calculated and shown in Tables 1-3.

In our study, the classification based on discriminant score provided sensitivity of 80% and specificity of 91.7% in discriminating negative culture and RAT from positive with an accuracy of 88.2% [Figure 3A], sensitivity of 16.7%, and specificity of 90% in discriminating negative culture and RAT from non-tonsillitis with an accuracy of 62.5% [Figure 3B], and sensitivity of 100% and specificity of 85% in discriminating positive culture and RAT from non-tonsillitis with an accuracy of 88% [Figure 3C].

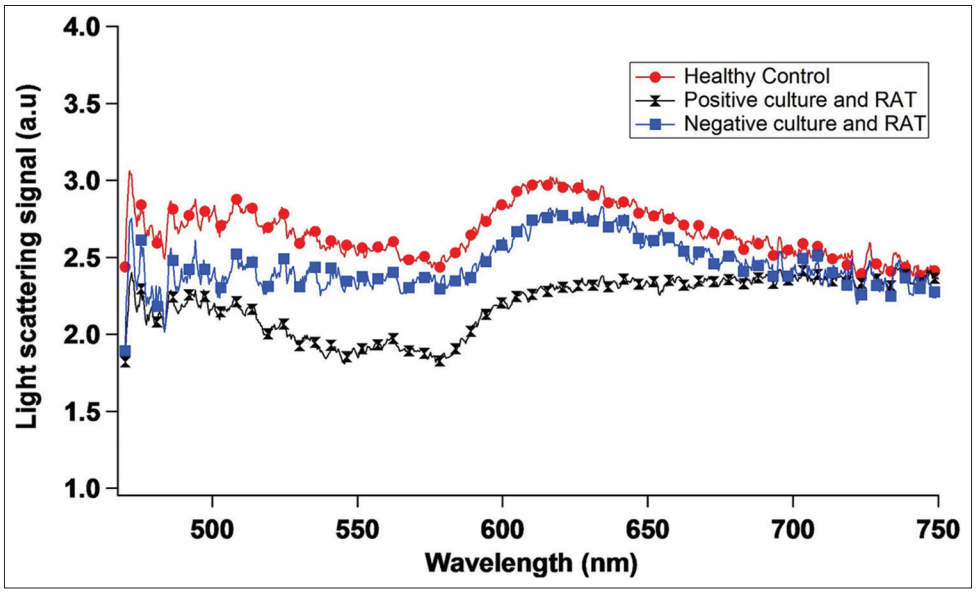

Figure 2: Corrected light spectra for positive culture and rapid antigen test (RAT), negative culture and RAT, and control subjects

Table 1: Specificity values of the system for differentiating acute tonsillitis and healthy control groups

Specificity	Positive culture and RAT	Negative culture and RAT	Healthy control
Positive culture and RAT	-		
Negative culture and RAT	0.917	-	
Healthy control	0.85	0.90	-

RAT: Rapid antigen test

Table 2: Sensitivity values of the system for differentiating acute tonsillitis and healthy control groups

Sensitivity	Positive culture and RAT	Negative culture and RAT	Healthy control
Positive culture and RAT	-		
Negative culture and RAT	0.80	-	
Healthy control	1.0	0.167	-

RAT: Rapid antigen test

Table 3: Area under curve values of the system for differentiating acute tonsillitis and healthy control groups

AUC	Positive culture and RAT	Negative culture and RAT	Healthy control
Positive culture and RAT	-		
Negative culture and RAT	0.85	-	
Healthy control	0.96	0.433	-

RAT: Rapid antigen test; AUC: Areas under the ROC curve

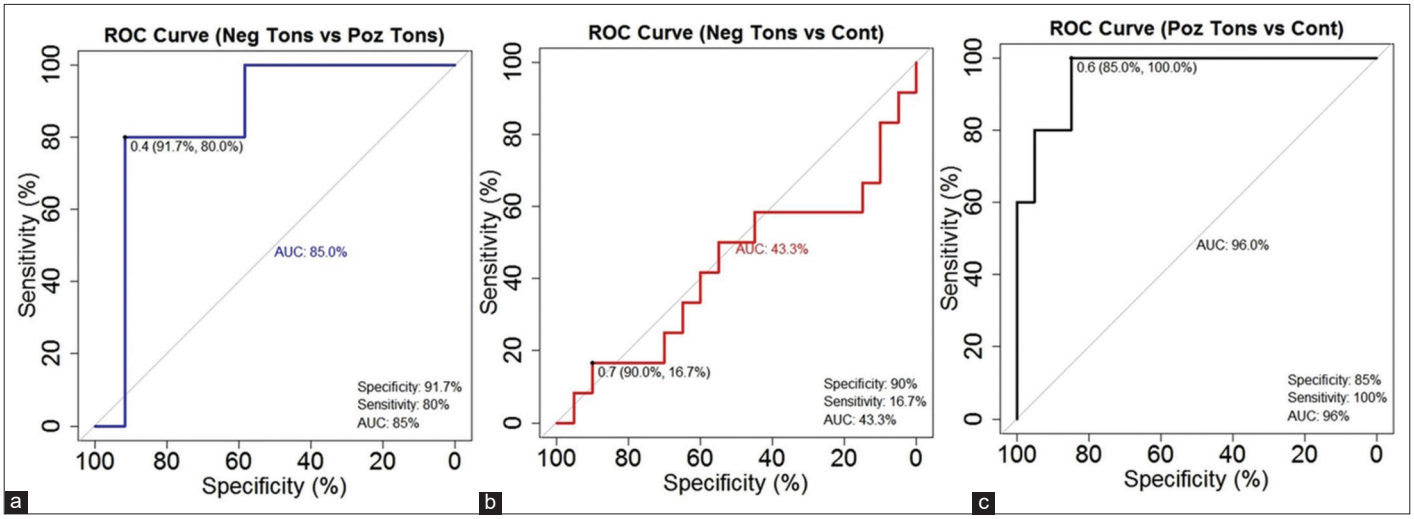

Figure 3: (a-c) Receiver operating characteristic curve, comparing positive culture and rapid antigen test (RAT), negative culture and RAT, and control subjects

DISCUSSION

In this study, we compared our spectral pattern with the culture and RAT results. A total of 37 (n = 17 patients with acute tonsillitis and n = 20 non-tonsillitis healthy control) volunteers were involved in the study, and 296 spectra were analyzed by PCA, LDA, and leave_one_out cross-validation. We compared acute tonsillitis with positive culture and RAT (bacterial etiology), acute tonsillitis with negative culture and RAT (viral etiology), and non-tonsillitis healthy control. We found the accuracy of 88.2% in discriminating negative culture and RAT from positive, the accuracy of 62.5% in discriminating negative culture and RAT from non-tonsillitis, and accuracy of 88% in discriminating positive culture and RAT from non-tonsillitis.

At present, diagnostic procedures for acute tonsillitis etiology consist of clinical evaluation, rapid diagnostic tests, and bacterial culture. In this study, a diagnostic scoring system according to signs and symptoms was suggested to predict the probability of tonsillitis caused by beta-hemolytic streptococci. If therapy is considered, a high score of clinical evaluation should lead to pharyngeal swab, culture, or RAT to identify beta-hemolytic streptococci. Blood tests do not have differential diagnostic value. When the patients were evaluated according to the clinical scores suggested by Mc Isaac and Centor, it is seen that at least 50% of the highly suspected patients are negative for the swab test.[12] The sensitivity and specificity of GABHS RAT range from 65.6% to 96.4% or 68.7% to 99.3%, respectively, depending on the user's performance.[13-15] In this study, the sensitivity and specificity values of the culture and RAT when employed by otorhinolaryngologist under office conditions were within the levels reported in the literature. RAT is a reliable and useful diagnostic tool but less sensitive than culture. Since microbiological culture is a time-consuming method, antibiotic treatment is started according to RAT results today.

In our study, it was seen that the fiber-optic method could contribute to the diagnosis when RAT tests and bacterial culture results were evaluated together.

The most important feature of the fiber-optic method is that it allows real-time evaluation and therefore it can be decided immediately whether to start antibiotic treatment or not. The most important limitations of the method are the difficulties in its application in patients with extremely sensitive gag reflexes and in non-cooperative pediatric patients. Another limitation of the fiber-optic method is that the measurements need to be analyzed by computer.

CONCLUSION

The study shows that this fiber-optic method could discriminate positive culture and RAT, negative culture and RAT, and healthy non-tonsillitis with high sensitivity value using multivariate statistical analysis. It can be concluded that the sensitivity (80%) of optical spectroscopy has the potential for use in the fast detection of whether the patient's tonsillitis whether viral etiology or a bacterial factor during the examination in real time. The pandemic process has shown how important such real-time diagnostic devices are in virus detection. This study paves the way for the studies of these types of methods with coronavirus patients.

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How to cite this article: Ceylan SM, Denkçeken T, Atak C, Erdoğan M, Demirbakan H. Assessment of acute tonsillitis using fiber-optic system. Int J Med Sci Public Health 2020;9(10):621-625.

Source of Support: Nil, **Conflicts of Interest:** None declared.