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Is adenotonsillectomy safe in covid-19 era? Investigation of sars-cov2 in adenoid and tonsil tissues^{☆, ☆ ☆}

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ABSTRACT

Objectives: COVID-19 has seriously altered physicians' approach to patients and diseases, with a tendency to postpone elective procedures. Tonsillectomy, alone or with adenoidectomy, is one of the most common surgeries performed by otolaryngologists. Although they are generally accepted as elective surgeries, they significantly improve the quality of life, and postponing these surgeries for a long time can have deteriorative effects on the patients. We aimed to investigate the presence of SARS CoV-2 in the adenotonsillectomy materials to find out if performing adenotonsillectomy is safe during the COVID-19 pandemic.

Methods: Forty-eight tissue samples from 32 patients that underwent tonsillectomy with or without adenoidectomy were investigated whose SARS-CoV-2 RT-PCR test in the samples obtained from nasopharyngeal (NP) and oropharyngeal (OP) swabs were negative within 24 h before the operation. While 16 patients underwent only tonsillectomy and one of their tonsils was investigated, 16 of the patients underwent adenotonsillectomy and their adenoid tissues were sent along with one of their tonsils. SARS-CoV-2 viral RNA was investigated with Real-Time PCR in tissue samples.

Results: Two (4.2%) tissue samples had positive PCR tests for SARS-CoV-2, while 46 of them were negative. One of the positive patients had undergone tonsillectomy with the indication of chronic recurrent tonsillitis, and the other patient had undergone adenotonsillectomy for obstructive adenotonsillar hypertrophy. PCR test was positive in the adenoidectomy specimen and negative in the tonsillectomy specimen in this patient.

Conclusions: Adenotonsillectomy can be done safely in asymptomatic patients without a history of Covid-19, with a negative PCR test result obtained within the last 24 h.

1. Introduction

Coronaviruses (CoVs) are enveloped, positive-sense single-stranded RNA viruses with helical symmetry. They are a large family of viruses that can cause a wide range of clinical symptoms; from self-limiting mild infections, like the common cold, to more serious infections such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS).^{1–3}

Cases of pneumonia of uncertain etiology were reported by the

World Health Organization (WHO) in the city of Wuhan, China in December 2019. On January 7, 2020, the causative agent was identified as a new coronavirus (2019-nCoV) and named SARS-CoV-2 due to its close resemblance to SARS-CoV. The disease caused by the virus was called coronavirus disease 2019 (COVID-19).^{4,5}

Until now, there have been over 210 million confirmed cases of COVID-19, including nearly 4.5 million deaths, reported to WHO.⁶ The transmission routes of the coronavirus are by direct contact and droplets, which may be the reason for the rapid spread of the virus. On the

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other hand, the tissue localization distribution of the virus is not clearly known. For SARS-CoV-2, penetration into the upper airways is the first step of infection.⁷ Upper airway epithelial cells were shown to express the highest levels of angiotensin-converting enzyme 2 (ACE2), which is working as the main entry receptor for SARS-CoV-2 following interaction with viral spike (S) protein.^{8,9} SARS-CoV-2 virus is bound to the ACE-2 receptor of the host cell with the spike (S) protein. Membrane fusion is provided by the transmembrane protease serine 2 (TMPRSS2) in the host cell. Also, ACE-2 receptors are abundantly expressed in the respiratory system, lungs, blood vessels, kidneys, small intestine, testes, heart muscle, colon, and thyroid gland.^{10,11} Accordingly, viral RNA of SARS-CoV-2 was detected in the respiratory tract and lung, salivary glands, heart, liver, kidneys, lymph nodes, spleen, gastrointestinal tract, and central nervous system.^{10,11} It has been shown in an in vivo study that the palatine tonsils, one of our first lines of defence, are also infected with SARS-CoV-2 and the virus replicates there.¹²

Adenotonsillectomy is one of the most common operations performed by otolaryngologists, which requires close contact with the patients' upper airway before, during, and after the operation. Although they are generally accepted as elective surgeries, they significantly improve the quality of life of the patients.¹³ Even most of the clinics ask for a negative PCR test before operating the patient, no study has been conducted on whether the virus is present in the adenotonsillar tissue. This study aimed to investigate the presence of SARS CoV-2 viral RNA in the adenotonsillectomy materials.

2. Material and methods

A prospective cross-sectional study was designed in our tertiary care education and training hospital. Permissions from the Ministry of Health (approval date: 02/05/2020; number: 2020-05-02T16-07-46) and the institutional review board were acquired (Date: 31.01.2021, Session No: 2021/01, Decision No: 01). The authors received no funding for the study. Written informed consent was obtained from all of the patients. Patients with a history of COVID-19 were not included in the study. The study was conducted before the public vaccination has started in our country, so the patients with any vaccine against SARS-CoV-2 were also not included in the study to maintain homogeneity of the study group. The patients were questioned in detail for COVID-19 symptoms preoperatively, and chest x-rays were taken, which is part of our anesthesia department's preoperative routine for patients that will receive general anesthesia.

2.1. Sample collection

Forty-eight tissue samples from 32 patients whose SARS-CoV-2 RT-PCR test in the samples obtained from nasopharyngeal (NP) and oropharyngeal (OP) swabs were negative within 24 h before the operation were included in the study. All surgeries were performed under general anesthesia; tonsillectomies by blunt dissection, and adenoidectomies with the help of an adenotome. Adenoid and/or tonsil tissues of the patients were taken into sterile viral transport medium (VTM) in the operating room under sterile conditions and were stored at -80°C until RT-PCR analysis.

2.2. Real-time reverse transcription PCR

RNA extraction from tissue samples was performed as described by Chomczynski et al.¹⁴ after the sample was homogenized with TRIzol® Reagent, chloroform was added. The homogenate was allowed to separate into three layers [(a clear upper aqueous layer (containing RNA), an interphase, and a lower layer (containing DNA and proteins)]. RNA was precipitated with isopropanol. The precipitated RNA was washed to remove impurities and then resuspended for use in RT-PCR.

Real-time reverse-transcription PCR was performed by using Bio-Speedy® SARS-CoV-2 Double Gene RT-qPCR Kit (Bioeksan, Istanbul,

Turkey) according to the manufacturer's instructions. A 20 μL reaction mix contained 5 μL of RNA, 5 μL of Oligo Mix (N and Orf1ab gene for SARS-CoV-2 detection, Rnase P gene for internal control), and 10 μL of 2XPrimer Script Mix containing DNA Polymerase, each deoxyribose triphosphates, reverse transcriptase, ribonuclease inhibitor, and reaction buffer. Positive control for amplification control and no-template control to assess contamination were used. Thermal cycling was performed at 52°C for 5 min for reverse transcription, followed by 95°C for 10 s and then 40 cycles at 95°C for 1 s, 55°C for 1 s in Rotor-Gene® 5 Plex instruments (Qiagen, Hilden, Germany). Cycle threshold (Ct) values of less than 38 were defined as positive. The sensitivity and specificity of the kit were reported as 99.64% and 100%, respectively, by the manufacturer.¹⁵

3. Results

The mean age of the patients was 15.4 ± 13.4 (3–59) years; 11 of the patients were female (34.3%) and 21 (65.7%) of them were male. While 16 of the patients underwent only tonsillectomy and one of their tonsils was sent to the microbiology department of our hospital, 16 of the patients underwent adenotonsillectomy and their adenoid tissues were sent along with one of their tonsils.

Two (4.2%) tissue samples had positive PCR tests for SARS-CoV-2, while 46 of them were negative. One of the positive patients was a 26-year-old male, who had undergone tonsillectomy with the indication of chronic recurrent tonsillitis. The other patient was a 6-year-old boy, who had undergone adenotonsillectomy for obstructive adenotonsillar hypertrophy. PCR test was positive in the adenoidectomy specimen and negative in the tonsillectomy specimen in this patient.

Both of the patients were tested for Anti-SARS-CoV-2 (Spike) antibodies 8 weeks after the operation. While no antibodies were detected in the 26-year-old patient, the 6-year-old patient showed high titers of antibodies which suggests previous asymptomatic infection.

4. Discussion

Acute and chronic-recurrent tonsillitis are the most common otolaryngological diseases, and, adenoidectomy and tonsillectomy constitute the main treatment of chronic or recurrent adenoids and tonsillitis that do not benefit from medical treatment alone.¹⁶ Since these operations are among the most common surgeries performed by an otolaryngologist, we need to know the potential risks to minimize the transmission risk of the virus as much as possible in the Covid era.

The COVID-19 pandemic has also caused the algorithms to change to reduce the risk of transmission in ENT emergencies and to use resources correctly. Treatment is now planned by targeting fewer hospitalizations.¹⁷ Coronavirus patients can also apply to the clinic with signs of tonsillitis. In a recent study, 13% of 193 COVID-19 patients had signs of tonsillitis.¹⁸ Since COVID-19 positivity has been detected in tonsillitis patients, it is clear that more data is needed in terms of surgical planning and creating an algorithm.

The diagnosis of SARS-CoV-2 is based on viral gene, antibody, and antigen detection, among which viral gene detection by RT-PCR has become the gold standard.¹⁹ Nasopharyngeal (NP), oropharyngeal (OP), or nasal swabs, upper and lower respiratory tract samples such as the sputum and BAL are used for diagnosis.²⁰ The viral load peak occurs on the fourth to sixth day after symptoms begin. It is known that the COVID-19 viral load is higher in the NP swab compared to the OP swab.²¹ Recent guidelines recommended that a single negative result at least 48 h before surgery is acceptable in asymptomatic patients,²² which is also the approach we use for all surgical procedures in our department.

In a recent study, 64.3% RT-PCR positivity was detected for patients presenting with COVID-19 symptoms, while in another study, RT-PCR showed positivity in 39.4% consistent with chest X-ray.^{23,24} The sensitivity of the RT-PCR test is closely related to the type of sample. Sample

collection technique, sampling time, and patient characteristics can also RT-PCR test results.²⁵ The real-life clinical sensitivity of SARS-CoV-2 RT-PCR testing was found to be “only moderate at best” by Kortela et al., with an overall sensitivity of 47.3%.²⁶ Our two asymptomatic cases with negative NP/OP swab RT-PCR results and positive RT-PCR results in tissue samples also support these findings.

Kadriyan et al. reported in their case report that, the SARS-CoV-2 RT-PCR result was found to be positive in the tonsillar biopsy sample and negative in the nasopharyngeal swab of a 26-year-old young female patient who underwent tonsillectomy surgery 3 weeks after the diagnosis of COVID-19. According to this result, it was determined that the virus could colonize the tonsils up to 3 weeks after the diagnosis of COVID-19.²⁷ In another study, it was determined that SARS-CoV-2 RNA can remain in feces much longer than in nasopharyngeal and oropharyngeal samples (the median duration of virus in stool was 22 days, interquartile range 17–31 days).²⁸ For these reasons, for the safety of both the surgeon and the patient, it was recommended that elective transoral surgeries such as tonsillectomy should be planned at least 4 weeks after the diagnosis of COVID-19.

PCR positivity was detected in 2 of 48 tonsil and adenoid specimens examined in our study. Considered together with the above reports, we think that it may be related to the latent stay of SARS-CoV-2 in the adenotonsillar tissue, not an acute infection, since the patients were completely asymptomatic with normal chest X-rays.

Forty-six out of 48 tissue samples (95.8%) had negative PCR tests for SARS-CoV-2. With these results, we think that the negative PCR test of nasopharyngeal and oropharyngeal swabs taken within 24 h in patients that are scheduled for tonsillectomy and adenoidectomy is sufficient for safe surgery.

Furthermore, postponing cases due to COVID-19 has had negative consequences not only for the health of patients but also for the training of the residents.²⁹ We also think that adenotonsillectomy, which is a basic operation in resident education, should be applied with these frameworks.

In conclusion, adenotonsillectomy can be done safely in asymptomatic patients without a history of Covid-19, with a negative PCR test result obtained within the last 24 h.

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