

COVID-19 AND ANATOLIAN PROPOLIS: A CASE REPORT

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ABSTRACT

Introduction: As an age-old folk remedy, it is widely accepted that propolis has natural anti-inflammatory properties. Anatolian propolis is a different form among bee products group. Propolis has taken its current place as a food supplement during the pandemic period and new studies on propolis against COVID-19 have gained momentum.

Case: 38-year-old male patient, who served as a medical secretary, first complained of a tickling in his throat. RT-PCR was requested from the patient who presented with this complaint and was in the high-risk profession. The routine blood values and Thorax CT results of the patient whose test was positive were normal. Medical treatment recommended in the Ministry of Health guidelines was initiated for the patient. The patient's cough complaint started 3 days later and his complaint got worse on the 5th day. A control thorax CT was requested from the patient whose fever did not decrease simultaneously and extensive bilateral ground glass areas were formed. The patient was hospitalized and moxifloxacin was added to his treatment; However, after 72 hours, the patient's fever continued. The patient started respiratory failure and his general condition worsened. It was decided to follow the patient in the intensive care unit (ICU) and tocilizumab and Continue positive airway pressure (CPAP) support was started. Although 2 days passed, the patient's oxygenation and clinic status did not improve. For this reason, BEEO'UP (bee&you) 30% Anatolian propolis 80 drops / day was applied to the patient. At the end of the third day, improvement began in the patient's oxygenation, blood parameters and radiological findings. For 5 days, the patient was followed up with IV moxifloxacin, 60 mg steroid, CPAP, inhaler treatments, low molecular weight heparin (LMWH) and BEEO'UP (bee&you) 30% (bee&you) Anatolian propolis. The patient's clinic improved and the patient was taken to the service on the 7th day of his admission to the ICU. The patient was discharged on the 10th day of hospitalization. At the health check-up 1 month later, the patient had no complaints except for forced exertion dyspnea, blood parameters normalized and abnormal radiological findings in Thorax CT completely regressed.

Discussion and conclusion: Surely, in this disease with many unknowns, it may not be correct to attribute the remarkable rapid and sequel-free recovery in this case to the use of Anatolian propolis alone. However, in such cases where there are no other treatment options left, in addition to the treatment recommended in the guideline, there is no harm in using Anatolian propolis, and even benefit will be gained due to its proven antioxidant and antiviral effect. This phenomenon has provided hope for further study plans.

As a result, Anatolian propolis can be added to the existing treatment protocol in patients diagnosed with COVID due to its easy, safe and low cost.

There is a need for multi-center, large-population studies on the use of Anatolian propolis in COVID-19 prophylaxis, treatment and post-covid-19 period, and even to prevent complications. With the promising picture created by this case, we continue our work more comprehensively. We look forward to announcing our results. It is hoped that in the future there will be drug studies that will provide definitive treatment with one or more of the specific compounds of Anatolian propolis.

Keywords: Anatolian propolis, COVID-19, food supplement.

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Introduction

As is known, the 2020 Pandemic is experienced due to COVID-19 caused by SARS-CoV-2. In epidemic, the first case of COVID-19 was diagnosed on March 10, 2020 in Turkey. The first death due to the virus was reported on March 15, 2020

On April 1, 2020 also was announced that the corona virus cases have been spread all over Turkey⁽¹⁾.

Studies on the virus with high pathogenicity have been carried out rapidly from the beginning of the pandemic all over the world. In this process, although our knowledge and experience about the

virus have increased, there is no evidence-level option for treatment yet. Since the disease can progress with a severe clinical picture and high mortality, serious fear and anxiety have occurred in people. Therefore, the use of alternative food supplements has increased⁽²⁾.

Anatolian propolis, whose antiviral and antioxidant activity was mentioned in many previous studies^(3,4,5); was used in a patient who was followed up with the diagnosis of COVID-19, where there was no other treatment option and developed severe respiratory failure. The case was shared considering that propolis had an interesting contribution in providing both clinical and radiological healing in the patient who developed severe lung involvement and respiratory failure due to COVID-19. The case was also presented to give an idea about the studies of Anatolian propolis on COVID-19 prophylaxis, treatment efficacy and complication prevention.

Case Presentation

The 38-year-old medical secretary requested RT-PCR test when his throat started to be tinged, since he was in the occupational risk group. The patient's test was positive. The patient had no additional symptoms, his vital signs were normal, and there were no abnormal findings in routine blood values and Thorax CT. The treatment recommended in the Ministry's algorithm (Hydroxychloroquine 2x200 mg and Favipiravir 2x1600 mg loading dose, 2x600 mg maintenance dose), low molecular weight heparin (LMWH) was started and the patient was placed in home quarantine.

The patient was isolated at home and was receiving regular treatment. Every day, the patient was interviewed by phone, questioned about symptoms and whether he received medical treatment regularly. The patient stated that a cough started on the 3rd day of medical treatment. Therefore, oropharyngeal mouthwash and short-acting beta-2 agonist were started. Cough became very severe on the 5th day of his treatment and the patient was called for control. Of the vital signs, when the pulse % SO₂ equal to 92, the temperature was 37.5 degrees and the symptoms developed under treatment, the patient was hospitalized. Routine blood values were lymphocyte = 0.76 10³ / U1 (19.4%), monocyte = 0.27 10³ / U1, white blood cell (WBC) = 3.4 10³ / uL, procalcitonin low risk in sepsis, CRP = 1, 4 mg / dl, platelet (PLT) = 147 10³ / UL, magnesium (Mg) 1.6 mg / dL. Ferritin, cardiac markers, D-dimer, vit B12, folate values were normal.

Thorax CT was reported as mild-moderate covid-19 pneumonia. It was decided to complete the current treatment for 10 days. In addition to treatment, 60 mg steroid and nebulizer treatment was added. When the patient's fever continued after 72 hours of his treatment, IV moxifloxacin was added to the current treatment.

Despite medical treatment, within two days, the patient developed shortness of breath and his cough increased. The patient could not speak normally due to coughing. During his follow-up, the pulse SO₂% of the patient decreased to 72, and his dyspnea increased. Routine blood values were lymphocyte = 0.67 10³ / UL, monocyte = 0.27 10³ / UL, PLT = 131 10³ / UL, CRP = 1.4 mg / dl and Thorax CT reported as moderate-severe covid-19 pneumonia (Figure 1a, 1b, 1c, 1d). The patient was referred to the intensive care unit.



Figure 1a, 1b, 1c, 1d: Thorax CT images when the patient is referred to the intensive care unit.

Intermittent CPAP support was immediately started in the intensive care unit. The patient was placed in the intermittent prone position. Tolizumab 400 mg 2x1 was additionally administered to the patient, who received steroid therapy since his first hospitalization. The next two days, the patient was also dyspneic, and although the patient was followed up with CPAP and received 10 lt / min oxygen support, SO₂ remained around 93%. Routine blood values were as lymphocyte = 0.66 10³ / UL, monocyte = 0.06 10³ / UL, PLT = 294 10³ / UL, CRP = 0.2 mg / dl.

After the patient was admitted to intensive care, it was decided to supplement the patient with BEE'OU P (*bee&you*) 30% Drops of Anatolian Propolis in addition to the current medical treatment. It was explained to the patient and his relatives that propolis was not a proven treatment / prophylaxis option, it was routinely used as a supplementary food, and that it would be given if they accepted, and written informed consent was obtained. BEE'OU P (*bee&you*) 30% Drops of Anatolian Propolis was obtained by the researcher from the pharmacy at an additional fee. When the patient gave written consent, an anterior wrist propolis allergy test was performed. For this, 5 drops of Anatolian Propolis was dropped on the wrist extensor and kept for 10 minutes.

When it was observed that there was no allergic reaction, Anatolian propolis was started to be given by dropping it into 20 drops of drinking water daily. The dose was increased to 80 drops / day in two days and continued in this way.

On the 3rd day of the patient's intensive care admission, the pulse% SO₂ started to increase slowly with the current treatment. The patient could breathe relatively easily with only oxygen support. Intermittent CPAP application was continued. In the following days, the patient's dyspnea and cough symptoms began to decrease significantly. In this way, he was followed up with intermittent prone position, CPAP, steroid, inhaler therapy and Anatolian propolis in the intensive care unit for 7 days. At the end of the 7th day, with only 2 lt / min nasal oxygen support, SO₂ had increased to around 96%. Routine blood values were lymphocyte = $1.00 \cdot 10^3$ / UL, monocyte = $0.29 \cdot 10^3$ / UL, PLT = $236 \cdot 10^3$ / UL, CRP = 0.1 mg / dl and the patient was taken to the normal service. Thorax CT was reported as severe viral pneumonia (Figures 2a, 2b, 2c, 2d).

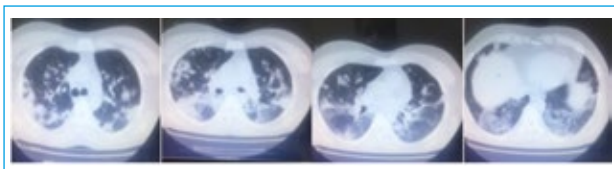


Figure 2a, 2b, 2c, 2d: Thorax CT images when the patient was taken to the service from the intensive care unit.

In service follow-up, the current medical treatment protocol was continued. Anatolian Propolis and other medications were applied. Without the need for CPAP support, oxygen support (2-3 lt / min) was followed in intermittent prone position. The patient's condition was getting better every day. His dyspnea was reduced and he had no cough. In this way, the patient was followed up in the service for 10 days and was discharged. Discharge recommendations were intermittent prone position, steroid, LMWH and BEE'O UP 30% Drop Anatolian propolis. The patient did not need oxygen support treatment at home, and oxygen-free SO₂ increased to 96%. Routine blood values, lymphocyte = $1.68 \cdot 10^3$ / UL, monocyte = $0.63 \cdot 10^3$ / UL, PLT = $260 \cdot 10^3$ / UL, CRP = 0 mg / dl, WBC = $8.78 \cdot 10^3$ / uL. The control thorax CT, which was evaluated in the service, was observed as diffuse ground glass consolidation areas and locally subsegmental atelectasis in both lungs, and it was reported as consistent with signs of severe viral pneumonia.

The patient was discharged after 10 days with a prescription (3a, 3b, 3c, 3d).



Figure 3a, 3b, 3c, 3d: Thorax CT images of the patient in service before discharge.

The patient who came to the outpatient clinic had only effort dyspnea. All blood parameters were within normal limits. The next check was done 15 days later; The patient's symptoms decreased further and routine blood parameters were within normal limits. It was recommended that the patient continue his current treatment.

In his check 1 month after his discharge; exertional dyspnea was alleviated, but continued, albeit slightly. Routine blood values were normal, lung involvement was completely regressed, and control Thorax CT was reported as normal radiological findings.

The patient is followed up as monthly polyclinic controls by continuing to use long-acting beta 2 agonist and inhaled corticosteroid, anticoagulant and BEE'O UP (*bee&you*) 30% drops of propolis 20 drops / day.

Discussion

The case developed severe respiratory failure due to COVID-19 and all of the recommended treatment protocols were applied. Since there were no other treatment options left and because there were publications about the antiviral effectiveness of propolis in previous studies and it was a natural and safe product, Anatolian propolis was started as a last chance for the patient.

Because studies with more samples are needed to confirm the pattern of improvement seen in this case. Actually is not possible understanding if the regression of lung infection is related with the propolis implementation therapy or the previous pharmacologic effect. In patients we follow in the COVID-19 subacute period, shortness of breath, chest pain, cough complaints and fibrotic change in Thorax CT are the main findings. However, in our case, these symptoms completely regressed with the addition of Anatolian propolis to the treatment and Thorax CT completely returned to normal^(6,7,8).

Propolis, one of the natural bee products, is

a resinous substance from which bees are collected from the leaves, stems and buds of plants, and is extremely rich in phenolic and flavonoid content. Bees use propolis to maintain a sterile environment in the hive. More than 300 compounds have been identified in the content of propolis, including polyphenols, terpenoids, amino acids, volatile organic acids, ketones, coumarin, quinones, vitamins and minerals⁽⁹⁻¹³⁾.

The structure of propolis varies according to the type of the plant it is collected, the way it is collected and used by the bee, the production method of the beekeeper and the methods used when making it suitable for human food. Propolis is not recommended to be consumed as it is produced in the hive. Because the bioavailability of consumed raw propolis occurs at a maximum level of 2%. For this reason, it must be made suitable for human consumption and processed in order for the body to benefit from this product sufficiently. This process, carried out under high technology and quality standards, is called extraction. On the other hand, with unhealthy extraction methods performed in places such as herbalists, the property and activity of propolis, which is a very valuable product, can be completely lost. Even these unhygienic production conditions can lead to unwanted health problems⁽²⁻⁸⁾. For this reason, propolis must be extracted by experts, with appropriate substructure, knowledge and technical equipment, and offered for human consumption⁽⁹⁻¹³⁾.

With the increasing interest in natural products in the current pandemic and with extensive literature knowledge and accumulation, the anti-inflammatory and positive effects on the immune system of bee products (raw honey, royal jelly, pollen) and propolis have come to the fore again. The main components of propolis have been studied in many studies as the main regulator of inflammatory and oncogenic processes. In studies conducted with Anatolian propolis; analgesic, antioxidant, antibacterial and antiviral efficacy has been demonstrated⁽⁹⁻¹³⁾. Anatolian propolis has 19 kinds and O-type (*Populus nigra* L. from botanical origin), propolis is the most abundant species in Turkey. O-type propolis has been shown to have a higher antioxidant effect than other types of propolis tested. Quercetin, caffeic acid, galangin and caffeic acid phenethyl ester (CAPE) have been found to significantly contribute to the antioxidant potential of Anatolian propolis⁽⁹⁾. On the other hand, as a recent development, the ability of caffeic acid phenyl ester (CAPE) to inhibit p-STAT3, which is a highly desirable target for anticancer drug develop-

ment, has also been identified⁽¹⁴⁻²⁰⁾.

Possible positive effects of these valuable compounds in the bioactive content of propolis against COVID-19 have been revealed in more than a dozen studies conducted with multiple *in vitro* and molecular modeling. In addition, as seen in this case propolis is expected to have positive effects on protein kinase-1 (PAK-1), which is known to have an effect on the regression of pulmonary fibrosis associated with respiratory failure and even in the prevention of cytokine storm⁽⁹⁻¹³⁾.

Recent studies also support the existing knowledge about propolis and suggest that it can be used in patients diagnosed with COVID-19 due to its antiviral effect. Certainly, more studies are needed to provide evidence of propolis positive effects against COVID-19⁽⁹⁾.

Conclusion

Anatolian propolis is thought to be beneficial in both symptom and radiological recovery in COVID-19 prophylaxis and post-COVID period. However, controlled, randomized and large population studies are needed for this.

Anatolian propolis can be added to the existing treatment protocol in patients diagnosed with COVID-19 due to its easy use, low cost and safety. It is recommended to use 20 drops of 30% propolis per day for normal individuals without health problems.

While choosing different supplementary foods (such as sumac, curcumin, black seed oil, *gonaderma lucidum*, herbal teas); it should be paid attention to the suitability of production conditions and should be used at recommended doses.

There is a need for multi-center, large population studies on the prophylaxis of Anatolian propolis against COVID-19, its use in the post-COVID-19 period with treatment and even to prevent complications. Animal experiments and cell culture studies are also necessary to clearly demonstrate the effect of propolis in the post-COVID period.

With the promising picture created by this case, we make comprehensive plans and continue our work. We look forward to announcing our results. We also hope that there will be drug studies in the future that will provide definitive treatment with one or more of the specific compounds of Anatolian propolis.

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