The use of ezpap in patients with Covid-19 pneumonia and multiple sclerosis

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Abstract
In patients with multiple sclerosis (MS) respiratory muscle weakness and related development of respiratory failure are important causes of mortality. Complications such as atelectasis and susceptibility to respiratory infections are common in these patients. In cases of atelectasis and hypoxemia that develop due to the weakness of inspiratory muscles, the use of EzPAP® positive airway pressure therapy system should also be kept in mind, in addition to nasal oxygen and NIMV treatment options. In this case, we aimed to present our patient with the diagnosis of MS who was followed up for severe Covid 19 pneumonia and for whom EzPAP® positive airway pressure therapy system was used for treatment.

Keywords: multiple sclerosis, COVID-19, EzPAP®, pneumonia

1. Introduction
Since December 2019, the disease called "Novel Coronavirus Disease (COVID-19)" caused by a novel type of coronavirus has first spread from Wuhan Province of China to other provinces and then to the whole world rapidly (1). The clinic of Covid-19 has a wide spectrum from asymptomatic infection to systemic involvement, even "Acute Respiratory Distress Syndrome (ARDS)" and multi-organ failure (2). In most patients, oxygen therapy under close monitoring is sufficient. Oxygen therapy can be applied with conventional low-flow methods or with high-flow nasal oxygen (HFNO) cannula. If the patient does not require immediate intubation, a non-invasive mechanical ventilator (NIMV) can be tried (3). Multiple Sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system. In these patients, besides the musculoskeletal and neurological problems, swallowing disorders, respiratory muscle weakness, and related development of respiratory failure are important causes of mortality. The main respiratory problems seen in MS patients are, decreased ventilation due to inspiratory muscle weakness, deterioration of effective coughing, and increased risk of aspiration and pneumonia. Due to the breaths with low tidal volume, atelectasis may develop in patients, the rate of right-to-left shunt increases, and subsequent hypoxemia may be observed (4). We aimed to present a patient with MS diagnosis, who was followed up in our clinic for severe Covid-19 pneumonia and for whom EzPAP® positive airway pressure therapy system was used for the treatment.

2. Case Report
A 71-year-old female patient was admitted to the emergency department with a complaint of shortness of breath for three days. Upon admission, the vital signs were as follows: fever: 36.2 °C, blood pressure: 120/80 mmHg, pulse: 79 bpm, and oxygen saturation: 85% at room air. It was learned that she had multiple sclerosis and hypertension diseases and she had been paraplegic for 25 years due to MS. Bilateral increased nonhomogeneous density areas were observed on chest radiography. In the laboratory findings, white blood cell count was 16100 / µl, lymphocyte count 1600/ µl, Na: 120 mEq / L, C-reactive protein (CRP): 166 mg / L, D-dimer: 0.45 mg / L, ferritin 300 ng / ml and cardiac troponin was normal. Concurrent Covid-19 Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) was positive. The patient was diagnosed with Covid-19 pneumonia, due to the presence of bilateral multilobar ground glass infiltration areas in thorax computed tomography (CT), and she was hospitalized in the Covid clinic. Favipiravir, methylprednisolone, low molecular weight heparin (LMWH) and nonspecific antibiotherapy treatments were initiated. Oxygen therapy of the patient, who was using an oxygen concentrator at home due to her current illness, was continued with nasal cannulae. On the sixth day of hospitalization, a control chest radiograph was obtained due to a decrease in the oxygen saturation of the patient. Because a progression was detected on the radiograph, HFNO and intermittent NIMV treatments were given. For the patient, whose oxygenation and control chest radiographs did not fully improve, EzPAP® positive airway pressure therapy system (Fig. 1) was used for the atelectasis. After EzPAP® treatment, the oxygen saturation of the patient was 90% and above, and a
significant regression was observed in the control chest X-ray (Fig. 2).

**Fig. 1.** EzPAP® positive airway pressure therapy system

**Fig. 2.** Chest radiographs (before (left) and after (right) treatment of EzPAP®)

3. Discussion

The virus that spread from Wuhan, China to the whole world in December 2019 and caused Covid-19 was named SARS-CoV-2. The main cause of mortality and morbidity in this disease is acute viral pneumonia that causes ARDS. In the Covid-19 disease, the clinic of the patient may range from asymptomatic infection to severe pneumonia. In patients with severe pneumonia, respiratory failure, shock, or several organ failures develops, and follow-up and treatment in intensive care units are required (5). The World Health Organization (WHO) recommends maintaining oxygen saturation ≥ 90%. Oxygen therapy can be given with conventional low-flow (<15 L / min) or high-flow methods (3). In adults with acute hypoxemic respiratory failure despite the conventional oxygen therapy, the use of HFNO therapy instead of conventional oxygen therapy is recommended. EzPAP® positive airway pressure therapy system is a portable and disposable system that is developed as an alternative to the inspiratory positive pressure therapy (Intermittent positive pressure breathing; IPPB) used in patients with spontaneous breathing. During its use, inspiration is supported by the flow, and PEP is applied during expiration. It provides the expansion of the lungs by increasing the functional capacity. Preliminary studies have shown its effectiveness in the treatment of atelectasis in patients in intensive care units (6-7). In a study by Rieg et al., a probable more effective improvement in pulmonary oxygenation was detected with oxygen therapy using the EzPAP® system, in patients at high risk of postoperative hypoxemia. Therefore, the EzPAP® system was presented as a well-tolerated, effective, cost-effective, and easy-to-operate system to improve postoperative oxygenation (8).

MS is an autoimmune central nervous system disease that is characterized by inflammation, demyelination, and axon damage. Commonly observed symptoms are weakness in the extremities, sensory symptoms, ataxia, bladder problems, fatigue, diplopia, visual symptoms such as blurred vision, dysarthria, and cognitive symptoms such as memory-concentration-attention disorder (9). Since MS is a chronic and usually progressive disease, many signs and symptoms which do not cause any disability at the beginning of the disease may cause further disabilities that affect the patient's functional activities after a while. Especially in multiple sclerosis patients with attacks, many drugs are widely used with the latest developments in the treatment of MS (10). However, all patients do not get the expected response with these treatments and some of the patients turn into a progressive form. In both acute and chronic periods, the most important cause of mortality and morbidity is the respiratory system being affected by neuromuscular diseases. Progressive weakness and mechanical disadvantage of respiratory muscles are responsible for the rapid and superficial breathing, and alveolar hypoventilation causes chronic CO2 retention in these patients. Respiratory muscle weakness causes impaired ventilation and accumulation of pulmonary secretions due to ineffective coughing. This situation leads to complications such as atelectasis and susceptibility to respiratory infections.

In the literature, it is emphasized that respiratory muscle weakness develops in the advanced stages of MS (11). Atelectasis may develop due to inspiratory muscle weakness and may cause a right to left physiological shunt. Chronic atelectasis increases respiratory workload by decreasing the compliance of the inspiratory system, and a vicious circle develops by the increased respiratory muscle weakness. The respiratory muscles can be helped by applying force manually or mechanically to the body or by applying intermittent pressure to the airway. Some devices help inspiratory muscles, while others facilitate coughing by mainly helping expiratory muscles (12).

In observational studies conducted in patients with neuromuscular disease who have acute respiratory failure and who need short-term mechanical ventilation, NIV was found to
reduce the need for IMV, shorten the length of stay in the intensive care unit and reduce mortality (13). In a prospective cohort study in which 17 patients with neuromuscular diseases who received NIV for acute respiratory failure were involved, a requirement of IMV did not develop in 79% of the patients (14). NIV may prevent or delay the progression of chronic respiratory failure in intermittent long-term NIV use in patients with nocturnal hypoventilation or early chronic respiratory failure (15).

In our case, there was respiratory muscle weakness due to being paraplegic for approximately 25 years. There was a history of regular oxygen support with a nasal cannula and intermittent NIMV use before the hospitalization with Covid 19 pneumonia. Impairment in oxygenation and radiological progression was detected in the patient, who received favipiravir, methylprednisolone, LMWH and nonspecific antibiotic treatments for Covid 19 pneumonia and who did not meet the cytokine storm parameters during follow-up. Atelectasis due to respiratory muscle weakness caused by the underlying disease was thought when and effective improvement was not observed with HFNO and intermittent NIMV treatments, so treatment of EzPAP® positive airway pressure therapy system was given.

After EzPAP® treatment, an improvement in oxygenation was observed in the first hour and a significant regression was observed in the first hour and a significant regression was not met with nocturnal hypoventilation. This treatment option can be tried in patient weakness, the use of EzPAP® positive airway pressure therapy was observed in the first hour and a significant regression was not observed in the first hour and a significant regression was not observed with nocturnal hypoventilation and early chronic respiratory failure (15). Atelectasis due to respiratory muscle weakness caused by the underlying disease was thought when and effective improvement was not observed with HFNO and intermittent NIMV treatments, so treatment of EzPAP® positive airway pressure therapy system was given.

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