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Abstract
Coronavirus disease 2019 (COVID-19) affects different organs and a severe pro-inflammatory response, denominated “cytokine storm” have been described as a key underlying mechanism. The lungs are the most affected organ, and a fibrotic response after infection by COVID-19 is often found. This case report demonstrates that 12 days of oral administration of Virlaza™, an herbal medicine developed in Israel (based on tinctures and natural antioxidants), was able to accelerate the lung recovery of a moderate/severe post-COVID-19 patient, who presents metabolic syndrome, characterized by grade II obesity, dyslipidemia, and hypertension.

After 12 days of hospitalization needing high flow nasal oxygen, non-invasive ventilation, awake (non-intubated) proning, the patient was discharged still presenting the following characteristics: 75% of ground-glass opacities of the lungs in computerized tomography (CT), severe reduction of the lung function, high levels of fractional exhaled nitric oxide (FeNO), leukopenia and neutrophilia, reduced respiratory muscle strength and peripheral muscle strength. So, a very quick recovery was observed after 12 days of Virlaza™, resulting in an improvement to 25% ground-glass opacities of the lungs in the CT, as well as an improvement for all parameters of lung function, FeNO, normalization of blood leukocytes and improvement of respiratory and peripheral muscle strength. So, Virlaza™ may be considered as an herbal medicine able to improve the recovery of post-COVID-19 patients and reduce COVID-19 comorbidities.

Keywords: COVID-19; Lung Function; Nitric Oxide; Peripheral Muscle Strength; Respiratory Muscle Strength; SARS-Cov-2

Introduction
The COVID-19 imposed a pandemic in the whole world, affecting more than 619 million cases and 6 million deaths due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The progression, severity, and mortality of COVID-19 differ from no, mild, or moderate symptoms in most of the patients, while up to 15% develop the severe and critical form of the disease with high mortality rates [2, 3]. Among the factors underlying the development of the severe and critical forms of COVID-19, advanced age [4], comorbidities such as obesity [4], hyperactivation of the immune system [4, 5] are proven to have a central role. In addition, hyperactivation of the immune system results in the cytokine storm, which is characterized by the synthesis and release of high levels of proinflammatory cytokines [4, 5]. In this way, cytokine storm plays a major role in COVID-19 pathogenesis,

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progression, and severity, impairing several organ functions, such as the lungs, heart, blood vessels, etc., [4, 5].

Case Presentation

A 50-year-old man, without any history of previous respiratory diseases or allergy, with historic of two cardiovascular surgeries, grade II obese (BMI 35.91), insulin resistance, flu-like symptoms, fatigue and breathlessness, partial oxygen saturation of 80%, chest CT of the lungs (>75% ground-glass opacities) and diagnosed with coronavirus disease 19 (COVID-19) by real-time polymerase chain reaction. After twelve days of hospitalization, under treatment with antibiotic (Amoxicillin 500mg/2x/day and Clavulanate Potassium 125mg/2x/day), corticosteroid (Prednisone 20mg/day) and sodium enoxaparin (100mg/day), the patient has been discharged from the hospital, still presenting 75% of ground-glass opacities of the lungs. After hospital discharged these symptoms remained: acute fatigue and breathlessness for minimal effort. The measurement of partial oxygen saturation at rest, lung function by spirometry (Masterscreen, Jaeger, Germany), according to ATS/ERS recommendations was performed by using forced maneuver [6]. Whole blood analysis (red and white cells) (automatic hematology analyzer Sysmex® XS-800i, Japan) [7], the levels of FeNO (NoBreath®, Bedfont Scientific, UK) [7], maximal inspiratory (MIP) and expiratory (MEP) pressure (analogical manovacuometer, Murenas®, Brazil) [7], and hand grip strength (analogical dynamometer, Jamar®, USA) [8] were performed before and after 12 days of use of Virlaza™ (20 drops, 2x/day). Virlaza™ is a tincture-based 10% concentration of: Clove Glycerin, Eucalyptus Glycerin, Basil Glycerin, Sage Glycerin, Maritime Pine Glycerin, Clove Ethyl Alcohol, Eucalyptus Ethyl Alcohol, Maritime Pine Ethyl Alcohol, Basilica Ethyl Alcohol, Sage Ethyl Alcohol. The results demonstrated that 12 days of Virlaza™ improved: lung function, forced vital capacity (FVC; 1.91 L x 2.31 L; 41.2% x 61.7% of predicted), forced expiratory volume in the first second (VEF1; 1.51 L x 1.68 L; 40.4% x 55.9% of predicted), inspiratory vital capacity (VC In; 1.59 L x 1.63 L, 36.3% x 46.7% of predicted), forced expiratory flow 25% (FEF25%; 0.47 L/s x 0.58 L/s, 35.8% x 58.3% of predicted), forced expiratory flow 50% (FEF50%; 1.42 L/s x 1.62 L/s, 37.4% x 41.9% of predicted), forced expiratory flow 75% (FEF75%; 2.91 L/s x 3.58 L/s, 48.3% x 49.7% of predicted), peak expiratory flow (PEF; 2.99 L/s x 3.97 L/s, 36.4% x 38%). The CT revealed a significant reduction in ground-glass opacities, reducing from >75% to 25% after 12 days of Virlaza™ (Figure 1). The levels of FeNO were initially of 28 parts per billion (ppb) to 11 ppb after treatment with Virlaza™. Partial oxygen saturation also presented significant improvement, from 92% to 99% after 12 days of treatment with Virlaza™. The hematological response was improved by Virlaza™ (platelets 250x10^10/mm^3 x 350x10^10/mm^3; total leukocytes 5.37/mm^3 x 9.77/mm^3; neutrophils 87% x 52.2%; lymphocytes 11% x 38%; eosinophils 0.9% x 0%; monocytes 2% x 0.1%; basophils 0.02% x 0.01%). The strength of respiratory muscles presented improvement after treatment with Virlaza™, where MIP was -100 cmH_2O x -120 cmH_2O and MEP 40 cmH_2O x 60 cmH_2O. Virlaza™ improved hand grip strength on right (28.9 Kg x 36.2 Kg) and left (19.8 Kg x 23.1 Kg) hands. Due to the reduction in the levels of FeNO demonstrating anti-inflammatory effects of Virlaza™, we point out the importance of controlling the lung inflammation to inhibit a poor prognosis during the recovery of COVID-19, which has been associated with lung fibrosis [9]. Such result is strengthened by the finding of a significant reduction in the lung ground opacities (>75% to 25%), followed by a very significant improvement in the lung function. As a study limitation, a longer period of follow up of the patient should be done. In conclusion, this case study reveals important beneficial effects of Virlaza™ on clinical and functional parameters of the severe post-COVID-19 patients.

Figure 1: In panel A (A.1 to A.5) the images referred to after treatment with Virlaza™, while in panel B (B.1 to B.5) the images referred to before treatment with Virlaza™.
Consent

This study was approved by Ethical Committee of Anhembi Morumbi University, registration number 5.193.830. Written and verbal consent was obtained from the patient for this case report.

Conflict of Interest

MARBR and CRF have no conflict of interest related to this study. DM and BB are the owners and scientific director of Libipharm™. RPV declares he has received consulting fee from Libipharm™.

Data Availability

All data obtained during the current study are not publicly available due to confidential issues but might be available at a reasonable request to the corresponding author.

Authors’ Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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