AUCTORES
Globalize your Research

Clinical Medical Reviews and Reports
Calixto Machado *

Open Access

Research Article

Early Prevention of Hypoxemia in COVID-19 Patients can avert the Cytokine Storm

Calixto Machado [1*], Alina Gonzalez-Quevedo [1], Yanín Machado [1], Mauricio Chinchilla [1], Jonathan Fellus [2], Arthur Schift [3], Beata Drobná Sániová [4] and Michal Drobný [4]

[1]Institute of Neurology and Neurosurgery, Havana, Cuba.

[2]MD, and Neurology Specialist in Morristown, NJ

[3]Emory University, Cuba.

[4]Commenius University in Bratislava

***Corresponding Author:** Calixto Machado, Institute of Neurology and Neurosurgery, 29 y D, Vedado La Havana, Cuba.

Received Date: December 03, 2021; **Accepted Date:** January 13, 2022; **Published Date:** January 20, 2022

Citation: Calixto Machado, Alina Gonzalez-Quevedo, Yanín Machado, Mauricio Chinchilla, Jonathan Fellus, Arthur Schift, Beata Drobná Sániová and Michal Drobný (2022) Early Prevention of Hypoxemia in COVID-19 Patients can avert the Cytokine Storm. *Clinical Medical Reviews and Reports.* 4(4); DOI:10.31579/2690-8794/118

Abstract

Background: In COVID-19, an exaggerated pro-inflammatory response, known as cytokine storm (CS). The anti-inflammatory system's CS–mediated response is an ineffective immunological control, leading to tissue damage, multiorgan failure, acute respiratory distress syndrome, and death.

Objectives: To review and discuss the tie relationship between hypoxemia and the CS, proposing an early avoidance of periods of hypoxemia to avert the CS.

Methods: We review the literature on this topic providing a pathophysiological background to support our proposal of avoiding periods of hypoxemia in the early stages of the disease.

Results: Cytokine-mediated lung endothelial and epithelial cell injury may damage the integrity of the blood–air barrier, promoting vascular permeability, alveolar edema, infiltration, and the presence of inflammatory cells, starving the blood of oxygen, causing hypoxemia. Hypoxemia triggers factors like HIF-1α, which regulates essential cellular processes, including cell proliferation, metabolism, and angiogenesis. HIF-1α is activated during the immune response and plays an indispensable role at the inflammation site by inducing pro-inflammatory cytokine production, finally resulting in CS. Short and slight periods of hypoxemia start even during the first manifestation of persistent cough and/or shortness of breath.

Conclusion: A more straightforward treatment strategy is to provide oxygen supply as early as possible, when the first respiratory symptoms begin, to prevent periods of hypoxemia outside the ICU. We have suggested using CPAP. Other methods such as Low or High-flow nasal oxygen HFNO therapy would provide the necessary oxygen at the lung alveoli to prevent gas exchange impairment, avoid hypoxemia, and therefore, avert CS.

Keywords: covid-19; sars-cov-2; cytokine storm; acute respiratory distress syndrome (ards); non-invasive ventilation; cpap

Introduction

A specific adaptive immune response is initiated during early incubation and non-severe stages after SARS-CoV-2 infection to exterminate the virus and halt disease progression. The second phase is characterized by the advent of systemic symptoms with unrestrained cytokine production, known as cytokine storm (CS) [1-3].

An exaggerated pro-inflammatory characterizes CS–mediated response and ineffective control by the anti-inflammatory system, leading to tissue damage, multiorgan failure, acute respiratory distress syndrome (ARDS), and death.[4-11].

Methods

We made a detailed review of the literature regarding the relationship between hypoxemia and CS in COVID-19 disease.

Results

Cytokine-mediated lung endothelial and epithelial cell injury may damage the integrity of the blood–air barrier, promoting vascular

permeability, alveolar edema, infiltration, and the presence of inflammatory cells. As tissue breaks down, the walls of the lungs' tiny air sacs become leaky and fill with fluid starving the blood of oxygen, causing hypoxemia [12-16].

Hypoxemia triggers factors like HIF-1α, which regulates essential cellular processes, including cell proliferation, metabolism, and angiogenesis. HIF-1α is activated during the immune response and plays an indispensable role at the inflammation site by inducing pro-inflammatory cytokine production, finally resulting in CS [1-4], [17-20].

Discussion

COVID-19 presents mildly in most patients, commonly beginning during the first days of clinical evolution with fever followed by a dry cough and flu-like symptoms. Nonetheless, short and slight periods of hypoxemia start even during the first manifestation of persistent cough and/or shortness of breath, as reported by authors using pulse oximetry and arterial gasometry.21 In some cases, during the second week of the clinical evolution, these symptoms may progress, leading to ARDS, closely related to the progressive increment of CS, which requires admission in intensive care units (ICU) with mechanical ventilation [1-3], [22-26]

Hence, the medical-scientific community is desperately trying to find treatments to avert CS. Several biologic interventions targeting inflammatory cytokines or related signaling pathways have been clinically evaluated with promising results, but without a final success to defeat this disease [27-36].
Hypoxemia is a decisive triggering factor for CS in COVID-19. CS generates additional hypoxia in tissues and organs, leading to a chain reaction between hypoxemia and CS [1, 2, 8, 9, 37, 38].

Conclusion

Therefore, a more straightforward treatment strategy is to provide oxygen supply as early as possible, when the first respiratory symptoms begin, to prevent periods of hypoxemia outside the intensive care units. Dr. Machado has suggested using CPAP.8 Other methods such as Low or High-flow nasal oxygen HFNO therapy, administered through nasal cannulae or a mask, would provide the necessary oxygen at the lung alveoli to prevent gas exchange impairment, avoid hypoxemia, and therefore, averting CS [3, 8].

Authors declare no conflicts of interest

References

1. Machado-Curbelo C. (2020) Silent or 'Happy' Hypoxemia: An Urgent Dilemma for COVID-19 Patient Care. MEDICC Rev; 22:85-6.
2. Machado-Curbelo C. (2020) Severe COVID-19 Cases: Is Respiratory Distress Partially Explained by Central Nervous System Involvement? MEDICC Rev; 22:38-9.
3. Machado C, González-Quevedo A. (2021) Hypoximia and cytokine storms in COVID-19: clinical implications. MEDICC Rev; 23:54–9.
4. Evans CE. (2019) Hypoxia and HIF activation as a possible link between sepsis and thrombosis. Thromb J; 17:16.
5. Dhont S, Derom E, Van Braeckel E, Depuydt P, Lambrecht BN. (2021) Conceptions of the pathophysiology of happy hypoxemia in COVID-19. Respir Res; 22:12.
6. Anirvan P, Narain S, Hajizadeh N, Aloor FZ, Singh SP, Satapathy SK. (2019) Cytokine-induced liver injury in coronavirus disease- (COVID-19): untangling the knots. Eur J Gastroenterol Hepatol; 2021;Publish Ahead of Print.
7. Lupon E, Lellouch AG, Zal F, Cetrulo CL, Jr., Lantieri LA. (2021) Combating hypoxemia in COVID-19 patients with a natural oxygen carrier, HEMO2Life(R) (M101). Med Hypotheses; 146:110421.
8. Machado C. (2021) Dangers and management of obstructive sleep apnea syndrome in COVID-19 patients. MEDICC Rev; 23.
9. Machado C, Gutierrez JV. (2020) Brainstem Dysfunction in SARS-COV2 Infection Can Be a Potential Cause of Respiratory Distress. Preprints; 2020040330.
10. Machado C, Mualem R, et al. (2020) It Is Imperative the use of Positive Air Pressure (CPAP) in Covid-19 Patients as Soon as the First Respiratory Symptoms Start. Frontiers Journal of Neurology and Neuroscience; 1:1-14.
11. Machado C, DeFina PA, Chinchilla M, Machado Y, Machado Y. (2020) Brainstem Dysfunction in SARS-COV-2 Infection can be a Potential Cause of Respiratory Distress. Neurol India; 68:989-93.
12. Wang X, Tu Y, Huang B, Li Y, Li Y, Zhang S, et al. (2020) Pulmonary vascular endothelial injury and acute pulmonary hypertension caused by COVID-19: the fundamental cause of refractory hypoxemia? Cardiovasc Diagn Ther; 10:892-7.
13. Saguil A, Fargo MV. (2020) Acute Respiratory Distress Syndrome: Diagnosis and Management. Am Fam Physician; 101:730-8.
14. Wang P, Luo R, Zhang M, Wang Y, Song T, Tao T, et al. (2020) A cross-talk between epithelium and endothelium mediates human alveolar-capillary injury during SARS-CoV-2 infection. Cell Death Dis; 11:1042.
15. Shao C, Liu H, Meng L, Sun L, Wang Y, Yue Z, et al. (2020) evolution of severe acute respiratory syndrome coronavirus 2 RNA test results in a patient with fatal coronavirus disease 2019: a case report. Hum Pathol; 101:82-8.
16. Nascimento Conde J, Schutt WR, Gorbunova EE, Mackow ER. (2020) Recombinant ACE2 Expression Is Required for SARS-CoV-2 To Infect Primary Human Endothelial Cells and Induce Inflammatory and Procoagulative Responses. mBio; 11.
17. AbdelMassih A, Yacoub E, et al. (2021) Hypoxia-inducible factor (HIF): The link between obesity and COVID-19. Obes Med; 22:100317.
18. Taniguchi-Ponciano K, Majluf A, et al. (2021) Increased expression of hypoxia-induced factor 1alpha mRNA and its related genes in myeloid blood cells from critically ill COVID-19 patients. Ann Med; 53:197-207.
19. Tian M, Liu W, Li X, Zhao P, Shereen MA, Zhu C, et al. (2021) HIF-1alpha promotes SARS-CoV-2 infection and aggravates inflammatory responses to COVID-19. Signal Transduct Target Ther; 6:308.
20. Yuan Y, Li Y, Qiao G, Zhou Y, Xu Z, Hill C, et al. (2021) Hyperbaric Oxygen Ameliorates Bleomycin-Induced Pulmonary Fibrosis in Mice. Front Mol Biosci; 8:675437.
21. Parasher A. (2020) COVID-19: Current understanding of its pathophysiology, clinical presentation and treatment. Postgrad Med J;
22. Network C-IGobotR, the C-ICUI. (2021) Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: a prospective cohort study. Intensive Care Med; 47:60-73.
23. Gonzalez-Martinez A, Fanjul V, Ramos C, Serrano Ballesteros J, Bustamante M, Villa Marti A, et al. (2021) Headache during SARS-CoV-2 infection as an early symptom associated with a more benign course of disease: a case-control study. Eur J Neurol;

24. Wang XH, Wang X, et al. (2021) High incidence and mortality of pneumothorax in critically Ill patients with COVID-19. Heart Lung; 50:37-43.
25. Leasa D, Group LVSfC-W. (2021) Knowledge translation tools to guide care of non-intubated patients with acute respiratory illness during the COVID-19 Pandemic. Crit Care25:22.
26. Bellani G, Grasselli G, Cecconi M, Antolini L, Borelli M, De Giacomi F, et al. Noninvasive Ventilatory Support of COVID-19 Patients Outside the Intensive Care Units (WARd-COVID). Ann Am Thorac Soc; 2021.
27. Ye Q, Wang B, Mao J. (2020) The pathogenesis and treatment of the `Cytokine Storm' in COVID-19. J Infect; 80:607-13.
28. Verma YK, Verma R, Tyagi N, Behl A, Kumar S, Gangenahalli GU. (2020) COVID-19 and its Therapeutics: Special Emphasis on Mesenchymal Stem Cells Based Therapy. Stem Cell Rev Rep;
29. Rehman MFU, Fariha C, Anwar A, Shahzad N, Ahmad M, Mukhtar S, et al. (2021) Novel coronavirus disease (COVID-19) pandemic: A recent mini review. Comput Struct Biotechnol J; 19:612-23.
30. Que Y, Hu C, Wan K, Hu P, Wang R, Luo J, et al. (2021) Cytokine release syndrome in COVID-19: a major mechanism of morbidity and mortality. Int Rev Immunol; 1-14.
31. Ong WY, Go ML, Wang DY, Cheah IK, Halliwell B. (2021) Effects of Antimalarial Drugs on Neuroinflammation-Potential Use for Treatment of COVID-19-Related Neurologic Complications. Mol Neurobiol; 58:106-17.
32. Li P, Lu Z, Li Q, Wang Z, Guo Y, Cai C, et al. (2021) Administration Timing and Efficacy of Tocilizumab in Patients With COVID-19 and Elevated IL-6. Front Mol Biosci; 8:651662.
33. Stoy N. (2021) Involvement of Interleukin-1 Receptor-Associated Kinase 4 and Interferon Regulatory Factor 5 in the Immunopathogenesis of SARS-CoV-2 Infection: Implications for the Treatment of COVID-19. Front Immunol; 12:638446.
34. Moradinasab S, Pourbagheri-Sigaroodi A. (2021) Mesenchymal stromal/stem cells (MSCs) and MSC-derived extracellular vesicles in COVID-19-induced ARDS: Mechanisms of action, research progress, challenges, and opportunities. Int Immunopharmacol; 97:107694.
35. Calabrese EJ, Kozumbo WJ, Kapoor R, Dhawan G, Jimenez PCL, Giordano J. (2021) NRF2 activation putatively mediates clinical benefits of low-dose radiotherapy in COVID-19 pneumonia and acute respiratory distress syndrome (ards): novel mechanistic considerations. Radiother Oncol;
36. Ciampa ML, O'Hara TA, Joel CLet al. (2021) Absence of "Cytokine Storm" in Hospitalized COVID-19 Patients: A Retrospective Cohort Study. Infect Dis Rep; 13:377-87.
37. Machado C,Cuspineda E, Machado Y. (2020) Continuous positive air pressure (CPAP) should be used in all COVID-19 patients when the first and mild respiratory symptoms commence. J Respir Dis Med 2:1-6.
38. Machado C.(2020) Early Prevention of Hypoxemia (Response to Peter S. Kim, Sarah W. Read, Anthony S. Fauci. Therapy for Early COVID-19: A Critical Need, published in JAMA. Published online. doi:10.1001/jama.2020.22813). JAMA;

DOI: 10.31579/2690-8794/118