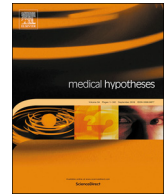




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to Editors

Transpulmonary electrotherapy for reduction of lung viral load of SARS-CoV-2 in patients with COVID-19



There are more than 9 million COVID-19 cases identified globally. Numerous observational studies have described the clinical course and outcomes of patients who have contracted SARS-CoV-2 and were subsequently hospitalized. The most common form of supportive care includes high flow nasal cannula up to invasive ventilation for moderate-to-severely ill cases. Beyond oxygen therapy, patients are also given a variety of pharmaceutical therapies including antiviral agents, protease inhibitors, immunosuppressive compounds, monoclonal antibodies and convalescent plasma therapy. However, no therapy has demonstrated a strong signal of improved clinical status. Several studies have demonstrated that established ICU protocols have failed to treat COVID-19 induced acute respiratory distress syndrome (ARDS) [1,2].

Considering the unique challenges of COVID-19 and lack of effective treatments, we propose the use of local bioelectronic therapy of lungs through electric fields to prevent the binding of spikes of SARS-CoV-2 to the ACE-2 receptors of lung epithelium. Several groups have previously studied the electric charges of viruses, including other coronaviruses, which demonstrated that a majority of viruses are electrically charged [3–8]. Indeed, the protein coat that surrounds the genome of the virus are made of amino acids with functional groups, such as amino and carboxylic acid groups. These protein coatings can be ionized depending on the pH of the solution in which they are immersed. This is extremely important in determining whether the viruses can bind to a cellular receptor and assemble themselves into an infective form. Viral structures must remain stable to enter the cell, whether it be through membrane fusion, endocytosis, or genetic injection. Neutralizing the charge of the virus is feasible to inhibit the binding affinity of the receptor for the virus, which could reduce the viral load potential as inhibiting viral host-cell entry inhibits viral replication.

In the context of COVID-19 we propose placing a unipolar pacing wire or catheter trans-esophageally, pulmonary, bronchially, or venously, and connecting it via an energy source. The energy course would create a low power electrical field locally in the lungs and may inactivate SARS-CoV-2 virions in the damaged lungs. The inactivation of the virions would inhibit further uninfected cells from infiltration. The procedure could be performed bedside and does not require imaging. However, there are several challenges to consider. For example, this approach could stimulate the vagus nerve and produce unwanted adverse events. In this instance, a trans-venous pulmonary route could be considered. This may prove to be more clinically meaningful and increase oxygenation. In both instances, a pacing catheter may be used,

and the electrodes maybe left during the course of treatment. Experimental studies will be underway to identify the therapeutic dose of energy that would be feasible and safe, and a dose that would not interfere with the electrical conduction of the heart. Finally, electric therapy does not preclude the use of conjunctive existing COVID-19 therapies. In fact, when combined with an existing medical therapy, especially antivirals and immunomodulating agents, concomitant bioelectronic and pharmaceutical therapy may prove to be the most effective approach. One caveat, however, warrants the attention that theoretically this bioelectronic procedure cannot be used in patients with ICD or permanent pacemakers. Ultimately, the planned experimental studies and early feasibility studies will demonstrate whether this is a worthwhile avenue to further explore.

Conflict of interest statement

The authors have no relevant industry relationships to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.110071>.

References

- [1] Richardson S, et al. JAMA 2020.
- [2] Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. JAMA 2020.
- [3] Belyi VA, Muthukumar M. Proc Natl Acad Sci USA 2006;103:17174–8.
- [4] Forrey C, Muthukumar M. 131; 2009: 105101.
- [5] Hu T, Zhang R, Shklovskii BI. Physica A 2008;387:3059–64.
- [6] Perlmutter JD, Hagan MF. Annu Rev Phys Chem 2015;66:217–39.
- [7] Roy S, et al. Adv Wound Care (New Rochelle) 2019;8:149–59.
- [8] Wang J, et al. Virol Sin 2016;31:49–56.

Nicholas Kipshidze^{a,*}, Valeri S. Chekanov^b, Nodar Kipshidze^c,
Vivek Y. Reddy^d, George Dangas^d

^a New York Cardiovascular Research, New York, NY, USA

^b Aurora Health Care, University of Wisconsin, Milwaukee, WI, USA
(Retired)

^c NYU Langone Health, New York, NY, USA

^d Icahn School of Medicine at Mount Sinai, New York, NY, USA

E-mail address: nicholas02@msn.com (N. Kipshidze).

* Corresponding author.