

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.



Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy



Methylene blue: Subduing the post COVID-19 blues!

ARTICLE INFO

Keywords COVID-19 Methylene blue Mitochondrial dysfunction Neurocognitive impairment Neuroinflammation Neuroprotection

Dear Editor,

We read with great interest the recent articles featured in the *Journal* elaborating a therapeutic role of methylene blue (MB) in coronavirus disease 2019 (COVID-19) [1,2]. However, the elaboration remains incomplete in the absence of discussion on the possibility of ameliorating the post COVID-19 blues (neurocognitive impairment) with the use of MB in this cohort peculiarly predisposed to neuroinflammation. The aforementioned becomes particularly relevant amidst an increasing recognition of cognitive and functional decline in the COVID-19 survivors [3].

There is an ever evolving comprehension of the pivotal role of mitochondrial dysfunction in neurodegenerative disorders characterized by neuroinflammation and neuronal death perpetuated in turn by the accompanying oxidative stress, endotheliitis and metabolic disturbances [4,5]. While the former can contribute significantly to the COVID-19 associated neurocognitive impairment [3,5], the proposition of improving brain mitochondrial respiration for neuroprotection and cognitive enhancement is doubtlessly pertinent even in the COVID-19 setting [6].

In this context, the mitochondrial protective effects of MB as the basis of the attributable neuroprotection in diverse clinical settings such as ischemic stroke, neurodegenerative diseases and chemotherapyinduced encephalopathy [7–9], captivate attention and enterprise a plausible role of the drug in attenuating post COVID-19 cognitive and functional decline. Moreover, literature also supports the role of MB as a redox-mediator in the electron-transport chain being at the cornerstone of the subsequent amelioration of the altered neurometabolomics [10]. A very recent description of a reduced incidence of postoperative cognitive disorders in the elderly patients undergoing major non-cardiac surgery, who received an intraoperative 2 mg/Kg MB infusion compared to the control group receiving saline in an open-label randomised controlled clinical trial by Deng et al [10], substantiates the matter furthermore.

The discussion strengthens the importance of highlighting the possible therapeutic options like MB with an augmented focus on the long-term outcomes which itself as in the case of neurocognitive impairment can potentially pose a challenging post-pandemic situation [3].

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References:

- Scigliano G, Scigliano GA. Methylene blue in covid-19. Med Hypotheses 2021;146: 110455. https://doi.org/10.1016/j.mehy.2020.110455.
- [2] Ghahestani SM, Shahab E, Karimi S, Madani MH. Methylene blue may have a role in the treatment of COVID-19. Med Hypotheses 2020;144:110163. https://doi.org/ 10.1016/j.mehy.2020.110163.
- [3] Magoon R. Impending cognitive and functional decline in COVID-19 survivors. Comment on Br J Anaesth 2021; 126: 44-7. Br J Anaesth. 2021;126:e113-e114.
- [4] Lin MT, Beal MF. Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases. Nature 2006;443(7113):787–95.
- [5] Magoon R, ItiShri, Kohli JK, Kashav R. Inhaled milrinone for sick COVID-19 cohort: a pathophysiology driven hypothesis! Med Hypotheses 2021;146:110441. https:// doi.org/10.1016/j.mehy.2020.110441.
- [6] Gonzalez-Lima F, Barksdale BR, Rojas JC. Mitochondrial respiration as a target for neuroprotection and cognitive enhancement. Biochem Pharmacol. 2014;88(4): 584–93.
- [7] Shen Q, Du F, Huang S, Rodriguez P, Watts LT, Duong TQ, et al. Neuroprotective efficacy of methylene blue in ischemic stroke: an MRI study. PLoS ONE 2013;8(11): e79833.
- [8] Alda M, McKinnon M, Blagdon R, Garnham J, MacLellan S, O'Donovan C, et al. Methylene blue treatment for residual symptoms of bipolar disorder: randomised crossover study. Br J Psychiatry 2017;210(1):54–60.
- [9] Küpfer A, Aeschlimann C, Wermuth B, Cerny T. Prophylaxis and reversal of ifosfamide encephalopathy with methylene-blue. Lancet 1994;343(8900):763–4.
- [10] Deng Y, Wang R, Li S, Zhu X, Wang T, Wu J, et al. Methylene blue reduces incidence of early postoperative cognitive disorders in elderly patients undergoing major non-cardiac surgery: an open-label randomized controlled clinical trial. J Clin Anesth 2021;68:110108.

Rohan Magoon^{*}, Noopur Bansal, Armaanjeet Singh, Ramesh Kashav Department of Cardiac Anaesthesia, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) and Dr. Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, New Delhi 110001, India

> ^{*} Corresponding author. *E-mail address:* rohanmagoon21@gmail.com (R. Magoon).

https://doi.org/10.1016/j.mehy.2021.110574 Received 26 February 2021; Accepted 14 March 2021 Available online 23 March 2021

0306-9877/© 2021 Elsevier Ltd. All rights reserved.

