

1 Commentary

2 Repurposing Diacerein, Omega 3 Fatty Acids and Pentoxifylline to Manage COVID-19

3 Relapse and Para COVID Syndrome

4 Mina T. Kelleni, MD, PhD

5 Pharmacology Department, College of Medicine, Minia University, Egypt.

6 Mobile: +201200382422

7 drthabetpharm@yahoo.com, mina.kelleni@mu.edu.eg

8 <https://orcid.org/0000-0001-6290-6025>

24 The persistence of troublesome symptoms, affecting different body systems, for more than
25 three weeks after the diagnosis of COVID-19 was suggested to be named Post COVID
26 syndrome with an incidence of 10 – 35% for non-hospitalized patients and up to 85% for
27 the hospitalized ones¹. Furthermore, an interesting study published at Journal of Infection
28 has suggested that 50% of COVID-19 patients might experience persistent symptoms for
29 10-14 weeks after disease onset². However, a relapse might be considered as a the proper
30 term if symptoms reappear in the first eight weeks after COVID-19 onset³ and we as a
31 compromise, we would like to recommend adoption of persistent symptoms for 10 weeks
32 after the initial diagnosis to be considered as Post COVID which is an evolving subject
33 with obscure pathogenesis and like COVID no current approved effective
34 pharmacotherapy. Notably, we have suggested that Para COVID syndrome might present
35 a more precise nomenclature and we will adopt it in this manuscript.

36 Relying on our academic expertise and our real-life daily clinical practice, we suggest that
37 COVID-19 non-targeted treatment might be revealed as the main cause of Para COVID
38 syndrome⁴. Importantly, intake of oral, parenteral and/or inhalational, corticosteroids as
39 well as favipiravir to manage mild-moderate COVID-19 was reported by most of our
40 managed relapsed and Para COVID patients and one Para COVID patient has also reported,
41 in addition to oral and parenteral corticosteroids, linezolid intake, though no blood culture
42 was performed, and her clinical condition did not warrant its prescription, as we suggest,
43 which might have added to the immunosuppressive effects of corticosteroids⁵.

44 We would like to report that we have repurposed diacerein 50 mg/day; a well-known
45 symptomatic slow-acting anti-inflammatory and immunomodulatory drug used in
46 osteoarthritis⁶, and omega 3 fatty acids in fish oil 1000 mg/day⁷ with or without NSAIDs⁸,
47 to safely manage relapsed and Para COVID patients who attended to our clinic mostly
48 complaining of persistent symptoms including some or all of the following: dry cough,
49 marked fatigue, chest pain, bone ache, headache, significant exercise intolerance and they
50 reported marked improvement starting from the first week of therapy and afterwards.
51 Moreover, we observed that the earlier the intervention, the shorter the duration of therapy
52 and one patient who complained for almost 6 months after she was first diagnosed with
53 COVID-19 has consulted us after her symptoms exacerbated after receiving the first dose

of ChAdOx1 nCoV-19 vaccine had to received diacerein, omega 3 fatty acids and lornoxicam 8 mg once or twice daily for three weeks during which gradual improvement was reported and we also advised her not to receive the other jab.

Taken together, we suggest that diacerein and omega 3 fatty acids possess the same potential properties^{6,7} that we have built upon our COVID-19 management protocol⁸ and we might consider either of them for our COVID-19 patients who might not tolerate NSAIDs due to peptic ulcers when the risk benefit ratio is favorable. Furthermore, we suggest that pentoxifylline should be also considered as another safe alternative for management of Para COVID⁹ and we have used it as an adjuvant treatment while managing selected cases of COVID-19¹⁰.

Funding

None

Competing interests

None

References

1. Pavli A, Theodoridou M, Maltezou HC. Post-COVID syndrome: Incidence, clinical spectrum, and challenges for primary healthcare professionals. Archives of Medical Research 2021.
2. Moreno-Pérez O, Merino E, Leon-Ramirez J-M, Andres M, Ramos JM, Arenas-Jiménez J, et al. Post-acute COVID-19 syndrome. Incidence and risk factors: A Mediterranean cohort study. Journal of Infection 2021;82:378-83.
3. Buskermolen M, te Paske K, van Beek J, Kortbeek T, Götz H, Fanoy E, Feenstra S, et al. Relapse in the first 8 weeks after onset of COVID-19 disease in outpatients: viral reactivation or inflammatory rebound? Journal of Infection.
4. Kelleni MT. Tocilizumab, Remdesivir, Favipiravir, and Dexamethasone Repurposed for COVID-19: a Comprehensive Clinical and Pharmacovigilant Reassessment. SN Compr Clin Med 2021;3:919-23.

- 81 5. Wang J, Xia L, Wang R, Cai Y. Linezolid and Its Immunomodulatory Effect: In
82 Vitro and In Vivo Evidence. *Frontiers in Pharmacology* 2019;10:1389.
- 83 6. de Oliveira PG, Termini L, Durigon EL, Lepique AP, Sposito AC, Boccardo E.
84 Diacerein: A potential multi-target therapeutic drug for COVID-19. *Med*
85 *Hypotheses* 2020;144:109920-.
- 86 7. Hathaway D, Pandav K, Patel M, Riva-Moscoso A, Singh BM, Patel A, et al.
87 Omega 3 Fatty Acids and COVID-19: A Comprehensive Review. *Infect Chemother*
88 2020;52:478-95.
- 89 8. Kelleni MT. NSAIDs/Nitazoxanide/Azithromycin Repurposed for COVID-19:
90 Potential Mitigation of the Cytokine Storm Interleukin-6 Amplifier via
91 Immunomodulatory Effects. *Expert Review of Anti-infective Therapy* 2021; DOI:
92 10.1080/14787210.2021.1939683
- 93 9. Seirafianpour F, Mozafarpour S, Fattahi N, Sadeghzadeh-Bazargan A, Hanifiha M,
94 Goodarzi A. Treatment of COVID-19 with pentoxifylline: Could it be a potential
95 adjuvant therapy? *Dermatol Ther.* 2020;33:e13733-e.
- 96 10. Kelleni M. NSAIDs/Nitazoxanide/Azithromycin Immunomodulatory Protocol
97 Used in Adults, Geriatric, Pediatric, Pregnant, and Immunocompromised COVID-
98 19 Patients: A Prospective Observational Study and Case-Series. *Authorea*
99 (Preprint) 2021; DOI: 1022541/au16212660115715282/v4.