Received: 27 May 2020 | Revised: 3 June 2020 | Accepted: 4 June 2020

DOI: 10.1111/dth.13792

SHORT PAPER

DERMATOLOGIC THERAPY WILEY

Omalizumab and COVID-19 treatment: Could it help?

Ayman Abdelmaksoud[1] | Mohamad Goldust[2,3,4] | Michelangelo Vestita[5,6]

[1]Mansoura Dermatology, Venerology and Leprology Hospital, Mansoura, Egypt

[2]Department of Dermatology, University of Rome G. Marconi, Rome, Italy

[3]Department of Dermatology, University Medical Center Mainz, Mainz, Germany

[4]Department of Dermatology, University Hospital Basel, Basel, Switzerland

[5]Unit of Plastic and Reconstructive Surgery, Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy

[6]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts

Correspondence
Ayman Abdelmaksoud, Mansoura Dermatology, Venerology and Leprology Hospital, 5-Amien Alsamanoudy Street, from Abdelsalam Aaref Street, Mansoura, Egypt.
Email: behcet.behcet@yahoo.com

Dear Editor,

Therapeutics that may assist to control current pandemic of coronavirus disease 2019 (COVID-19) rapid spread and reduce its high mortality rates are urgently needed. It might be prudent to look into existing therapies used in dermatology that could be effective against this virus. Omalizumab (OMZ), a recombinant humanized monoclonal immunoglobulin G1 (IgG1) antibody, blocks IgE binding to its high-affinity FcεRI receptor. By this mechanism, it secondarily reduces free IgE and IgE-mediated reactions. The reduction of free IgE also results in downregulation of the FcεRI expression. The drug is Food and Drug Administration-approved for treatment of moderate-to-severe allergic asthma and H1-antihistamine refractory chronic spontaneous urticaria (CSU).[1]

The current threat of COVID-19 pandemic may cause close to half a billion deaths, that is, 6% of the global population—and potentially more.[2] The nasal epithelium is one of the first sites of infection with SARS-CoV-2. Angiotensin-converting enzyme 2 (ACE2) is a cellular receptor which has been proven to bind to SARS-CoV-2 spike protein and promote internalization of the virus into human cells, thus inhabitating and replicating in the nasal and pharyngeal mucosa. SARS-CoV-2, like other coronavirus species, is primarily attacked by immune cells, such as mast cells (MCs) that are located in the submucosa of the respiratory tract and in the nasal cavity and involved in prevention of microinvasion. Activation of MCs results in release inflammatory agents, such as histamine and protease, in addition to pro-inflammatory cytokines including interleukin (IL)-1, IL-6, and IL-33.[3]

OMZ has showed reduction of local nasal mucosal inflammation and improving nasal respiration, in addition to improvement of sinonasal function in patients with chronic rhinosinusitis,[4] a mechanism that could be essential for the initial combating of COVID-19. OMZ can be used in treatment of patients with different types of MCs disorders, even in low-dose,[5] mitigating viral-triggered release of the pro-inflammatory mediators and risk of subsequent serious complications in COVID-19 patients. Researchers noted OMZ treatment in vivo restored interferon alpha responses to both rhinovirus and influenza via OMZ-reduced expression of FcεRIα on the cell surface secondary to OMZ-reduction of free serum IgE levels, denoting an antiviral potential of OMZ.[6]

Furthermore, excessive synthesis of pro-inflammatory cytokines such as IL-6, IL-1β, and tumor necrosis factor alpha (TNF-α) is induced by activated neutrophils and alveolar macrophages, which attracts more neutrophils and results in further release of chemokines and cytokines. Pro-inflammatory mediators and upstream nuclear factor kappa β (NF-kβ) signaling pathways might have a key role in COVID-19-related acute lung injury (ALI) pathogenesis. Interestingly, these cytokines are significantly elevated when lung tissue is exposed to SARS-CoV.[7] Infiltration of inflammatory cells into lung parenchyma is a crucial process in acute lung injury with subsequent acute respiratory distress syndrome (ARDS). OMZ has not only anti-IgE effect, but also have inhibitory effects on inflammatory cells, such as neutrophil, and coagulation in patients with CSU.[8]

In addition to clinical manifestations of COVID-19, such as fever, fatigue, myalgia, headache, diarrhea, dry cough, dyspnea that may lead to ARDS and death, it may manifest with cutaneous signs. Among the cutaneous manifestations of COVID-19 in hospitalized patients, urticaria has been reported, which may be widespread, according to reports from Wuhan, China, and Lombardy.[9,10] Infected COVID-19 patients have a hypercoagulable state presented with vascular skin symptoms, such as acroischemia and chilblain-like lesions.[11] OMZ may be tried for COVID-19 patients manifested with urticaria or vascular lesions.

In an experimental study, Wang et al noted that intramuscular injection of OMZ-small peptide segment (SPT) could inhibit the synthesis of

IL-6, IL-1β, and TNF-α in bronchoalveolar lavage fluid (BALF), and thereby attenuate acute inflammation in female C57BL/6 mice suffering from lipopolysaccharide-induced ALI. Also, OMZ-SPT could inhibit the synthesis of periostin (which modulates pulmonary inflammation) in BALF. Furthermore, OMZ-SPT could inhibit activation of the NF-kβ signaling induced by lipopolysaccharide in mouse lungs. Also, OMZ-SPT has a suppressive effect on total expression of NF-kB in RAW264.7 cells.[12]

On the basis of current evidence at this time, and according to the experts, the use of ACE inhibitor should be maintained for the control of blood pressure and not to be discontinued.[13] In only one report, ACE inhibitors have shown to sustain CSU exacerbations and to annul the therapeutic effect of OMZ in two patients who had been previously responding to the drug.[14] Whether that therapeutic resistance was dose dependent or patient specific remains to be studied in accumulating similar cases.

OMZ may be worth to try in the treatment of COVID-19 by international research groups. With possible home administration of OMZ, the patients would refrain from usual clinic visits and keep on the recommended social distancing.[15]

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

The authors worked equally in preparing this manuscript for submission to *Dermatologic therapy*. All the authors collected the scientific data and shared in writing the initial draft. All the authors reviewed and approved the final draft. First author submitted the final draft.

ORCID

Ayman Abdelmaksoud https://orcid.org/0000-0003-4848-959X
Mohamad Goldust https://orcid.org/0000-0002-9615-1246
Michelangelo Vestita https://orcid.org/0000-0002-2203-0353

REFERENCES

1. Giménez-Arnau AM. Omalizumab for treating chronic spontaneous urticaria: an expert review on efficacy and safety. *Expert Opin Biol Ther*. 2017;17(3):375-385.
2. Grech V. Unknown unknowns—COVID-19 and potential global mortality. *Early Hum Dev*. 2020;144:105026. https://doi.org/10.1016/j.earlhumdev.2020.105026.
3. Kritas SK, Ronconi G, Caraffa A, et al. Mast cells contribute to coronavirus-induced inflammation: new anti-inflammatory strategy. *J Biol Regul Homeost Agents*. 2020;34(1). https://doi.org/10.23812/20-Editorial-Kritas.
4. Pinto JM, Mehta N, DiTineo M, Wang J, Baroody FM, Naclerio RM. A randomized, double-blind, placebo-controlled trial of anti-IgE for chronic rhinosinusitis. *Rhinology*. 2010;48(3):318-324.
5. Berry R, Hollingsworth P, Lucas M. Successful treatment of idiopathic mast cell activation syndrome with low-dose omalizumab. *Clin Transl Immunol*. 2019;8(10):e01075.
6. Gill MA, Liu AH, Calatroni A, et al. Enhanced plasmacytoid dendritic cell antiviral responses after omalizumab. *J Allergy Clin Immunol*. 2018;141(5):1735-1743.e9.
7. Yoshikawa T, Hill T, Li K, Peters CJ, Tseng CTK. Severe acute respiratory syndrome (SARS) coronavirus-induced lung epithelial cytokines exacerbate SARS pathogenesis by modulating intrinsic functions of monocyte-derived macrophages and dendritic cells. *J Virol*. 2009;83(7):3039-3048.
8. Acer E, Erdogan HK, Çanakçı NY, et al. The effect of omalizumab on hematological and inflammatory parameters in patients with chronic spontaneous urticaria. *Cutan Ocul Toxicol*. 2019;38(1):5-8.
9. Zhang JJ, Dong X, Cao YY, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan. *China Allergy*. 2020. https://doi.org/10.1111/all.14238.
10. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. *J Eur Acad Dermatol Venereol*. 2020;34:e212-e213. https://doi.org/10.1111/jdv.16387.
11. Bouaziz JD, Duong T, Jachiet M, et al. Vascular skin symptoms in COVID-19: a French observational study. *J Eur Acad Dermatol Venereol*. 2020. https://doi.org/10.1111/jdv.16544.
12. Wang T, Hou W, Fu Z. Preventative effect of OMZ-SPT on lipopolysaccharide-induced acute lung injury and inflammation via nuclear factor-kappa B signaling in mice. *Biochem Biophys Res Commun*. 2017;485(2):284-289.
13. Schiffrin EL, Flack J, Ito S, et al. Hypertension and COVID-19. *Am J Hypertens*. 2020;33(5):373-374. https://doi.org/10.1093/ajh/hpaa057.
14. Asero R. ACE inhibitors may interfere with omalizumab in chronic spontaneous urticaria. *J Eur Acad Dermatol Venereol*. 2017;31(8):e358-e359.
15. Shaker MS, Oppenheimer J, Grayson M, et al. COVID-19: pandemic contingency planning for the allergy and immunology clinic. *J Allergy Clin Immunol Pract*. 2020;8(5):1477-1488.e5. https://doi.org/10.1016/j.jaip.2020.03.012.

How to cite this article: Abdelmaksoud A, Goldust M, Vestita M. Omalizumab and COVID-19 treatment: Could it help? *Dermatologic Therapy*. 2020;33:e13792. https://doi.org/10.1111/dth.13792