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.

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Letter to Editors

As a potential treatment of COVID-19: Montelukast

A B S T R A C T

It has been hypothesized that Montelukast, a cysteinyl leukotriene (cysLT) receptor antagonist, with effects of anti-inflammatory, suppress oxidative stress and reduce affect cytokine production, may limited progression of the disease on COVID-19 infection.

To the Editor:

The pandemia, emerged with the new coronavirus 2019 (COVID-19), has not yet been brought under control, despite serious measures taken all over the world and efforts to control and treat the disease. Up till now, a specific treatment for COVID-19 infection is not available. We believe that new approaches to treatment should be considered in cases of COVID-19. Here, the treatment approach of COVID-19 infection may include monteluksat, a cysteinyl leukotriene (cysLT) receptor antagonist, and the possibility of decrease severe COVID-19 progression will be mentioned.

The clinical process features of COVID-19 can range from asymptomatic cases to acute respiratory distress syndrome (ARDS) and multi-organ dysfunction. The disease can progress to pneumonia, respiratory failure and death when severe, and in this case, acute complications include acute lung injury, ARDS, sepsis and shock. This progression is thought to be related to excessive increase in proinflammatory cytokine levels [1,2].

In addition, as it is known, COVID-19 reaches the cell through angiotensin-converting enzyme (ACE) receptors and leads to severe pneumonia and thus increased mortality rates during infection by binding to human ACE2 [3,4]. The cough that can develop with ACE inhibition is caused by increased bradykinin and its bronchoconstrictor effect, and montelukast, a selective LTD4 antagonist, has an inhibitory effect on bradykinin-induced airway hypersensitivity [5,6]. Although it is unclear how this effect came about, it is thought to be through ACE receptors.

The most important cause of COVID-19 related deaths is respiratory failure, which is progressive and unresponsive to treatment [2,4]. ARDS, which frequently occurs in these patients, is an acute inflammatory lung injury, a clinical condition that is not well understood due to its complex pathogenesis, and is a result of widespread alveolar injury caused by intense inflammation. IL-6 and IL-8, the tumor necrosis factor (TNF) and IL-1 produced in the early phase and other pro-inflammatory cytokines that occur in the later stages of the disease, induce leukocyte migration to the region. Then, leukocytes accumulating in the lungs are activated and secretive reactive oxygen species and proteases that damage capillary endothelium and alveolar epithelium. Montelukast therapy has been shown in recent studies to reduce TNF-α, IL-6 and IL-1b levels [3,4]. The pronounced inhibitory effect of montelukast against bradykinin-induced tracheal smooth muscle contraction has also been demonstrated, which supports the interaction between bradykinin and leukotriene mediators [3,6].

Montelukast is a potent cysteinyl leukotriene (cysLT) receptor antagonist with anti-inflammatory effects and has been proven to significantly suppress oxidative stress. Also, CysLTs can affect cytokine production. In high doses and i.v. administration of montelukast, IL-4, IL-5, IL-13 reduced protein expression in the lungs exerts its anti-inflammatory effect through the suppression of T-helper type-2 cytokines. Consequently, use of high-dose montelukast as an anti-inflammatory agent has been shown to be effective in acute asthma [7]. In addition, the use of montelukast is known to have a decreasing effect on the frequency and severity of wheezing in patients with clinical episodic wheezing (wheezing after an upper respiratory tract infection caused by adenovirus, influenza, metapneumovirus, coronavirus). In these patients, montelukast does not prevent these viral infections, but seems to limit the upper respiratory tract [5,8].

In the light of these informations, montelukast has an effect on events developing with ACE receptors, and also has an anti-inflammatory effect with bradykinin and leukotriene antagonism; Because of COVID-19 has entry into the cell through ACE receptors and caused mortality due to excessive inflammatory processes, it was thought that montelukast may have a limiting effect on the progression of the disease on COVID-19 infection. It suggests that it may be effective to use it, possibly at high doses, in order to reduce its severity during the course of the disease or before the disease occurs fully in people at risk. The healing effects of montelukast on these damages can be seen.

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.

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Appendix A. Supplementary data

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References

[1] Rodriguez-Morales AJ, Cardona-Ospina JA, Gutierrez-Ocampo E, Villamizar-Pena R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis 2020:101623. PubMed PMID: 32179124. Epub 2020/03/18. eng.

[2] Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy 2020. PubMed PMID: 32077115. Epub 2020/02/23. eng.

[3] Chen X, Zhang X, Pan J. Effect of Montelukast on Bronchopulmonary Dysplasia (BPD) and Related Mechanisms. Medical science monitor : int Med J Exp Clin Res 2019 Mar 13; 25: 1886-93. PubMed PMID: 30862773. Pubmed Central PMCID: PMC6427930. Epub 2019/03/14. eng.

[4] Sarzi-Puttini P, Giorgi V, Sirotti S, Marotto D, Ardizzone S, Rizzardini G, et al. COVID-19, cytokines and immunosuppression: what can we learn from severe acute respiratory syndrome? Clin Exp Rheumatol 2020;38(2):337–42. PubMed PMID: 32202240. Epub 2020/03/2eng.

[5] Bisgaard H, Flores-Nunez A, Goh A, Azimi P, Halkas A, Malice MP, et al. Study of montelukast for the treatment of respiratory symptoms of post-respiratory syncytial virus bronchiolitis in children. Am J Respir Critical Care Med 2008;178(8):854–60. PubMed PMID: 18583576. Epub 2008/06/28. eng.

[6] Noor A, Najmi MH, Bukhtiar S. Effect of Montelukast on bradykinin-induced contraction of isolated tracheal smooth muscle of guinea pig. Indian J Pharmacol 2011;43(4):445–9. PubMed PMID: 21845003. Pubmed Central PMCID: PMC3153711. Epub 2011/08/17. eng.

[7] Wu AY, Chik SC, Chan AW, Li Z, Tsang KW, Li W. Anti-inflammatory effects of high-dose montelukast in an animal model of acute asthma. Clin Exp Allergy 2003;33(3):359–66. PubMed PMID: 12614451. Epub 2003/03/05. eng.

[8] Brodlie M, Gupta A, Rodriguez-Martinez CE, Castro-Rodriguez JA, Ducharme FM, McKean MC. Leukotriene receptor antagonists as maintenance and intermittent therapy for episodic viral wheeze in children CD008202. PubMed PMID: 26482324. Pubmed Central PMCID: PMC6986470. Epub 2015/10/21 Cochr Database Syst Rev2015.

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