MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Renin Angiotensin System and Covid-19

Ataie A[1] and Ataee R[2]*

[1]Department of Toxicology and Pharmacology, Babol University of medical Sciences, Iran

[2]Pharmaceutical Sciences Research Center, Mazandaran University of Medical Sciences, Iran

*Corresponding author: Ramin Ataee, Km18, Khazarabad road, Mazandaran University of Medical Sciences, Pharmacy School, Pharmaceutical Sciences Research Center, Iran, Tel: +98 911 323 2804; Email: Iran.raminataee1349@gmail.com

Abstract

Covid-19 is a new clinical complication in the world and many efforts for its treatment have been done. Renin Angiotensin System (RAS) may have an important role in the control of Covid-19. ACE2 is approved as Covid receptor in lungs and many other organs. Down regulation and up regulation of ACE2 is critical roles in viral infusion into the cells also ACE2 has an important in the level of Angiotensin 2 (ANG2) concentration in the lungs , the high levels of ANG2 may increase inflammation and proliferation and cytokine storms in lung. Angiotensin Receptor Blocker (ARB) such as Losartan may be useful in prophylaxis of lung injury, in this paper we explain about RAS and covid-19 managements in early stages.

Keywords: ACE2; Renin Angiotensin System; Angiotensin Receptor Blocker; Covid-19; ADRS

Introduction

Some studies indicated the role of ACEIs/ARBs in Covid-19 infections [1] and showed the lower rates of death and intubation in patients administrated with ACEIs during hospitalization. ACE2 is a receptor for SARS–CoV-2 infusion, and down regulation or up regulation of this receptor could affect on the severity of Covid-19 infections. The pulmonary effect of renin angiotensin system (RAS) on covid-19 infection is controversial. Also renin blocker could down regulate ACE2 receptors in animal studies [2,3]. ACE2 is an enzyme that converts angiotensin2 to angiotensin (1-7). ACE2 expression protects from lung injury, an action which is down regulated by binding of SARS-CoV via its spike protein [3]. Also RAS blockers could up regulate ACE2 and antagonize inflammatory effects of Covid-19 virus on the lungs. On the other hands long uses of RAS inhibitors such as ARBs and ACE1 inhibitors could increase ACE2 expression and increase the binding sites of Covid-19 in lungs and infection. According guideline it was approved to continue RAS blockers in covid-19 patients also in healthy patients it could be used prophylactically .Only in pulmonary problems

and sever conditions its used must be restricted and blood pressure and kidney function must be monitored [3]. ANG II also be produced by other pathways [4]. The main enzyme involved in ANG II generation in tissue-specific RAAS are serine proteases (especially kallikrein-like enzymes also called tonins), and also cathepsin G and chymase [5]. In the kidneys, 40% of ANG II is produced by this pathways, and in heart, coronary arteries, chymase generate ANG II [5]. ACE2 is homologues of ACE converts ANG 1 to ANG 1-9 and ANG2 to ANG1-7 [6]. TMPRSS2 is serine protease, with ADAM-17. ADAM-17 function is production a form of active sACE2 that cleave ANG2 and block viral particle [7]. Therefore, the balance between the two sACE2 forms generated by enzymes is important role in COVID-19 infection [7].

Effect of Losartan on Covid-19

It was accepted that ACE2 is a hydrolyzing enzyme that convert ANG2 to ANF1-7. After binding virus to ACE2 as its receptor, ACE2 internalization is occurred and down regulated on cell surface. The role of AT1R in ADRS was approved [8] also activation of AT1 is responsible for cytokine

storm [8]. Therefore the use of ARBs such as losartan may be useful in the treatment of covid-19 infection. Also ACE2 is not inhibited by captopril and lisinopril [8]. One of product of ACE2 is ANG (1-7). ANG (1-7) has antioxidant and anti-inflammatory and anti proliferative and anti-fibrotic properties and is vasodilator and antithrombotic properties [9]. Some studies demonstrated that angiotensin II receptor blocker (ARB) losartan could decrease some symptoms of acute lung injury in SARS-CoV [10]. In one of study on mice, it was shown that IL-6, was also significantly down-regulated in losartan-treated group [10]. Also significant recovery of ACE2 expression and down-regulation of ACE in lung tissues of losartan-treated mice were also shown 48 h after H5N1 virus infection [10]. Therefore stimulation of AT1R induce lung inflammation through pro-inflammatory, cytokine and induce proliferative, thrombotic and tissue destructive effects as well as activating platelet derived growth factor receptor (PDGFR) [11].

Conclusion

According to some recent studies, there are some evidences about role of ACEIs and ARBs in prevention and prophylaxis of corona virus infections but some more studies are necessary for confirmation of this opinion.

References

1. Kuba K, Imai Y, Rao S, Gao H, Guo F, et al. (2005) A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. Nat Med 11(8): 875-879.

2. Henry C, Zaizafoun M, Stock E, Ghamande S, Arroliga AC, et al. (2018) Impact of angiotensin-converting enzyme inhibitors and statins on viral pneumonia. Proc (Bayl Univ Med Cent) 31(4): 419-423.

3. Messerli FH, Siontis GCM, Rexhaj E (2020) COVID-19 and Renin angiotensin Blockers Current Evidence and Recommendations. Circulation 141(25): 2042-2044.

4. Atlas SA (2007) The Renin-Angiotensin Aldosterone System: Pathophysiological Role and Pharmacologic Inhibition. J Manag Care Pharm 13(8): 9-20.

5. Ihara M, Urata H, Kinoshita A, Suzumiya J, Sasaguri M, et al. (1999) Increased hymase-dependent angiotensin II formation in humanatherosclerotic aorta. Hypertension 33(6): 1399-405.

6. Zisman LS (2005) ACE and ACE2: A tale of two enzymes. Eur Heart J 26(4): 322-324.

7. Zipeto D, Palmeira J da F, ArgañarazGA, Arganaraz ER (2020) ACE2/ADAM17/TMPRSS2 Interplay May Be the Main Risk Factor for COVID-19. Front Immunol.

8. Nejat R, Sadr AS, Are losartan and imatinib effective against SARS–CoV2 pathogenesis? A pathophysiologic–based in silico study In Silico Pharmacology 9(1): 1.

9. Watanabe T, Barker TA, Berk BC (2005) Angiotensin II and the endothelium: diverse signals and effects. Hypertension 45(2): 163-169.

10. Kuba K, Imai Y, Rao S, Gao H, Guo F, et al. (2005) A crucial role of angiotensin converting enzyme 2 (ACE2) in sars coronavirus-induced lung injury. Nat Med 11: 875-879.

11. Kelly DJ, Cox AJ, Gow RM, Zhang Y, Kemp BE, et al. (2004) Platelet-derived growth factor receptor transactivation medi-ates the trophic efects of angiotensin II in vivo. Hypertension 44(2): 195-202.