Annals of Pharmacology and Pharmaceutics

Review Article
Published: 17 Jan, 2022

Medications Used for SARS-CoV-2 Prophylaxis and Treatment

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Abstract

The initial part of human body influenced by the virus is the lung epithelial cells and the 1st traipse of viral infection encloses its attaching to angiotensin converting enzyme-2 receivers delineated on the host cells pursued by budding with the cell membrane. Hydroxychloroquine can obviate viral attachment and entry into host cells by injuring glycosylation of angiotensin converting enzyme-2, thus rupturing the interaction between S protein and angiotensin converting enzyme-2. Chloroquine is known to obviate virus infection by escalating endosomal pH required for virus endosome fusion and release of viral deoxyribonucleic acid or ribonucleic into the cytosol. Dexamethasone would confines the generation and injuring outcome of the cytokines, but will also obviate the protective work of T cells and downgrade the capability of B cells to synthesize antibodies. Heparin has been revealed to de-escalate the expression of proinflammatory mediators in human alveolar macrophages damaged by lipopolysaccharide and to de-escalate the NF-κB pathway in alveolar cells.

Keywords: Medications; Prophylaxis; SARS-CoV-2; NF-κB pathway

Abbreviations

ACE2: Angiotensin-Converting Enzyme 2; 3CLpro: Chymotrypsin-Like protease; CPM: Chlorpheniramine Maleate; COX-2: Cyclooxygenase-2; COVID-19: Coronavirus Disease 2019; DMARD: Disease-Modifying Antirheumatic Drug; HCQs: Hydroxychloroquine; IFN: Interferons; IL-1: Interleukins; MERS-CoV: Middle East Respiratory Syndrome Coronavirus-2; PLpro: Papain-Like protease; RA: Rheumatoid Arthritis; SARS-CoV-2: Acute Respiratory Syndrome Coronavirus-2; SLE: Systemic Lupus Erythematosus; TGF-β: Transforming Growth Factor Beta

Introduction

The coronavirus disease 2019 pandemic has disseminate across the world with millions infected and hundreds of thousands dead. Coronavirus disease 2019 antecedent by heavy-handed acute respiratory syndrome coronavirus-2 is credent to have originated from the Huanan Seafood Wholesale Market, Wuhan, Hubei province, China which was announced as a pandemic by the WHO [1]. The initial part of human body influenced by the virus is the lung epithelial cells and the 1st traipse of viral infection encloses its attaching to ACE-2 receivers delineated on the host cells pursued by budding with the cell membrane [2], The SARS-CoV-2 spike protein attaches to a receiver on the human cell surface called ACE2, which is most predominant in the type II alveolar cells of the lungs [3,4]. The relation emplacements between ACE2 and SARS-CoV-2 are fascinating therapeutic targets with the intention of obviating or revamping the ACE2 receptor. It is indispensable to memorandum that ACE2 has a compulsory lung protective work [5] and is, thereupon, of restrained use as a target as it has to vindicate its physiological work. ACE2 inhibitors will go hand-in hand with one-sided destruction of this lung safeguard. Chloroquine and the least toxic HCQ are of specific significance, as it interposes with the glycosylation of ACE2 which is thought-outsole of the cellular receptors of SARS-CoV [6]. Relating to phylogeny, these viruses can be categorized into 4 geniuses: α-coronavirus, β-coronavirus, γ-coronavirus, and δ-coronavirus. Amid this genus, the α-coronaviruses and β-coronavirus chiefly contaminate mammals, and ordinarily influence to respiratory malady in humans and gastritis in animals. Differently, the γ-coronavirus and δ-coronavirus are capable to contaminate birds [7]. Nowadays, there are multiplex strains of coronavirus that infect humans: HCoVHKU1, HCoV-NL63, HCoV-229E, SARS-CoV and MERS-CoV [8]. The comprehensive genome resulting revealed that the virus belonged to a great family of coronavirus and is terminate affiliated to SARS-CoV. It encodes for dual great polyproteins that are greater proceeding by virally encoded cysteine proteases, namely, the PLpro and the 3CLpro. The proceeding of the viral polyprotein is crucial for growth and infectivity of the virus [9].

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Received Date: *10 Dec 2021*
Accepted Date: *05 Jan 2022*
Published Date: *17 Jan 2022*

Citation:
Bereda G. Medications Used for SARS-CoV-2 Prophylaxis and Treatment. Ann Pharmacol Pharm. 2022; 7(1): 1203.

Hydroxychloroquine

HCQ has been used triumphantly as an anti-inflammatory agent DMARD in unspecified autoimmune and rheumatic circumstances such as systemic lupus, rheumatoid arthritis, Sjogren's syndrome, antiphospholipid antibody syndrome, and connective tissue disarrangements [10,11]. Hydroxychloroquine sulfate is a chloroquine analogous, ubiquitously used for malaria, RA, and SLE. It attributes myriad anti-inflammatory and immunomodulatory properties, enclosing suppression of cytokine (IL-1 and IL-6) generation, suppression of phospholipase A2 and matrix metalloproteinase's, and reduction of B and T cell work [10]. The implicit function of HCQS defend SARS-CoV-2 could be owing to its capability to escalate lysosomal pH, which reduces the cellular metabolism of iron, thereby de-escalating its intracellular accumulation, which in turn inactivates glycosyltransferases and glycosylation enzymes, more obviating glycosylation of SARS-coronavirus [12]. HCQS and chloroquine wait to pick up concentrated in tissues; there is a implicitly that extended incubation periods perhaps influence to escalated intracellular medication accumulations sequencing in augmented antiviral consequences [13]. Hydroxychloroquine can obviate viral affection and penetrate into host cells by injuring glycosylation of ACE2, thus rupturing the relation between S protein and ACE2 [14,15]. Chloroquine is known to obviate virus infection by escalating endosomal pH needed for virus/endosome budding [14], and delivery of viral deoxyribonucleic acid or ribonucleic acid into the cytosol. Furthermore, chloroquine has immunomodulatory outcomes, obviating the generation/delivery of TNF-α, IL-1β, and IL-6 [16], which perhaps synergistically heighten its antiviral outcome *in vivo*. It also functions as a novel group of autophagy suppressor [17].

Anti-histaminic agents

Anti-histaminic agents such as chlorpheniramine maleate have been displayed to effectively obviate viral dissemination of a wide activity of influenza viruses through the respiratory mucosa [18]. They do not interpose with the viral adsorption on to the cell surface, but suppress the procedure of endocytosis, by which the virus penetrates into the host cell [18], SARS-CoV-2 viruses, though they bind onto cells using a non-identical cell surface protein [2], have an identical procedure of endocytosis [19], and thereupon CPM can lessen the peril of obtaining the COVID-19 infection. In HCWs with allergies and great IgE, this can be implicitly advantageous as a prophylaxis. Anti-histaminic medications such as olopatadine and azelastine are also medicines which particularly obviate H1 histamine receptors, identical to CPM. Olopatadine, additionally, has a mast cell stabilizing property too. Both azelastine and olopatadine are also applicable as nasal sprays permitting for simple and targeted operation to the nasal mucosa [20,21]. We commit launching the medicine in consultation with their allergy-immunology and ENT specialists as the dosage and generic medicine has to be discerned and titrated based on individual necessitates, tolerability and security profile. Histamine is a potent inflammatory mediator, ubiquitously consociated with allergic reactions, advancing vascular and tissue revamps and attributing more chemoattractant spectrum. The usage of particular H4R ligands and/or inhibition of H1 and H4 receptor synergism perhaps further effective in the management of inflammatory circumstances of the lung. Histamine also inhibits the inflammatory reaction by deed on distinctive cellular populations, in human lung macrophages. The attaching of histamine to H1R initiates generation of proinflammatory cytokine IL-6 and β-glucuronidase. Obviating H4R in a model of pulmonary fibrosis alleviates the inflammatory response, downgrading COX 2 expression and activity, leukocyte infiltration, generation of TGF-β (profibrotic cytokine), and collagen precipitation [22].

Bromhexine or bromhexine hydrochloride

Bromhexine or bromhexine hydrochloride (N-cyclo-N-methyl-(2-amino-3,5-dibromo-benzyl) amine hydrochloride) is derived from Vasicine, a plant-derived ingredient and alkaloid that was advanced from the Indian lung herb, Adhatoda vasica, and is a brominated aniline and benzylamine derivative [23]. Bromhexine hydrochloride deed as a mucolytic (decomposition mucus and supports vivid chest congestion) and is attested in multiplex countries as an OTC medication. It is described by less adverse drug reactions.

Trehalose

Trehalose, an easy plant based sugar known to inhibit autophagy [24,25], is also a broadly used ocular pharmaceutical agent that is used as an eye drop. It is known for its anti-viral properties, such as induction of type 1 interferon's [26], facilitating lysosomal breakdown of intracellular virus [27], downgrading viral penetration by de-escalating the description of host cell surface proteins that facilitates the adsorption of virus to the cells [28], and de-escalating cathepsin spectrum [29].

Interferons

Interferons (IFNs) are endogenous proteins which have anti-viral spectrum by obviating viral protein production and break downing viral RNA [30]. The use of type 1 IFN in the treatment of SARS-CoV and MERS-CoV has been well examined and has been found to indispensably de-escalate viral shedding [31,32].

Povidone-iodine

Povidone-iodine has been revealed to have potent virucidal spectrum defend a number of viruses, enclosing SARS-CoV and MERS-CoV coronavirus [33,34].

Dexamethasone

Dexamethasone would confines the generation and injuring outcome of the cytokines [29], but will also obviate the forfend work of T cells and downgrade the capability of B cells to synthesize antibodies [35]. Corticosteroid treatment perhaps ameliorates tissue damage in SARS antecedent by unrestrained generation of proinflammatory cytokines (e.g., interferon-gamma, tumor necrosis factor, IL-1 and IL-6 as an inflammatory reaction to viral infection [36,37].

Protease Inhibitors

Lopinavir and ritonavir

Lopinavir and ritonavir have firstly revealed ameliorated clinical consequences in patients with SARS in a nonrandomized trial and although, it is yet to be determined whether HIV PIs could effectively obviate the 3-chymotrypsin-like and papain-like proteases of 2019-nCoV [38].

Heparin

Heparin also has distinctive pharmacological actions of implicit benefit enclosing suppression of inflammatory cytokines showed in COVID-19 and the suppression of inflammatory cell recruitment into tissues through obviating multiplex of the key adhesion

molecules characterized on vascular endothelium, amelioration in lung work and escalated NO release [39-43]. Heparin has been revealed to de-escalate the description of proinflammatory mediators in human alveolar macrophages damaged by lipopolysaccharide and to de-escalate the NF-κB pathway in alveolar cells [44]. Additionally, nebulizer heparin downgrades pro-inflammatory cytokines in lung tissue and the description of NF-κB and TGF-β effectors in alveolar macrophages [44,45]. Heparin, through van Haren et al. Critical Care (2020) 24:454 Page 4 of 11 multiple actions enclosing suppression of adhesion molecules and heparanase activity, has also been displayed to decrease the infiltration of inflammatory cells into a range of tissues, enclosing the lung, activities that are independent of its anti-coagulant properties [46].

Conclusion

The SARS-CoV-2 lance protein attaches to a receptor on the human cell surface called ACE2, which is most predominant in the type II alveolar cells of the lungs. The implicit function of HCQs defend SARS-CoV-2 could be owing to its capability to escalate lysosomal pH, which inhibits the cellular metabolism of iron, thereby de-escalating its intracellular accumulation, which in turn inactivates glycosyltransferases and glycosylation enzymes, more obviating glycosylation of SARS-coronavirus. Corticosteroid treatment perhaps ameliorate tissue damage in SARS antecedent by unrestrained generation of pro inflammatory cytokines (e.g., interferon-gamma, tumor necrosis factor, Interleukins (IL)-1 and IL-6) as an inflammatory reaction to viral infection. Povidone-iodine has been revealed to have potent virucidal spectrum defend a number of viruses, enclosing SARS-CoV and MERS-CoV coronavirus.

Acknowledgment

The author extends his gratitude to those all who support him amid manuscript preparation by bestowing constructive information.

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