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Covid-19 Spike Protein Physiological Pathogens through Vesicular H^+-Adenosine Triphosphatase

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Abstract

The mini-review synthesizes the blood-borne Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) human pathogens in its clinical significance through Vesicular H^+-Adenosine Triphosphatase (V-ATPase) that lead to pericarditis-induced sudden deaths with acute myocarditis, blood clots, and etc. Early symptoms may arise through rapid acidification in the blood and may guide patient self-awareness and clinical practices. A Phase III clinical trial is reviewed on its phase IV implications, and potentials of experimental medicine in inhibiting V-ATPase protons for Coronavirus Disease 2019 (COVID-19) transmembrane treatment. The mini-review calls for animal tests on Bafilomycin A1 treatment on SARS-CoV-2.

Keywords: bafilomycin a1; precarditis; proton inhibition; sars-cov-2; v-atpase

Introduction

The developments of vaccines for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) only focused on its Spike 1 (S1) protein for its targeting on human Angiotensin-converting enzyme 2 (ACE2) receptor [1], and serologic assays do not support vaccines sterilizing immunity [2]. The adolescent age group clinical trial evidenced SARS-CoV-2 spike proteins circulating in mRNA-vaccinated individuals' plasma who developed myocarditis symptoms despite of antibody generated [3]. With the ancestral SARS-CoV strain's Spike 2 (S2) protein's structural similarities with Human Immunodeficiency Virus-1 (HIV-1) gp41 and transmembrane fusion capacities, the clinical evidence suggests S2 proteins consist and induce the key human pathogen regardless of vaccines [4,5,6]. Palliative care approaches in managing lethal physiological symptoms in combination of anti-fusion therapeutic approaches become the rational clinical practice.

Physiological Cause

The Omicron variant's immune escape capacities with S2 protein are signatory of the potential and plausible immune attack mutational directions in intruding the blood-brain barrier (BBB) in natural immunity's gateway reflex [7,8,9]. Backtracking physiological symptoms to immune attacks is paramount for effective medical treatment. The *post hoc* condition for SARS-CoV-2 membrane fusion cell infection is an acid pH of 6.2 to 6.8 [10], and RNA hibernation independent of receptors creates further uncertainties in viral concentration targeting in case-by-case endocytic pathways [11]. The physiological infection paths in stem cells [7] invoke clinical focus on the circulatory system for treatment and pharmacokinetic solutions. The fusogenic causes in the circulatory system with known receptors in ACE2, Transmembrane protease, serine 2 (TMPRSS2), and cluster of differentiation 147 (CD147) [1,12,13] alert the early symptoms with sores, premature pericarditis that might lead to myocarditis symptoms, defused and concentrated pain in the chest, intestine, and kidney [7], and more later severe concerns in disorientation and headaches with the pericytes paths [14].

Pharmacokinetic Strategies

The physiological lethalities in SARS-CoV-2 human pathogens mainly arise from organ-specific over-concentration of viral loads in the circulatory carriers, and stalling strategies focus on preventing the cross of BBB. Unlike pharmacokinetic tumor and cancer

targeting, unless with specific antiviral drugs in early symptoms for statistical advantages [15,16], viral diffusion and salvaging natural immunity are the optimal relatively long-term strategies. In pericarditis symptoms, endocytic fusogens are the key cardiac health threats, with subsidiary risks in vein scratches and internal bleeding that led to blood clots. Vesicular H^+-Adenosine Triphosphatase (V-ATPase) is then seen as the optimal strategic point on the hydrophobic virus [6,17,18]. Blood flow controls with receptor inhibition and transmembrane proton inhibition are adopted in the clinical trial for treatment [19], aprotinin is evidenced to inhibit viral entry during activation and prevent cytokine storm that leads to acute lung injury [16,20,21], and naringenin has further effects in ameliorating radiation-induced lung fibrosis [22].

Two respective rationales have been present in the pharmacokinetic solutions. One takes the immune reflexes as compromised and the treatment aims to restore, and the other takes the immune reflexes as given and delivers antiviral medicine without regarding the former. For the clinical trial, medicine actions function alongside the vagus nerve in innate immune reflexes and reflex-based homeostasis [23,24], and innate immunity becomes of the physiological risks in organ-specific pathogens, such as Angiotensin II (ANG II) and cytokine storm from natural immune responses [19,25]. The advantage of the antiviral approach is concentrated efficacy in treatment cycles which requires early treatment and precision for statistical advantage, and the advantage of the clinical trial is discretion and empiricism, with thoroughness that may compensate for ignored hibernation in specific organs during activation and treatment. Current antiviral approaches, including vaccination mandates, take Coronavirus Disease 2019 (COVID-19) as acute illness, and the clinical trial takes it as chronic disease. The former can be contributed by People's Republic of China (PRC)'s consistent downplay and politicization of SARS-CoV series ever since it initially caught international attentions in 2002 - 2003 outbreak [26,27].

Neurotransmitter and Immune Reflexes

Pharmacokinetic readjustment of the natural immune reflex requires more attentive care than acute illness treatment or its initial methodological designs in blocking transmembrane fusogenicity and plausibly alleviating viral membrane insertion depth, with its S2 similarities to HIV-1 gp41 [28]. The V-ATPase focused method below the BBB does not interfere with the brain proton productions, but the transmembrane fusogenic inhibition may change neurotransmitters in immune reflexes [17,18,29]. In the neurodiverse clinical case with autism spectrum disorder (ASD), the intervention with proton-pump inhibitor (lansoprazole) in the endocytic solutions, apart from other psychological factors, may have caused clinical depression with the exocytic renal hemodialysis processes by glucose metabolism changes [19,30], and the involvement of the vagus nerve both in ASD and immune reflexes makes the clinical trial's phase IV prospect questioning [24,31].

Bafilomycin has been the experimental medicine promising in the fusogenic intervention rationale for treating SARS-CoV-2 [32,33], but the V0 and V1 domains in V-ATPase for neurotransmitters and immune reflexes pose further uncertainties in the physiological effects from the change in proton extruders, through synaptic vesicle [29,34,35]. However, the inhibition of autophagy and induction of apoptosis can be positive in preventing infection cycles and blood clot formation [36], and the exocytosis alkalinization may counteract the rapid acidification of SARS-CoV-2 [17,35]. The intersectional effects of synaptic vesicle in SARS-CoV-2 neurological infection and non-infected brains may justify and need to be tested through animal trials before clinical considerations.

Conclusion

With cautions for adverse effect potentials in neurodiversity and depression, the mini-review concludes that the clinical trial NCT05711810 may enter phase IV after 1 month of observation, for treating SARS-CoV-2 induced pericarditis and myocarditis with ACE inhibitor, beta blocker, and proton-pump inhibitor, with cautions on ACE inhibitor's dangers to persons with diabetes [19,37]. It further calls for animal-based clinical trials in Bafilomycin A1 treatment on SARS-CoV-2 infection in its various stages, to access its benefits and risks in potential human trials. Neurodiversity needs to be accounted for in the immune attack viral treatments. The mini-review inclines to consider COVID-19 as chronic disease instead of acute illness, in calling on patient and healthcare awareness.

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