Brief Communication

Pulmonary Covid Fibrosis a New Pharmaceutic Approach

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Abstract

Background: Patient's post-COVID may develop chronic irreversible respiratory failure with "widespread signs of pulmonary fibrosis." Our study analyzed the causes of this fibrosis to propose a therapeutic protocol. **Methods:** Identification of the biochemical causes of fibrosis in COVID-19 analysing the literature and chest CT. **Results:** The CT imaging shows pulmonary fibrosis. The viral infection produces "interleukin-6", which binds to its receptor, in MUC1 of lung epithelial cells. The biochemical response of the cells promotes an over-expression of MUC1 with fibrosis. Interleukin6 also causes a metabolic imbalance in NO that promotes clots and atherosclerosis of the pulmonary vessels. These results show to promote NO endothelia's formation to block both the excessive expression of MUC1 and the atherosclerosis effect of the vessels. **Conclusions:** This study proposes to inhibit phosphodiesterase by vasodilatation of the pulmonary vascular bed and the MUC1 over expression by interleukin6, the Sildenafil with the SGLT2 and N-Acetylcysteine.

Keywords: *COVID 19, fibrosis, lung*

Introduction

"Patients discharged after contracting Covid-19 may become chronically ill due to respiratory complications".[1] Many, about a 30% of them, return to the hospital and present embolism, phlebitis, vacuities, and lung relics. It is very likely to have a cohort of patients with fibrotic remnants in the lungs. These fibrotic patients show large scars on the lung with irreversible respiratory impairment, which creates respiratory problems even after a simple walk". This also occurs in young patients, with an incidence ranging from 30 to 75 percent of the assessed cases. We think that pulmonary fibrosis may be the danger post COVID, needs for specific clinical screening dedicated to the follow-up of patients post COVID especially who had cures for lung complications especially the most severe and the frailest.[2] These will need active pharmacological treatment 1nd dedicated rehabilitation pathways.[3] We also expect to do chest X-rays, respiratory function tests, 6-minute walking tests, chest and cardiac ultrasound and chest CT to investigate if a diffuse interstitial neuropathy or pulmonary embolism is present. Our study aims find with the analysis of the literature and the radio diagnostic imaging of the fibrosis in COVID, its most plausible biochemical causes to propose the most right therapeutic protocol.

Results

Many patients discharged from COVID-19 return to the hospital with signs of respiratory failure have a typical CT scan image of pulmonary fibrosis, [see Figure 1]. The CT scan on the first day of admission revealed tissue or fluid blocking blood vessels in both lungs, although at this stage it was mainly limited to the right lower lobe. The CT images fade to the fifteenth day, but the blurred patches in the lower left lung indicate tissue filled with fluid and not air, which can cause further damage. It is important to check the biochemical mechanisms that trigger the fibrosis process. Viral infection produces various inflammatory compounds in excess, the most important of which is interleukin 6. Our study hypothesizes that interleukin-6 binds to cells that have its IL-6R receptor on the surface, triggering many pro-inflammatory actions, including: Production of the VEGF protein by fibroblasts, with the consequent response of endothelial blood vessel cells and increased permeability of the vessels themselves.[4] It is also possible to hypothesize that interleukin 6 induces to form a process of atherosclerosis

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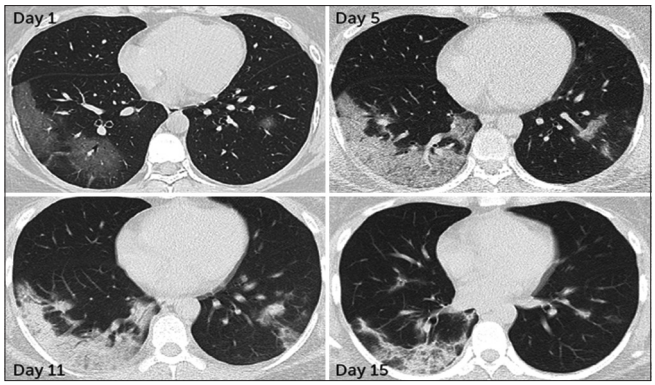

Figure 1: TAC of lungs in 65-year-old women with COVID-19

of the vessels: Interleukin-6 (IL-6) in fact could influence the endothelial interaction of nitric oxidesynthase (eNOS) -caveolin-1[5] and decide a reduced bioavailability of nitric oxide in the context of inflammation, contributing both to the narrowing of the lumen and to the fibrosis of the same.[6] Many of the effects of IL-6 on vascular function and structure are representative of the loss or to cut the nitric oxide (NO) biodisponibilty. IL-6 has direct effects on the activity and expression of nitric oxide endothelial synthase as well as on the increase in vascular superoxide, which rapidly inactivates NO and thus limits bioavailability. The report of IL-6 involving its IL6R receptor, mediates a range of effects in the vascular wall, including endothelial activation, vascular permeability, immune cell recruitment, endothelial dysfunction, as well as vascular hypertrophy and fibrosis. Our study demonstrates an aberrant production of MUC1 during the inflammatory cascade that produces fibrosis.[6] The MUC1 protein has an N-terminal subunit (also called KL-6) consisting of a variable extracellular number of units (VNTR).[7] We hypothesize that interleukin 6 interacts with its receptor IL-6R present on the extracellular domain of MUC1, translating and amplifying the signal for a new synthesis of MUC1 The excess of interleukin 6 causes over-expression of MUC1 and formation of fibrosis.

Our study show restores the balance to form the endothelial NO so to block both the over expression of MUC1 and the atherosclerotic effect of the vessels. We propose Sildenafil, a selective inhibitor of phosphodiesterase type 5 cGMP-specific (PDE5).[8] To inhibit the PDE5 causes vasodilatation of the pulmonary vascular bed: High levels of cGMP show a decrease in intracellular Ca2+ deposits with relaxing action on the endothelial cells. Sildenafil can be decisive both in the acute phase to prevent the formation of clots through the vasodilator and both for a antiaggregant effect in the chronic and fibrotic phase for the restoration in the biosynthesis of NO…[8,9] In this literature review work we have reviewed how recent research has studied the effects of antidiabetic compounds on periarterial fibrosis In particular Empagliflozin belonging to the class of sodium-glucose carrier inhibitors type 2, SGLT2 which the physicians use in non-insulin-dependent type 2 improves periarterial and tubulointerstitial fibrosis in the kidney.[10] Empagliflozin suppresses advanced glycation end products (AGE), restores endothelial nitric oxide synthase (eNOS) activation and reduces interstitial and periarterial nitrous-oxidative stress.[10,11] The fibrotic conditions involve over expression of MUCA5c; we acetylcysteine[12] that improves inflammations as well prevents mucin's production. Its use in post COVID-19 fibrosis is important; it is known that in diabetics where lung complications are commonly present this class of compounds SGLT2 stimulates surfactant production in alveolar type 2 cells as well as for mucin.[12]

Conclusions

This study proposes to promote NO endothelia's formation to block both the excessive expression of MUC1 and the atherosclerosis effect of the vessels. This study proposes to inhibit phosphodiesterase by vasodilatation of the pulmonary vascular bed and MUC1 over-expression by interleukin6. the use of Sildenafil with SGLT2 and N-Acetylcysteine The protocol give sildenafil citrate 25 mg/die, acetyl cysteine 600 mg × 3/die empagliflozin 100 mg/die.

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Conflicts of interest

There are no conflicts of interest.

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