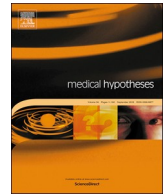




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Fenofibrate increases the amount of sulfatide which seems beneficial against Covid-19



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ABSTRACT

Fenofibrate, which is a PPAR- α agonist, increases the level of sulfatide. In this letter we hypothesize on the background of various findings that this is beneficial against COVID-19. Fenofibrate has been used for decades against hypercholesterolemia and has no serious side effects. Therefore, a trial giving fenofibrate to patients with corona virus infection is recommended.

It has been somewhat strange and unexplainable that patients with hypertension and/or metabolic syndromes have been more hurt by the coronavirus pandemic. Partly plausible has it been that hypertension patients treated with ACE inhibitors are more sensitive because, compensatory, they develop more ACE2 molecules which actually have been found to be the receptor of coronaviruses. However, only 1/3 of the hypertension patients take these drugs meaning that for 2/3 of the patients the higher sensitivity is not understood.

Also, it is odd that children and even small kids who usually are very sensitive to virus infections, are not sensitive to the infection or do not develop serious symptoms after infection of the coronavirus. How can these obvious paradoxes be explained?

Sulfatide has been connected to various infections. Sulfatide is a glycosphingolipid consisting of two fat chains on the backbone of a ganglioside molecule consisting of serine. To this is attached sugar molecules and in the case of sulfatide it is galactose. The length of the fat chains can vary. Thus the molecule consist of a hydrophobic end and a hydrophilic end thus it is a detergent. Among other organs it is synthesized in the liver and it depends on the supply of serine which is a non-essential amino acid. It is ubiquitously present in the neural system as it is an important component of sphingomyelin which insulate the nerve fibers. Also it is present in the beta cells in which it has important role for manufacturing and secretion of insulin [1]. It is present in the blood and it is easy to determine by mass spectrophotometry. Due to its physical properties as described and due to its presence on many cell surfaces mostly in the carvioli crypts, it has been considered whether sulfatide might be a virus receptor, which has turned out not to be the case [2]. However, highly interesting sulfatide regulates negatively the fusion process for the entrance of a virus through the cell membrane [3]. In beta cells, sulfatide has a role in exocytosis of insulin by fusing the membranes of secretory granules to the cell membrane [1]. In contrast, sulfatide seems to play a role in the opposite process of infusion of human paravirus influenza type 3 [3]. This has been shown by a three times lower infection of Cos cells after loading these with sulfatide. Also treatment of sulfatide containing cells with monoclonal sul-

fatide antibodies highly enhanced infection status of the cells [3].

It has been described that patients being part of the lowest one third percentile of sulfatide in the blood, have a two times increased risk of hypertension compared to persons with the highest sulfatide amount [4]. This has further been elaborated by Guo et al. who found that patients with hypertension and/or metabolic syndromes display lower amount of sulfatide in their blood [5]. Furthermore, there is no precise data on the amount of sulfatide in children, but both in rats and in mice, young offsprings before puberty have higher levels of sulfatide than adults [6].

Thus, hypertension is associated with low amount of sulfatide, whereas kids might have high levels. Regarding Corona virus, it could be that high amounts of sulfatide (children) might reduce the infection ability or the disease severity, whereas low levels (hypertension) may do the opposite. This could quite easily be examined in an experimental virus laboratory. Also in a population, treatment with agents that increase sulfatide levels such as fenofibrate or serine [7,8] should be investigated for a beneficial effect against coronavirus infection.

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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.110127>.

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