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Letter to the Editor

Monkeypox is a global public health emergency: The role of repurposing cholesterol lowering drugs not to be forgotten

On July 23, 2022, World Health Organization (WHO) declared the current monkeypox outbreak a Public Health Emergency of International Concern (PHEIC).[1] Less than a week later New York and San Francisco declared a state of emergency due to an alarming rise in the number of monkeypox cases.[2, 3] By July 29, 2022; 22, 141 cases of monkeypox had been reported globally in the countries that have not been reported this disease historically.[4] Of these cases 4,906 were reported from the USA.

As a preventive measure effective smallpox vaccination is currently offered in many countries as Pre-Exposure Prophylaxis for risk groups to prevent monkeypox but it is not widely available and vaccination programs have only just been initiated.[5] Thus, the number of monkeypox patient cases will continue to rise. There are several antiviral medications including cidofovir, brincidofovir, and tecovirimat to treat monkeypox.[6] Of these, the most effective medication against monkeypox is tecovirimat which inhibits the function of a major envelope protein required for the production of extracellular virus. Tecovirimat thus prevents the mature virus from leaving an infected cell. The recommended duration of tecovirimat treatment is 14 days.[6] Currently there is very little data of the effectiveness of tecovirimat treatment against monkeypox although several clinical trials are ongoing.[6,7]

It can be expected that clinical trials regarding effectiveness of tecovirimat will last very long. So, at the current situation repurposing of cholesterol lowering drugs as adjuvants to tecovirimat, including statins, PCSK9 inhibitors and fenofibrates is an attractive strategy and has already been applied in the COVID-19 pandemic.[8-10]

The interest to repurposing cholesterol lowering drugs, particularly statins, is best known among COVID-19 patients.[11] Moreover, there are several examples of this repurposing strategy regarding other severe infections. Statins have been repurposed in the treatment of influenza and Ebola.[12] With Ebola infection, statins may result in the production of fusion-inefficient Ebola virus particles.[13] PCSK9 inhibitors have been used to treat Dengue virus infection because PCSK9 inhibitors enhance secretion of type I interferons.[14] Fenofibrate has been shown to decrease mortality and morbidity among Japanese encephalitis patients.[15] Compared to Japanese encephalitis vaccination Sehkal and coauthors mention the potential usefulness of fenofibrate especially when treating endemic infections.[15]

While currently there is clearly a lack of studies repurposing cholesterol lowering drugs for the treatment of Monkeypox more attention needs to be given how such viral infections effect the re-distribution of cellular cholesterol.[16] For example, the efficient endosomal re-distribution of cholesterol is essential for viral life cycles. If this cholesterol redistribution can be disrupted the viral life cycles may be inhibited or even collapse.[16] Fenofibrate also seems to have this ability, at least *in vitro*.[17] Taken together, monkeypox appears to become yet another global public health problem, and, as such, it is a reminiscent of the current COVID-19 pandemic and its predecessors. Therefore, the potential beneficial role of repurposing cholesterol lowering drugs should not be forgotten in this newly emerging viral outbreak. Patients with severe hypercholesterolemia should not stop taking cholesterol-lowering medication after contracting Monkeypox. If tecovirimat medication is started for Monkeypox, simvastatin should be changed to another statin, analogously when treating SARS-CoV-2 infection with Paxlovid.[18]

Declaration of Competing Interest

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