Colchicine May Interfere With the Efficacy of the Adenoviral Vector–Based Vaccine for COVID-19

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ABSTRACT: Under the ongoing COVID-19 pandemic, vaccines have become the crucial players to reduce the spread of the infection. Among them, the ChAdOx1 nCoV-19 vaccine is an adenoviral vector vaccine with an overall efficacy of 70.4% in protection. The engineered adenovirus contains the SARS-CoV-2 spike protein gene and pushes its DNA into the vaccinated cell's nucleus and subsequently, the spike protein can be made. During vaccination, the genome transition of adenovirus is influenced by the architecture and dynamics of the microtubule. Colchicine can alter microtubule dynamics by suppressing microtubule dynamics at lower concentrations and inducing depolymerization of microtubules at higher concentrations. Accordingly, the delivery of the genome to the vaccinated cell's nucleus by the adenoviral vector could be hindered under the presence of colchicine. Nevertheless, colchicine is a common medication for gout therapy worldwide, and though not recommended by guidelines, colchicine has even been taken into consideration as a possible therapeutic option for COVID-19 infection. Given the above reasons and the worldwide use of colchicine, the impact of colchicine on the efficacy of the COVID-19 vaccine via adenoviral vector should be viewed cautiously.

KEYWORDS: COVID-19, adenoviral vector vaccine, colchicine, microtubule

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Dear Editor:

Under the health-threatening ongoing COVID-19 pandecmic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), vaccines have become key in calming the spread of infection. Currently, several vaccines for SARS-CoV-2 are under development or in clinical process and some of them (Pfizer/BioNTech, Moderna, Janssen and Covaxin) have gained emergency use authorization (EUA) listing by the World Health Organization, while the ChAdOx1 nCoV-19 vaccine (AZD1222) developed at the University of Oxford partnered with the British-Swedish company AstraZeneca[1] received EUA by European Medicines Agency (EMA) on January 29, 2021.[2]

The ChAdOx1 nCoV-19 vaccine is an adenoviral vector vaccine with an overall efficacy of 70.4% in protection after two doses and 64.1% after at least one standard dose.[1] The engineered adenovirus contains the SARS-CoV-2 structural surface glycoprotein antigen (spike protein) gene and pushes its DNA into the vaccinated cell's nucleus and subsequently, the spike protein can be made by messenger RNA of the vaccinated cell to induce immunity. During vaccination, the genomes of adenovirus are carried in capsids across the membranes of host cells to gain access to their internal networks.[3] The virus will mimic the behavior of the intracellular crowd for achieving directed movements along the cytoskeletal network of filamentous proteins. Interestingly, the adenovirus uses the architecture and nucleotide-dependent conformational changes of the dynein motor and its cofactor dynactin for movements along microtubules,[3-5] so the transition in the cytoskeletal network for adenovirus to target the nucleus for genome release is influenced by the microtubule architecture and dynamics.

Microtubules are filamentous polymers that form one of the major components of the cytoskeleton while also providing transportation for cellular messages and are involved in intracellular signaling. Several compounds currently in clinical use alter microtubule dynamics, including taxane, vinca alkaloid, or colchicine.[6] The colchicine-binding site is located in the center of the tubulin dimer, right at the interface of α- and β-tubulin monomers.[7] Binding to the colchicine site is followed by a conformational change involving an intradimer bending, where the tubulin monomers undergo twisting around the interface. This change in the conformation allows the inclusion of colchicine-tubulin complex inside the microtubule filament and then suppresses microtubule dynamics at lower concentrations and induces depolymerization of microtubules at higher concentrations.[6,7]

Accordingly, the delivery of the genome to the nucleus of the vaccinated individual's cell by the adenoviral vector could be hindered under the presence of colchicine. In addition, there was in vivo evidence on the effect of colchicine inhibiting the gene delivery of adenovirus to the neuron.[8] Colchicine is a common medication for gout therapy. Furthermore, colchicine could be taken as a therapeutic option for COVID-19 infection under the current pandemic in inhibiting the immune system to prevent cytokine storms.[9,10] Given the above reasons and the worldwide use of colchicine, the impact of colchicine on the efficacy of COVID-19 vaccine using adenoviral vector

should be viewed cautiously and further precise investigations are warranted.

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Author Contributions

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