Antiviral activity of aminocaproic acid against SARS-CoV-2: review of the literature and results of the first experimental study

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Conflict of interest: none

BACKGROUND. The SARS-CoV-2 pandemic has a significant impact on the global health care system, so effective treatments for coronavirus disease (COVID-19) are urgently needed. Nowadays, drug repurposing is widely considered for COVID-19 therapy; significant attention is paid to inhibitors of transmembrane serine proteases (TMPRSS2), which ensure the penetration of SARS-CoV-2 into the human cells and contribute to their infection. ε-aminocaproic acid (ACA), which has been used worldwide for many years to correct blood loss as a fibrinolysis inhibitor, is also known for its ability to block TMPRRS2. It is approved by the Ministry of Health of Ukraine for the treatment of influenza and acute respiratory viral infections.

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OBJECTIVE. The aim of our study was to evaluate the antiviral effect of ACA *in vitro* by staining of SARS-CoV-2 viral antigen (spike protein) and by visual scoring of cytopathogenic effect (CPE).

RESULTS AND DISCUSSION. Using immunohistochemistry assay it was found that the mean value of EC50 for ACA on Caco-2 cells was 2.5 mg/ml and on Calu-3 cells – 17.3 mg/ml. Using CPE assay it was identified that the mean value of EC50 for ACA on Caco-2 cells was 6.4 mg/ml and on Calu-3 cells – 8.7 mg/ml. Additional analysis was shown that ACA has low cytotoxicity with CC50 values of >50 mg/ml on Caco-2 cells after 24h and 48h incubation and 37,57 and 41,29 mg/ml on Calu-3 cells after 24h and 48h incubation, respectively. Antiviral activity of ACA was detected when using non-toxic concentrations of the drug and did not depend on the time of introduction of ACA (before the introduction of the virus simultaneously with the pathogen after 1-hour incubation). ACA can be recommended for further *in vivo* studies on laboratory animals.

KEY WORDS: SARS-CoV-2, COVID-19, transmembrane serine proteases, TMPRSS2 inhibitor, ε-aminocaproic acid.