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Proteolysis inhibitor e-aminocaproic acid is effective drug for prevention and treatment of influenza and other acute respiratory viral infections in children and adults

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Abstract:
The proteolytic cleavage is the universal mechanism of specific proteins activation. The activation of proteolysis plays the important role in the pathogenesis of many diseases including viral infections. The results of our previous research and the scientific data have made it possible to formulate the conception concerning “vicious circle” forming: virus activates the proteolytic systems, which in turn assist the development, generalization and aggravation of infectious process at the expense of influence on the etiological and pathogenetical factors. The inhibitors of proteolysis (IP) may prevent the forming or to destroy this “vicious circle”. Usually IP E-aminocaproic acid (E-ACA) is used for hemostasis when fibrinolysis contributes to bleeding. E-ACA is low toxic drug. The intravenous and oral LD50 of E-ACA are 3.0 and 12.0 g/kg respectively in the mouse. E-ACA prevents the enhancement of proteolysis during the interaction of virions with cell membranes, decreases penetration of virions into sensitive cells. It brings down proteolytic cleavage of HA precursor to HA-1 and HA-2 and reduces the infectious virus harvest. High levels of E-ACA anti-influenza efficacy in vitro were shown on subtypes H1N1; H2N2; H3N2 of human, H5N3 and H7N3 avian influenza A viruses and on influenza B viruses. E-ACA promotes the intensification of specific antibodies production and cell immunity, prevents vessels’ permeability and hemorrhagic phenomena and decreases the destruction of bronchi’s epithelium. Mice treated by E-ACA after primary infection were more protected to re-infection. E-ACA decreased the virus reproduction in lungs and also enhanced the humoral immune response when used in the prevention and treatment of influenza. On the basis of our experimental research and clinical trials Ukrainian Ministry of Public Health has allowed using E-ACA as antiviral for prevention and treatment influenza and other acute respiratory viral infections (ARVI) in children and adults. The results of including of E-ACA in the therapeutic complex for treatment of influenza and other ARVI in children were decrease of duration of intoxication symptoms on 2-3 days, of fever on 1.5-3 days, of catarrhal symptoms on 1.5-2 days. Quantity of complications reduced to 17%. It is known that using of agents with different mechanisms of antiviral actions may
have as result synergistic effect. Our studies of anti-influenza activity *in vitro* and *in vivo* show that the results of combination action of E-ACA with Tamiflu are synergistic antiviral effects.

**Conclusions**

E-aminocaproic acid is effective drug for prevention and treatment of influenza and acute respiratory viral infections in children and adults. The combination using of proteolytic inhibitor E-Aminocaproic acid with neuraminidase inhibitor Tamiflu have good perspectives in anti-influenza protection and therapy.