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Metered dose inhaler containing aprotinin, a protease inhibitor, as a drug against influenza

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Influenza virus is activated by host respiratory proteases to maintain infection in respiratory epithelium and pathogenesis of disease. Inhalations of aprotinin, a natural protease inhibitor, were found to provide therapeutic effect in influenza. Antiviral efficacies of inhalations of aprotinin aerosol generated by meter dose manual inhaler (MDI) were studied in influenza patients. Clinical trials were performed during outbreak in Moscow region caused with pandemic Influenza H1N1pdm09 virus. Propellant type MDI (AerusTM, Russia) containing aprotinin as an active substance was used. Patients inhaled nasally 2 aerosol doses of aprotinin (160 Kallikrein-inhibiting Units (KIU)) each 2 hours for 5 days. In comparison group, patients were treated with ingavirinTM (a synthetic peptidoamine with unknown antiviral target), 90 mg per day for 5 days. On day 2 after treatment, virus loads in nasal-pharyngeal washes were determined by real time PCR. Because amounts of host cells in nasopharyngeal washes varied from patient to patient, amounts of viral RNA were normalized to host ribosomal 18S RNA determined by real time PCR with human ribosome specific primers. About 10 fold decrease of virus load in aprotinin patients were determined in comparison to ingavirin patients. Duration of clinical symptoms, such as headache, sore throat, cough, sore thorax, rhinorrhea, weakness, fever, was 1-2 days shorter in aprotinin then in ingavirin group. About 35 patients were observed and no side effects were documented in aprotinin-treated patients. Aprotinin MDI can be recommended as a drug of choice against Influenza caused by different viruses because phenomenon of virus activation by host proteases is a major pathogenesis mechanism in all influenza viruses.

Biography

Oleg Zhirnov graduated 1'st Moscow Medical Institute and defended PHD theses and Degree of Doctor of science at the D.I.Ivanovsky Institute of Virology (Moscow, Russia). Currently, he is professor and a head of the laboratory of viral pathogenesis at the D.I.Ivanovsky Institute of Virology (Moscow, Russia). Awards: Stipendium of European Molecular Biology Organization (EMBO), Moscow Mayer's Award for the development of a new method of Influenza therapy. Grants: German Research Foundation (DFG), NATO Research Grant, Scholarship of Howard Hughes Medical Institute (USA), Grants of Russian Foundation of Basic Research (Russia). Research interests: molecular biology of viruses, molecular pathways of cell death (apoptosis; autophagy), antivirals and viral pathogenesis, viral vaccines design and design of oncolytic viruses.

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Notes: