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Antibodies to interferon-gamma in ultra-low doses: a new option for pandemic influenza

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Objectives: To assess antiviral activity of antibodies to interferon gamma in ultralow doses (ULDabIFNg) against influenza A/H1N1 viruses.

Methods: Antiviral activity of ULDabIFNg (Anaferon for children®) was studied in experimental models of lethal infection of mice infected by different influenza A/H1N1 virus strains. Studies were conducted in Influenza Research Institute (Russia) and in APcis (France) in 2009. In Influenza Research Institute 100 female outbred mice (16-18 g., 20 mice/group) were infected intranasally with 10LD50 of influenza virus A/California/07/2009swl. In APcis 60 female Balb/c mice (10-12 g., 20 mice/group) were infected intranasally with 3LD50 of influenza virus A/NewCaledonia/20/99. In both studies ULDabIFNg given as water solution were administered according to prophylactic/treatment regimen (5 days before and 12 days after inoculation) via oral gavage (0.2 ml/mice 2 times/day). Besides ULDabIFNg were given instead of drinking water. Control mice were given distilled water according to the same schedule. In negative control group mice were neither infected nor treated. In Influenza Research Institute efficacy of combination of ULDabIFNg with oseltamivir against monotherapy with oseltamivir was also studied. Oseltamivir was administered according to prophylactic/treatment regimen (25 hours and 1 hour before and 3 days after inoculation) via oral gavage (0.2 ml/mice 2 times/day at dose 20 mg/kg/day) or (APcis) from 1 hour to 5 days after inoculation (10 mg/kg/day). Combination of ULDabIFNg with oseltamivir was prepared by dissolving oseltamivir in water solution of ULDabIFNg. Mortality rate and body weight change were evaluated.

Results: In Influenza Research Institute ULDabIFNg significantly reduced mortality. In control group survival was 12.5%, in oseltamivir group – 10%, in ULDabIFNg group – 50%, in oseltamivir+ULDabIFNg group – 35%. In the second study (APcis) in the control group inoculation caused deaths 60% of mice on day 7, treatment with ULDabIFNg resulted in a later disease onset (on day 5 in ULDabIFNg group mortality was 15% vs 40% in control group). In both studies mean body weight of alive mice was constantly a positive function of time in group treated with ULDabIFNg.

Conclusion: Antiviral activity of ULDabIFNg against two strains of influenza A/H1N1 viruses including the pandemic one is comparable to oseltamivir. Combination of ULDabIFNg with oseltamivir increases the efficacy of monotherapy with oseltamivir.