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Protective effect of bacterial preparation CM in experimental influenza infection

Julia Serkedjieva, Emilia Ivanova
Institute of Microbiology, Bulg Acad Sci, Sofia, Bulgaria

The combined use of selective viral inhibitors and substances with immunopotentiating effect is a promising approach in experimental antiviral chemotherapy. Previously it was shown that the cytoplasmic membranes of E. coli WF^+ stable protoplast type L - forms (CM) exhibited a pronounced stimulating effect on the cellular and humoral immune response in intact experimental animals. In the course of sublethal influenza infection with virus A/Aichi/2/68 (H3N2) in mice, CM applied intraperitoneally 7 days before virus inoculation in a single dose of 25 mg/kg stimulated the peritoneal macrophage and polymorphonuclear functions in infected animals. The immunostimulating and immunorestaurating effect of CM was related to the presence of a lypopolysaccharide in the preparation. In the course of lethal influenza in-fection in mice with the same virus, CM applied in a single dose of 25 mg/kg 1 - 8 days before virus inoculation reduced mortality rate of experimental animals (protection index 59.5) and prolonged mean survival times (1.8 - 2.3 days). The protective effect was best expressed when the substance was inoculated 7 days before virus infection. The combined application of CM with rimantadine hydrochloride resulted in synergistic protective effect (protection index 88.8%). The protective effect of CM in experimental influenza infection in mice was attributed mainly to its pronounced immunostimulating activity. Our results clearly show that in experimental influenza infection in mice the appropriate combined use of a selective antiviral agent with an immunomodulator results in increased protection of infected animals.

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Combination Effects of Picornavirus Replication Inhibitors

L. Nikolaeva and A. S. Galabov. Department of Virology, Institute of Microbiology, Bulgarian Academy of Sciences, Sofia, Bulgaria

Various picornavirus replication inhibitors with known mechanisms of action, i.e. guanidine hydrochloride, HBB, S-7, arildone, disoxaril and enviroxime, as well as ribavirin, were examined for their combination effects on poliovirus 1 (Mahoney) replication in FL cells. The plaque-reduction test was used following the requirements of Prichard & Shipman's model (1990) to analyze drug-drug interactions, revealing the dose-response surface. The results obtained could be summarized as follows: 1. synergysm was observed when enviroxime and disoxaril, enviroxime and S-7, disoxaril and HBB, HBB and S-7 were combined; 2. ribavirin produced antagonistic effects when combined with all tested substances; 3. effects of the rest of combinations could be characterized as additive ones. Synergistic combinations were tested on other members of the enterovirus genus (Coxsackie B1, ECHO13). As regard to the perspectiveness of the combination of enviroxime and disoxaril further experiments were carried out in order cross resistance to be studied. For that purpose enviroxime and disoxaril-resistant poliovirus mutants were selected. Resistance followed only two passages in the presence of disoxaril and ten passages with enviroxime (40 μmol/l each). The effects of both of the substances were tested on the parental Mahoney strain and the resistant ones. Results revealed lack of cross-resistance which is very encouraging for further investigations.