VIROLOGY

Inhibitory Effect of No-Spa on Parainfluenza Virus Replication

I. N. Zhilinskaya, I. P. Ashmarin, and O. I. Kiselev

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No-Spa (20 μg/ml) effectively inhibits replication of parainfluenza viruses in cultured chick chorioallantoic membrane culture and *Macaca rhesus* kidney cells. Mechanism of the antiviral effect of vasodilator drugs is discussed.

Key Words: *vasodilator drugs*; *parainfluenza virus*; *replication*

Some vasodilator drugs possess antiviral activity. Previous studies demonstrated a potent antiviral effect of papaverine on cytomegalovirus, measles virus, and HIV [6] and that of No-Spa on influenza viruses [1]. Our aim was to study the effect of No-Spa on replication of parainfluenza viruses (PV). Similar to influenza viruses, PV belongs to the myxovirus family, which evokes a variety of acute respiratory infections, in particular, in infants.

MATERIALS AND METHODS

No-Spa (Chinoin) and 3 types of PV Sendai (type I), ALTBcc 2056 (type II), and III-v-2932 (type III) were used in this study.

Replication of type I (Sendai) PV was investigated using chick chorioallantoic (CA) membrane culture. The antiviral effect was assessed by ID_{50}, i.e. a concentration inhibiting virus replication by 50% in comparison with the control. Hemagglutination titer was determined using 1% chick erythrocyte. Replication of type II and III (ALTBcc 2056 and III-v-2932) PV strains were examined using cultured *Macaca rhesus* kidney cells. The inhibitory effect was also estimated by ID_{50} (hemagglutination titer in the culture medium and hemabsorption of infected cells with 1% guinea pig erythrocyte suspension).

Institute of Grippe, Russian Academy of Medical Sciences, St. Petersburg; Department of Human and Animal Physiology, M. V. Lomonosov Moscow State University

RESULTS

No-Spa in a dose of 20 μg/ml efficiently inhibits replication of Sendai viruses. Remantadin used as the reference anti-influenza drug had no effect on PV type I replication.

In contrast to remantadin, No-Spa in therapeutic doses exhibits antiviral activity against PV types II and III (Table 1).

Thus, No-Spa exhibits *in vitro* antiviral activity toward all PV types (I, II, and III), which is of theoretical and practical interest.

Concerning the mechanisms of this effect, we started with the hypothesis that vasodilators stimulate the synthesis of NO which possesses antimicrobial and antiviral activities. However, L-arginine, the main source of NO in cells, less effectively inhibits influenza virus replication in comparison with No-Spa. It is likely that apart from stimulation of NO synthesis, vasodilator agents modulate other biochemical processes, which are more critical for virus replication. Experimental data accumulated during the last decade on the action of vasodilator drugs and on replication of virus strains suggest that the cross point of these processes may be associated with cAMP-dependent intracellular events. It is established that vasodilators

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Table 1. Effect of No-Spa on Parainfluenza Virus Replication

Preparation	Concentration, μg/ml	Antiviral activity, lg ID_{50}		
		PV type I (Sendai)	PV type II (ALTBcc 2056)	PV type III (III-v-2932)
Control		6.3	3.5	7
No-Spa	20	3	0	1.5
Remantadin	25	6	3	7

inhibit phosphodiesterases and induce accumulation of cAMP in the cell [6]. Replication of certain viruses, myxoviruses included, depends on cAMP synthesis. The lower the content of cAMP in the cell, the more intense the replication, and vice versa [2-5,7,8]. Accumulation of cAMP results in protein kinase (p68) activation, which catalyses phosphorylation of the α subunit of the eukaryotic initiation factor IF-2, natural substrate of protein kinase, and inhibits protein synthesis at the transcription level [5,7]. This is the most likely mechanism of inhibition of virus replication by vasodilators. The hypothesis on the mechanism of No-Spa antiviral activity calls for further experimental verification.

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