Effect of Trekrezan on Immunogenesis under Experimental Conditions

M. G. Voronkov, Yu. G. Pavel, A. L. Karus, Yu. A. Kumar, T. K. Shattshneider, E. Yu. Myuirsepp, Kh. Yu. Pavel, E. Poverina, and M. M. Rasulov

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 138, No. 8, pp. 196-197, August, 2004
Original article submitted January 11, 2004

We studied the dynamics of immune reactions to trekrezan in mouse pups after vaccination of adult mice during pregnancy and mouse pups at different terms after birth with *Salmonella typhimurium* 34-96. The preparation modulated activity of the immune system and stimulated antibody production in the pre- and postnatal period.

Key Words: *Trekrezan; immunity; pre- and postnatal development*

Much attention is given to a new class of tris(2-hydroxyethyl)ammonium salts of arylheteroacetic acids [2]. We previously studied pharmacological properties of biological stimulator trekrezan (2-methyl-phenoxyacetate tris(2-hydroxyethyl)ammonium, $2CH_3C_6H_4OCH_2COONH(CH_2CH_2OH)_3$) [1-6]. Trekrezan has no toxic activity, acts as an adaptogen [2], immunomodulator, and hemomodulator [4], stimulates reproductive activity in animals [1], improves intrauterine development of embryos, increases viability of the offspring [5], and accelerates the development and growth of chicks [3]. The preparation increases activity of regenerating cells in the liver [6], possesses cardioprotective properties, and can be used for the therapy of tuberculosis. The effects of trekrezan on embryogenesis and viability of the offspring in animals are determined by stimulation of the immune system in fetuses and maternal immune status. Several properties of trekrezan were estimated in our previous experiments [5]. Here we studied the effect of trekrezan on prenatal immunogenesis and development of the immune system in mice over the first weeks after birth.

Irkutsk Institute of Chemistry, Siberian Division of the Russian Academy of Sciences; Tartu University; Estonian Agricultural University, Tartu. ***Address for correspondence:*** maksud@bk.ru. Rasulov M.M.

MATERIALS AND METHODS

Experiments were performed on immunologically heterogeneous outbred albino mice. The "maternal effect" of trekrezan was studied by the method of vaccination. Female mice and mouse pups were divided into the control and 2 experimental groups.

Adult male mice were housed together with virgin females. On days 1 and 7, group 1 females were intraperitoneally vaccinated with *Salmonella typhimurium* 34-96 (0.7×10^9 cells) and received subcutaneous injection of trekrezan (1 mg in 0.5 ml physiological saline). Trekrezan in the same dose was administered to group 2 mice. Control animals received physiological saline.

The offspring was examined until the period of maturity (body weight ≥20 g). Newborn mice of group 1 were vaccinated on days 1 and 4 after birth. Group 2 animals were vaccinated on day 1 after birth. Group 1 and 2 mice received trekrezan on days 1 and 4 after birth. The vaccine and trekrezan were administered in doses similar to those used in experiments on adult animals.

Control mouse pups did not receive the vaccine and trekrezan.

Antibody production was assayed by a unified method for studying the antigen-antibody reaction (-lg antibody titer).

Experimental groups were small (8 mice per group) and were physiologically heterogeneous. Hence, the re-

0007-4888/04/1382-0172

TABLE 1. Ratio of the Immune Response in Mouse Pups (%, *M*±*m*)

Day, group		Non-responding	Response		
			weak	moderate	strong
day 1	1st	100	0	0	0
	2nd	100	0	0	0
	3rd	100	0	0	0
day 4	1st	75	12.5	12.5	0
	2nd	62.5	37.5	0.	0
	3rd	100	0	0	0
day 7	1st	0	25	62.5	12.5
	2nd	0	25	62.5	12.5
	3rd	0	87.5	12.5	0
day 10	1st	0	12.5	62.5	25
	2nd	0	62.5	25	12.5
	3rd	0	75	25	0

sults were analyzed according to the directive of the Russian Veterinary Legislation.

RESULTS

Some treated mice were responders on day 4 of postnatal period. In control animals antibody production was not detected (Table 1).

Vaccination of group 1 animals during embryogenesis had a moderate stimulating effect in the early stage of antibody production (compared to group 2 mice receiving trekrezan). A similar tendency was observed at the late stage of antibody production (days 7 and 10).

Trekrezan also stimulated antibody production in group 2 mice.

The total ratio of immune reactions in normal responders and hyperresponders of group 1 was much higher compared to that in group 2. These differences were probably related to the fact that group 2 animals were not revaccinated on day 4 of life.

Our results indicate that trekrezan possesses immunomodulatory activity during embryogenesis and improves the "maternal effect".

REFERENCES

1. M. G. Voronkov, A. P. Dyban, V. M. D'yakov, and N. A. Simbirtsev, *Dokl. Ros. Akad. Nauk*, **364**, No. 5, 703-707 (1999).
2. M. G. Voronkov, A. N. Mirskova, and G. G. Levkovskaya, *Ibid*., **386**, No. 3, 411-414 (2002).
3. M. G. Voronkov, Kh. N. Mukhutdinova, M. K. Nurbekov, and M. M. Rasulov, *Dokl. Ros. Akad. Sel'skokhoz. Nauk*, No. 2, 39-41 (2003).
4. O. P. Kolesnikova, O. G. Kudaeva, T. V. Suzhenko, *et al*., *Dokl. Ros. Akad. Nauk*, **391**, No. 3, 410-412 (2003).
5. Yu. G. Pavel, A. L. Karus, Yu. A. Kumar, *et al*., *Ibid*., **385**, No. 3, 419-421 (2002).
6. M. M. Rasulov, I. G. Kuznetsov, A. G. Zabozlaev, *et al*., *Izv. Akad. Nauk SSSR*, No. 2, 235-243 (1993).