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Vitamin C – a challenge in the management of rabies

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Studies in experimental animals have shown that protection from rabies seems to be related not only to the high antigenicity of the vaccine but also to induction of interferon [1–4]. It has also been established that vitamin C enhances the interferon response to the chemical interferon inducers poly (rI) and poly (rC) [3, 5] as well as to some viruses [2].

Our study was conducted on humans in the course of post-exposure treatment of rabies in a region endemic for animal rabies. The aim of the study was to establish whether an enhancing effect of vitamin C on interferon induction could be demonstrated in patients vaccinated against rabies. As vaccination alone is not always effective in treated patients [6], a further improvement of the post-exposure treatment of rabies would be welcome. The existence of a huge reservoir of rabies in animals almost all over the world and the occurrence of human cases of rabies are reasons for continuing research on protection against rabies [7, 8].

The course of the study

Sixteen healthy adult patients entered the study. The mean age of the patients was 32 years (minimum 20 years, maximum 46 years, median 30 years). Written informed consent was obtained. The patients were randomly allotted to two groups and were treated with the vaccine alone (group 1) or vaccine plus vitamin C (group 2).

Risk of infection with rabies virus was assessed using a standardised questionnaire. The criteria for exposure to rabies demanded that the patients had a break in the skin due to the bite of an animal with an unknown owner or an animal suspected to be rabid in the endemic animal rabies area. The patients were not previously vaccinated against rabies and they had no immunodeficiency disorders or immunosuppressive treatment. Commercially available inactivated rabies vaccine prepared in human diploid cells, Vaccine Rabique (Pasteur Mérieux, Lyon, France) was used in the study. Rabies immunoglobulins were not added. All patients were immunized with 2 ml – 1 ml – 1 ml on the days 0,7 and 21 [9]. The second group received a single oral dose of 2 g of vitamin C powder dissolved in water in addition to the first dose of vaccine.

Alpha interferon levels were measured in the sera before the start of the treatment, at 24 hours and at 21 days after the start of the vaccinations. Assessment of the level of alpha interferon was done using interferon alpha ELISA assay (Endogen Inc, USA). Statistical analysis was done by EPI-Info 6.

Baseline mean level of interferon in groups 1 and 2 of patients (Table 1) was comparable, being 24.5 in group 1 and 23.9 in group 2. 24 hours after the start of the treatment, mean interferon alpha level had increased only in the group 2.

Vitamin C has a significant influence on the production of interferon alpha in patients vaccinated against rabies on the first day after the start of the treatment (Odds ratio 23.20; 95% confidence limits for OR 7.49 <OR <83.52; Chi-Squares Yates corrected 47.69; P-values highly significant <0.001).

21 days after the start of the treatment the influence of vitamin C on the level of interferon alpha was not statistically apparent (Odds ratio 1.63; confidence limits for OR 0.51 <OR <5.38; Chi-Squares Yates corrected 0.42; P-values 0.52).

The immunization with human diploid cell vaccines against rabies is the gold standard for prevention of rabies in exposed persons [10]. However, some deaths in treated patients have been reported [6, 11, 12].

We have demonstrated that vitamin C is an effective stimulator of interferon production in humans and could therefore be used for stimulation of an enhanced interferon response to rabies vaccine. Simultaneous inoculation of rabies vaccine and administration of vitamin C could improve the post-exposure immunization especially in the case of rabies immunoglobulin shortage.

We assume that at the beginning of treatment, when the antibody levels against rabies virus are not present or are not protective, a high level of interferon could have protective role.

Table 1

Level of interferon alpha (pg/ml) in the sera of patients during the course of treatment.

Patients			Mode of treatment	Period after vaccination		
Number	**Gender**	**Age**		**0 day**	**24 hours**	**21 day**
1	male	30	Vaccine alone (group 1)	0	10.8	13.4
2	male	40		6.6	0	5.4
3	male	35		0	0	8.6
4	male	20		25.3	39.4	ND*
5	male	44		17.8	0	0
6	male	29		18.5	2.7	ND*
7	male	26		158	0	5
8	female	46		0	0	0
9	female	45		18.4	0	9.1
10	female	38		0	0	24
Mean				**24.5**	**5.2**	**8.2**
SD				**47.9**	**12.5**	**7.8**
11	female	32	Vaccine + vitamin C (group 2)	0	45.6	21
12	female	26		0	11.2	5.4
13	male	28		0	20.2	0
14	male	29		19.5	11.5	0
15	female	30		0	91.3	13.8
16	female	20		124	514	37
Mean				**23.9**	**115.6**	**12.9**
SD				**49.6**	**197.5**	**14.4**

*ND = not done

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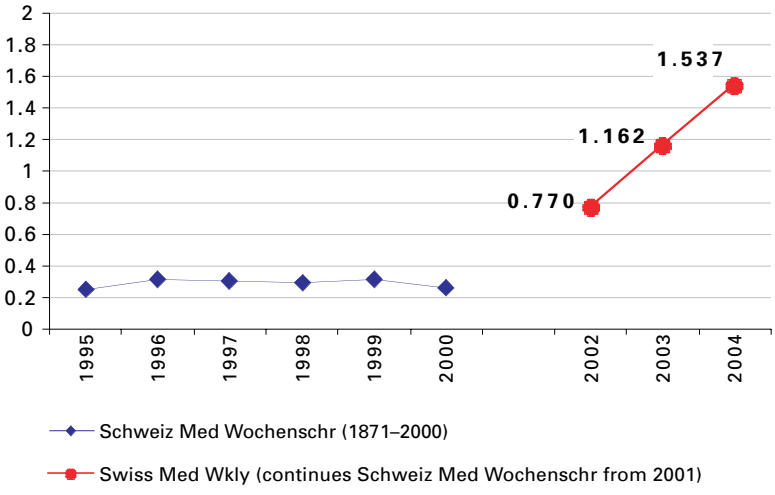

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