Asian Biomedicine Vol. 1 No. 2 August 2007

Brief communication

Accelerated neutralizing antibody response to rabies vaccination six month after a single intramuscular pre-exposure dose

Porntep Suandork[a], Chitsanu Pancharoen[b], Sanit Kumperasart[c], Araya Sungdee[c], Sirima Pattamadilok[c], Pathom Sawanpanyalert[c], Usa Thisyakorn[b]

[a]*Bangkok Hospital Medical Center, Bangkok 10330;* [b]*Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330;* [c]*Department of Medical Sciences, Ministry of Public Health, Nonthaburi 11000, Thailand*

Background and objective: Rabies is still a serious public health problem in much of Asia. Management of severe exposures includes use of immunoglobulin which is expensive and scarce in regions where needed the most. Pre-exposure vaccination of subjects at risk eliminates need for immunoglobulin in case of an exposure. Pre-exposure vaccination schedules require 3 injections of tissue culture vaccine over 2-4 weeks. It would be desirable to learn if a reduced dose might be able to induce an adequate immune response.

Method: Thirteen volunteers received one intramuscular dose of a WHO recognized commercial rabies vaccine. All had detectable neutralizing antibodies six months later and developed an accelerated immune response when given a simulated post-exposure rabies vaccine series.

Results: This study suggests that one intramuscular injection of purified vero cell rabies vaccine provides immune memory for at least 6 months. This study needs to be repeated with a larger number of subjects for a longer period of time as it may be of interest for selected populations.

Keywords: Pre-exposure prophylaxis, short regimens, rabies.

The rabies advisory committee of the World Health Organization (WHO) mandated the use of rabies immunoglobulin for post exposure prophylaxis (PEP) for severely rabies exposed patients [1]. Human rabies immunoglobulin is virtually unavailable in countries where it is needed the most. Equine immunoglobulins are now being produced in some rabies endemic countries, but are in short supply and not well distributed throughout Asia. Travelers to rabies endemic countries, particularly children who are more likely to be exposed, are advised to have pre-exposure vaccination [1, 2]. Many travelers do not have the time to complete a full series prior to departure and may be exposed for only weeks to months. It would therefore be desirable to shorten the pre-exposure course and yet have the assurance that no immunoglobulin will be needed in the event of an exposure [1, 2].

Correspondnec to: Dr. Porntep Suandork, Bangkok Hospital Medical Center, Bangkok 10330, Thailand; E-mail: Porntep.su@bgh.co.th

Materials and methods

We recruited 40 medical students between the age of 22 and 25 with a male/female ratio of 1/1 for a randomized controlled trial. Thirty one of the recruited students were able to complete the entire study. All subjects provided informed written consent and the study was approved by the ethics committee of King Chulalongkorn Memorial Hospital. The students were divided into two groups. Group A received one full ampoule (0.5 mL) of rabies vaccine into deltoid muscle (Purified vero cell rabies vaccine, PVRV, Sanofi-Pasteur, Lyon, lot RO101, potency 4.35 IU per 0.5 mLampoule). Group B was given one subcutaneous dose of measles-mumps-rubella vaccine. After 180 days, both group received a full course of a simulated post-exposure rabies vaccination (PEP) (PVRV 0.5 Ml intramuscularly on days 180, 183, 187, 194 and 208). Serum was drawn prior to the initial vaccination to assure that they did not have any previous rabies vaccine. Serum was then collected on day 180 (day 0 prior to the first simulated PEP) and on days 3, 5, 7, 14. 28 and 42

Table 1. GMTs and percentage of subjects with titers above 0.5 IU/ml six months after one pre-exposure intramuscular rabies vaccine injection.

		Day 180	183	185	187	194	208	222
Group A (n=13) PVRV 0.5 mL IM	Mean GMT (IU/mL)	0.3* (0.11-0.77)	0.41* (0.13-0.86)	2.14* (0.5-4.05)	24.21* (6.12-67.3)	56.88* (74.8-121.4)	36.56* (12.6-60.3)	42.82* (29.5-61.1)
	Percentage of NAB above 0.5 IU/mL	15.4	38.5	100	100	100	100	100
Group B (n=18) MMR 0.5 mL SC	Mean GMT (IU/mL)	< 0.03*	< 0.03*	< 0.03*	0.37* (0.13-1.11)	12.15* (4.9-43.1)	9.64* (2.9-38.3)	14.51* (4.1-60.3)
	Percentage of Nab above 0.5 IU/mL	0	0	0	16.7	100	100	100

PVRV: Sanofi-Pasteur, Lyon, lot RO101, potency 8.7 IU/mL (4.35 IU/ 0.5 mL Amp). MMR: One subcutaneous dose of measles-mumps-rubella vaccines. One subcutaneous dose of measles-mumps-rubella vaccine. $p < 0.05$ (Student's t test).

after that. Neutralizing antibodies were determined at the Department of Medical Science, Ministry of Public Health of Thailand, using the rapid fluorescent focus inhibition test (RFFIT) [3]. Exclusion criteria were prior rabies vaccination and medications or illnesses that may suppress the immune response.

Results

All 13 subjects in group A who completed the study had detectable antibody titers on day 180 (before the first simulated PEP injection) and all had titers above the WHO minimum recommended level of 0.5 IU/mL on day 5,7,14,28 and 42; representing an accelerated antibody response (**Table 1**). Group B subjects showed no detectable titers on days 180 but they became detectable by day 7 and rose above the WHO acceptable levels (>0.5 IU/mL) after that. This is as one would expect in not previously rabies vaccinated subjects who receive a post-exposure vaccine series [1, 2]. Adverse side effects were minor, transient and in accordance with previous experiences using modern tissue culture rabies vaccines.

Discussion and conclusion

One intramuscular injection of a full dose commercial purified vero cell rabies vaccine confers sufficient immune memory to last at least 6 month and possibly longer. In the event of a rabies exposure during this period of time, one can expect an accelerated immune response to post-exposure vaccination. This would eliminate the need for administering immunoglobulin. A recently published study by a different group of investigators came to similar conclusions [4]. These studies need to be repeated using other tissue culture rabies vaccines, a larger number of subjects and wider age range. These data may be of interest to travel medicine advisors who deal with tourists, NGOs or military personnel traveling to rabies endemic regions for periods of time less than 6 month.

Acknowledgement

This study was supported by a grant from the Thai Medical Association. None of the authors have any conflicts of interest to declare. Drs. Pakamatz Khawplod and Henry Wilde provided helpful suggestions for the design and conduct of this study.

References

1. World Health Organization. Eighth report of the expert committee on rabies. Tech Rep Series 824. Geneva: WHO, 1992.
2. Wilde H, Khawplod P, Khamoltham T, Hemachudha T, Tepsumethanon V, Lumlerdacha B, et al. Rabies control in south and southeast Asia. Vaccine. 2005; 23:2284-89.
3. Smith J. Yager PA, Baer GM. A rapid fluorescent focus inhibition test (RFFIT) for determining rabies virus-neutralizing antibody. In: WHO Laboratory techniques in rabies. Meslin FX, Kaplan MM, Koprowski H, eds. Geneva:World Health Organization, 1996.
4. Khawplod P, Wilde H. Immunogenicity study of abbreviated rabies preexposure vaccination schedules. Proceedings of the WHO/OIE/EU Rabies Conference, OIE HQ, Paris, May 2007.