

Kinetic of Protective Antibodies After Small Doses of Purified Chick Embryo Cell Rabies Vaccinated Intradermally for Mild Rabies Post-Exposure Treatment

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Abstract

The immunogenicity and tolerability of purified chick embryo cell rabies vaccine (PCEC) given intradermally (id) as post-exposure treatment was observed in seven vaccinees, aged between 4-49 years old, who exposed to laboratory proven rabid dogs. PCEC was administered id 0.1 ml each into two sites at both deltoid areas on days 0, 3 and 7 and one site at right or left site on day 28. The severity of exposure was mild by nibbling or licking on questionable abraded skin. All patients had detectable neutralizing antibody from day 14 until 1 year after immunization which similar to those whom received the intramuscular regimen. The id vaccination schedule was well tolerated. This economically simplified alternative intradermal regimen would reduce the total dose of PCEC to 20-25% of the conventional scheme. (*J Infect Dis Antimicrob Agent 1994;11:5-8*)

Key words : Neutralization test, Protective antibody, Rabies Vaccine, vaccine.

เรื่องย่อ

ระดับแอนติบอดีคุ้มกันโรคพิษสุนัขบ้าภายหลังฉีดวัคซีน PCEC ขนาดน้อย เข้าในผิวหนัง จันทพงษ์ วะสี พ.บ.* ปรมเสวร์ ชัยประสิทธิ์กุล วท.ม.* ประเสริฐ เอื้อวารกุล พ.บ., ปร.ด.* ประเสริฐ ทองเจริญ พ.บ., ปร.ด.*

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คณะผู้วิจัยได้ติดตามศึกษาาระดับแอนติบอดี อาการแทรกซ้อนและประสิทธิผลในการป้องกันโรค ภายหลังฉีดวัคซีนป้องกันโรคพิษสุนัขบ้า เตรียมจากตัวอ่อนของลูกไก่ (PCEC) เข้าในผิวหนังขนาด 0.1 มล. ที่บริเวณเดลทอยด์สองข้าง ๆ ละ 1 ตำแหน่ง ในวันที่ 0, 3 และ 7 และฉีดเข้าในผิวหนัง 0.1 มล. 1 ตำแหน่ง ที่เดลทอยด์ขวาหรือซ้ายในวันที่ 28 ผู้ได้รับวัคซีนอายุระหว่าง 4-49 ปี มีประวัติถูกสุนัขที่ตรวจพบว่าเป็นโรคพิษสุนัขบ้ากัด หรือเลียผิวหนังที่อาจมีรอยถลอก ทุกรายมีระดับแอนติบอดีคุ้มกันโรคตรวจวัดได้ในวันที่ 14 จนถึง 1 ปี เช่นเดียวกับระดับแอนติบอดีที่ตรวจพบภายหลังฉีดวัคซีน PCEC เข็มกล้ำเนื้อตามตารางแบบธรรมดา หลังติดตาม 1 ปี พบว่าผู้รับการฉีดวัคซีนทุกรายปลอดภัย ไม่พบอาการแทรกซ้อน การฉีดวัคซีนขนาดน้อยเข้า ในผิวหนังสามารถลดขนาดวัคซีนที่ใช้เหลือเพียงร้อยละ 20-25 ของขนาดที่ใช้ฉีดเข้ากล้ามเนื้อ (*วารสารโรคติดเชื้อและบาดานจุลชีพ 2537;11:5-8*)

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INTRODUCTION

At present, cell culture rabies vaccines with high potency and safety are available but costly. Protective efficacy of the multiple sites intradermal vaccination in post-exposure prophylaxis have been documented for the human diploid cell strain vaccine (HDCV), the purified chick embryo cell rabies vaccine (PCEC) and the purified vero cell rabies vaccine (PVRV) (1-3). Hereby we report our observation in vaccinees who received intradermal post-exposure prophylactic regimen of PCEC. The kinetic of antibody responses and adverse reactions were studied. This practical schedule would be more cost effective than the conventional intramuscular regimen in mild exposure cases and in clinics where many exposed victims were seen in a day.

MATERIALS AND METHOD

In January 1990, six members (case No. 1-6) in the same family were exposed to one month old rabid dog (fluorescent rabies antibody proven). They were nibbled or licked by the puppy either on the intact skin or questionable abraded skin. Primary post-exposure immunization with 0.1 ml of PCEC (Behringwerke AG, FRG), vaccine lot No. 516053 with antigenic value of 10 IU/ml, was administered intradermally into two sites at both deltoid areas on days 0, 3, 7 and one site at right or left deltoid on day 28.

Subsequently another patient (case No. 7) was exposed to a proven rabid dog. The severity was mild with few nibbling abrasions. The same i.d. PCEC regimen was also given to this patient. Blood samples were collected on day 0 before vaccination and on days 7, 14, 28, 56, 180 and 365. Neutralizing antibody levels were

measured by rapid fluorescent focus inhibition test (RFITT) (4) at the Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University.

During the same period, conventional intramuscular schedule of the same lot of PCEC were given to 16 vaccinees as a control group to another study regimen (5).

RESULTS

Neutralizing antibody (NTAb) levels in 7 vaccinees (aged 4-49 years, median 13 years) were found to be satisfactory. All vaccinees had positive NTAbs on day 7 and levels greater than 5.46 IU/ml on day 14 (Table 1). The peaks of antibody levels were on day 56 and maintained until one year after vaccination. All patients reported no significant adverse effect. These seven patients remained healthy throughout the observation period.

Comparison of NTAbs response in intradermal and intramuscular groups of vaccinees is illustrated in Figure 1.

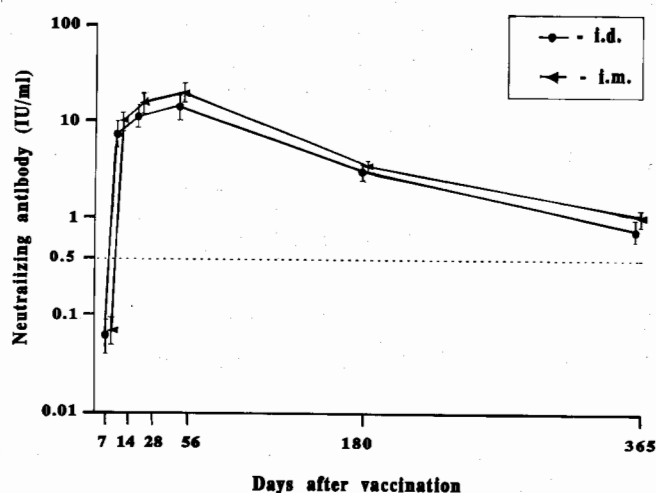


Fig.1 GMTs (IU/ml) of NTAbs after PCEC i.m. and i.d. vaccination.

Table 1: Rabies NTAbs of 7 vaccinees after PCEC ID 2-2-2-0-1 vaccination

Case No	Sex	Age (Yrs)	Rabies NTAbs (IU/ml) on days					
			Day 7	Day 14	Day 28	Day 56	Day 180	Day 365
1.	F	36	0.03	6.88	10.00	10.32	2.53	0.78
2.	M	11	0.06	8.67	17.17	21.81	4.34	1.08
3.	M	10	0.04	5.46	7.35	10.82	2.50	0.57
4.	M	9	0.10	13.77	14.52	15.02	3.63	0.81
5.	F	15	0.10	8.67	14.52	15.87	3.54	1.13
6.	M	49	0.06	5.46	9.48	9.90	2.37	0.62
7.	M	4	0.06	5.46	10.00	18.77	3.15	0.62
GMT			0.06	7.35	11.41	14.05	3.08	0.78
95% CI			0.04-0.09	5.34-10.12	8.63-15.08	10.53-18.74	2.49-3.81	0.60-1.00

DISCUSSION

Rabies is a fatal disease, once the symptoms appear the grave prognosis is expected. The only way to save life of the rabies exposed case is by giving the appropriate wound treatment and vaccinating the victims promptly with or without rabies immune globulin (6). In the historic record, nervous tissue vaccines had been used for century and saved lives of millions of people (7). The improved treatment of rabies exposure by tissue culture vaccine has success in this decade. However, the cost of vaccine are relatively expensive for people in developing countries which are rabies endemic area. In many instances such as case No. 1-6, exposure to rabid animal at a time involved many people which the family could not afford for the cost of full dose vaccine.

Alternative schedules have been developed for economic purpose. All schedules showed higher antibody responses than the nervous tissue vaccines given full course (8-10). The conventional Essen scheme given one full dose i.m. on days 0, 3, 7, 14 and 28, and optional for the booster dose on day 90 gave the satisfactory results (11) and the multisite intradermal regimens could be alternative with special precaution (6). In most cases of vaccinees who received primary vaccination, the NTA_b was detectable on days 7 to 14, the peak of antibody response appeared on day 14-30 after vaccination and then declined (1-3, 8-10). After booster, rapid rising of antibody was shown on day 7 and persisted at high level for 1-2 months then decline. Since the incubation period in most human rabies cases varied from 7 days to one year (12, 13), keeping detectable level of antibody for at least a year is suggested (13).

In our observation, 7 vaccinees were given PCEC i.d. schedule as 2-2-2-0-1 on days 0, 3, 7 and 28 (omitted day 14). This schedule was similar to the Thai Red Cross-intradermal regimen except we did not give booster dose on day 90. We found good antibody response in all vaccinees on days 14 and onward. The antibody persisted over detectable level of 0.5 IU/ml at one year. The kinetic of antibody response elicited by i.d. regimen was comparable with NTA_b after receiving conventional regimen (Figure 1). In this study the number of i.d. vaccinees is too small for the power of statistical calculation.

This study regimen consumes only 20-25% of the total volume of vaccine used in the conventional regimen.

The results of the neutralizing antibody determination, which is the best available indicator for protection indicated that all vaccinees had detectable levels of neutralizing antibody from days 14 to 1 year after immunization. These findings suggest that the simplified schedule of intradermal regimen could be another alternative for rabies post-exposure prophylaxis. However, this method of vaccination is useful when several patients with mild degree of exposure visit the clinic at the same time. Since saving the unused portion of vaccine may run to the risk of contamination and partially potency loss. Another important consideration is the antigenic value of the vaccine which should be higher than minimal requirement (>2.5 IU/dose). In this vaccine lot, the potency was 10 IU/dose. The conventional schedule is still highly recommended in small clinic setting and in victims who can afford the cost of vaccine.

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