Three-Year Experience with 4-Site Intradermal Booster Vaccination with Rabies Vaccine for Postexposure Prophylaxis

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For booster vaccination of previously immunized persons with potential exposure to rabies, the World Health Organization recommends 2 doses of cell-culture vaccine administered intramuscularly or intradermally on days 0 and 3. We believe that four 0.1-mL intradermal booster doses given on a single day could be used at no risk to the recipient. We studied use of a single booster vaccination on day 0 followed by four 0.1-mL intradermal doses of cell-culture rabies vaccines, and we determined that this is a safe, convenient, and economical regimen for postexposure treatment of previously vaccinated individuals.

Rabies is a fatal infectious disease in developing countries where animal immunization and control of dogs are inadequate. A person who is bitten or scratched by a rabid animal should receive postexposure rabies immunization, which induces rapid production of a high level of immunity that is maintained throughout the lengthy incubation period of rabies virus infection. The World Health Organization recommends booster vaccination if there is an additional occurrence of potential exposure. In this event, 2 booster doses of cell- or avian-culture vaccine, administered either intramuscularly or intradermally, should be given on days 0 and 3 of treatment [1]. Presumably, the dose given on day 3 is meant to be a “reserve booster dose” and may somewhat enhance the speed of booster response [2]. Studies published elsewhere have proven that a single booster dose of cell-culture rabies vaccine given on day 0, administered via either the intramuscular or intradermal route, successfully induces high titers of rabies-neutralizing antibody (Nab) in healthy adults who had previously been vaccinated with cell-culture rabies vaccine [2–10]. We believe that a single booster vaccination with cell-culture vaccine administered on day 0 for subsequent postexposure rabies treatment may be appropriate in previously vaccinated persons.

Our recent study showed that four 0.1-mL intradermal booster doses of purified Vero-cell rabies vaccine (PVRV) administered on day 0 induced significantly higher titers of Nab than did 2 booster doses given intramuscularly to subjects who had received preexposure rabies vaccination with cell-culture rabies vaccine 1 year previously [3]. Moreover, the Nab response associated with the 4-site intradermal booster regimen clearly appeared more rapidly than did the response associated with the conventional intramuscular booster regimen, and it was also shown to be consistently high 1 year after the booster vaccination [3]. Because the safety and cost of vaccination are the prime concern, shortening the postexposure schedule for previously vaccinated persons may be appropriate in our country. Since 1998, in the institution’s guidelines for subsequent postexposure rabies treatment of previously vaccinated individuals (i.e., persons who have received pre- or postexposure rabies vaccination), the Scientific Committee of the Queen Saovabha Memorial Institute (Bangkok, Thailand) has recommended use of either (1) the four 0.1-mL booster doses of cell-culture rabies vaccine given intradermally on day 0, or (2) the conventional schedule of 2 booster doses given on days 0 and 3.

From 1998 through 2000, a total of 1871 previously vaccinated patients who had possibly been exposed to rabies virus (the risk of rabies exposure was classified as World Health Organization category III in 1145 of these subjects) were given four 0.1-mL intradermal booster doses of either PVRV or purified chick embryo–cell rabies vaccine (PCECV) on day 0. An animal, which was proven to be rabid by means of fluorescent antibody testing, had bitten 90 patients who had received pre- or postexposure vaccination 1–10 years previously (median time since vaccination, 3 years). All of these patients received four 0.1-mL intradermal booster vaccinations within 72 h after rabies exposure. All patients who had been bitten by animals that were proven to be rabid were followed up for ≥3 months, and 68 of those patients were contacted by investigators 1–2 years after booster vaccination. No patients died of rabies infection, and no serious adverse reactions were reported.
reactions were seen in any of our patients, although some patients experienced mild adverse reactions, such as pain or itching at the inoculation sites.

To determine the Nab response after receipt of four 0.1-mL intradermal doses of booster vaccination, we obtained peripheral blood samples on day 0 and 1 year after booster vaccination from 20 patients (age range, 17–42 years) who volunteered to participate in our study. All of these patients had received either pre- or postexposure rabies vaccination, without rabies immunoglobulin, 1–10 years earlier. Informed consent was obtained from all subjects (approved by the Ethics Committee of the Science Division, Thai Red Cross Society, Bangkok), and the guidelines of the Queen Saovabha Memorial Institute for experimentation with humans were followed in the conduct of this study.

Nab to rabies virus was measured on days 0 and 360 with the rapid fluorescent focus inhibition test. Table 1 shows the ranges of Nab titers in patients who received four 0.1-mL booster doses of PVRV (Institute Mérieux; commercial lot number, N0367; antigenicity, 10.8 IU/mL) and PCECV (Chiron Behring GmbH & Co.; lot number, 219011; antigenicity, 7 IU/mL). All subjects had Nab titers of >0.5 IU/mL, which is considered acceptable for protection against rabies 1 year after receipt of the booster vaccination.

In Thailand, the incidence of human deaths caused by rabies has decreased significantly during the past decade, owing to the introduction of safe and effective (but costly) modern postexposure treatment. The number of persons who have received postexposure prophylaxis for rabies with cell-culture rabies vaccines has increased each year (>200,000 cases per year); however, although potent modern cell-culture rabies vaccines are administered, treatment failures are still reported after primary immunization. The only way to prevent postexposure treatment failure in areas where rabies is endemic and where rabies immunoglobulin is not widely available would be to preimmunize the entire potentially exposed population. Booster vaccination after reexposure to rabies virus can rapidly evoke high titers of antibody as protection against rabies, and there have been no reports of treatment failure occurring after booster vaccination. Because the number of persons in Thailand who require booster vaccination for postexposure treatment of rabies has increased each year, the practice guidelines for postexposure treatment in previously immunized persons could be simplified, at no risk, to include the entire booster vaccination with a small total dose of vaccine given on a single day. We found that the use of 4-site intradermal inoculation for booster vaccination can reduce the cost and speed up the immune response for rabies virus, compared with intramuscular inoculation [3]. In previously vaccinated patients, a single booster vaccination (four 0.1-mL doses of cell-culture rabies vaccines given intradermally on day 0) is a safe, convenient, and economical method of rapidly stimulating a Nab response after potential exposure to rabies virus. This alternative regimen would reduce the postexposure schedule and cost of vaccination in previously vaccinated persons, which is of paramount importance in developing countries.

Acknowledgments

We thank Dr. Donna Robinson, for reviewing the manuscript, and Mrs. Panutda Khumniphat, for secretarial support.

References

