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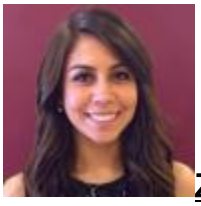
Intradermal Rabies Vaccine Noninferior to Intramuscular Vaccine



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Intradermal administration of the rabies vaccine may produce similar antibody titers at a fraction of the intramuscular administration dose, according to results of a study published in the *Journal of Infectious Diseases.*

In most regions of the world, rabies is enzootic and causes an estimated 55,000 deaths annually. When the recommended 3-dose vaccination schedule for rabies is administered, it is well tolerated and provides an antibody response in 100% of individuals with durable immunity for years. In the United States, the current pre-exposure prophylaxis (PrEP) is comprised of three 1.0-mL intramuscular injections of the rabies vaccine on days 0, 7, and 21 or 28. However, due to the high cost and limited supply of cell-cultured vaccines, other strategies are being investigated to extend the supply without reducing immune response.

Intradermal administration of the vaccine has immunologic advantages over intramuscular administration via presenting an antigen or live virus directly to dendritic cells for immunologic processing and presentation. This offers the potential for intradermal administration to significantly reduce the volume of vaccine required. Therefore, this randomized open-label single-center trial characterized the serologic and proteomic immune response to a shorted dose schedule and intradermal administration relative to the current licensed schedule for rabies PrEP.

A total of 60 participants (mean age 32.4 years; 64.4% women) at the State University of New York Upstate Medical University in Syracuse were included in the study and randomly assigned to 1 of 6 groups: 12 participants each in groups 1 through 4 and 6 participants each in control groups 5 and 6. Groups 1 and 3 received the vaccine via intramuscular administration and groups 2 and 4 received the vaccine via intradermal administration.

The primary objective was to assess the serologic immune response to various dosing regimens (2 vs 3 doses; intramuscular vs intradermal administration) based on rabies neutralizing antibody titers at days 28 and 365 after the first dose of the vaccine, and 7 days post-booster administered at 1 year (372 days). The licensed RabAvert® vaccine (produced by GSK Vaccines GmbH, Marberg, Germany) was used. For the intramuscular administration, the recommended dose of 1 mL per injection was used. For the intradermal administration, 0.1 mL of the vaccine or 0.25 IU rabies antigen per dose was used. The 2-dose groups received vaccination on days 0 and 7; the 3-dose groups received vaccination on days 0, 7, and 21 or 28. A titer of >0.5 IU/mL against rabies virus was considered acceptable.

Results showed that intradermal administration resulted in high antibody titers at day 14 and day 28. All participants in groups 1 through 4 demonstrated acceptable titer levels by days 14, 28, and 372. At day 365, protective titer levels were reached by the following: 70% in the 3-dose intramuscular group; 60% in the 3-dose intradermal group; 40% in the 2-dose intramuscular group, and 50% in the 2-dose intradermal group. More related adverse events (local and systemic) occurred in groups receiving the intradermal vaccine (groups 2 and 4; 91.7% and 90.9%, respectively) compared with groups receiving the intramuscular vaccine (groups 1 and 3; 66.7% each). The most common adverse events included pain, itching and swelling at the injection site, fatigue, low-grade fever, and muscle aches. No serious adverse events were reported.

Overall, the study authors concluded that, “Our results support larger studies that show [intradermal] delivery of a rabies vaccine is equivalent to [intramuscular] vaccination at a fraction of the dosing.”

Reference

Endy TP, Keiser PB, Wang D, et al. Serologic response of two versus three doses, intradermal versus intramuscular administration of a licensed rabies vaccine for pre-exposure prophylaxis [published online December 6, 2019]. *J Infec Dis*. doi:0.1093/infdis/jiz645/5658469