

Long-term immunogenicity of measles vaccine after coadministration with live attenuated Japanese encephalitis vaccine

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Background

Japanese encephalitis (JE) is the leading cause of viral neurological disease and disability in Asia.¹ Some 70% of children with clinical JE die or have long-term neurologic sequelae. One dose of live attenuated SA 14-14-2 JE vaccine (LJEV) has been shown to provide greater than 96% protection for up to 5 years, and single-dose immunization of LJEV with measles vaccine (MV) would provide a simplified prevention strategy.²

To address the key question of whether LJEV can be coadministered with MV at 9 months of age, we conducted a noninferiority study at the Research Institute for Tropical Medicine in Manila, Philippines in 2006-2007 to evaluate MV immunogenicity after coadministration with LJEV versus MV given alone. Results of that study showed a one-month seroprotection rate in the coadministration group that was statistically noninferior to that in the MV alone group (96% versus 100%, respectively).³ We now report results of long term follow-up among those who seroconverted for measles to assure that measles antibody levels acquired after coadministration of the two vaccines will remain equivalent to those acquired after MV alone.

Methods

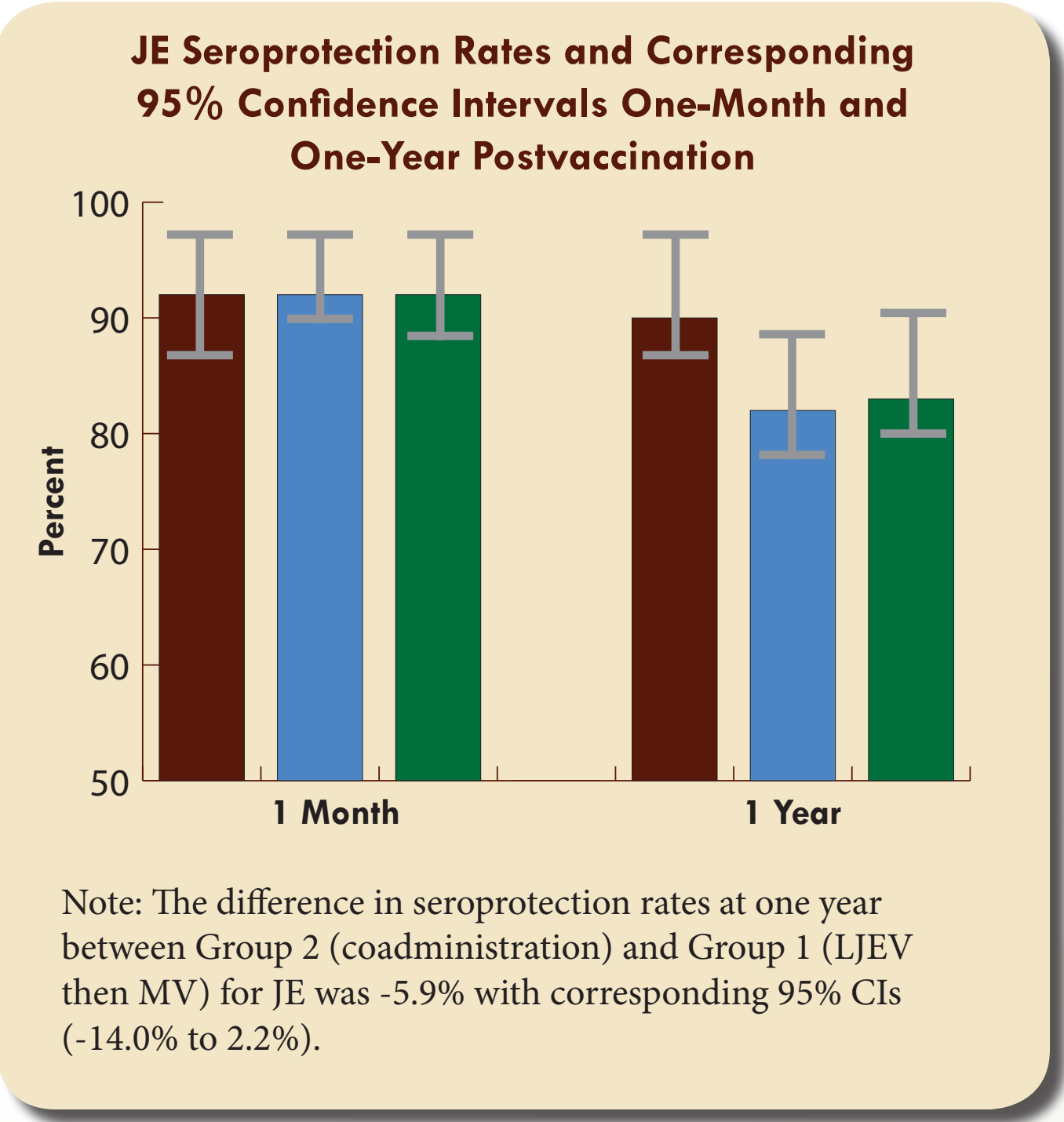
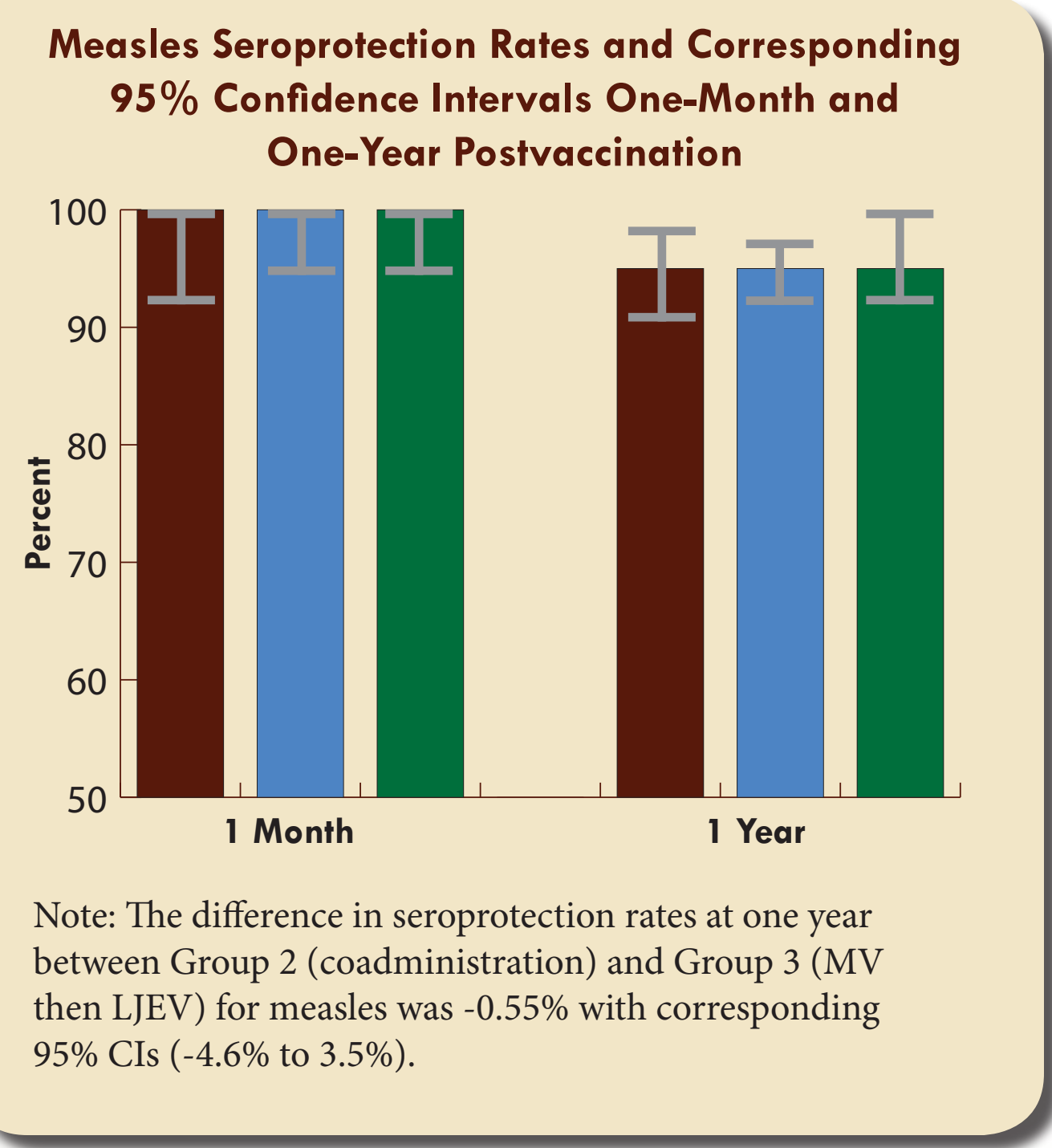
In the original study, healthy infants were randomized to receive either LJEV at 8 months of age and MV at 9 months [Group 1 (n=100)], LJEV and MV coadministered at 9 months [Group 2 (n=250)], or MV at 9 months and LJEV at 10 months [Group 3 (n=250)]. In this long-term follow-up study, only infants whose one month postvaccination blood samples demonstrated seroprotective levels of measles antibodies (anti-measles concentration ≥ 340 mIU/mL) by Enzyme Linked Immunosorbent Assay were included. One month and one year measles geometric mean concentrations (GMCs) and seroprotection rates were then compared. One month and one year geometric mean titers (GMTs) and seroprotection rates ($\geq 1:10$) for JE were also measured by JE Plaque Reduction Neutralization Test.

Results

Among those infants who seroconverted for measles antibodies by one month postvaccination, one month GMCs for measles antibodies in Groups 1, 2, and 3 were 3159, 2861, and 3417, respectively. For Groups 2

Anti-Measles Geometric Mean Concentrations (GMCs) One Month and One Year Postvaccination with Measles Vaccine (MV) Coadministered with Live JE Vaccine (LJEV) or Administered Alone			
1 Month Postvaccination	Group 1 (LJEV then MV) (N = 88)	Group 2 (Coadministered) (N = 205)	Group 3 (MV then LJEV) (N = 208)
	Anti-Measles GMCs (mIU/mL) and Corresponding 95% Confidence Intervals		
	3159 (2839-3514)	2861 (2627-3115)	3417 (3182-3668)
1 Year Postvaccination	804 (692-936)	738 (671-812)	692 (632-758)

Anti-JE Geometric Mean Titers (GMTs) One Month and One Year Postvaccination with Measles Vaccine (MV) Coadministered with Live JE Vaccine (LJEV) or Administered Alone			
1 Month Postvaccination	Anti-JE GMTs and Corresponding 95% Confidence Intervals		
	256 (189-347)	210 (172-256)	196 (162-238)
1 Year Postvaccination	145 (98-216)	141 (111-179)	119 (96-148)



and 3, the primary comparison groups, GMCs displayed nonoverlapping confidence intervals. However, at one-year postvaccination, the anti-measles GMCs for Groups 2 and 3 were 738, and 692, respectively, and were then not statistically significantly different. At one year postvaccination, measles seroprotection rates were 95.5% (Group 1), 95.1% (Group 2), and 95.7% (Group 3), and JE seroprotection rates were 89.8% (Group 1), 83.9% (Group 2), and 86.1% (Group 3).

Conclusions

One year postvaccination, measles seroprotection rates were still high after receipt of measles vaccine administered with or without live JE vaccine among infants who originally seroconverted for measles by one month. Measles seroprotection rates in 9-month-old infants have varied widely in developing country populations. Our high rates are similar to those in populations from Oman, Indonesia, and a number of African countries.⁴⁻⁷ Additionally, although the anti-measles GMC for the coadministered group at one month had been significantly lower than that for measles vaccine given alone group, the one year anti-measles GMC in this group was similar to that for measles vaccine given alone group. Therefore, concerns of reduced immunogenicity at one month should be mitigated by the equivalence at one year. These results, combined with those from our original study, increase confidence that introduction of live JE vaccine with measles vaccine at 9 months of age in routine EPI programs will not substantially interfere with measles elimination programs and will eliminate the need of an additional JE vaccination visit. Moreover, introduction of live JE vaccine into the EPI schedule with measles vaccine has the potential to increase coverage rates of measles, which are quite low in many JE endemic regions.

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