Immunogenicity of 2-dose pre-exposure rabies vaccine co-administered with quadrivalent influenza vaccine in children

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Introduction

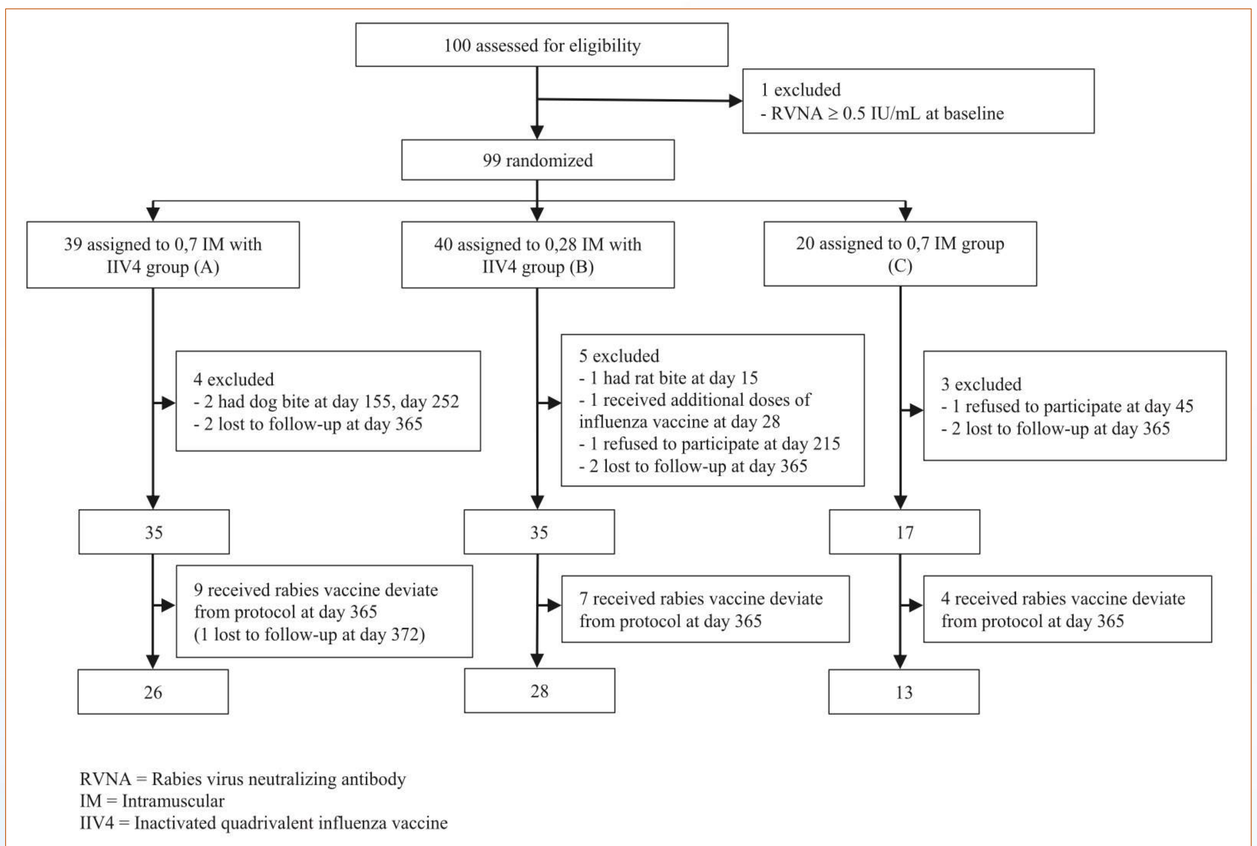
The World Health Organization recommends a 2-dose rabies pre-exposure prophylaxis (PrEP) regimen. Annual influenza vaccine visits provide an opportunity to add rabies PrEP as concomitant immunization without any additional cost for transportation or minimal additional health care worker manpower.

Objectives

This study aimed to compare the immunogenicity of rabies PrEP regimens co-administered with inactivated quadrivalent influenza vaccine (IIV4).

Methods

Children aged 3 to 9 years were randomly assigned (2:2:1) to receive 0.25 mL of chromatographically purified Vero cell rabies vaccine (CPRV) intramuscularly. Group A at day 0, 7 with IIV4; Group B at day 0, 28 with IIV4; Group C at day 0, 7. A booster-dose of CPRV was given on day 365. Primary outcome was the proportion of children with protective rabies virus neutralizing antibody (RVNA) ≥ 0.5 IU/mL, on day 42- and 7-days post-booster.

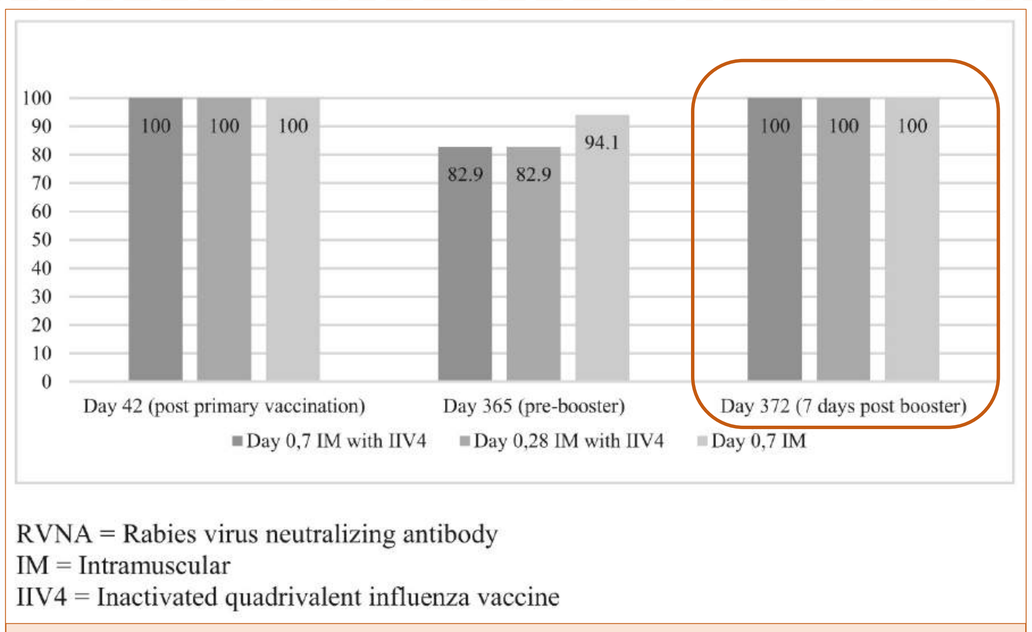


Study diagram (CONSORT flow diagram).

Results

From November 2019 to January 2020; 100 children with a median age (IQR) of 5.4 years (4.8-7.3) were enrolled. All participants achieved protective RVNA titers on day 42 and 7-day post booster.

Geometric mean titer (GMT) at day 42 were Group A, 8.98 (95%CI 7.06-11.42); Group B, 23.89 (95%CI 19.33-29.51); Group C, 9.94 (95%CI 7.03-14.06). Likewise, RVNA GMT at 7 days post-booster were Group A, 42.53 (95%CI 18.41-66.64); Group B, 23.19 (95%CI 17.28-29.10); Group C, 57.75 (95%CI 35.86-79.67).



The proportion of participants with RVNA titers ≥ 0.5 IU/mL at day 42, day 365, and day 372.

GMT of Rabies virus neutralizing antibody (RVNA) compared between groups

	IU/mL	0,7 IM with IIV4 (Group A)	0,28 IM with IIV4 (Group B)	0,7 IM (Group C)	P-value
Day 42 (N=97)	N	39	38	20	
	GMT(95%CI)	8.98 (7.06-11.42)	23.89 (19.33-29.51)	9.94 (7.03-14.06)	<0.001
	Min-Max	1-136.59	7.38-128	2.38-54.17	
Day 365 (N=87)	N	35	35	17	
	GMT(95%CI)	1.90 (0.88-2.93)	1.12 (0.85-1.39)	2.69 (0.89-4.49)	0.04
	Min-Max	0.27-17.45	0.11-3.67	0.44-14.67	
Day 372 (total) (N=82)[a]	N	32[b]	35	15	
	GMT(95%CI)	25.83 (21.44-30.23)	23.19 (17.28-29.10)	45.75 (30.53-61)	0.002
	Min-Max	4.05-56.57	6.82-91.7	10-100	
Day 372 (per-protocol) (N=63)[a]	N	24	28	11	
	GMT(95%CI)	24.26 (19.05-29.47)	24.15 (16.93-31.37)	48.21 (27.38-69.03)	0.02
	Min-Max	4.05-45.85	6.82-91.7	10-100	
Day 372 (full dose booster of CPRV) (N=19)	N	8	7	4	
	GMT(95%CI)	30.55 (21.23-39.87)	19.35 (10.24-28.47)	39 (14.3-63.71)	0.02
	Min-Max	21.81-56.57	9.17-36.68	25.9-56.57	

P-value from ANOVA; IM = Intramuscular; IIV4 = Inactivated quadrivalent influenza vaccine; GMT = Geometric mean titer; CPRV = Chromatographically purified Vero cell rabies vaccine

[a] Potential outlier removal results

[b] One participant lost to follow-up at day 372

Conclusion

This study revealed a 100% adequate RVNA response to 0.25 mL of intramuscular chromatographically purified Vero cell rabies vaccine without interference with influenza vaccine in healthy children 3 to 9 years old. This finding suggests that 2 doses of IM CPRV with either 0,7 or 0,28 regimens could be administered concomitantly with IIV4 in rabies-endemic countries.

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Reference

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