COMPARISON OF SUBCUTANEOUS VERSUS INTRADERMAL ADMINISTRATION OF MVA VACCINE BOOSTER DOSE

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BACKGROUND

The third-generation smallpox vaccine, MVA-BN, is now considered the primary preventive measure against mpox infection. A booster dose administered at least two years after the primary vaccination significantly enhances both humoral and cellular immunity. Assessing whether the subcutaneous (SC) or intradermal (ID) administration route influences the magnitude of the response may inform public health strategies for maximizing dose savings.

In smallpox vaccine-naïve individuals, a booster dose administered at least two years after the primary cycle is strongly immunogenic, rapidly increasing IgG and nAb titers and enhancing T-cell response. The intradermal dose-sparing route elicits higher nAb titers than the subcutaneous route.

METHODS

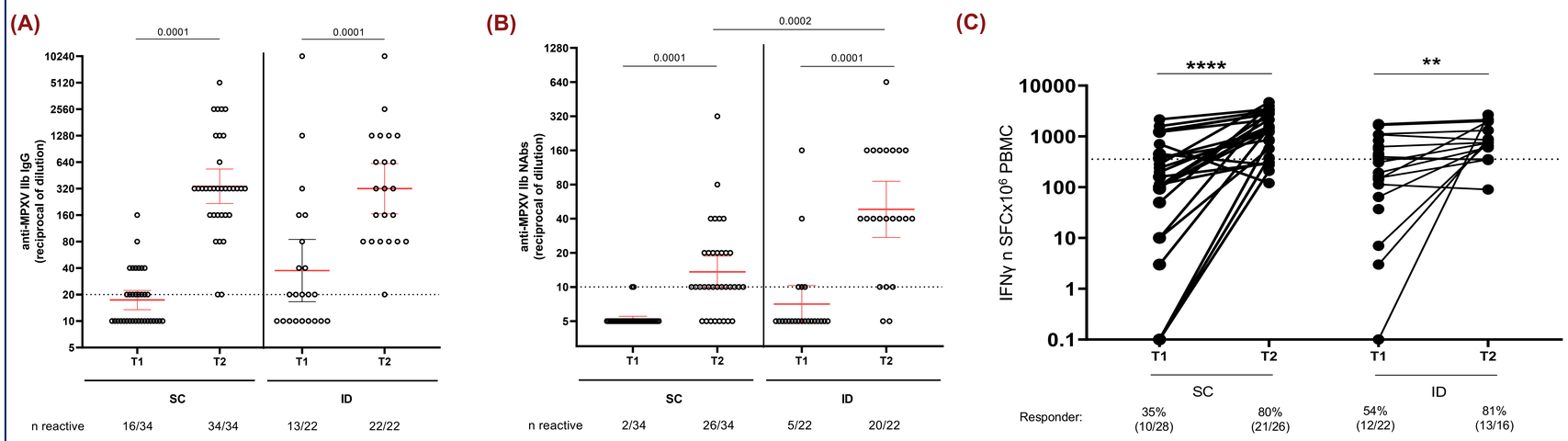
We conducted a prospective observational study in individuals who had completed a two-dose primary MVA-BN vaccination cycle and received a booster dose either subcutaneously (SC, 0.5 mL) or intradermally (ID, 0.1 mL) two years after. Individuals who had previously received the smallpox vaccine were excluded from analysis. Blood samples were collected at the time of booster administration (T1) and after 4 weeks (T2). Anti-MPXV IgG titers were measured by immunofluorescence assay (IFA, clade IIb), neutralizing antibodies (nAb) by PRNT50 (clade IIb), and MVA-responsive T-cells by IFN-γ ELISpot. Clinical and immunological features were compared between SC and ID groups using the Wilcoxon paired and Mann-Whitney tests.

Table 1. Main characteristics of the study population

Characteristic	Overall (N=56)	Subcutaneous (N=34)	Intradermal (N=22)	p-value[1]
Male at birth	56 (100%)	34 (100%)	22 (100%)	Nd
Age[2]	43,7 [36,6;50,0]	44,0 [38,0;50,0]	43,0 [36,0;51,0]	0,575
Risk factor				0,457
Living with HIV	8 (14,3%)	5 (14,7%)	3 (13,7%)	
PrEP	48 (85,7%)	29 (85,3%)	19 (86,4%)	
CD4 T-cells at vaccination[3]				0,826
<500 cells/µL	2 (25,0%)	1 (20,0%)	1 (33,3%)	
>500 cells/µL	6 (75,0%)	4 (80,0%)	2 (66,7%)	
Viral load at vaccination[3]				0,362
<30 copies/mL	6 (75,0%)	4 (80,0%)	2 (66,7%)	
>30 copies/mL	2 (25,0%)	1 (20,0%)	1 (33,3%)	
Previous smallpox vaccination	2 (3,6%)	2 (5,9%)	0 (0%)	0,38

Nd=not determinable; [1]Wilcoxon-Mann-Witheny U test, Fisher's Exact test as appropriate; [2]median [IQR]; [3]among people with HIV.

FIGURE 1. Evaluation of MPXV-specific IgG (A), neutralising antibodies (nAbs) (B) and MVA-BN T-cell specific response (C).



Dot lines represent the detection limit for IgG (1:20), nAbs (1:10) and median values of T-cell response evaluated in 10 healthy controls matched for age and sex. Geometric mean IgG and nAbs titers (GMT-95% CI) are shown for each time range or study group.

RESULTS

Among the 56 participants included, 34 (61%) received SC and 22 (39%) ID. All individuals were males, with a median age of 43.7 years [IQR 36.6–50.0]; 8 of them (14%) were people with HIV (PWH). From T1 to T2, IgG titers increased significantly in both SC and ID groups ($p < 0.001$). Reactive sera varied from 47% to 100% in SC and 59% to 100% in ID. No difference in IgG titer increase was found between groups (Figure 1A). Additionally, nAb titers significantly increased from T1 to T2 ($p < 0.0001$), with reactivity ranging from 6% to 77% for SC and from 23% to 91% for ID. Comparison between groups showed a significant advantage for ID over SC in the increase of nAb titers ($p = 0.0002$) (Figure 1B). MVA-specific T-cell response also improved from baseline to one month after administration in both the SC ($p<0.0001$) and ID ($p<0.002$) groups. No evidence of a difference in response variation between the two groups was found (Figure 1C).

CONCLUSIONS

Both subcutaneous and intradermal routes of administration of the MVA-BN booster dose elicit strong humoral and cellular responses, with a clear advantage for the intradermal route in improving the neutralizing response. These results support the use of the intradermal route for booster administration to conserve vaccine resources and optimize the possibilities for intervention in high-risk populations.

PLAIN LANGUAGE SUMMARY

An mpox vaccine booster strongly increases immune responses. When given intradermally, a smaller dose produces stronger virus-blocking (neutralizing) antibodies than the standard injection, while other immune responses are similar.

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