

VAC_07 - Comparison of systemic immunity following intranasal/intramuscular and intramuscular immunization with meningococci antigens

Amanda Izeli Portilho¹; Victor Araujo Correa¹; Elizabeth De Gaspari¹.

¹Adolfo Lutz Institute/University of São Paulo.

Introduction: Intranasal (IN) immunization could be explored for meningococcal vaccines, however, it would be interesting if these vaccines induced systemic protection mediated by bactericidal antibodies and a Th2 response, which are considered the better mechanisms of protection.

Objective: This study compared the systemic immune response to IN/intramuscular (IM) and IM/IM delivery of meningococcal outer membrane vesicles (OMVs).

Methodology: A/Sn (H2^a) mice were immunized with 4 subsequent IN doses (0.2 µg OMVs+0.1 µg Cholera toxin subunit B [CTB]) (Sigma-Aldrich) and one IM booster (0.2 µg OMVs+0.2 µg CTB) after 15 days. For comparison, another group received 2 IM doses, 15 days apart (0.2 µg OMVs+0.1 mM Aluminium hydroxide [AH]). Control groups received only adjuvants. Antigen control received 2 IM doses (0.2 µg OMVs), 15 days apart. The humoral response was assessed by ELISA and serum bactericidal assay (SBA) and the cellular response, by ELISpot.

Results: OMVs+CTB had increased IgG titers compared to pre-immune control after the IN doses ($p<0.05$) and, after booster, it increased even more ($p<0.01$). OMV+AH was superior to pre-immune ($p<0.001$) and AH ($p<0.05$) controls after 2 doses. OMVs alone did not elicit statistically higher titers, although it was higher than pre-immune sera. There was no significance in IgG2a titers, while IgG1 was increased in OMV+CTB and OMV+AH compared to controls ($p<0.05$ for all). OMVs alone were not bactericidal, while OMV+CTB and OMV+AH were (SBA titers 1/8 and 1/16, respectively). ELISpot was conducted when mice were elderly (after 475) to assess immunologic memory. IL-4 release after antigenic stimuli was higher in OMV+CTB and OMV+AH groups than in OMVs group. The immunization also induced IL-17 release, especially by the OMV+CTB group.

Conclusion: Low antigenic doses of OMVs were immunogenic and induced immunologic memory. 4 IN doses were effective to induce systemic IgG. Adjuvants were needed to increase IgG titers and to guarantee bactericidal activity. AH and CTB modulated a Th2 response, with higher IgG1 titers and IL-4 secretion. The IN/IM approach was comparable to the IM/IM one to induce systemic immunity.

Keywords: Prime-booster immunization; Outer membrane vesicles; Meningococci