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Adjuvant properties of outer-membrane-vesicle in hepatitis B surface based vaccine

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Objective: The outer membrane vesicle of Neisseria meningitidis serogroup B (OMV) is among the more studied components with microbial origin, which could be applied as an adjuvant. In the present study, OMV of N. meningitidis serogroup B was applied as an adjuvant co-administrated with the HBs Ag to evaluate the efficiency of this immunization strategy for the promotion of efficient humoral/cellular responses against Hepatitis B virus.

Methods: OMVs were prepared as previously described. In brief, N. meningitidis serogroup B strain (CSBPI, G-245) was grown under controlled submerge cultural condition in a fermentor containing modified Frantz medium. The outer membrane vesicles (OMVs) were extracted in Tris-HCl buffer, containing EDTA and deoxycholate. Purification of the OMVs was done by sequential centrifugation at 20, 000 followed by ultracentrifugation at 125, 000. Purified recombinant hepatitis B surface antigen (HBsAg) was prepared from the production and research complex of Pasteur Institute of Iran (Karaj, Iran). Four animal groups were immunized by intranasal inoculation with HBs, HBs+OMV mixture, HBs+complete/incomplete Freund's adjuvant (C/IFA) and OMV. Two booster immunizations were carried out three and six weeks after the first immunization. Indirect enzyme-linked immunosorbent assay (ELISA) was applied to assess total and subtype antibody responses against HBsAg.

Results & Conclusion: Analysis of anti-HBsAg responses elicited in immunized BALB/c mice following different immunization regimens indicated OMV+HBsAg as an immunopotent combination which significantly induced anti-HBsAg IgG with IgG2a dominancy. In accordance to previous study, evaluation of humoral responses following the immunization with HBsAg, HBsAg+C/IFA and HBsAg+OMV indicated the potency of HBsAg vaccine in all the administrated formulations to efficiently induce humoral responses against HBsAg. Although the highest level of antibodies was raised in HBsAg +C/IFA injected animals, however, the promoted response in HBsAg +OMV immunized group was comparable with HBsAg +C/IFA, indicating the capability of HBsAg +OMV immunogen for humoral response induction. All of these responses are TH1 oriented with IgG2a sub-type predominance. The highest IgG2a titer has been detected in the sera of mice immunized with HBsAg +C/IFA respectively followed by HBsAg +OMV and HBsAg. Although the most augmented anti-HBs humoral responses were detected in the sera of HBsAg +C/IFA-immunized mice, however, titer of total anti-HBs antibody and raised IgG2a was significantly increased by the application of OMV adjuvant and was comparable with the HBsAg +C/IFA regimen. Considering that OMV is a human-compatible adjuvant, this finding argues in support of probable application of OMV in HBsAg -based vaccine. According to our study, HBsAg combined with OMV seem to be a promising adjuvant in vaccine development against hepatitis B virus.

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