In vitro immunogenic and immunostimulatory effects of zwitterionized 23-valent pneumococcal polysaccharide vaccine compared with nonzwitterionized vaccine.

ABSTRACT

Background: It was hypothesized that the observed slight immunostimulatory effect of the 23-valent pneumococcal polysaccharide (pneumo-23) vaccine might be due to the presence of low levels of zwitterionic motifs. Therefore, it was hypothesized further that introducing zwitterionic motifs experimentally into polysaccharides of pneumo-23 vaccine might render it an effective immunostimulatory agent. Objective: This study was conducted to assess the in vitro immunostimulatory effect of zwitterionized pneumo-23 (Z-P23) vaccine compared with the nonzwitterionized commercial pneumo-23 (C-P23) vaccine. Methods: In vitro proliferation, ELISA-based in vitro cytokine synthesis (interleukin [IL]-2, interferon [IFN]-γ, and IL-10), and immunofluorescence microscopy-based immune cell profiling (CD4+, CD8+, and CD21+ cells) assays were used to evaluate the immunostimulatory effect of Z-P23 on peripheral blood mononuclear cells (PBMC) of immunosuppressed cancer (IC) patients and healthy control subjects in comparison with PBMC exposed to C-P23, concanavalin A (positive control), and phosphate-buffered saline (PBS) (negative control). Results: Z-P23 induced proliferation of PBMC in the IC (81.1%) and control (75.1%) groups significantly higher than that achieved with concanavalin A in the IC group (51.0%; $P = 0.01$) but not in the control group (89.2%; P = NS). This was also significantly higher than that achieved with C-P23 in the IC (4.8%; $P < 0.001$) and control (6.2%; $P < 0.001$) groups. Z-P23 induced IL-2 and IFN-γ synthesis in the IC group (0.61 and 0.45 ng/mL, respectively) significantly more than that with C-P23 (0.4 and 0.45 ng/mL; $P = 0.002$ and $P <0.001$), concanavalin A (0.45 and 0.31 ng/mL; $P = 0.021$ and $P = 0.03$), and PBS (0.41 and 0.29 ng/mL; $P = 0.005$ and $P = 0.04$) but not the control group. Z-P23 induced expansion of CD4+, CD8+, and CD21+ lymphocytes (39.3%, 42.7%, and 8.1%, respectively) in the IC group higher than that with C-P23 (28.3%, 30.1%, and 5.5%; $P = 0.01$, $P = 0.003$, and P = NS), concanavalin A (27.2%, 35.8%, and 4.1%; $P = 0.02$, $P = 0.048$, and $P = 0.035$), and PBS (25.6%, 31.9%, and 4.2%; $P = 0.018$, $P = 0.02$, and $P = 0.045$). Conclusion: The in vitro immunostimulatory potential of Z-P23 was clearly observed on PBMC of IC patients as well as, to a lesser extent, healthy control subjects, stimulating the synthesis of core cytokines of T-helper 1, and primarily inducing CD4+ and CD8+T cells.

Keyword: Polyvalent pneumococcal vaccine; Pneumo-23; Zwitterionic; Cancer; Immunostimulatory; Immune suppression.