Antibody responses in genital secretions and serum after mucosal vaccination in humans

Lotta Wassen, Departments of Obstetrics and Gynecology and Medical Microbiology and Immunology, Sahlgrenska Academy at Göteborg University, Göteborg, Sweden

The overall aim of this thesis was to study the induction of B-cell immune responses in genital secretion and serum after mucosal vaccination in women. Oral inactivated B subunit whole-cell (B-WC) cholera vaccine and recombinant cholera toxin B subunit (CTB) alone were used as model immunogens.

Cervical secretion was shown to be a suitable specimen for determination of IgA and IgG antibodies in the genital tract. Three vaginal doses of B-WC vaccine induced prominent CTB-specific IgA antibody responses in 6 of 7 women, and 5 of 7 individuals responded with IgG antitoxin titer rises in cervical secretions. Only 3 of 7 orally vaccinated women demonstrated genital tract antibody responses. Nasal vaccination was superior in inducing CTB-specific IgA antibody responses in vaginal fluids, whereas only modest responses were seen in the cervix. These findings indicate that there is a compartmentalization within the genital tract, and that the induction of specific antibodies in cervical secretion is regulated in a different manner from that in vaginal fluid. Systemic antibody responses were less frequent and weaker than those displayed in genital secretions after vaginal vaccination.

Two vaginal doses of B-WC vaccine were found to be far more efficient than a single dose in generating IgA and IgG antitoxin responses in cervical secretions, and a third dose did not further increase the responses. Twelve months after vaccination, increased IgA and IgG antitoxin levels could still be detected in half of the women who had initially responded to the vaccine.

Biweekly vaginal vaccination on days 10 and 24 of the menstrual cycle induced stronger CTB-specific antibody responses in cervical secretions than biweekly vaccination initiated at random time. Exogenously administered steroid hormones did not seem to have any impact on the production of specific antibodies in the genital tract. A majority of women using monophasic oral contraceptives, progesterone-containing intra-uterine devices and women without hormonal contraceptive methods exhibited strong CTB-specific IgA and IgG antibody responses in genital secretions after vaginal vaccination.

In conclusion, vaginal vaccination was superior to both oral and nasal vaccination in generating local IgA and IgG antibodies in cervical secretions. The effective induction and long-term duration of cervical antibodies suggest that CTB and probably also other antigens linked to CTB may be used for vaginal vaccination. Our observations may be of relevance for future development of vaccines against sexually transmitted diseases as well as human immunodeficiency virus.

Key words: genital immunity, antibodies, mucosal vaccination, cervical secretions, vaginal fluids,

ISBN 91-628-6701-6

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Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Göteborgs Universitet kommer att offentligen försvars i aulan, Kvinnokliniken, Sahlgrenska Universitetssjukhuset/Östra, Göteborg, fredagen den 9 december, 2005, kl 9.00

Av

Lotta Wassen
Leg. Läkare

Fakultetsopponent: Professor Dan Danielsson, Örebro

Avhandlingen baseras på följande arbeten:

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