CLIPPINGS

Theme: Immunization

Interventions to improve oral vaccine performance (*Lancet Infect Dis. 2019;19:203-14*)

Oral vaccines underperform in low- and middle-income countries in comparison to high-income countries. This systematic review and meta-analysis aimed to assess efficacy of interventions designed to increase oral vaccine efficacy or immunogenicity.

Of 2843 studies identified, 87 were eligible for qualitative synthesis and 66 for meta-analysis. Twenty-two different interventions were assessed for oral poliovirus vaccine (OPV), oral rotavirus vaccine (RVV), oral cholera vaccine (OCV), and oral typhoid vaccines. There was generally high heterogeneity. Seroconversion to RVV was significantly increased by delaying the first RVV dose by 4 weeks (RR 1·37, 95% CI 1·16 to 1·62); for OPV, the seroconversion increased with monovalent or bivalent vaccine compared with trivalent vaccine (RR 1·51, 95% CI 1·20 to 1·91). There was some evidence that separating RVV and OPV increased RVV seroconversion (RR 1·21, 95% CI 1·00 to 1·47), and that higher vaccine inoculum improved OCV seroconversion (RR 1·12, 95% CI 1·00 to 1·26). There was no evidence of effect for anti-helminthics, antibiotics, probiotics, zinc, vitamin A, withholding breastfeeding, extra doses, or vaccine buffering.

Comments: Delayed RVV administration and altered OPV valence were the only effective approaches identified from the available evidence. The mechanism for increased immunogenicity when RVV is delayed is probably a combination of a lesser degree of interference from maternal antibodies and maturation of immune system. Delayed RVV administration might also mitigate the inhibitory effect of OPV. There is a need to change administration practices of RVV, particularly the RV1 that is a purely human strain and more susceptible to maternal antibodies than all other available RVVs.

Maternal pertussis immunization (Tdap) as the first infant dose (*Lancet Infect Dis. 2019;19:392-401*)

In this open-label, parallel, randomized, controlled trial, pregnant women aged 18-40 years from Netherlands received Tdap vaccination either at 30-32 weeks of pregnancy (maternal Tdap group, *n*=58) or within 48 h after delivery (control group, *n*=60). Cord blood, and infant blood samples were collected at age 2 months, 3 months, 6 months, 11 months, and 12 months. The primary endpoint was serum IgG pertussis toxin (PT) antibody concentrations at the age of 3 months.

The GMC of PT antibodies were higher in infants in the maternal Tdap group than in the control group infants at age of 3 months (GMC ratio 16·6, 95% CI 10·9 to 25·2) and 2 months. However, after primary vaccination, antibody concentrations for PT, FHA, and pertactin were significantly lower at all time points in infants of the maternal Tdap group than in infants in the control group, suggesting maternal antibody interference in infant after primary and booster vaccinations with Tdap.

Comments: The trial explores the possibility of adding maternal pertussis immunization to the vaccination schedule as a first infant dose in order to reduce the possibility of infection before the first dose administered to the infant. However, it also suggests that the infant vaccination needs to be delayed beyond 3 months of age, in order to minimize interference with maternal antibodies. Introduction of a delayed infant pertussis immunization schedule would place neonates of unvaccinated women in a more vulnerable situation, and maternal coverage needs to be higher to protect all babies from pertussis from the first day of their life. Moreover, the study only addresses vaccination schedules using acellular pertussis vaccines in industrialized countries. The situation is completely different in LMICs where whole-cell pertussis (wP) vaccines are used in primary vaccination schedule and maternal immunization is still not well established. The blunting effect of maternal Tdap on wP containing primary vaccine series may be different from the findings in the current study.

Immunogenicity and safety of monovalent acellular pertussis vaccine at birth (*JAMA Pediatr. 2018;172: 1045-52*)

This randomized clinical trial was conducted at 4 sites in Australia to compare IgG antibody responses to vaccine antigens at 6, 10, 24, and 32 weeks of age between newborn infants receiving the monovalent acellular pertussis (aP) vaccine and hepatitis B vaccine (HBV) or HBV alone. At 6, 16, and 24 weeks, infants received a hexavalent vaccine with IPV, as well as the PCV-10.

A total of 440 infants were randomized to receive the aP vaccine plus HBV (*n* = 221) or HBV only (control group, *n*=219). At 10 weeks, 192 of 206 infants who received the aP vaccine (93.2%) had detectable antibodies to both pertussis toxin (PT) and pertactin *vs* 98 of 193 infants in the control group (50.8%) (*P*< .001), with the geometric mean concentration (GMT) for PT IgG 4-fold higher among the group that received the aP vaccine. At age 32 weeks, all infants who received the aP vaccine at birth had detectable PT IgG and significantly lower IgG GMT for Hib, hepatitis B, diphtheria and tetanus antibodies.

Comments: The time between birth and initiation of the primary pertussis vaccination series at 6 to 8 weeks of age is the period of the greatest morbidity and mortality associated with pertussis disease. This study demonstrates that monovalent aP vaccine is immunogenic and safe in neonates, and may prove valuable for newborns whose mothers did not receive the Tdap vaccine during pregnancy. A birth dose of aP vaccine would significantly narrow the immunity gap between birth and 3 months of age, marking the critical period when infants are most vulnerable to severe pertussis infection. Thus, now we have two approaches to provide immunity cover to very young infants against pertussis – the maternal Tdap and aP at birth. Which one is superior? Can we utilize both the approaches in a synergistic way? However, both the options have undesirable impact on future infant immunization. The blunting effect of maternal Tdap on infant pertussis vaccination schedule even after booster dose, and the significantly reduced GMCs of the concomitantly administered antigens at 32 weeks with birth aP, are two main concerns. Furthermore, there is some evidence of a lower pertussis antibody level after completion of the primary vaccine series in infants born to mothers who had received Tdap within the 5 years prior to delivery.

VIPIN VASHISHTHA
vipinipsita@gmail.com