Poster #0604

IMMUNIZATION RESPONSE IN INFANTS BORN TO HBSAG+ AND HBEAG+ MOTHERS RECEIVING TDF

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Background

- The use of hepatitis B (HB) immune globulin (HBIg) in newborns and HB immunization starting with a birth dose (passive-active immunization) decreases the risk of perinatal transmission of HBV. However, pregnant women with high HBV DNA loads remain at risk of transmission.
- The addition of antiviral prophylaxis during the last trimester of pregnancy further decrease transmission (1-2).
- It is unknown whether maternal antiviral prophylaxis affects infant vaccine response.

Objective

- To compare the immunization response (anti-HBs antibody levels) in infants whose mothers were randomized to receive either tenofovir disoproxil fumarate from 28 weeks' pregnancy or a matching placebo

Study population

- Infants born to HBV chronically infected mothers participating in a double-blind, randomized, controlled trial to assess the efficacy of tenofovir disoproxil fumarate (TDF) in preventing mother to child transmission of HBV (iTAP study, NCT01745822).
- The mothers were randomized to receive either TDF or a matching placebo from 28 weeks gestation to 2 months postpartum in 17 hospital sites in Thailand.
- We included 315 infants born in this study and measured for anti-hepatitis B antibody at least 1 time after birth, except 3 (placebo group) who were confirmed HBV infected.
- All infants received passive-active immunization, as follows:
  - HBIg immediately after birth
  - birth dose immediately after birth (monovalent vaccine) at a different body site
  - dose at 1 month of age (monovalent vaccine)
  - at 2, 4 and 6 months as part of multivalent vaccine

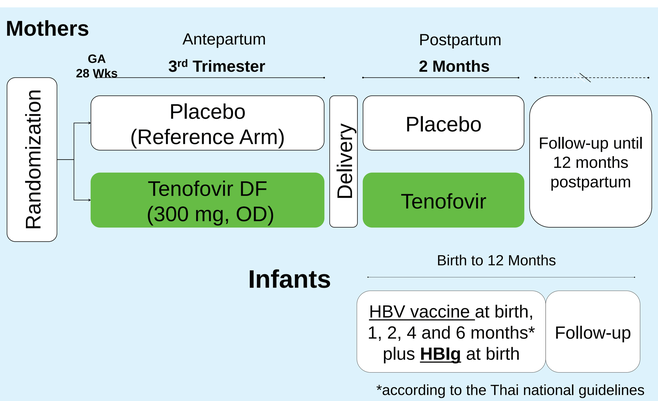


Figure 1: iTAP-1 STUDY Design

Methods

- Anti-HBs antibody titers were measured at 1, 2, 4, 6, 9 and 12 months of age using Monolisa Anti-HBs PLUS kit (Biorad, France).
- Anti-HBs levels were compared between arms using the Wilcoxon rank sum test.

Results

- 315 infants (162 TDF, 153 placebo) were included in the analysis. 166 were male and 149 female (see Table).
- Infant characteristics were unremarkable.
- The distribution of maternal and infant characteristics were similar in the two arms.

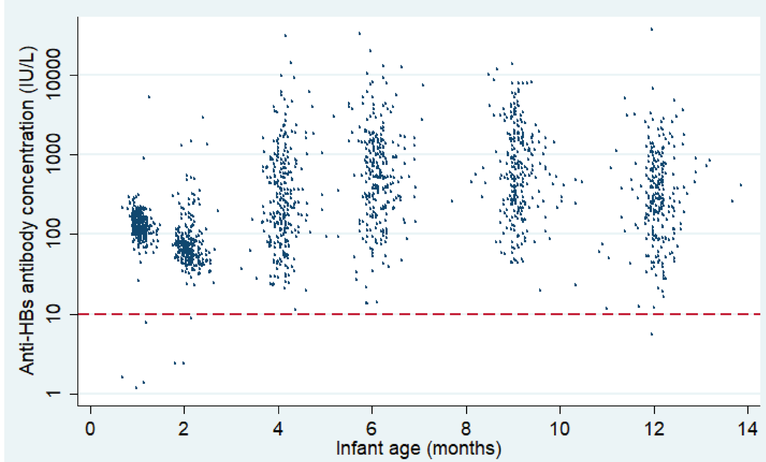
Table 1: Maternal and Infant Characteristics at Delivery/Birth (N=315)

	n (%) or median (IQR)	
	Placebo (n=153)	Tenofovir (n=162)
Mothers		
Body weight (kg)	65.0 (59.0 – 73.2)	66.0 (60.1 – 75.0)
Gestational age (weeks)	39.0 (38.1 – 40.0)	39.0 (38.3 – 39.7)
Infants		
Male	81 (53%)	85 (52%)
Birth weight (kg)	3.1 (2.9 – 3.4)	3.0 (2.8 – 3.3)
Length (cm)	50.8 (49.0 – 52.0)	50.0 (49.0 – 52.0)
Time from birth to HB vaccine (hours)[a]	1.2 (0.8 – 2.4)	1.2 (0.8 – 2.0)
Time from birth to HBIg (hours)[b]	1.3 (0.8 – 2.5)	1.3 (0.8 – 2.4)

IQR, Interquartile range; HBIg, Hepatitis B immune globulin
[a] Time of vaccine birth dose missing for 3 infants
[b] 2 infants did not receive HBIg and time was missing for another infant

Immune Response

- Geometric mean concentrations of anti-HBS Ab (95% CI) at 1 , 2, 4, 6, 9 and 12 month visits are provided in Figure 2.
- **All infants had anti-HBs titers > 10 IU/L except 4 of 311 (1.3%) at 1 month of age, 3 of 303 (1.0%) at 2 months, and 1 of 274 (0.4%) at 12 months.**
- No significant differences in anti-HBs titers between treatment arms (TDF versus placebo), at 6 months and thereafter.



Geometric mean concentration (95% CI):

Mean	123	71	268	556	595	294
95% CI	(115-132)	(66-77)	(228-315)	(477-648)	(512-691)	(253-342)

Figure 2. Anti-HBs geometric concentrations according to age

Conclusions

- Maternal antiviral prophylaxis had no effect on the infant response to HB vaccine.
- HBIg hid the response until 2 months, after which anti-HB antibody titers increased until 9 months (3 months after last vaccine dose administration).
- Immunization was effective in >99% of the infants aged 4 to 12 months.

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