PROLONGED SHEDDING OF ROTAVIRUS VACCINE VIRUSES DOES NOT ASSOCIATE WITH LEWIS AND SECRETOR STATUS AND ROTAVIRUS IMMUNOGLOBULIN A RESPONSE

Markkula J.¹, Hemming-Harlo M.¹, Gröhn S.¹, Heinimäki S.¹, Vesikari T.¹

¹ Vaccine Research Center, University of Tampere, Tampere, Finland

INTRODUCTION

- Live oral rotavirus (RV) vaccine RotaTeq® was introduced exclusively into National Immunization Program in Finland in September 2009.
- Shedding of RotaTeq® vaccine strains is common after each dose of the vaccine.
  - Prolonged shedding (over 14 days) has been found to be common in previously healthy children.
  - **The cause and the clinical significance of prolonged shedding have remained unclear.**
- Histo-blood group antigens Lewis (FUT3) and secretor (FUT2) have been found to have a role in RV attachment to cell in strain-specific manner.
  - Positive Lewis and secretor statuses may predispose to infection caused by VP4 genotype P[8].

We investigated the Lewis and secretor status and rotavirus IgA seroconversion of children in comparison to duration of shedding of RotaTeq® vaccine viruses.

Table 1. Distribution of Lewis (Le) and secretor (se) types in children with normal and prolonged (>14 days) shedding.

	Duration of shedding		Total, n	p-value
	Short (n=94)	Prolonged (n=24)		
Le+	60 (76.9 %)	18 (23.1 %)	78	0.302 χ ² -test
Le-	34 (85.0 %)	6 (15.0 %)	40	
se+	31 (72.1 %)	12 (27.9 %)	43	0.122 χ ² -test
se-	63 (84.0 %)	12 (16.0 %)	75	

MATERIAL AND METHODS

- 133 infants were given RotaTeq® vaccine according to 2, 3, and 5 months schedule.
- Stool samples were collected:
  - 5-10 days after the 1st vaccine dose and 0-7 days before the 3rd dose.
  - Further stool samples 6 and 12 weeks after the 3rd dose, if a previous stool sample was RV positive.
- Stool samples were studied for RV VP7, VP4 and VP6 by RT-PCR.
- All children provided a saliva sample at the age of 1 to 2 years. Saliva FUT2 and FUT3 enzyme expression was studied with ELISA.
- Serum rotavirus VP6 IgA was measured with ELISA from children who continued to shed vaccine strains for at least 4.5 months.

Table 2. Lewis (Le) and Secretor (se) status of children with normal and prolonged (>14 days) shedding.

	Duration of shedding		Total, n (%)
	Short (n=94)	Prolonged (n=24)	
Le+, se+	25	11	36 (30.5)
Le+, se-	35	7	42 (35.6)
Le-, se+	6	1	7 (5.9)
Le-, se-	28	5	33 (28.0)
p-value	0.335, χ ² -test		118 (100.0)

RESULTS

- Out of the 133 children, 126 (94.7 %) provided at least 2 stool samples.
  - **118 (93.7 %) shed the vaccine strains after the 1st dose.**
  - **24 (20.3 %) continued and 94 (79.7 %) halted shedding before the 3rd dose of the vaccine**
- Serum RV VP6 IgA was positive in 6 out of 7 (85.7 %) children with long-term shedding for at least 4.5 months.
- There were no difference the duration of shedding in neither Lewis positive and negative nor secretor positive and negative children (Table 1).
- We detected no statistically significant (p<0.05) difference in the FUT2 and FUT3 status between children with normal and prolonged shedding of vaccine virus strains (Table 2).

CONCLUSIONS

- ❖ **Short- (93.7%) and long-term (20.3 %) shedding are common after RotaTeq vaccine, and are both signs for successful inoculation.**
- ❖ **We found no association between Lewis or secretor status and prolonged shedding of RotaTeq® vaccine strains.**
- ❖ **Majority of the children with prolonged shedding seroconverted by rotavirus IgA indicating that lack of antibody response was not the reason for prolonged shedding.**