Retrovirology

Poster presentation

A guinea pig model for cytomegalovirus congenital infection: dose-effect and vertical transmission rate

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Backgrounds and objectives

Animal models are necessary to test new antiviral drugs to prevent CMV materno foetal transmission [1]. Among the small animal CMV models, the guinea pig CMV (GPCMV) has the ability to cross the placenta [2], causing disease in utero [3,4]. The objective was to study the relation between inoculum doses of guinea pig cytomegalovirus (GPCMV) and the natural history of congenital disease in the pregnant guinea pig model, by means of updated ultrasound and virological methods.

Methods

1) Development of ultrasound examination for precise assessment of the gestational age based on fetal crown-rump length (CRL) measure.

2) Development of a real time PCR Taqman® GPCMV based on the amplification of a sequence of the UL83 gene and determination of its sensitivity.

3) Subcutaneous administration at mid-gestation of two doses (10^6 DI50 in group 1 and 10^8 DI50 in group 2 of GPCMV strain obtained by cell culture in CMV-seronegative pregnant Hartley strain guinea pigs. Serial sacrifice of the animals were performed in the second part of the gestation up to collect maternal tissues, maternal blood, amniotic fluid, placenta and fetal tissues and to determine the GPCMV load. Conventional histological examination of the fetal infected tissues was performed.

Results

18 pregnant guinea pigs were included in group 1 and nine in group 2.

1) Ultrasound examinations allowed the diagnosis of gestations in the totality of the cases. A growth curve of fetuses based on CRL was built.

2) The real time PCR GPCMV developed had sensitivity at 50% and 95% of 200 copies/mL and 2500 copies/mL respectively, with a wide linear ranges up to 10^6 copies/mL.

3) CMV infections were observed in 14/18 females in group1 and in 9/9 females in group 2.

GPCMV maternal viremia was observed in 28% and 70%, the median viral load was 100 and 700 copies/ml in groups 1 and 2 respectively. The proportion of female with at least one infected fetus in their litter was 0/18 and 2/9 (22.22%) in group 1 and 2 respectively (p= 0.103, Fisher Exact Test).

Conclusions

We developed an effective animal model using ultrasound for determination of gestational age and a sensitive real time GPCMV PCR for the diagnosis of GPCMV neonatal infections. The acute infection with GPCMV in the guinea-pig was reproduced in this model with materno-foetal transmission. We show that the kinetics and the intensity of the primary infection in the pregnant females as well as the vertical transmission rate are related to the inoculum's viral load. This model will be useful for further antiviral CMV drug assays.

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