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Chemotherapy of EHV-1 induced abortion in a murine model.

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We have developed a murine model to study particular aspects of the pathogenesis of and immune response to equine herpesvirus-1 (EHV-1). The most important clinical manifestation of EHV-1 in horses is abortion. Vaccines are available but have not been fully effective in preventing abortion. We have shown that intranasal inoculation of pregnant mice with EHV-1 results in premature parturition (Awan *et al.* 1991). Abortion was noted when virus was inoculated in the late second or early third week of gestation while inoculation in the first week led to fetal death and fetal resorption. Virus crossed the placenta, virus antigens were detected in the fetal tissues and virus was isolated from the placentae and aborted offspring. Antiviral compounds (*S*)-1-(3-hydroxy-2-phosphonylmethoxypropyl) adenine (HPMPA) and (*S*)-1-(3-hydroxy-2-phosphonylmethoxypropyl) cytosine (HPMPC) were found to be particularly effective in inhibiting virus replication in the respiratory tissues (lungs and turbinates) and reducing viraemia in mice (Field & Awan, 1990; Gibson *et al.* 1992). Here we report the effects of HPMPA and HPMPC in the EHV-1 murine abortion model. HPMPA was given from one day before virus inoculation at 25 mg/kg s.c. twice per day for five days. HPMPA therapy, however, interfered with the gestation, and thus proved unsatisfactory. In the second experiment a single dose of HPMPC (50mg/kg) was given one day before virus inoculation. HPMPC markedly reduced the abortion, transfer of virus to the fetuses and mortality compared to the infected placebo-treated controls. The effect of these drugs on EHV-1 induced abortion and virus transmission across the placenta will be discussed.

References

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The effect of (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl) cytosine (HPMPC) against EHV-1 in mice: primary and secondary infections.

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Equine herpesvirus-1 (EHV-1) is an important infection endemic in horses worldwide, associated with respiratory disease, abortion and paresis. Although vaccines exist their efficacy is controversial and the possibilities of chemotherapy have been investigated. Several active antiviral agents have been identified, notably the phosphonyl derivatives including PMEA, HPMPA and HPMPC. Infact, HPMPC shows considerable activity in both horses and mice after a single administration (Gibson *et al.*, 1992), making experiments and the development of chemotherapeutic regimens more feasible. In the present work, we characterise further the interactions between HPMPC and EHV-1 in a murine model which shares many features in common with the natural infection. In particular, we were interested in the ways in which HPMPC might modulate the host response to EHV-1 infection. In the principal experiment described, mice were divided into groups and given intranasal inoculations of live or inactivated EHV-1 or uninfected cell extract; inoculations associated with different degrees of immunopathology on untreated re-infection. Half the mice were given HPMPC (single dose, s.c., 20 mg/kg) on the day before infection; others received a placebo preparation. Three months later, all mice were challenged with live EHV-1 i.n., with or without HPMPC (single dose, s.c., 20 mg/kg on the day before infection). Clinical signs, virus replication in target organs and histopathology were monitored and used to assess the extent to which HPMPC alters protective immunity and immunopathology in primary and secondary infections. Independent effects at each of the three main compartments of virus replication, turbinates, lungs and blood, are described.

Reference:

Gibson *et al.* (1992). Antiviral Res. **19,** 219-232.