

**OTR 02 - Use of small interfering RNA (siRNA) as a viral replication inhibitor of Human Herpesvirus 1 in BALB/C mice with keratoconjunctivitis**

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**Introduction:**

Herpetic keratoconjunctivitis (HK) is mainly caused by Human Herpes virus 1 (HHV-1) and is the most common cause of infectious blindness in developed countries, with an incidence of 21/100,000 cases per year and a prevalence of 149/100,000. In Southeast Brazil an study found an herpetic keratoconjunctivitis positivity of 26,8% in patients with keratoconjunctivitis. Patients with HK present blepharoconjunctivitis, ocular pain, dry eye sensation, dendritic ulceration, loss of sensation in injured areas, intermittent conjunctivitis and the persistence of infection could cause corneal destruction and vision loss by corneal opacification leading to corneal transplantation. Nowadays, HK treatment has encountered difficulties such as utilization of antivirals with elevated toxicity, metabolic side effects and HHV-1 resistance. An alternative to antivirals is the use of small interfering RNA (siRNA) as viral replication inhibitor.

**Objective:**

The aim of this study was the evaluation of siRNA anti-HHV-1 as an alternative for treatment of HK in BALB/C mice.

**Methodology:**

20 BALB/C mice were inoculated via intraocular with HSV-1 and treated with siRNA anti-HHV-1. Mice were divided in 5 groups to evaluate the siRNA treatment and number of administered doses (one, two and four doses) of siRNA anti-HHV-1. Besides that, HK clinical signs, mortality and viral replication inhibition in brain, trigeminal ganglia, serum, left eye and right eye were evaluated to measure siRNA therapy.

**Results:**

Animals treated with one dose and two doses of siRNA did not lose weight. The viral replication inhibition was high in trigeminal ganglia (96.95%), left eye (99.63%) and right eye (99.35%) of animals treated with one dose of siRNA anti-HHV-1. Animals treated

with two doses of siRNA anti-HHV-1 showed viral replication inhibition of 91.25% in trigeminal ganglia, 98.84% in left eye and 97.80% in right eye; and in animals treated with four doses the replication inhibition in brain was of 81.02%, in trigeminal ganglia was of 96.81%, in serum was of 67.88%, in left eye was of 99.46% and in right eye was of 99.82%.

**Conclusion:**

These findings demonstrated that siRNA can inhibit HHV-1 replication in mice with herpetic keratoconjunctivitis. However, further studies need to be undertaken to confirm if siRNA can be a potential alternative HK treatment.

**Keywords: HSV-1; Herpetic Keratoconjunctivitis; siRNA**