16th March 2021

Equine Herpesvirus-1 therapy

Lutz Göhring, Karsten Feige, Marianne Sloet, Dominique De Clercq, Vinzenz Gerber, Orsolya Korbacska-Kutasi, Ignacio Corradini, Fernando Malalana, Ruth Morgan, Lisa Katz, René Van den Hoven, Marco Duz, Jessika-M. Cavalleri, Anne Couroucé

Once biosecurity/quarantine guidelines have been followed, there are numerous medical options for treatment of Equine Herpesvirus-1 (EHV-1) positive horses with and without clinical signs of Equine Herpesvirus Myeloencephalopathy (EHM). If a horse begins to show clinical signs of EHM, it is important to consider that intensive and committed nursing care plays a pivotal role in the management of these cases. This may include provision of soft bedding and helmets to protect the horse from head trauma, the use of indwelling urinary catheters and manual evacuation of the rectum and assisting the horse to stand (using slings) if possible. If the horse is unable to stand the horse should be maintained in sternal recumbency, and rolled to different sides every 2-4 hours. Monitoring and maintaining hydration is vitally important.

Table 2: Commonly used drugs for EHV-1 positive horses, both with and without clinical signs of EHM.

		when to apply:				
	compound	**pre-viremia**	**viremia**	**post-viremia /EHM**	**recommendations**	**level of evidence: 1 (poor) – 10 (good)**
1	Valaciclovir	✓	✓	✓	Loading dose of 30mg/kg PO TID for 2 days, then 20mg/kg PO BID up to 14 days (Maxwell et al. 2017)	
	Claims: i) decreases severity of EHM signs when treatment starts early; decreases magnitude of viremia (Maxwell et al. 2017); ii) does not influence viremia (Garré et al. 2009). Comments: i) unlikely to have side-effects; ii) unlikely to interfere with other drugs; iii) most effective at reducing severity of abnormal neurological signs when given early during an infection, ideally pre-viraemic. iv) Acyclovir is not recommended due to poor bioavailability in horses.					7 (i) RCT 9 (ii) RCT
2	NSAIDs		✓	✓	Cox-2 specific: full-dose during febrile days, half-dose for 3–5 days beyond fever (Goehring et al. 2017)	
	Flunixin meglumine (1.1mg/kg IV BID), Firocoxib (0.09mg/kg IV SID or 0.1mg/kg PO SID), or other suitable NSAID (phenylbutazone 2.2–4.4mg/kg IV/PO BID). Claims: i) decreased concentration of inflammatory mediators during viremia may decrease frequency of lymphocyte-endothelial cell interaction. Comments: likely to interfere with/potentiate effect of other drugs: 3), 4), 5)					2 (i) *in vitro* model

3	Dexamethasone			✓	0.05–0.07mg/kg once daily for 5 days; do not combine with NSAID (Goehring et al. 2017)	
	Claims: i) decreased concentration of inflammatory mediators during viremia may decrease frequency of lymphocyte-endothelial cell interaction; ii) stabilizing vasculature during vasculitis; however, not tested during EHM. Comments: likely to interfere with/potentiate effect of other drugs (eg. NSAIDs)					2 (i) *in vitro* model 1 (ii) clinical experience
4	Unfractionated (unfrx)/ Low-molecular-weight (LMW) heparin		✓		50 (unfrx) – 80 (LMW) IU/kg SQ BID for 2 – 3 days (Walter et al. 2016, Stokol et al. 2018)	
	Claims: i) interferes with platelet activation (Stokol et al. 2018); ii) interferes with thrombus formation (Walter et al. 2016). Comments: likely to interfere with/potentiate effect of other drugs: 2), 3), 5); as spinal cord hemorrhage is a hallmark finding during EHM, use with caution!					2 (i) *in vitro*/*ex vivo* model 2 (ii) clinical experience
5	Aspirin	✓	✓		5mg/kg PO q48hrs for up to 10 days	
	Claims: i) decreased concentration of inflammatory mediators during viremia may decrease frequency of lymphocyte-endothelial cell interaction (Goehring et al. 2017); ii) clinical observation. Comments: likely to interfere with/potentiate effect of other drugs: 2), 4)					2 (i) *in vitro* model 2 (ii) clinical experience
6	Lidocaine CRI		✓		IV Bolus (1.3mg/kg) followed by CRI maintenance (0.05mg/kg/minute)	
	Claims: i) decreased concentration of inflammatory mediators during viremia may decrease frequency of lymphocyte-endothelial cell interaction (Goehring et al. 2017); ii) decreases leukocyte extravasation during post-ischemic events (Cook et al. 2008); however, EHM was not included as a disease. Comments: unlikely to interfere with other drugs; requires continuous observation and special equipment (CRI!); unknown effects during periods of blood-brain barrier breeches as can occur during EHM.					2 (i) *in vitro* model, 2 (ii) projected pathogenesis
7	Zinc supplementation	✓			70-200mg/500kg horse/day PO	
	Claims: i) supplementation prior to an EHV-1 outbreak may decrease risk of development of EHM (Traub-Dargatz et al. 2013). Comments: excessive Zinc supplementation can cause copper deficiency, particularly in young horses					1 (i) retrospective cohort study
8	Vitamin E	✓	✓	✓	1000 – 2000 IU PO once daily	
	Claims: i) anti-oxidant, not evaluated during EHM Comments: unlikely to interfere with other drugs; unlikely to have side-effects.					1 (i) clinical experience
8	DMSO		✓	✓	1L of 5-8% solution IV (once – BID) for up to 3 days.	
	Claims: i) free radical scavenger, anti-osmotic. Can cause haemolysis, cause nephron/hepatotoxicity and teratogenic effects.					1 (i) clinical experience

RCT: Randomised Control Trial; CRI: Constant Rate Infusion; DMSO: Dymethyl sulphoxide;

References

Cook VL et al. (2008) Attenuation of ischaemic injury in the equine jejunum by administration of systemic lidocaine. *Eq Vet J.* 40:353-357

Garré B et al. (2009) Evaluation of orally administered valacyclovir in experimentally EHV1-infected ponies. *Vet Microbiol.* 135:214-221

Göhring L et al. (2017) Anti-inflammatory drugs decrease infection of brain endothelial cells with EHV-1 in vitro. *Eq Vet J.* 49(5):629-636

Maxwell LK et al. (2017) Efficacy of the early administration of valacyclovir hydrochloride for the treatment of neuropathogenic equine herpesvirus type-1 infection in horses. *Am J Vet Res.* 78(10):1126-1139

Stokol T et al. (2016) Unfractionated and Low-Molecular-Weight Heparin and the Phosphodiesterase Inhibitors, IBMX and Cilostazol, Block Ex Vivo Equid Herpesvirus Type-1-Induced Platelet Activation. *Front Vet Sci.* 17:99

Traub-Dargatz et al. (2013) Case-Control Study of a Multistate Equine Herpesvirus Myeloencephalopathy Outbreak. *J Vet Int Med.* 27(2):339-346

Walter J, et al. (2016) Prevention of equine herpesvirus myeloencephalopathy - Is heparin a novel option? A case report. *Tierarztl Prax Ausg G Grosstiere Nutztiere*. 44:313-317