|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Species** | **Neurokinin1 receptor antagonist (route)** | **Effect on “nausea- like behaviour” as defined by authors** | **Behaviour(s) measured** | **Additional details of stimulus** | **Comment** | **Reference** |
| **Cisplatin (low dose)** |
| Dog | Maropitant (i.v.) | Onset of signs of nausea delayed and VAS scores reduced at three time points between 3.7 and 4.5h post cisplatin but AUC over 7h not significantly reduced. | Composite score of lip licking, lethargy, restlessness or turning /circling signalling that vomiting is imminent. |  | Also showed that vasopressin secretion was reduced by maropitant. | Kenward et al., 2017 |
| **Doxorubicin (5 days)** |
| Dog | Maropitant (s.c.) | No significant effect | Appetite, protracted salivation, lip smacking |  |  | Rau et al., 2010 |
| **Opiate receptor agonists** |
| Dog | Maropitant (s.c.) | No significant difference in signs of nausea but reduction in number with nausea | Ptyalism, lip licking, increased swallowing | Morphine(s.c.) | Salivation incidence unaffected; metaclopramide also no effect on “nausea -like behaviours” | Lorenzutti et al., 2016, 2017 |
| Dog | Maropitant(s.c.) | No significant effect but reduction in incidence | Excessive lip licking and swallowing, hunched posture | Hydromorphone (i.m.) | No effect on increased panting; maropitant increased ptyalism- salivation not included in nausea score | Claude et al., 2014 |
| Dog | Maropitant (s.c.) | Significantly decreased with 60 min pre-dose | Salivation, lip-licking | Hydromoprphone (i.m.) | Effect on “N” only seen with 60min pre-dose | Hay Kraus 2014 |
| Cat | Maropitant (s.c.) | No significant effect on sialorrhea but decrease in lip licking | Sialorrhea, lip licking | Dexmedetomidine +morphine (i.m.) |  | Martin-Flores et al., 2016 |
| **Tranexamic acid** |
| Dog | Maropitant (i.v.) | No significant effect on severity | Visual analogue scale | Fibrinolytic |  | Kantyka et al., 2020 |
| **Brimonidine** |
| Cat | Maropitant(p.o.) | No significant effect | Sialorrhea, lip licking | α2 agonist sedative given as eye drops |  | Kanda et al., 2020 |
| **Motion** |
| Cat | CP-99,994 (s.c.) | No significant effect | Suri et al., 1979 symptom scale | Ferris Wheel |  | Lucot et al., 1997 |
| **Lycorine (s.c.)** |
| Dog | Maropitant (s.c.) | No significant effect | Increased salivation, lip licking, frequent/exaggerated swallowing motions, lethargy, restlessness and /or panting | Alkaloid from daffodils |  | Kretzing et al., 2011 |

**Supplementary Table 1.** A summary of the results of preclinical studies reporting the effects of neurokinin1 receptor antagonists on the “nausea –like behaviours” in response to a range of emetic stimuli in species capable of vomiting.

**References**

Claude, A.K., Dedeaux, A., Chiavaccini, L. & Hinz, S. (2014). Effects of maropitant citrate or acepromazine on the incidence of adverse events associated with hydromorphone premedication in dogs. *Journal of Veterinary Internal Medicine*, 28, 1414-1417.

Hay-Kraus, B.L. (2014) Efficacy of orally administered maropitant citrate in preventing vomiting associated with hydromorphone administration in dogs. *Journal of the American Veterinary Medicine Association*, 15, 1164-1169.

Kanda, T., Toda, C., Morimoto, H., Shimizu, Y., Otoi, T., Furumoto, K., Okamura, Y., & Iwata, E. (2020). Anti-emetic effect of oral maropitant treatment before the administration of brimonidine ophthalmic solution in healthy cats. *Journal of Feline Medicine and Surgery,* 22,557-563.

Kantyka, M.E., Meira, C., Bettschart-Wolfensberger, R., Hartnack, S., & Kutter, A.P.N. (2020). Prospective, controlled, blinded, randomized crossover trial evaluating the effect of maropitant versus ondansetron on inhibiting tranexamic acid-evoked emesis. *Journal of Veterinary Emergency Critical Care,* 30, 436-441.

Kenward, H., Elliott, J., Lee, T., & Pelligrand, L. (2017). Anti-nausea effects and pharmacokinetics of ondansetron, maropitant and metoclopramide in a low-dose cisplatin model of nausea and vomiting in the dog: a blinded crossover study. *BMC Veterinary Research*, 13, 244.

Kretzing, S., Abraham, G., Seiwert, B., Ungemach, F.R., Krügel, U., Teichert, J., & Regenthal, R. (2011). In vivo assessment of antiemetic drugs and mechanism of lycorine -induced nausea and emesis. *Archives of Toxicology,* 85, 1565-1573.

Lorenzutti, A.M., Martin-Flores, M., Literio, N.J., Himelfarb, M.A., Invaldi, S.H., & Zarazaga, M.P. (2016). Evaluation of the antiemetic efficacy of maropitant in dogs medicated with morphine and acepromazine. *Veterinary Anesthesia and Analgesia,* 43, 195-198.

Lorenzutti, A.M., Martin-Flores, M., Literio, N.J., Himelfarb, M.A., Invaldi, S.H., & Zarazaga, M.P. (2017). A comparison between maropitant and metoclopramide for the prevention of morphine-induced nausea and vomiting in dogs. *Canadian Veterinary J*ournal,58, 35-38.

Lucot, J.B., Obach, R.S., McClean, S., & Watson, J.W. (1997). The effect of CP-99994 on the responses to provocative motion in the cat. *British Journal of Pharmacology,* 120, 116-120.

Martin-Flores, M., Sakai, D.M., Learn, M.M., Mastrocco, A., Campoy, L., Boesch, J.M., & Gleed, R.D. (2016). Effect of maropitant in cats receiving dexamethasone and morphine. *Journal of the* *American Veterinary Medicine Association,* 248, 1257-1261.

Rau, S.E., Barber, L.G., & Burgess, K.E. (2010). Efficacy of maropitant in the prevention of delayed vomiting associated with administration of doxorubicin in dogs. *Journal of Veterinary Internal Medicine*, 24, 1452-1457.