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Effect Of Melatonin On Prednisolone Eye Disposition In Cats

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Footnotes

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Abstract

Purpose:

To characterize prednisolone (PRED) ocular and systemic pharmacokinetics in cats after oral administration and to study the effect of concomitant administration of melatonin (MEL) on PRED disposition.

Methods:

Six (6) castrated young physically and ophthalmologically healthy male European Short Hair cats were orally administrated with a single dose (10 mg) of PRED or a single dose of PRED (10 mg) and MEL (3 mg) in tablet. In anesthetized cats 2 mL of blood and 450 µL of aqueous humor (AH) were obtained from preplaced cephalic antebrachial intravenous catheters and from one eye by direct puncture, respectively, at: 0.25, 0.5, 1, 1.5, 2, 3, 4 and 5 h after administration. Plasma and AH samples were assayed for PRED by HPLC. A two-compartment model was used to simultaneously fit PRED plasma and aqueous concentration *vs.* time data using ADAPT 5. The estimated pharmacokinetic (PK) parameters included the absorption rate constant (ka),

elimination rate constant from the central compartment (kc), intercompartment rate constants between plasma and aqueous humor (kpa), apparent volume of distribution of the central compartment (Vc/F). PK parameters were compared between groups (PRED *vs*. PRED+MEL) by means of Wilcoxon matched pairs test ($p<0.05$).

Results:

The model adequately fitted the data and the estimated median (interval) PK parameters are shown in Table 1. No significant difference was observed in the PK parameters when comparing between groups of treatments ($p>0.05$).

Conclusions:

These results indicated that MEL does not modify PRED systemic or ocular disposition in cats when both are administrated simultaneously. A possible synergic pharmacological effect may be account for different mechanisms of action, but not for pharmacokinetic synergism and will be further studied.

Table 1. Plasma and aqueous humor (AH) pharmacokinetic parameters (median and interval) for prednisolone (PRED) after oral administration of PRED (10 mg) alone or PRED (10 mg) plus melatonin (MEL; 3 mg) to cats.

Pharmacokinetic parameters	Plasma		AH	
	PRED	PRED/MEL	PRED	PRED/MEL
ka (h^{-1})	**1.02** (0.55 - 1.87)	**1.90** (0.72 – 3.43)		
C_{max} (ng/mL)	**213.1** (117.4 - 607.7)	**315.9** (227.2 – 532.4)	**84.6** (37.6 – 210.6)	**122.2** (67.5 – 174.5)
T_{max} (h)	**1.25** (0.50 – 2.00)	**1.00** (0.50 – 2.00)	**2.50** (1.00 – 3.00)	**1.50** (1.50 – 2.00)
AUC (ng h/mL^{-1})	**458.4** (235.1 – 932.1)	**434.8** (350.0 – 745.5)	**259.8** (102.1 – 474.4)	**252.4** (185.8 – 407.4)
Vc/F (L)	**11.2** (5.1 – 18.2)	**15.1** (7.5 – 26.3)		
kc (h^{-1})	**1.88** (1.72 - 2.66)	**1.91** (0.77 - 2.37)		
kpa (h^{-1})	**1.08×10^{-4}** (2.87×10^{-5} – 2.58×10^{-4})	**1.26×10^{-4}** (5.63×10^{-5} – 1.99×10^{-4})		

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Keywords: corticosteroids • melatonin • antioxidants