

ABCB1 Deletion Mutation & Drug Reactions in Cats

P-glycoprotein (P-gp) is the product of the *ABCB1* (formerly *MDR1*) gene. Dogs with the *ABCB1-1Δ* mutation are at increased risk for serious adverse reactions to P-gp substrate drugs. The goal of this study was to sequence the coding region of the gene in cats that experienced adverse reactions to P-gp substrate drugs (eg, macrocyclic lactones, loperamide, vinca alkaloids). Eight cats that had clinical signs of central nervous system (CNS) toxicosis after receiving ivermectin ($n = 2$), combination moxidectin and imidacloprid ($n = 3$), combination praziquantel and emodepside ($n = 1$), or selamectin

($n = 2$) at doses not expected to cause adverse reactions were tested. DNA was also collected from 1 cat treated with praziquantel-emodepside that did not develop CNS toxicity. DNA from 105 non-phenotyped cats was also obtained from a DNA bank.

The most significant finding was a nonsense (deletion) mutation in 1 of the ivermectin-treated cats. This cat was homozygous for the deletion mutation. The other cats were all homozygous for the wild-type allele. The nonsense mutation was identified in 4/105 non-phenotyped cats (1 homozygous and 3 heterozygous). The authors conclude that cats with the described nonsense mutation would be expected to show susceptibility to adverse effects of P-gp substrate drugs, similar to dogs with the *ABCB1-1Δ* mutation.

Commentary

Genetic predisposition to macrocyclic

lactone sensitivity is widely reported in dogs, and testing is available for the *ABCB1* deletion in this species. This study represents the first report of genetic associations with adverse drug reactions to P-gp substrates in cats. Although the most significant *ABCB1* mutation had a low prevalence in a phenotypically normal population of cats (4%), clinicians should be aware that clinical signs can occur in these cats even at therapeutic doses of macrocyclic lactones. It is also possible that cats with this mutation could be at higher risk for adverse drug reactions to other P-gp substrate drugs. Currently, genetic testing is not commercially available for cats. Hopefully, future studies will further elucidate the role of genetics in feline macrocyclic lactone sensitivity.—*Jennifer Reinhart, DVM, MS, DACVIM (SAIM)*

Source

Mealey KL, Burke NS. Identification of a nonsense mutation in feline *ABCB1*. *J Vet Pharmacol Ther*. 2015;38(5):429-433.

Managing Feline Stress Through Diet

Cats are susceptible to external stressors (eg, environmental changes, forced confinement, unpredictable handling by unfamiliar humans, changes in routine, continued exposure to high-frequency sounds). Studies have shown that cortisol secretion increases when cats are exposed to these events chronically. Ingestible, bioactive peptides (eg, alpha-casozepine, tryptophan) have been reported to have a calming effect on humans. Alpha-casozepine is derived from a major protein in milk, which is believed to cause an anxiolytic effect by binding to gamma amino butyric acid (GABA) receptors. Tryptophan is the precursor for the neurotransmitter serotonin (5-HT) and kynurenine. The

anxiolytic effects of dietary tryptophan are likely facilitated by central 5-HT synthesis and signaling.

In this study, 21 healthy, client-owned cats were divided into 2 groups. The control group ($n = 11$) was fed a balanced commercial diet, and the study group ($n = 10$) was fed a novel balanced prescription diet that contained alpha-casozepine and tryptophan. Plasma and urine cortisol levels were measured before the study and after 8 weeks. Plasma cortisol levels served as an indicator of acute stress. Urine cortisol levels were used to estimate change in cortisol over the 8-week study period. There was no significant change in plasma cortisol levels in either group. The cats treated with the study diet had a 40% reduction in urinary cortisol levels after 8 weeks, whereas those in the control group had no significant change in urinary cortisol levels.

Commentary

The concept of feeding diets to reduce

stress is novel in veterinary prescription nutrition. It is an ancient concept in Traditional Chinese medicine, in which certain foods or herbal medicine can be given to treat stress. This study points out that by elevating levels of certain compounds (eg, an essential amino acid), a client can possibly change the biochemical nature of the cat's central nervous system so that it reacts to stress differently. These types of interventions may be useful in the management of the indoor-only cat and especially in stress-mediated conditions (eg, feline idiopathic cystitis). Further studies are warranted to evaluate foods and supplements to better understand how they work and the clinical situations in which they would be most beneficial.—*Heather Troyer, DVM, DABVP, CVA, CVPP*

Source

Miyaji K, Kato M, Ohtani N, M Ohta. Experimental verification of the effects on normal domestic cats by feeding prescription diet for decreasing stress. *J Appl Anim Welf Sci*. 2015;18(4):355-362.