

VETERINARY TECHNICAL DATASHEET

Multidrug Resistance 1, (MDR1)



Mutation Found In :Australian Shepherd , Miniature American Shepherd, Border Collie, Collie, English Shepherd, German Shepherd Dog, Herding Breed Cross, Long-haired Whippet, McNab, Mixed Breed, Old English Sheepdog , Shetland Sheepdog , Silken Windhound

Disorder Type

- Drug response

Disease Severity

- Moderate

Background

A mutation in the multidrug resistance 1 (MDR1) gene alters a dog's ability to limit the absorption and distribution of many medications. Affected dogs are slower to eliminate these drugs from the body and can suffer side effects when exposed to certain medications. This condition is sometimes called "ivermectin sensitivity." However, the name is a misnomer as several other drugs pose a risk to MDR1 positive dogs. Adverse reactions can occur when affected dogs are exposed to some common drugs, however, all FDA approved heartworm preventatives are safe to administer to MDR1 positive dogs. This mutation is inherited in a dominant fashion though dogs with two copies of the mutation will exhibit more severe clinical signs.

Key Signs

- Some medications may cause prolonged sedation
- stupor
- coma
- seizures.

Clinical Description

Dogs that carry this mutation are asymptomatic until they are exposed to a medication that uses the pump that is rendered defective by the mutation in the MDR1 (also called ABCB1) gene. Drugs known to use this P-glycoprotein pump are macrocyclic lactones (antiparasitic drugs), loperamide (antidiarrheal), erythromycin (antibiotic), acepromazine (tranquilizer), butorphanol (opioid), and certain drugs used in cancer treatment (vincristine, vinblastine, and doxorubicin). When these medications are administered, they accumulate in the brain which results in the adverse reactions. Typical symptoms include tremors, loss of balance, seizures, obtundation, excessive salivation, dilated pupils, and bradycardia. If untreated, the condition may lead to respiratory arrest, coma or death. Because dogs with one copy of the mutation will have some P-glycoprotein function, the most severe cases tend to occur in dogs that two copies of the mutation and therefore lack any functional P-glycoprotein pumps. However, the condition can still be very severe in dogs that have only one copy of the mutation.

Mode of Inheritance

- autosomal dominant

Gene Name

- MDR1/ABCB1

Next Steps

For dogs with copies of the MDR1 mutation it is important to be aware of medications which may result in an adverse reaction. These include: Acepromazine, Butorphanol, Doxorubicin, Doramectin, Emodepside, Erythromycin, Ivermectin, Loperamide, Milbemycin, Moxidectin, Paclitaxel, Rifampin, Selamectin, Vinblastine, Vincristine. It is best to explore alternative medications that will not use this P-glycoprotein pump or, at minimum, consider reduction of the dose to levels safe for an MDR1 positive dog.

References

Mealey KL, Bentjen SA, Gay JM, Cantor GH. Ivermectin sensitivity in collies is associated with a deletion mutation of the *mdr1* gene. *Pharmacogenetics* 11:727-33, 2001.