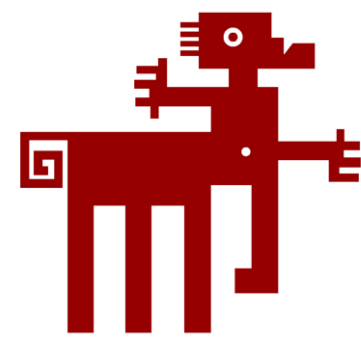


Mutation of the MDR1 gene in dogs. Anesthetic implications and possible complications.



Ernest Martínez Martínez

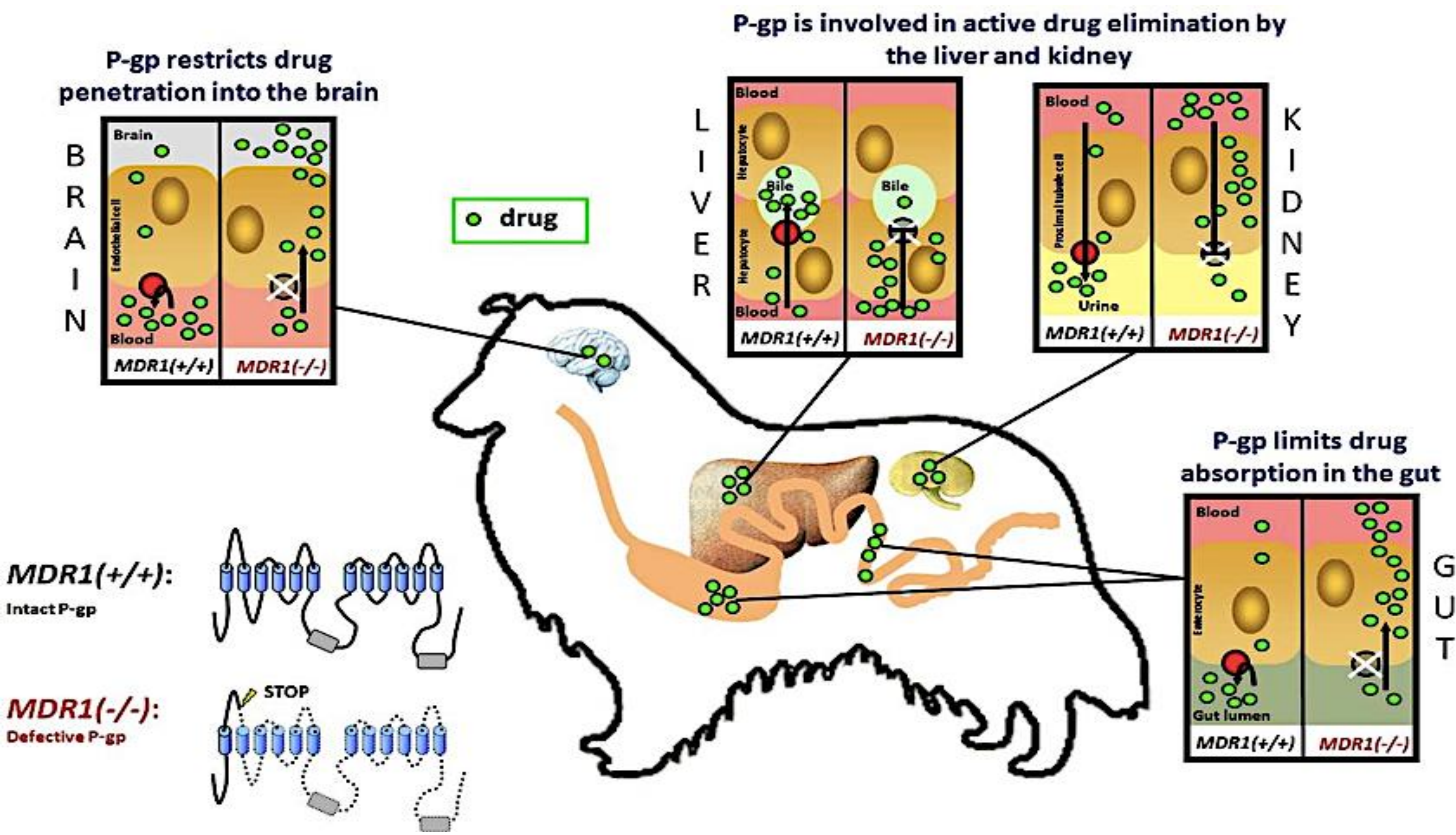
Faculty of Veterinary Medicine - Final degree project. June 27, 2019

Introduction

The MDR1 gene encodes P-glycoprotein (P-gp), a drug transporter that plays a great role in drug disposition. P-gp is a component of the blood-brain barrier (prevents the CNS from excessive exposition to toxic compounds) and also promotes drug excretion through bile and urine. Some individuals have a mutation in this gene, which can lead to potentially fatal adverse drug reactions. This mutation has been mainly documented in herding dogs. The genetic factor of a patient is one of the variables between animals that can condition the result of an intervention. Thus, some individuals may require a different anesthetic management.

Objectives

The aim of this bibliographic review is to determinate the implications of the MDR1 gene in the dogs anesthesia, specifically hypnotics, analgesics and other drugs that could be used in a anesthetic protocol. Moreover, it pretends to stablish a safe protocol for the dogs that suffer from this mutation of the MDR1 gene.



Geyer and Janko 2012



Affected breeds

The main affected breeds are **Collies (Rough and Smooth)**, **Shetland Sheepdog**, **Australian Shepherd**, **Miniature Australian Shepherd**, **Longhaired Whippet**, **Silken Windhound**, **Border Collie**, **Wäller**, **German Shepherd**, **English Shepherd**, **McNab** and **Bobtail**.

* Breeds in bold are the ones with more incidence of the mutation.

Despite this, the popular belief among the veterinarians is that Border Collie is one of the main affected breeds: *white feet don't treat*.

Drugs involved

Drug	P-gp substrate	MDR1 mutated dogs affected
Morphine	✓	✓
Methadone	✓	✗
Butorphanol	✓	✓
Buprenorphine	✓	✓
Fentanyl	✓	✗
Acepromazine	✓	✓
Midazolam	✓	✗
Lidocaina	✓	✗
Vercuronium bromide	✓	✗



Conclusion

A safe anesthetic protocol for dogs with the mutation of MDR1 consists in a 50% reduction of the normal dose with the drugs involved, specially morphine, butorphanol, buprenorphine and acepromazine. Another option is choosing drugs that are not substrates of the P-gp instead, for example, NSAIDs for the analgesia and $\alpha 2$ -adrenergic agonists (dexmedetomidine).

Bibliography

Geyer J, Janko C. 2012. Treatment of MDR1 mutant dogs with macrocyclic lactones. Current Pharmaceutical Biotechnology. 13(6):969-986.
Melanie. 2017. Dog Breed Corner - Border Collie | Mad Paws Blog. [accessed 2019 may 28]. <https://www.madpaws.com.au/blog/dog-breed-corner-border-collie/>.