Application of a sedation scoring system in dogs following premedication

Thesis is submitted by Deepti Deshpande
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To Mom, Dad and Prathmesh,

You have been my inspiration and my strength. Thank you for being a part of my life!
Acknowledgements

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Abstract

Pharmacogenetics is the study of how variations in the genome influence drug pharmacokinetics (the body's effect on the drug) and pharmacodynamics (the drug's effect on the body). The MDR1 gene codes for a membrane-bound drug transporter protein, P-glycoprotein (P-gp) that transports drugs across the cell membrane using an energy-dependent mechanism. Anecdotal reports in the literature suggested that dogs with a mutation in the MDR1 gene (MDR1-1Δ) show increased sensitivity to routinely used veterinary sedatives such as acepromazine and butorphanol, resulting in increased duration and depth of sedation. This study has 3 aims. First is to gain experience with a sedation scoring system that can be used to assess the level of sedation. The second aim is to assess the difference in sedation of dogs premedicated with dexmedetomidine and acepromazine. The third aim is to investigate the effect of acepromazine (n=29) and a combination of acepromazine and butorphanol (n=12) on MDR1 genotyped rough-coated collies.

In the study assessing the sedation of dogs premedicated with dexmedetomidine and acepromazine, 30 dogs scheduled for orchidectomy were divided into two groups; the DEX group (n=15) and the ACE group (n=15). Dogs in the DEX group received dexmedetomidine (125 μg/m²) and morphine (0.5 mg/kg) while the dogs in the ACE group received acepromazine (0.04 mg/kg) and morphine (0.5 mg/kg). The dogs were sedation scored at 0, 10, 20 and 30 minute intervals. The dogs in the DEX group had a statistically higher sedation score at 30 minutes than the dogs in the ACE group (p value =0.0189). Dogs premedicated with dexmedetomidine had a higher sedation score than dog's premedicated acepromazine at 30 minutes. The heart rate, respiratory rate and mean arterial blood pressure were not different between the DEX and the ACE group at 30 minutes post administration of premedication agent.

The second study investigated the effects of acepromazine and a combination of acepromazine and butorphanol in dogs carrying the MDR1-1Δ mutation. Genotyping for the MDR1-1Δ mutation was performed in 31 rough-coated collies. Dogs were considered healthy based on clinical history, physical examination, complete blood count, serum chemistry and urinalysis. Twenty-nine of the 31 rough coated collies were deemed healthy and were enrolled in the sedation trial assessing the effects of
acepromazine on the *MDR1-1Δ* mutants. A subset of the 29 rough coated collies was enrolled in the study assessing the effects of combination of acepromazine and butorphanol. The rough coated collies were divided in 3 groups based on their genotype: homozygous mutants, heterozygous carriers and normal group. After administration of acepromazine (0.04 mg/kg, IV) or a combination of acepromazine (0.04 mg/kg) and butorphanol (0.05 mg/kg), sedation scoring was performed at 0, 30 minutes, 60 minutes, 90 minutes, 2, 2.5, 3, 4 and 6 hour intervals by an observer blinded to the results of the *MDR1* genotype. Following administration of acepromazine, homozygous mutant collies (*MDR1 -/-*) (n = 10) reached a greater level of sedation and remained sedated for a longer duration as compared to the heterozygous carriers (*MDR1 +/-*) (n = 10) and wild-type collies (*MDR1 +/+*) (n = 9) (p= 0.0176). A subset of 12 dogs was sedated with a combination of acepromazine (0.04 mg/kg) and butorphanol (0.05 mg/kg). Heterozygous carriers (*MDR1 -/+*) had significantly higher sedation scores than homozygous mutants (*MDR1 -/-*) and normal groups (*MDR1 +/+*) when sedated with the combination (p=0.0423). This unexpected result may have been due to the small number of dogs tested. The author recommends lower dosing of acepromazine and butorphanol in dogs that are homozygous mutants to the *MDR1-1Δ* mutation and recommends the constant monitoring of sedation.
# Table of Contents

Acknowledgements ............................................................................................................................... 4  
Abstract.................................................................................................................................................. 5  
Lists of tables ....................................................................................................................................... 10  
Lists of Figures .................................................................................................................................... 12  
Abbrevations ....................................................................................................................................... 14  

1. Introduction ..................................................................................................................................... 16  
   1.1 Balanced Anaesthesia ..................................................................................................................... 16  
   1.2 Premedication ................................................................................................................................. 18  
      1.2.1 Anticholinergics ....................................................................................................................... 18  
         A. Atropine ................................................................................................................... ............. 19  
         B. Glycopyrrolate ............................................................................................................. ......... 19  
      1.2.2 Pre-emptive analgesia ............................................................................................................... 21  
         Neurobiology of pain..................................................................................................................... 21  
      1.2.3 Sedatives ................................................................................................................................... 23  
         A. Phenothiazines ............................................................................................................. ......... 23  
         Acepromazine........................................................................................................................... 24  
         B. Alpha-2-adrenergic agonist ................................................................................................. .. 25  
         Dexmedetomidine .......................................................................................................................... 27  
         C. Benzodiazepines ............................................................................................................ ....... 27  
         D. Opioids.................................................................................................................... .............. 28  
   1.3 Sedation: clinical implications ........................................................................................................ 31  
   1.4 Sedation Scoring Scales .................................................................................................................. 32  
   1.5 Pharmacogenetics ........................................................................................................................... 36  
      Basic Genetics Concepts ............................................................................................................... 37  
      CYP2D15 in Beagles..................................................................................................................... 38  
      CYP2D11 in greyhounds............................................................................................................... 39  
      Thiopurine Methyltransferase (TPMT) in Giant Schnauzers and Alaskan Malamutes .................. 39  
      Malignant Hyperthermia................................................................................................................ 40  
      MDR1 Gene ................................................................................................................................. 40  
      Overview of P-glycoprotein ............................................................................................................. 41  
      ABC transporters ........................................................................................................................... 42  
      Structure of P-glycoprotein ........................................................................................................... 42  

2. Material and Methods: .................................................................................................................. 62

2.1 Comparison of sedation in dogs following administration of dexmedetomidine plus morphine to acepromazine plus morphine ................................................................................................................ 62

2.1.1 Animals .................................................................................................................................... 62

2.1.2 Pre-surgical work up ................................................................................................................ 62

2.1.3 Sedation Scoring ....................................................................................................................... 62

2.1.4 Anaesthesia and Surgery protocol ............................................................................................ 63

2.1.5 Recovery ................................................................................................................................... 63

2.1.6 Sedation System ....................................................................................................................... 63

2.2 Pharmacogenetic effects of MDR1-1Δ mutation on sedation of rough coated collies with acepromazine and a combination of acepromazine and butorphanol. .................................................. 67

2.2.1 Animals .................................................................................................................................... 67

2.2.2 Buccal Swabs ........................................................................................................................... 67

2.2.3 Genotyping ................................................................................................................................ 68

2.2.4 Pre-sedation work up ................................................................................................................ 68

A. History ......................................................................................................................................... 69

B. Blood Testing ............................................................................................................................... 69

C. Urine analysis ............................................................................................................................... 69
D. Physical Examination....................................................................................................... 70

2.2.5 Sedation Scoring....................................................................................................................... 70

A. Sedation scoring following administration of acepromazine alone........................................... 70
B. Sedation scoring following administration of a combination of acepromazine and butorphanol 71

2.3 Statistical Analysis:......................................................................................................................... 72

A. Comparison of sedation in dogs following administration of dexmedetomidine plus morphine to acepromazine plus morphine ....................................................................................................................... 72
B. Pharmacogenetic effects of MDR1-1Δ on the level of sedation following administration of acepromazine alone................................................................................................................................................... 73
C. Pharmacogenetic effects of MDR1-1Δ on the level of sedation following administration of combination of acepromazine and butorphanol. .............................................................................................................................. 73

3. Results: Comparison of sedation in dogs following administration of dexmedetomidine plus morphine to acepromazine plus morphine ........................................................................................................ 75

4. Results: .............................................................................................................................................. 82

4.1 Pharmacogenetic effects of MDR1-1Δ mutation on sedation of rough coated collies with acepromazine ........................................................................................................................................... 82
4.2 Pharmacogenetic effects of MDR1-1Δ mutation on sedation of rough coated collies with combination of acepromazine and butorphanol. ........................................................................................................ 90

5. Discussion: ....................................................................................................................................... 98

5.1 Comparison of sedation in dogs following administration of dexmedetomidine plus morphine to acepromazine plus morphine ....................................................................................................................... 98
5.2 Pharmacogenetic effects of MDR1-1Δ mutation on sedation of rough coated collies with acepromazine ................................................................................................................................................... 101
5.3 Pharmacogenetic effects of MDR1-1Δ mutation on sedation of rough coated collies with a combination of acepromazine and butorphanol. ........................................................................................................ 106
5.4 Conclusion .................................................................................................................................... 108

6. References ...................................................................................................................................... 110
Lists of tables

Table of Contents.................................................................................................................................................. 7
Table 1.1: Opioid Receptor Activity (Adams, 2001), (Pleuvry, 2005) ................................................................. 30
Table 1.2: Sedation scoring system (Hofmeister, Chandler, & Read, 2010). ......................................................... 35
Figure 1.1: Topological map and domain organisation of P-gp, predicted from its primary sequence (Higgins et al., 1997). ......................................................................................................................... 44
Figure 1.2: P-glycoprotein expression and function in various tissues (Fromm, 2004)......................................... 46
Table 1.3: Selected P-gp substrates (Martinez et al., 2008). ............................................................................... 53
Figure 1.3: Partial (bases 275±708) sequence comparison of wild-type (top) and mutant (bottom) MDR1 cDNAs. .................................................................................................................................................. 55
Figure 1.4: Diagrammatic representation of the transmembrane structure of P-glycoprotein (P-gp) (Mealey et al., 2001). ........................................................................................................................................ 56
Table 2.1: Sedation Scoring System, modified from (Hofmeister et al., 2010) .................................................... 66
Table 3.1: Mean + SD Age (years) and Bodyweight (Kg) of dogs in DEX and ACE groups. 76
Table 3.2: Breeds of dogs enrolled in DEX groups. .............................................................................................. 76
Table 3.3: Breeds of dogs enrolled in ACE groups. .............................................................................................. 77
Figure 3.1: Comparison of sedation scores between dogs premedicated with dexmedetomidine (DEX) and acepromazine (ACE). ................................................................................................................. 78
Figure 3.2: Comparison of heart rates (HR) between dogs in DEX and ACE group following induction with propofol. .......................................................................................................................... 79
Figure 3.3: Comparison of systolic arterial blood pressure (SAP) between dogs in DEX and ACE following induction with propofol. ................................................................................................. 80
Table 4.1: Name, age, sex and genotype data of 31 rough coated collies in the study. ........................................ 83
Table 4.2: Number of dogs, sex, age and weight data from 29 rough coated collies in the trial assessing the effect of MDR1-1∆ mutation on the level of sedation following the IV administration of acepromazine alone. ......................................................... 84
Figure 4.1: Mean sedation scores during acclimation period. ................................................................................ 85
Figure 4.2: Individual sedation scores of 29 rough coated collies. ......................................................................... 86
Figure 4.3: Comparison of the median recalculated (R) sedation scores and genotypes in the trial assessing the effect of MDR1-1∆ mutation on the level of sedation following IV administration of acepromazine alone. .............................................................................................................. 87
Figure 4.4: Comparison of the median heart rate and genotypes in the study assessing the effect of MDR1-1∆ mutation on the level of sedation following IV administration of acepromazine alone. ....................................................................................................................... 88
Figure 4.5: Comparison of the median respiratory rate and genotypes in the study assessing the effect of MDR1-1∆ mutation on the level of sedation following IV administration of acepromazine alone. ....................................................................................................................... 89
Figure 4.6: Comparison of the median mean arterial blood pressure and genotypes in the study assessing the effect of MDR1-1∆ mutation on the level of sedation following IV administration of acepromazine alone. ....................................................................................................................... 90
Table 4.3: Number of dogs, sex, age and weight data from 12 rough coated collies in the trial assessing the effects of MDR1-1∆ mutation on the level of sedation following IV administration of acepromazine and butorphanol combination. .............................................................................................................. 91
Figure 4.7: Mean sedation score during acclimation period. ................................................................................ 92
Figure 4.8: Comparison the median recalculated (R) sedation scores and genotypes in the study assessing the effect of MDR1-1Δ mutation on the level of sedation following IV administration of combination of acepromazine and butorphanol. .......................................................... 93

Figure 4.9: Comparison of the median heart rate and genotypes in the study assessing the effect of MDR1-1Δ mutation on the level of sedation following IV administration of a combination of acepromazine and butorphanol. .......................................................... 94

Figure 4.10: Comparison of the median respiratory rates and genotypes in the study assessing the effect of MDR1-1Δ mutation on the level of sedation following IV administration of a combination of acepromazine and butorphanol. .......................................................... 95

Figure 4.11: Comparison of the median mean arterial blood pressure and genotypes in the study assessing the effect of MDR1-1Δ mutation on the level of sedation following IV administration of a combination of acepromazine and butorphanol. .......................................................... 96

Table 5.1: Table shows the allelic distribution of MDR1-Δ mutation published in other studies and in the current study. ........................................................................................................ 101
Lists of Figures

Table of Contents .................................................................................................................. 7
Table 1.1: Opioid Receptor Activity (Adams, 2001), (Pleuvry, 2005) .................................. 30
Table 1.2: Sedation scoring system (Hofmeister, Chandler, & Read, 2010). ....................... 35
Figure 1.1: Topological map and domain organisation of P-gp, predicted from its primary sequence (Higgins et al., 1997). ............................................................. 44
Figure 1.2: P-glycoprotein expression and function in various tissues (Fromm, 2004)....... 46
Table 1.3: Selected P-gp substrates (Martinez et al., 2008). .............................................. 53
Figure 1.3: Partial (bases 275±708) sequence comparison of wild-type (top) and mutant (bottom) MDR1 cDNAs. ................................................................. 55
Figure 1.4: Diagrammatic representation of the transmembrane structure of P-glycoprotein (P-gp) (Mealey et al., 2001). .............................................................. 56
Table 2.1: Sedation Scoring System, modified from (Hofmeister et al., 2010) ..................... 66
Table 3.1: Mean + SD Age (years) and Bodyweight (Kg) of dogs in DEX and ACE groups. 76
Table 3.2: Breeds of dogs enrolled in DEX groups. ............................................................. 76
Table 3.3: Breeds of dogs enrolled in ACE groups. ............................................................. 77
Figure 3.1: Comparison of sedation scores between dogs premedicated with dexmedetomidine (DEX) and acepromazine (ACE). ......................................................... 78
Figure 3.2: Comparison of heart rates (HR) between dogs in DEX and ACE group following induction with propofol. ................................................................. 79
Figure 3.3: Comparison of systolic arterial blood pressure (SAP) between dogs in DEX and ACE following induction with propofol. ......................................................... 80
Table 4.1: Name, age, sex and genotype data of 31 rough coated collies in the study....... 83
Table 4.2: Number of dogs, sex, age and weight data from 29 rough coated collies in the trial assessing the effect of MDR1-1Δ mutation on the level of sedation following the IV administration of acepromazine alone................................................. 84
Figure 4.1: Mean sedation scores during acclimation period. .............................................. 85
Figure 4.2: Individual sedation scores of 29 rough coated collies .................................... 86
Figure 4.3: Comparison of the median recalculated (R) sedation scores and genotypes in the trial assessing the effect of MDR1-1Δ mutation on the level of sedation following IV administration of acepromazine alone................................................. 87
Figure 4.4: Comparison of the median heart rate and genotypes in the study assessing the effect of MDR1-1Δ mutation on the level of sedation following IV administration of acepromazine alone................................................. 88
Figure 4.5: Comparison of the median respiratory rate and genotypes in the study assessing the effect of MDR1-1Δ mutation on the level of sedation following IV administration of acepromazine alone................................................. 89
Figure 4.6: Comparison of the median mean arterial blood pressure and genotypes in the study assessing the effect of MDR1-1Δ mutation on the level of sedation following IV administration of acepromazine alone................................................. 90
Table 4.3: Number of dogs, sex, age and weight data from 12 rough coated collies in the trial assessing the effects of MDR1-1Δ mutation on the level of sedation following IV administration of acepromazine and butorphanol combination ................................................. 91
Figure 4.7: Mean sedation score during acclimation period.............................................. 92
Figure 4.8: Comparison the median recalculated (R) sedation scores and genotypes in the study assessing the effect of MDR1-1Δ mutation on the level of sedation following IV administration of combination of acepromazine and butorphanol ................................................. 93
Figure 4.9: Comparison of the median heart rate and genotypes in the study assessing the effect of \( MDR1-1\Delta \) mutation on the level of sedation following IV administration of a combination of acepromazine and butorphanol. ................................................................. 94

Figure 4.10: Comparison of the median respiratory rates and genotypes in the study assessing the effect of \( MDR1-1\Delta \) mutation on the level of sedation following IV administration of a combination of acepromazine and butorphanol. .................................................. 95

Figure 4.11: Comparison of the median mean arterial blood pressure and genotypes in the study assessing the effect of \( MDR1-1\Delta \) mutation on the level of sedation following IV administration of a combination of acepromazine and butorphanol. .................................................. 96

Table 5.1: Table shows the allelic distribution of \( MDR1-\Delta \) mutation published in other studies and in the current study. ........................................................................................................................ 101
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC</td>
<td>ATP Binding Cassette Transporter Proteins</td>
</tr>
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<td>ACE</td>
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<td>ATP</td>
<td>Adenosine Triphosphate</td>
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