

HYPOTENSION IN HEALTHY DOGS
UNDERGOING ELECTIVE
DESEXING

Submitted by

RENATA SAMPAIO COSTA

BVM, Grad Dip Ed

This thesis is presented for the degree of Master of Philosophy,

Murdoch University

2014

DECLARATION

I declare that this thesis is my own account of my research and contains as its main content work which has not previously been submitted for a degree at any tertiary education institution.

Renata Sampaio Costa

2014

DISCLAIMER

This Master in Philosophy (MPhil) thesis consists of chapters that have been prepared as stand-alone manuscripts. These manuscripts have either been published or have been submitted for publication. As a consequence, there may be some repetition between chapters and differences in formatting.

The manuscript “Frequency of hypotension in a historical cohort of anaesthetised dogs undergoing elective desexing” has been published in the Australian Veterinary Practitioner in June, 2013:

- Costa RS, Rasis A, Musk GC and Hosgood G (2013) Frequency of hypotension in a historical cohort of anaesthetised dogs undergoing elective desexing. Aust Vet Pract 43(2), 414-419.

GENERAL ABSTRACT

Hypotension is the most common complication during anaesthesia of dogs and contributes to anaesthetic-related morbidity. The frequency of hypotension reported in anaesthetised dogs is quite variable due to the lack of a standardised definition of hypotension and the number of different factors present in each study that could influence the results. In addition, there is no study in the veterinary literature that has attempted to identify animal factors that may influence perioperative mean arterial blood pressure (MAP).

The aims of this thesis were to document the proportion of healthy dogs developing hypotension during elective desexing at Murdoch University Veterinary Hospital (MUVH) and investigate patient factors influencing perioperative MAP during a surgical plane of anaesthesia. To achieve these aims, a historical cohort study and two prospective studies were performed. These studies were approved by the Murdoch University Animal Ethics Committee (AEC R239611).

The historical cohort study reviewed anaesthetic records from dogs desexed in general practice (GP) between 2007 and 2011. The aim was to determine the frequency of hypotension and explore associations between gender, age, body mass, heart rate and anaesthetic drugs with MAP. Hypotension was defined as MAP <60 mmHg for ≥ 10 minutes. Records from 188 dogs were included, 87/188 developed hypotension and the frequency of hypotension was higher in younger dogs. However, this study had limitations such as the use of a non-invasive technique for measuring MAP and various anaesthetic protocols were utilised. Prospective studies were thus performed to clarify the previous findings. These studies used invasive blood pressure monitoring (the most accurate method of measuring blood pressure) and a standardised anaesthetic protocol.

A prospective study was performed in dogs undergoing elective desexing in student neutering clinics between 2011 and 2012. To determine the proportion of hypotensive dogs, the average of 10 consecutive MAP measurements were recorded every five minutes. Hypotension was defined as above. To investigate factors that influenced MAP, the area under the MAP*time curve (AUC) from 10 minutes before to 40 minutes after the start of surgery was calculated using the trapezoidal method. Association of explanatory variables including gender, age, body mass, urine specific gravity (USG), packed cell volume and total solids with the AUC were explored using regression models. Thirty five of 71 dogs developed hypotension. The combination of age and USG best explained the MAP with age being positively and USG being negatively associated with MAP.

A second prospective study was performed to determine if the findings of the previous study could be corroborated in dogs undergoing desexing in GP, where dogs were hospitalised for a shorter period and surgery was performed by experienced veterinarians. As duration of anaesthesia was shorter, the AUC was calculated from 5 minutes before to 30 minutes after the start of surgery. Association of explanatory variables with AUC were explored. The proportion of hypotensive dogs was higher than in student neutering clinics with 17 of 24 dogs developing hypotension. Urine specific gravity was also found to be negatively associated with MAP, which was consistent with the previous study.

The observed proportions of hypotensive dogs support the recommendation for blood pressure monitoring during anaesthesia in healthy young dogs and the presence of subclinical dehydration suggested by increases in USG support the administration of intravenous fluids.

TABLE OF CONTENTS

DECLARATION	2
DISCLAIMER.....	3
GENERAL ABSTRACT	4
TABLE OF CONTENTS	6
LIST OF FIGURES	8
LIST OF TABLES.....	9
ACKNOWLEDGEMENTS	12
ABBREVIATIONS	13
CHAPTER 1 – LITERATURE REVIEW.....	15
Introduction	15
Definition of normal and abnormal blood pressure	16
Regulation of blood pressure.....	18
Factors influencing blood pressure regulation during anaesthesia	23
Summary and Aims	33
References	34
CHAPTER 2 – FREQUENCY OF HYPOTENSION IN A HISTORICAL COHORT OF ANAESTHETISED DOGS UNDERGOING ELECTIVE DESEXING.....	47
Abstract	47
Introduction	48
Materials and methods	49
Results	52
Discussion	57
Acknowledgments	62
References	62
CHAPTER 3 – HYPOTENSION IN ANAESTHETISED DOGS UNDERGOING ELECTIVE DESEXING IN STUDENT NEUTERING CLINICS	66
Abstract	66
Introduction	67
Materials and methods	68
Results	74
Discussion	80
Acknowledgments	85
References	85
CHAPTER 4 – HYPOTENSION IN ANAESTHETISED DOGS UNDERGOING ELECTIVE DESEXING IN GENERAL PRACTICE	90
Abstract	90
Introduction	91

Materials and methods	92
Results	98
Discussion	104
Acknowledgments	108
References	108
CHAPTER 5 – GENERAL DISCUSSION AND CONCLUSIONS	111
Further work	119
References	120
APPENDICES	124

LIST OF FIGURES

Chapter 2

Figure 1. Dose of acepromazine (mg/kg) across body mass (kg) in 188 healthy dogs undergoing desexing.....57

Chapter 3

Figure 1. Fit plot for age and cumulative mean arterial blood pressure calculated from 10 minutes before surgery to 40 minutes after surgery (AUC_{-10-40}) ($p=0.038$, $r=0.319$) in 60 dogs undergoing elective desexing in student neutering clinics at Murdoch University Veterinary Hospital. The regression line (solid line) and the 95% confidence interval (dotted lines) of the fitted line is depicted.....79

Figure 2. Fit plot for urine specific gravity (USG) and cumulative mean arterial blood pressure calculated from 10 minutes before surgery to 40 minutes after surgery (AUC_{-10-40}) ($p=0.126$, $r=-0.224$) in 60 dogs undergoing elective desexing in student neutering clinics at Murdoch University Veterinary Hospital. The regression line (solid line) and the 95% confidence interval (dotted lines) of the fitted line is depicted.....79

Chapter 4

Figure 1. Fit plot for urine specific gravity (USG) and cumulative mean arterial blood pressure calculated from 5 minutes before to 30 minutes after start of surgery (AUC_{-5-30}) in 16 dogs undergoing elective desexing in at Murdoch University Veterinary Hospital. The regression line (solid line) and the 95% confidence interval (dotted lines) of the fitted line is depicted.....104

LIST OF TABLES

Chapter 1

Table 1. Summary of the definition of hypotension used in anaesthetised dogs.....	17
--	----

Chapter 2

Table 1. Signalment (gender, age and body mass) of 188 healthy dogs undergoing desexing. Dogs were categorised according to mean arterial pressure recorded during anaesthesia (hypotension, MAP <60 mmHg; mild hypotension, MAP 60-79 mmHg; normotension, MAP 80-120 mmHg). Frequencies are reported with proportions in parentheses and age and mass are summarised as median (range). *Indicates significantly different from other MAP categories (P ≤0.017, Bonferroni-adjusted).....	53
---	----

Table 2. Anaesthetic drugs (premedicants and induction agents) used and heart rate of 188 healthy dogs undergoing desexing. Dogs have been categorised according to mean arterial blood pressure recorded during anaesthesia (hypotension, MAP<60mmHg; mild hypotension, MAP 60-79mmHg; normotension, MAP 80-120mmHg). Frequencies are reported with proportions in parentheses. bpm = beats per minutes.....	55
--	----

Table 3. Median (range) dose of premedicants and induction agents (mg/kg) used for 188 healthy dogs undergoing desexing. Dogs have been categorised according to mean arterial blood pressure recorded during anaesthesia (hypotension, MAP<60mmHg; mild hypotension, MAP 60-79mmHg; normotension, MAP 80-120mmHg). ACP = acepromazine.....	56
--	----

Chapter 3

Table 1. Median (interquartile interval) of age and body mass and mean (95% confidence interval) of anaesthesia duration, surgery duration, dose of isoflurane and cumulative mean arterial blood pressure calculated from 10 minutes before to 40 minutes after the start of surgery (AUC₋₁₀₋₄₀) of 71 healthy dogs undergoing elective desexing in student neutering clinics at Murdoch Veterinary Hospital.....77

Table 2. Mean (95% confidence interval) of urine specific gravity (USG), packed cell volume (PCV) and total solids (TS) of healthy dogs undergoing elective desexing in student neutering clinics at Murdoch Veterinary Hospital.....78

Table 3. Best subset regression models explaining the cumulative mean arterial blood pressure calculated from 10 minutes before to 40 minutes after start of surgery (AUC₋₁₀₋₄₀) in 60 dogs undergoing elective desexing in student neutering clinics at Murdoch Veterinary Hospital. The complete subset included age, gender, body mass (BM), urine specific gravity (USG), packed cell volume (PCV) and total solids (TS). The model including age and USG was considered the best fit subset based on C(p), R² and biologic plausibility.....78

Chapter 4

Table 1. Median (interquartile interval) of age and body mass and mean (95% confidence interval) of anaesthesia duration, surgery duration, dose of isoflurane and cumulative mean arterial blood pressure calculated from 5 minutes before to 30 minutes after start of surgery (AUC₋₅₋₃₀) of 24 healthy dogs undergoing elective desexing in general practice at Murdoch University Veterinary Hospital.....101

Table 2. Mean (95% confidence interval) of urine specific gravity (USG), packed cell volume (PCV) and total solids (TS) of healthy dogs undergoing elective desexing in general practice at Murdoch Veterinary Hospital.....102

Table 3. Best subset regression models explaining the cumulative mean arterial blood pressure calculated from 5 minutes before to 30 minutes after start of surgery (AUC₋₅₋₃₀) in 16 dogs undergoing elective desexing in general practice at Murdoch University Veterinary Hospital. The complete subset included age, gender, body mass (BM), urine specific gravity (USG), packed cell volume (PCV) and total solids (TS). The model including USG was considered the best fit subset based on C(p), r^2 and biologic plausibility.....103

ACKNOWLEDGEMENTS

I would like to express my gratitude to my supervisors Dr Anthea Raisia, Dr Gabrielle Musk and Professor Giselle Hosgood for the valuable comments towards improving my thesis. I would like to thank Murdoch University Research Studentship for providing financial assistance in the form of a scholarship and Interpath services, Epicchem and Boehringer Ingelheim for acknowledging our hard work and awarding me prizes throughout my candidature.

Thank you general practice, clinical pathology laboratory and student neutering clinics' staff (especially Ann, Sue and Tania) for your support. I also want to thank the Anaesthesia department at Murdoch University Veterinary Hospital for the kind care and for allowing me to be part of this great team of professionals.

Thank you my dear friends from the Bat Cave and the Dungeon, especially Chelsea, Narelle and Kat, for all your support. Thank you my friends from the Cat Haven. Thank you, Anthea, for sharing your expertise, for your guidance, ethic and friendship.

I would like to express my deepest gratitude to my family, especially my parents Raimundo and Vania, my sister Vanessa, and my husband Joao, for their unconditional love and for always believing in me. Joao, thank you for your patience and for always being by my side, helping me through hard times and celebrating each accomplishment. Thank you all for being such an amazing family.

This thesis represents the work, ideas and assistance from many individuals. To all of you who have been involved in this study, I express my greatest thank you.

ABBREVIATIONS

ACP	Acepromazine
AEC	Animal Ethics Committee
ANP	Atrial natriuretic peptide
ASA	American Society of Anesthesiologists
ATP	Adenosine triphosphate
AUC	Area under the curve
BM	Body mass
BSA	Body surface area
CI	Confidence interval
CO₂	Carbon dioxide
ETCO₂	End-tidal carbon dioxide
GP	General practice
HR	Heart rate
HZ	Hertz
IBP	Invasive blood pressure
IM	Intramuscular
IV	Intravenous
l	Length
MAP	Mean arterial blood pressure
mmHg	Millimetres of Mercury
MUVH	Murdoch University Veterinary Hospital
η	Blood viscosity
NIBP	Non-invasive blood pressure
NO	Nitric oxide
O₂	Oxygen

P	Pressure
PCV	Packed cell volume
pH	Potential of hydrogen
Qt	Cardiac output
<i>r</i>	Radius
R	Resistance
SAP	Systolic blood pressure
SpO₂	Oxyhaemoglobin saturation
SV	Stroke volume
SVR	Systemic vascular resistance
T	Ventricular wall tension
TS	Total solids
USG	Urine specific gravity
<i>α</i>	Alpha
<i>β</i>	Beta
<i>π</i>	Constant 3.14