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# Surgical stress response in dogs diagnosed with pyometra undergoing ovariohysterectomy

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Kirurgisk stress på hundar diagnostiserade med pyometra  
som genomgår ovariehysterektomi

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## **ABSTRACT**

The aim of this study was to investigate the intraoperative surgical stress response in dogs undergoing ovariohysterectomy and to compare acepromazine and medetomidine as premedications. 15 dogs diagnosed with pyometra were used in this study. Blood pressure and heart rate were used as parameters to measure surgical stress response. The surgery was divided into four phases. Phase 0 was the period 10 minutes before the skin incision, phase 1 was skin incision and opening of abdomen, phase 2 was manipulation of uterine horns, ligation and transection of mesovarium and phase 3 was ligation of cervix, removal of organs and closing the abdomen.

The results showed that phase 2 was the most intense phase of surgical stress, regardless of which premedication the dogs received.

When acepromazine and medetomidine were compared the results showed that within phase 3, all dogs that were given medetomidine had higher blood pressure compared to dogs that were given acepromazine.

The dogs that were given acepromazine had higher heart rate than the dogs that were given medetomidine in phase 0, phase 2 and phase 3.

## **SAMMANFATTNING**

Målet med denna studie var att undersöka intraoperativ kirurgisk stress hos hundar som genomgår ovariehyστεrektomi och att jämföra acepromazin och medetomidin som premedicinering. 15 hundar som diagnosticerats med pyometra användes i denna studie. Blodtryck och hjärtfrekvens användes som parametrar för att mäta den kirurgiska stressen. Kirurgin delades in i fyra faser. Fas 0 var perioden 10 minuter före hudsnittet, fas 1 var hudsnittet och öppnandet av buken, fas 2 var manipulation av livmoderhornen och ligering av mesovariat och fas 3 var ligering av cervix, borttagande av organ och stängning av buken.

Resultatet visade att fas 2, ligering av mesovarie och borttagande av äggstockar, var den mest intensiva faser av kirurgisk stress, oavsett vilken premedicinering hundarna fick.

När acepromazin och medetomidin jämfördes visade resultaten att inom fas 3, ligering av cervix, borttagande av organ och stängning av buk, hade alla hundar som fått medetomidin högre blodtryck i jämförelse med hundar som fått acepromazin.

Hundar som fick acepromazin hade högre hjärtfrekvens än hundar som fick medetomidin i fas 0, fas 2 och fas 3.

## **INTRODUCTION**

Pyometra is a common disorder in female dogs in Sweden as few bitches are routinely spayed and therefore most bitches are intact. Nearly 25% of all insured bitches develop the illness before 10 years of age in Sweden (R. Hagman, 2004). The best and most effective way to treat the disease is surgery.

Surgical stress response is a physical response to trauma and surgery and has an important role in the recovery period after surgery. The duration and extent of the stress response are proportional to the development of complications, such as sepsis (J.P. Desborough, 2000). Most of the veterinary research that has been performed in this area has focused on preoperative or postoperative stress response and pain assessments in healthy animals. In this study, the intraoperative stress response in dogs diagnosed with pyometra was measured based on heart rate, blood pressure and the consumption of anesthetic gas.

The aim of this study was to investigate the intraoperative surgical stress response in dogs diagnosed with pyometra that were premedicated with either acepromazine or medetomidine and undergoing ovariohysterectomy.

## **LITERATURE STUDY**

### **Pyometra – background**

Pyometra is a common disease that almost 25% of insured bitches develop before 10 years of age in Sweden. In high risk breeds, for example Golden Retriever, Rottweiler, Cavalier King Charles Spaniel, Bernese Mountain Dog and rough-haired Collie, the proportion is higher and can be as high as over 50% (R. Hagman, 2004). According to S. Jitpean et al. (2012) the top five high breeds at risk for developing pyometra before ten years of age in Sweden are Bernese Mountain Dog, Great Dane, Leonberger, Rottweiler and Irish Wolfhound.

The disease is defined by a uterine infection that most often appears in metoestrus, with purulent fluid that accumulates in the uterus and different degrees of inflammatory cells in the endometrium and at times the myometrium (Small Animal Internal Medicine, 2009). Pyometra can be classified as either open-cervix or closed-cervix, where the closed-cervix pyometra often is more acute and has to be treated immediately (S.D. Pretzer, 2008). Pyometra is also characterized by uterine changes such as edema in variable degrees and necrosis and ulceration of the endometrium. It is a life threatening disease in severe cases as a bitch with pyometra can develop septicemia and endotoxemia in a very short period of time (Small Animal Internal Medicine, 2009).

The clinical features of pyometra are versatile where dehydration, polydipsia, polyuria, mucopurulent vaginal discharge, anorexia, vomiting, lethargy, abdominal pain, fever, hypothermia and raised heart and respiratory rates are common symptoms (S.D. Pretzer, 2008).

The diagnosis of pyometra is based on anamnesis, physical examination, diagnostic imaging (both ultrasound and radiography are helpful) and laboratory findings. On diagnostic imaging a fluid-filled, enlarged uterus is demonstrated, typically with echogenic fluid compared to mucometra and hydrometra where the fluid generally is anechoic. The most common findings in laboratory tests are neutrophilia with a left shift, white blood cell toxicity and monocytosis (R.W. Nelson et al., 2009).

Pyometra develops from several complex factors and the infection is in most cases (62-90%) caused by *Escherichia coli*. *E. coli* exists in the natural environment of the vagina and has the ability to reach the uterus during proestrus and oestrus (R. Hagman, 2004). Aetiological factors that predispose for pyometra are hormonal influences on the uterus, where progesterone and oestradiol are important. Virulence of the bacteria, the capacity of the host's immune system and the animal's sensitivity to inflammatory and bacterial products also affect whether the bitch is developing pyometra or not (R. Hagman, 2004; S.D. Pretzer, 2008).

Surgical treatment of pyometra is curative. Traditionally ovariohysterectomy is performed, where the patient is subjected to midline celiotomy, the uterus is removed whereafter the incision is closed.

### **Surgical stress response**

Stress response is the definition of a wide range of systemic reactions to injury and trauma. The stimulation of afferent neural pathways from the wound site is the most important regulation and initiation of the neuroendocrine stress response to trauma and surgery. The impulses travel along sensory nerve roots, via the spinal cord to the medulla and hypothalamus is activated. Both hormonal and metabolic changes are initiated. The evolutionary background is considered a protective mechanism by allowing injured animals to catabolize stored body fuels and therefore increase chance of survival (J.P. Desborough, 2000).

The endocrine part of the response is a general activation of the sympathetic nervous system and an increase in catabolic hormones (J.P. Desborough, 2000; Sibanda et al., 2006). These hormones include Adrenocorticotrophic hormone (ACTH), cortisol, catecholamines, glucagon and growth hormone (Sibanda et al., 2006; Ogawa et al., 2000). These changes lead to mobilization of substrates for energy sources, as well as salt and water retention for maintenance of fluid volume and cardiovascular homeostasis. The degree of surgical trauma and the hypersecretion of ACTH and cortisol are well correlated (Naitoh et al., 2002; Newsome N.H. 1971)

The metabolic changes in response to surgery are also meant to function as a survival mechanism where the animal could survive without food intake until the injury was healed. Blood glucose may increase during surgery because of the increased insulin resistance, glycogenolysis in the liver, increased gluconeogenesis, stimulated by cortisol and catecholamines. Also protein catabolism is stimulated. Increased cortisol levels also stimulate

protein catabolism. Skeletal muscles are broken down to release amino acids (J.P. Desborough, 2000).

Water and electrolytes are retained in the body because of increased release of ADH (Arginin vasopressin) and renin, as a response to surgery. Renin is synthesized and released from the kidneys and in turn stimulates aldosterone release. Aldosterone affects Na<sup>+</sup> and water reabsorption from the tubules in the kidney, to preserve sufficient body fluid volumes (J.P. Desborough, 2000).

## **Regulation of heart rate (HR) and blood pressure (BP)**

The heart rate is controlled by impulse generation in the SA (SinoAtrial) node, regulated by the autonomic nervous system as well as hormones. Via stimulation of the sympathetic nerves and consequently increased release of epinephrine, the heart rate increases. The reverse effect is caused by stimulation of the parasympathetic nervous system and the heart rate decreases. The balance between these two systems regulates the heart rate (Sjaastad et al., 2010).

Acetylcholine is released when the SA node and AV (AtrioVentricular) node is stimulated by the vagal nerve. The effect of the neurotransmitter is short because of the enzyme acetylcholinesterase, one of the contents in the SA and AV nodes, which breaks down acetylcholine (Sjaastad et al., 2010).

The sympathetic nervous system is regulated by norepinephrine from the postsynaptic sympathetic nerve endings and by epinephrine from the adrenal medulla. These hormones affect the adenylyl cyclase system, cAMP system, which affects the heart rate. Most of the norepinenephrine is transported back into the nerve endings directly after the release (Sjaastad et al., 2010).

Blood pressure depends on several factors such as the elasticity of the arteries, cardiac output, respiration cycle, resistance to blood flow and blood volume. Changes in emotions and physical activity can contribute to blood pressure changes. There is a short-term and long-term regulation of blood pressure (Sjaastad et al., 2010).

The short-term regulation is controlled by the cardiovascular center in the brain stem. A decrease in blood pressure is registered by baroreceptors located in the aortic arch and nerve endings in the carotid sinus. Baroreceptors act as a negative feedback system, where any changes in blood pressure gives signals to the brain stem that analyzes the information, compare the result to a reference level and if the pressure differs from normal levels, it is changed towards normal mean arterial pressure (MAP) (Sjaastad et al., 2010).

If the blood pressure falls rapidly, the sympathetic system increases and the parasympathetic system decreases. The activated sympathetic system leads to contraction of the veins, which causes increased venous return and thus increased stroke volume. Increased sympathetic activation results in increased heart rate and contraction of the arterioles leads to increased TPR (Total Peripheral Resistance). All these changes increase the blood pressure:  $MAP = CO$



× TPR (Mean Arterial Pressure = Cardiac Output × Total Peripheral Resistance). If the blood pressure on the other hand increases quickly, the brain stem will send opposite signals as described above, to decrease the pressure towards MAP.

The kidneys are responsible for the long-term regulation of the blood pressure. When the arterial pressure increases, the filtration of the kidneys also increases and the blood volume is adjusted to reach normal pressure levels (Sjaastad et al., 2010).

## **Effects of drugs on heart rate and blood pressure**

### ***Acepromazine***

Acepromazine is a neuroleptic substance that blocks the post-synaptic dopamine receptors in the Central Nervous System (CNS). The drug is mostly used as a tranquilizer in veterinary medicine. Among its adverse effects it causes hypotension and bradycardia (D.C. Plumb, 2011).

### ***Butorphanol***

Butorphanol acts as a partial opiate agonist/antagonist. It is used in small animal practice as analgesic, premedication, antiemetic and antitussive. Butorphanol decreases the heart rate by increased parasympathetic stimulation and therefore also decreases the arterial blood pressure (D.C. Plumb, 2011).

### ***Carprofen***

Carprofen is a Non-steroidal anti-inflammatory drug (NSAID) that has anti-inflammatory, antipyretic and analgesic effects. The substance is a weak cyclo-oxygenase (COX) inhibitor; the mechanism behind its main anti-inflammatory effect is unknown. No perioperative adverse effects on the cardiac system have been reported at recommended dosages (D.C. Plumb, 2011; Boström, Nyman et al., 2002).

### ***Medetomidine***

Medetomidine is an alpha-2 ( $\alpha_2$ ) adrenergic agonist that has sedative and analgesic effects. Some of the adverse effects are cardiac vasoconstriction, bradycardia and hypotension, but the effects on blood pressure vary (D.C. Plumb, 2011). Also the vasoconstrictive effects of Medetomidine may attenuate the hypotension induced by anesthetic agents (Väisänen 2002).

### ***Meloxicam***

Meloxicam is an NSAID and has no reported adverse effects on either heart rate or blood pressure (D.C. Plumb, 2011).

### ***Methadone***

Methadone is an opiate agonist ( $\mu$ -receptor agonist) and work as a non-competitive inhibitor of NMDA-receptors (N-Methyl-D-Aspartate receptors). Methadone also decreases the re-

uptake of serotonin and norepinephrine which may influence the analgesic effects of this drug. One of the adverse effects of methadone is bradycardia (D.C. Plumb, 2011).

### **Measurements of blood pressure - Oscillometric method**

Blood pressure can be measured with different techniques. When measured noninvasively, an external pneumatic cuff is placed around one limb, usually the front limb, and occludes a major artery by increasing the pressure in the cuff. When the pressure inside the artery is lower than the pressure in the cuff, the artery collapses. The pressure in the cuff slowly decreases and when the pressure in the cuff reaches below systolic pressure, the blood starts to flow through the artery and the systolic pressure is estimated. As the blood flows constantly through the artery, the diastolic blood pressure is estimated (C.F. Babbs, 2012).

The oscillometric method detects the small vibrations, or oscillations, at every cardiac contraction and the information is transferred to a computer. The oscillations increase as the cuff pressure drops between systolic pressure and mean arterial pressure. In the same way, the oscillations decrease when the cuff's pressure falls below mean arterial pressure. The point where the maximal oscillations are measured is very close to the mean arterial pressure. By use of an algorithm, the computer estimates both systolic and diastolic blood pressures (C.F. Babbs, 2012).

## **MATERIALS AND METHODS**

### **Animals**

Animals used in this study were bitches diagnosed with pyometra. Dogs of different breeds and ages were used (Table 1a and 1b). The dogs were privately owned and admitted to the university animal hospital (UDS) for treatment. All dogs were examined by an experienced veterinarian and diagnosis was confirmed with ultrasound and/or radiographs.

### **Premedication**

The dogs were given two different premedications, acepromazine or medetomidine. Which premedication the dogs received was decided by the surgeon. Dogs that were examined with ultrasound the same day as the surgery received medetomidine. 8 dogs had acepromazine and 5 dogs had medetomidine as premedication. 2 of the dogs had no premedications due to their severely affected general condition.

Different analgesia were used and the choice of analgesia was decided by the treating surgeon. The dogs received butorphanol, carprofen, meloxicam or methadone as analgesic agent, or a combination of these drugs.

Anesthesia was induced by intravenous infusion of propofol (PropoVet Multidose, 10mg/ml, Orion Pharma Animal Health) at symptomatic dosage and maintained with inhalation of isoflurane mixed in air at 2-3%. The concentration of administered isoflurane was controlled by the veterinary assistant who monitored the anesthesia.

## **Anesthetic monitoring**

Life Window is an anesthetic monitoring device which uses an oscillometric method for measuring blood pressure with a non-invasive technique. An automatic pneumatic cuff was placed on the distal forelimb. The device measured the systolic pressure, diastolic pressure and Mean Arterial Pressure. Life Window also measured heart rate and concentration of anesthetic gas (EtAgas) (C.F. Babbs, 2012). The device saved the data every minute and transferred it to an excel file.

## **Protocol**

A protocol was designed and used for following the different parts of the surgery in the anesthetic monitoring file. For comparison and evaluation of the surgical stress response the surgery was split into four phases: 10 minutes immediately before skin incision (phase 0), skin incision and opening of abdomen (phase 1), manipulation of uterine horns, ligation and transection of mesovarium (phase 2), ligation of cervix, removal of organs and closing (phase 3). Other actions by the surgeon that could affect the surgical stress response were noted in the protocol. The exact time when all procedures were performed were noted in the protocol.

## **Surgery**

The surgery was performed by different surgeons. The animal's abdomen was clipped and cleaned and the dog was placed in dorsal recumbency. A ventral midline incision 2-3 cm cranial to umbilicus was made and extended caudally. The uterus was located and the ovaries were identified and a hole was made in the mesovarium. Hemostat forceps were placed across the ovarian pedicle. One or two ligatures were placed proximal to the ovary. An absorbable suture size 2-0 or 3-0 was used. A ligature was also placed over the broad ligament. The procedure was repeated on the contralateral side. The uterine body was ligated at the cranial tip of the cervix. The ligated tissue was observed for hemostasis. The abdominal wall was closed in three layers (linea alba, subcutaneous tissue and skin).

## **Statistics**

The effects of different premedications and surgery on heart rate, systolic blood pressure and end-tidal concentration of Isoflurane were analyzed using mixed linear models for repeated measured data (Littell R.C et al., 2006; Fitzmaurice G.M et al., 2004). The least square means (and standard error of least square means) were computed and compared (SAS, Procedure mixed) for each phase. The means or least square means of each phase is reported (Table one: mean. Others: LS mean). Level of significance was set to  $P < 0.05$ .

## RESULTS

Physical parameters and results of imaging of the 15 dogs in the study are presented in table 1a and 1b.

**Table 1a**

Physical parameters and findings of the 15 dogs

Dog	Age	Breed	Weight	Vital signs*	HR**	Temp	Premed
1	8	Border Terrier	8,3 kg	NAD***	72	38,3°	Medetomidine Methadone
2	8	Labrador Retriever	30,3 kg	Stressed, wheezy	180	39,3°	Medetomidine Methadone Butorphanol
3	1	Golden Retriever	26,9 kg	NAD	80	38,7°	Acepromazine Methadone
4	6	Giant Schnauzer	35,9 kg	Dull	-	38,9°	Acepromazine Methadone
5	4	Australian Kelpie	12,6 kg	NAD	-	39,0°	Acepromazine Methadone
6	12	Golden Retriever	38,7 kg	General condition ↓, wheezy	104	38,7°	Methadone
7	6	Mixed-breed	30 kg	General condition slight ↓	72	38,8°	Medetomidine Methadone Meloxicam
8	6	Shetland Sheepdog	9,4 kg	NAD	-	38,6°	Acepromazine Methadone Carprofen
9	6	Airedale Terrier	23,2 kg	NAD	-	38,4°	Acepromazine Methadone
10	8	Labrador Retriever	36 kg	General condition ↓, sore abdomen	100	38,7°	Methadone
11	1	Shih Tsu	6,6 kg	General condition mildly ↓	120	38,3°	Medetomidine Methadone
12	7	English Springer Spaniel	20,8 kg	General condition moderate ↓, dehydrated	96	39,1°	Acepromazine Methadone
13	8	Cavalier King	9,5 kg	NAD (heart murmurs)	130	38,7°	Acepromazine Methadone

14	3	Charles Spaniel Bernese Mountain Dog	46,5 kg	NAD (2,5 weeks before surgery)	-	38,3 (2,5 weeks before surgery)	Acepromazine Methadone
15	10	Border Collie	20,2 kg	NAD	-	-	Medetomidine Methadone Buthorphanol

\*Such as general condition, stress or anxiety

\*\*HR = Heart Rate

\*\*\* NAD = No Abnormalities Detected

**Table 1b**

Physical parameters and findings at examination of the urogenital apparatus of the 15 dogs

Dog	Vaginal discharge	Diagnosed by Radiograph	Diagnosed by Ultrasound	Complications to surgery
1	No	No	Fluid seen in uterus, normal size	No
2	No	No	Mildly enlarged uterus, fluid contents	No
3	Yellow-white	Uterine fluid, anechoic and hyperechoic	Small amounts of anechoic fluid. Endometrium irregular and thickened.	No
4	No	No	Enlarged uterus, mild amount of fluid in left uterine horn	3 weeks post surgery: Lethargy. Unknown cause.
5	Yes	No	Enlarged uterus, anechoic fluid	3 weeks post surgery: Lethargy, polydipsia, fever. Unknown cause.
6	Brown-bloody	Enlarged uterus	No	UTI
7	No	Dilated uterine horns, anechoic fluid	No	No
8	Bloody	No	Mild inflammatory changes of the uterus, anechoic fluid	No
9	No	No	Fluid in uterus, 3-4 cm	No
10	Purulent, smelly	Uterus 1,5-2 cm	Enlarged fluid-filled uterus, possible peritonitis	No
11	No	Normal abdomen	Focally enlarged area with hypoechoic content, uterus 1,2 cm	No
12	No	Enlarged uterus	No	No
13	Yes,	No	Enlarged uterus, 2,5 cm, echoic	No

	moderate.		fluid	
14	No	No	Mild amount fluid, endometrium cysts	No
15	No	No	Mildly enlarged uterus, anechoic fluid.	No

The mean values of systolic blood pressure, heart rate and EtAgas from all 15 dogs are shown in table 2.

**Table 2**

Systolic blood pressure, Heart rate and EtAgas (means) of the 15 dogs included in the study

All dogs	Phase 0	Phase 1	Phase 2	Phase 3
Syst BP	91,5	90,9	114,8	105,6
Heart rate	89,4	91,6	101,9	101,4
EtAgas	1,9	1,8	2,1	2,0

## Results systolic blood pressure (BP)

### ***Acepromazine as premedication:***

Dogs that were given acepromazine (n=8) as premedication had significantly higher blood pressure during phase 2, than all other phases (phase 0, 1 and 3). In phase 3, the dogs had significantly higher blood pressure compared to phase 0. See table 3.

### ***Medetomidine as premedication:***

Dogs that were given medetomidine (n=5) as premedication had significantly higher blood pressure during phase 2, compared to phase 0 and phase 1. Also phase 3 showed significantly higher blood pressure than phase 0 (table 3).

### ***Comparison between groups***

Within phase 3, all dogs that were given medetomidine (n=5) had higher blood pressure compared to dogs that were given acepromazine (n=8) as premedication (table 3).

**Table 3**

Systolic blood pressure (LSMean) in dogs diagnosed with pyometra and subjected to ovariohysterectomy.

Premed	Phase 0	Phase 1	Phase 2 <sup>a,b</sup>	Phase 3 <sup>a,b</sup>	n
Acepromazine	87,1	86,8	113,5 <sup>a,b</sup>	101,0 <sup>a,b,c</sup>	8
Medetomidine	101,4	99,0	131,8 <sup>a,b</sup>	135,0 <sup>a,c</sup>	5
No premed	91,2	101,0	106,2 <sup>a</sup>	92,6 <sup>b</sup>	2

Significant differences were calculated by the mixed procedure (SAS) with Tukey-Kramer's adjustment ( $P < 0.05$ ).

<sup>a</sup> = differ significantly compared with phase 0

<sup>b</sup> = differ significantly compared with previous phase

<sup>c</sup> = differ significantly between groups

## Results heart rate (HR)

### ***Acepromazine as premedication***

All dogs that were given acepromazine (n=8) had significantly higher heart rate during phase 2, compared to phase 0 and phase 1. The heart rate of phase 3 was higher compared to phase 0 (table 4).

### ***Medetomidine as premedication***

The dogs in the medetomidine group (n=5) had significantly higher heart rate in phase 2 and phase 3, in comparison to phase 0.

### ***Comparison between groups***

The dogs in the acepromazine group (n=8) had significantly higher heart rate than the medetomidine group in phase 0, phase 2 and phase 3 (table 4).

**Table 4**

Heart rate (LSMean) in dogs diagnosed with pyometra and subjected to ovariohysterectomy.

Premed	Phase 0	Phase 1	Phase 2 <sup>a,b</sup>	Phase 3 <sup>a</sup>	n
Acepromazine	95,3 <sup>d</sup>	94,1	108,0 <sup>a,b,d</sup>	107,9 <sup>a,d</sup>	8
Medetomidine	66,4	73,1	77,0 <sup>a</sup>	78,0 <sup>a</sup>	5
No premed	121,4 <sup>d</sup>	120,0 <sup>d</sup>	114,5	115,1	2

Significant differences were calculated by the mixed procedure (SAS) with Tukey-Kramer's adjustment ( $P < 0.05$ ).

<sup>a</sup> = differ significantly compared with phase 0

<sup>b</sup> = differ significantly compared with previous phase

<sup>c</sup> = differ significantly between groups

<sup>d</sup> = differ significantly from Med within phase

## Results EtAgas

The concentration of isoflurane that was used during surgery was significantly higher in the acepromazine group ( $n=8$ ) during phase 2, compared to phase 0, phase 1 and phase 3. See table 5.

**Table 5**

EtAgas concentration (LSMean) during surgery in dogs with pyometra subjected to ovariohysterectomy.

Premed	Phase 0	Phase 1	Phase 2	Phase 3	n
Acepromazine	1,9	1,9	2,1 <sup>a,b</sup>	2,0 <sup>b</sup>	8
Medetomidine	2,0	2,0	2,0	2,0	5

Significant differences were calculated by the mixed procedure (SAS) with Tukey-Kramer's adjustment ( $P < 0.05$ ).

<sup>a</sup> = differ significantly compared with phase 0

<sup>b</sup> = differ significantly compared with previous phase



## DISCUSSION

The aim of this study was to investigate the intraoperative surgical stress response in dogs diagnosed with pyometra undergoing ovariohysterectomy. Acepromazine and medetomidine as premedications were also compared. The surgery was divided into four phases for comparison and evaluation of the surgical stress response. Blood pressure and heart rate increased at removal of ovaries.

The results showed that all dogs had highest blood pressure during phase 2, highest heart rate during phase 2 and phase 3. The amount of used EtAgas was highest during phase 2 in dogs premedicated with acepromazine. EtAgas could not be measured in the two dogs without premedications and is therefore not evaluated. Phase 2, ligation of mesovarium and removal of ovaries was the most intense phase of surgical stress, regardless of which premedication the dogs received.

When acepromazine and medetomidine as premedication were divided into two groups, the data varied more. The blood pressure increased at removal of the ovaries in dogs premedicated with medetomidine. Additionally their blood pressure remained at a higher level in phase 3 compared in dogs premedicated with acepromazine. This was unexpected in view of the results of Väisänen (2002) where blood pressure in the medetomidine group decreased at the end of the surgery. One possible explanation for the unexpectedly high blood pressure in the medetomidine group was differences in time from premedication to surgery. Most of the dogs that were diagnosed with ultrasound and were subjected to surgery on the same day were premedicated with medetomidine. If the premedication with medetomidine began to lose its effect at time of surgery, a higher blood pressure compared to that of acepromazine would be expected which is in agreement with the results of this study. Another possible explanation to the higher blood pressure in phase 3 in the medetomidine group is the shorter half-life of medetomidine compared to acepromazine following i.v. administration (medetomidine: 1,2h, acepromazine: 4-5h or up to 7h) (Fass vet. 2013; Hashem A. et al., 1992). It could be hypothesized that the level of medetomidine in the blood was too low to affect the blood pressure in phase 3. A comparison to the group without premedication should be cautious as the group was small (n=2).

The heart rate had a relatively small increase during phase 2 and phase 3 compared to phase 0 in the medetomidine group. At removal of ovaries the heart rate was lower compared to other groups. A possible explanation could be that the concentration of medetomidine in the body was high enough to affect the heart rate but too low to affect the blood pressure.

According to Väisänen (2002), the powerful bradycardic effects of medetomidine could explain the lower heart rate in the medetomidine group compared to the acepromazine group. But opioids might have contributed to the effects. Väisänen's study (2002) suggested that the great hypotensive actions of acepromazine and its milder sympathetic attenuation could explain the higher heart rates in the acepromazine group compared to the medetomidine group.

An increased symptomatic dosage of anesthetic gas was demonstrated at removal of the ovaries in the acepromazine group. Removal of ovaries is considered maximum noxious stimuli (Bubalo et al., 2008; Höglund et al., 2011). Attempts to reduce the noxious stimuli at removal of the ovaries by adding local anesthetic to the mesovarium has been investigated with no proven benefit in dogs (Bubalo et al., 2008) but with positive effects shown in cats (Zilberstein et al., 2008).

There were study limitations. The dogs used in this study were few and individual variations may have affected the results. The time between administration of premedication and surgery varied.

Another variable that could have influenced the result is the dog's general condition. Their status of pain, blood pressure and endotoxin influence before surgery varied and this could have affected the premedication's effect on blood pressure and heart rate. No measurements of heart rate or blood pressure were made before or after surgery.

## **CONCLUSION**

Blood pressure and heart rate increased at removal of the ovaries in dogs diagnosed with pyometra and subjected to ovariectomy, both in the acepromazine group and the medetomidine group.

When acepromazine and medetomidine were compared the results showed that within phase 3, all dogs that were given medetomidine had higher blood pressure compared to dogs that were given acepromazine.

The dogs that were given acepromazine had higher heart rate than the dogs that were given medetomidine in phase 0, phase 2 and phase 3.

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