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PHYSIOLOGY OF PREGNANCY AND ANESTHESIA FOR CESAREAN SECTION IN DOGS

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Introduction

All major body systems undergo adaptation during pregnancy and many of these changes have a significant impact on anesthetic management. Some data is extrapolated from humans and some data has been published based on dogs studies, but much less is known about cats.

The Cardiovascular System.

Significant cardiovascular changes, which continue to progress until term, have been documented as early as mid-pregnancy in dogs. There is a decrease in blood pressure and an increase in heart rate and cardiac output [1]. Although total blood volume increases, red blood cells do not keep pace with plasma expansion resulting in anemia, the severity of which is correlated with the number of puppies [2]. The fetus is vulnerable to changes in the mother’s cardiovascular system because fetal blood flow is not autoregulated and uterine perfusion is pressure-dependent. The consequences of maternal changes are obvious when it is understood that uterine blood flow is directly proportional to the arterial-venous blood pressure difference and inversely proportional to systemic vascular resistance. Anesthetic drugs, dehydration and intra-operative fluid losses will result in maternal hypotension. Fear, stress, excitement and pain can all cause increased sympathetic nervous system activity resulting in vasoconstriction and increased systemic vascular resistance; all of which will adversely affect the fetus. Pregnant animals appear to have blunted cardiovascular responses and are less able to tolerate hypovolemia [3]. Hypotension occurs more rapidly after hemorrhage in pregnant bitches compared with non-pregnant dogs. In addition, resuscitative efforts with vasopressors or chronotropic drugs are less effective [4]. Intra-operative fluids were administered to only 53% of canine caesarean sections [5] suggesting that cardiovascular support for these patients is an area that can be improved.

The Respiratory System

Pregnant patients are at risk for hypoxemia especially during induction of anesthesia if oxygen supplementation has not been provided in advance of hypoventilation or apnea. The functional residual capacity (FRC) acts as a reservoir in the lungs and this volume is decreased in pregnant animals making them more susceptible to rapid hemoglobin desaturation. Because total lung volume is lower, atelactasis is more likely. In addition, pregnant animals have an increased oxygen demand, which they meet with an increase in minute ventilation. Three to five minutes of pre-oxygenation with a facemask should be attempted in all pregnant patients to increase oxygen reserves, and prolong the time taken for hemoglobin to desaturate if apnea occurs, or a difficult intubation is anticipated; for example in a brachycephalic breed. “Sighing” is recommended during surgery as it may decrease the degree of atelectasis. Closing the pop-off valve on the anesthetic circuit and squeezing the reservoir bag briefly (1 to 2 seconds) at a pressure of 15-20 cm H_2O achieves this. Maternal hypoventilation can lead to fetal hypoxia and acidosis and either manual or mechanical intermittent positive pressure ventilation may be required. However, overzealous ventilation causing hypocapnia ($PaCO_2$ < 32 mm Hg) is detrimental because alkalosis increases uterine vascular resistance and a left shift of the oxygen dissociation curve so that there is less fetal unloading of oxygen. Obviously, there is a critical balance between too much and too little respiratory support and careful patient monitoring is important. Pulse oximeters should be used to evaluate oxygen saturation and capnometers to indicate the adequacy of ventilation. These monitors are especially useful in pregnant patients because these patients are, first, more likely to become hypoxemic than a non-pregnant patient and secondly, because they have a smaller tidal volume and higher respiratory rate, it is challenging to diagnose hypoventilation based solely on clinical signs.

The Central Nervous System

Pregnant animals have reduced requirements for inhalant agents and this can lead to over dosage or apparent “sensitivity”. The sedative effects of circulating progesterone [4] and analgesic actions of elevated -endorphin levels [6] are thought to be responsible for this phenomenon which has been demonstrated clearly in humans, sheep and dogs. The dose of inhalant agents such as isoflurane [7] and halothane [8] (as measured by minimum alveolar concentration [MAC] studies) for pregnant patients can decrease by as much as 25-40%. The clinical implications of reduced anesthetic requirements, plus the more rapid uptake of inhalant agents because of the high minute ventilation in pregnant animals are obvious. These differences may be most apparent if a mask induction is performed; under those circumstances a rapid loss of unconsciousness would be expected. Drugs must be given to effect and the depth of anesthesia must be carefully and frequently assessed.

The Gastrointestinal System

Gastric reflux is more likely because of the increased intra-abdominal pressure created by the fetuses pressing on the diaphragm and a hormone-induced relaxation of the gastro-esophageal junction [9]. Gastric emptying is delayed by pregnancy and the stomach contents are more acidic. Loss of laryngeal reflexes at induction of anesthesia makes aspiration and pneumonitis a possible sequel if rapid intubation is not achieved. In humans, this complication which is referred to as Mendelson's syndrome can be life-threatening [9]. Moon et al [5] reported that 5 out of 9 bitches whose death was associated with caesarean section had pneumonia suggesting that aspiration is also an important risk factor in dogs. This information justifies the recommendation for rapid airway control with an endotracheal tube after anesthetic induction. It is also important to question the owner for a history of vomiting and, on presentation, to closely evaluate lung fields, so prompt treatment can be initiated if aspiration has occurred. Damage to the pulmonary tree is primarily caused by the acidity of the aspirate and although antibiotics should not be withheld, their value in this situation is controversial. Vomiting and regurgitation during recovery are also possible so the endotracheal tube should not be removed until the patient regains adequate control of their airway.

Survival rates

Immediate survival rate of puppies delivered by Caesarean-section is reported as 92% falling to 87% and 80% at two hours and 7 days, respectively [10]. Although this is much improved from reports in the 1960's when mortality rates were as high as 36% [11], it is still much greater than infant mortality following C-section in women [12]. Mortality rates for bitches undergoing caesarean section have dropped from approximately 13% [11] to 1% [5, 10] over the past 40 years but is high compared to women in developed countries where overall maternal mortality has dropped to approximately 1 in 10,000 deliveries. Much of this improved success in women is attributed to better anesthetic management [13]. We must strive for higher survival rates in our veterinary patients and their offspring.

Preparation for surgery

Over half of canine cesarean sections are emergency procedures [10]. Puppy mortality is 12.7% in an emergency situation compared to 3.6% when the procedure is elective. When labour is prolonged, dehydration, hypovolemia, sepsis, stress, exhaustion, and hypocalcaemia may be present leading to worse outcomes. Elective procedures should be considered in Bulldogs which constitute 17% of all cesarean sections [5]. In an elective situation there is time for a complete physical examination and blood work. In an emergency there may be no time to await results of all blood work, but a hematocrit, total protein, blood urea nitrogen, and blood glucose should always be measured before embarking on surgery. At least one intravenous catheter should be placed and fluids given to dehydrated, hypovolemic or hypotensive patients before induction; larger breeds may require 2-3 liters of crystalloid fluids and, in most circumstances; any balanced electrolyte solution can be used. All bitches should receive intra-operative fluids at a rate of 10-20 mls/kg/hour to compensate for the substantial fluid losses associated with surgery.
Aortocaval compression in the supine position producing maternal hypotension is well documented in pregnant women. It has been suggested that because the dog's uterus is bicornuate, this does not occur in this species. In anesthetized small breed dogs, pregnant dogs had lower blood pressures than non-pregnant dogs, irrespective of position [14]. In another study, healthy Golden Retriever bitches remained normotensive in both dorsal and lateral recumbency regardless of pregnancy status [15]. This suggests that pregnant patients may be prone to hypotension and that this susceptibility is not always related to patient positioning. It is important to note that these studies were performed on healthy dogs weighing less than 27 kg. However, most caesarean sections in practice are not elective and 45% of the bitches in one report weighed over 27 kg and 25% weighed more than 41 kg [5]. Therefore, the impact of dorsal positioning for a specific case scenario is unpredictable.
Clipping and preparing the surgical site prior to induction of anesthesia decreases the time between induction and delivery of puppies. Administration of sedatives and analgesics to anxious, aggressive, or fractious dams decreases maternal stress and accompanying vasoconstriction, and allows clipping and administration of oxygen. Many clinicians are concerned that premedication causes neonatal depression. However, this concern was not borne out in a study correlating different anesthetics with puppy mortality (with the exception of xylazine) [10] or vigor [10]. Xylazine was associated with increased puppy mortality [10]. All other common premedicants and opioids were used successfully [10]. If properly dosed based on maternal status, premedicants may decrease maternal anxiety, provide analgesia (for labor pain and surgical pain), reduce anesthetic requirements, and smooth induction and recovery.

Anesthetic management

In humans, the improvements in epidural and spinal techniques are given credit for the current low mortality rates for both mothers and offspring [9]. In veterinary medicine there are insufficient data to state whether general or regional anesthesia is safer. Placental drug transfer occurs with all injectable and inhalant anesthetic agents. Careful titration of drugs to provide adequate analgesia for the dam but minimal depression of the fetus is one essential skill the anesthetist must learn.

Local anesthetic techniques

Epidural or spinal anesthesia using local anesthetic agents with or without an opioid may be used as the sole technique and produce minimal fetal depression. However, local anesthetics placed in the epidural or subarachnoid space produce systemic vasodilation and hypotension [16]. Prior fluid loading and continued fluid administration during surgery is essential to prevent decreased uterine perfusion and fetal compromise. The ideal patient for this technique is the healthy bitch, but in practice few patients will tolerate being placed in dorsal recumbency while fully conscious. Debilitated and exhausted dams that may tolerate this technique can become severely hypotensive because of pre-existing hypovolemia. In a non-pregnant animal 1 milliliter of 2% lidocaine per 5 kg of body weight deposited epidurally will produce a block up to the level of L2 [17]. In the pregnant animal, this dose may produce a higher block because distended epidural veins, a consequence of increased intra-abdominal pressure, decrease the size of the epidural space. Lidocaine is the agent of choice, as this will provide 60-90 minutes of surgical analgesia, sufficient for a caesarean section and allowing rapid return to normal function. A danger of this technique is that the airway is not protected and regurgitation and vomiting are possible when the bitch is placed in dorsal recumbency. Local infiltration (line block) with a local anesthetic without epinephrine along the midline before making the incision is a worthwhile technique in anesthetized animals. It is easy and quick to perform, and may reduce anesthetic requirements and improve immediate post-operative comfort.

General anesthesia

Propofol and thiobarbiturates have the advantage of rapid onset and short duration with minimal residual fetal depression [18], but can cause cardiovascular depression and decreased uterine blood flow. Transient apnea is common following administration and may result in fetal hypoxia and acidemia if the mother is not pre-oxygenated, rapidly intubated, and ventilated. Propofol is associated with better puppy vigor than barbiturates [19]. Maintenance of anesthesia with propofol is not yet recommended in humans because of lower neurological and adaptive capacity scores in the offspring compared to thiopental [20]. However, when compared to isoflurane, total intravenous anesthesia with propofol in pregnant ewes resulted in superior hemodynamics [21].

The dose of all induction agents and therefore their side-effects can be reduced by first giving intravenous lidocaine (0.25-0.5 mg/kg), diazepam (0.1-0.4 mg/kg), or midazolam (0.1-0.3 mg/kg). Ketamine (4-6 mg/kg i.v.) combined with diazepam (0.1-0.4 mg/kg i.v.) or midazolam (0.1-0.3 mg/kg i.v.) is an alternative induction technique that provides good cardiovascular support. Ketamine combinations do not affect overall puppy survival but have necessitated more vigorous resuscitative efforts [19]. In compromised dams, etomidate (2 mg/kg i.v.) is recommended because of its minimal cardiovascular effects. When used alone etomidate may cause gagging or retching but when used in combination with a benzodiazepine, these side-effects are reduced. Opioids provide analgesia and reduce anesthetic requirements. Morphine, methadone, oxymorphone, hydromorphone and buprenorphine can all be used. Vomiting is least likely with buprenorphine, methadone and meperidine. Detrimental side-effects from opioids are rare, but include respiratory depression and bradycardia both of which can be managed with respiratory support and anticholinergics respectively. If bradycardia occurs after opioids have been administered to the dam, atropine (0.02-0.04 mg/kg i.v. or i.m.) is the anticholinergic of choice because glycopyrrolate does not cross the placental barrier and the opioid-induced bradycardia may also be present in the fetuses. Opioids were not a risk factor during C-section in the dog [10].

Xylazine is associated with higher neonatal mortality after caesarean section. Although xylazine was the only alpha2-agonist evaluated in this study, the implication is that none of the drugs in this class can be recommended. Halothane did not have a positive or negative effect on caesarean-derived puppies and isoflurane was associated with improved neonatal survival [10]. There is no data for sevoflurane.
For an uncomplicated C-section, induction with propofol followed by maintenance with isoflurane with or without premedication with acepromazine and an opioid is recommended. In critically ill dams, a small i.v. dose of fentanyl (5-10 µg/kg i.v.) prior to induction with etomidate (1-2 mg/kg i.v.) is suggested. In both situations, a line block with local anesthesia is advocated and an analgesic can be administered as soon as the puppies are removed. Induction of anesthesia with inhalant agents is not recommended because of the delay in protecting the airway and possible maternal excitement and struggling that would be detrimental to uterine blood flow.

Intra-operative management

The two most important functions to maintain within normal limits are maternal oxygen delivery and uterine blood flow. Since these cannot be easily measured we rely on the assumption that an adequate hematocrit, heart rate, blood volume, and blood pressure will maintain these at acceptable levels. Intravenous fluids should be administered pre-, intra- and also post-operatively in some critical cases. Simply increasing the rate of fluid administration and decreasing anesthetic delivery can treat mild hypotension. Adding analgesic agents (e.g.fentanyl) to an inhalation protocol will permit a decrease in vaporizer setting and usually results in an improved blood pressure. Refractory hypotension should be treated with ephedrine (0.04-0.1 mg/kg i.v.) because of its ability to maintain or improve uterine blood flow despite its vasoconstrictive properties. Dopamine (1-5 µg/kg/min i.v.) or dobutamine (1-5 µg/kg/min i.v.) can also be used. Epinephrine will dramatically decrease uterine blood flow and should only be used to save the life of the mother in catastrophic situations such as rupture of the uterine artery. If the dam becomes bradycardic, look for an underlying cause (deep anesthesia, hypothermia, hypoxia, etc). If the bradycardia is opioid-induced, atropine should be used for the reasons described above. Other causes of bradycardia can be temporarily alleviated with glycopyrrolate (0.01-0.02 mg/kg i.v.) because it will not cross the blood brain barrier and will not result in unnecessary fetal tachycardia.

Blood loss during a caesarean section is typically not enough to be life-threatening and can be treated with crystalloids at three times the volume of estimated blood loss. However, 25% of pregnancy-related deaths in women are associated with hemorrhage [22] and such life-threatening situations can occur in the dog. Bleeding can be rapid and severe and under emergency circumstances it is unlikely that a suitable cross-matched donor is readily available. In pregnant sheep, hemorrhage caused maternal hypotension and reduced oxygen content without any change in blood gas measurements [23]. There was a drop in uterine blood flow and fetal oxygenation fell causing fetal acidosis. In this situation, maternal blood pressure can be restored by hetastarch 6%, autologous blood or a hemoglobin based oxygen carrier such as a polymerized bovine hemoglobin solution. Only the latter two fluids can restore fetal oxygenation [23]. Hypothermia can lead to increased bleeding and post-operative wound infection in the dam and effects on the fetus include lower core temperature and acidosis. When mothers were warmed with forced warm air systems there was significantly less post-operative shivering, and babies were warmer and had higher umbilical vein blood pH [24].

Post-operative management

A painful dam may not let her puppies nurse and an overly sedated dam may be unable to care for her offspring. Opioids can be administered pre- and post- operatively. Non-steroidal anti-inflammatory agents can provide excellent analgesia but should not be given in the face of hypotension or hypovolemia because they interfere with renal perfusion. Postoperatively, continuous assessment of the dam's condition is required to determine the need for cardiovascular support, oxygen supplementation, a warmer environment or any other intervention.

References

1. Pascoe, P.J. and P.F. Moon, Periparturient and neonatal anesthesia. Vet Clin North Am Small Anim Pract, 2001. 31(2): p. 315-40, vii.
2. Kaneko, M., et al., Relationship between the number of fetuses and the blood constituents of beagles in late pregnancy. J Vet Med Sci, 1993. 55(4): p. 681-2.
3. Brooks, V.L. and L.C. Keil, Hemorrhage decreases arterial pressure sooner in pregnant compared with nonpregnant dogs: role of baroreflex. Am J Physiol, 1994. 266(4 Pt 2): p. H1610-9.
4. Camann, W.R. and G.W. Ostheimer, Physiological adaptations during pregnancy. Int Anesthesiol Clin, 1990. 28(1): p. 2-10.
5. Moon, P.F., et al., Perioperative management and mortality rates of dogs undergoing cesarean section in the United States and Canada. J Am Vet Med Assoc, 1998. 213(3): p. 365-9.
6. Gintzler, A.R., Endorphin-mediated increases in pain threshold during pregnancy. Science, 1980. 210(4466): p. 193-5.
7. Gin, T. and M.T. Chan, Decreased minimum alveolar concentration of isoflurane in pregnant humans. Anesthesiology, 1994. 81(4): p. 829-32.
8. Chan, M.T., P. Mainland, and T. Gin, Minimum alveolar concentration of halothane and enflurane are decreased in early pregnancy. Anesthesiology, 1996. 85(4): p. 782-6.
9. Dresner, M.R. and J.M. Freeman, Anaesthesia for caesarean section. Best Pract Res Clin Obstet Gynaecol, 2001. 15(1): p. 127-43.
10. Moon, P.F., et al., Perioperative risk factors for puppies delivered by cesarean section in the United States and Canada. J Am Anim Hosp Assoc, 2000. 36(4): p. 359-68.
11. Mitchell, B., Anaesthesia for caesarean section and factors influencing mortality rates of bitches and puppies. Vet Rec, 1966. 79(9): p. 252-7.
12. MacDorman, M.F., et al., Infant and neonatal mortality for primary cesarean and vaginal births to women with "no indicated risk," United States, 1998-2001 birth cohorts. Birth, 2006. 33(3): p. 175-82.
13. Cooper, G.M., G. Lewis, and J. Neilson, Confidential enquiries into maternal deaths, 1997-1999. Br J Anaesth, 2002. 89(3): p. 369-72.
14. Probst, C.W. and A.I. Webb, Postural influence on systemic blood pressure, gas exchange, and acid/base status in the term-pregnant bitch during general anesthesia. Am J Vet Res, 1983. 44(10): p. 1963-5.
15. Probst, C.W., R.V. Broadstone, and A.T. Evans, Postural influence on systemic blood pressure in large full-term pregnant bitches during general anesthesia. Vet Surg, 1987. 16(6): p. 471-3.
16. Chan, W.S., et al., Prevention of hypotension during spinal anaesthesia for caesarean section: ephedrine infusion versus fluid preload. Anaesthesia, 1997. 52(9): p. 908-13.
17. Skarda, R., Local and Regional Anesthetic Techniques: Dogs, in Lumb & Jones' Veterinary Anesthesia., T.W. Thurmon JC, Benson GJ, Editor. 1996, Williams & Wilkins: Baltimore. p. 426-447.
18. Siafaka, I., et al., A comparative study of propofol and thiopental as induction agents for elective caesarean section. Clin Exp Obstet Gynecol, 1992. 19(2): p. 93-6.
19. Moon-Massat, P. and H. Erb, Perioperative factors associated with puppy vigor after delivery by cesarean section. J Am Anim

Hosp Assoc, 2002. 38(1): p. 90-96.
20. Yau, G., et al., Propofol for induction and maintenance of anaesthesia at caesarean section. A comparison with thiopentone/enflurane. Anaesthesia, 1991. 46(1): p. 20-3.
21. Gaynor, J.S., et al., A comparison of the haemodynamic effects of propofol and isoflurane in pregnant ewes. J Vet Pharmacol Ther, 1998. 21(1): p. 69-73.
22. Klein, H.G., The prospects for red-cell substitutes. N Engl J Med, 2000. 342(22): p. 1666-8.
23. Moon, P.F., et al., Fetal oxygen content is restored after maternal hemorrhage and fluid replacement with polymerized bovine hemoglobin, but not with hetastarch, in pregnant sheep. Anesth Analg, 2001. 93(1): p. 142-50.
24. Horn, E.P., et al., Active warming during cesarean delivery. Anesth Analg, 2002. 94(2): p. 409-14, table of contents.