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Abstract

Cesarean sections are a common procedure in veterinary medicine and specific anesthesia techniques have been recommended. Anesthesia for non-obstetric surgery during pregnancy is very rare. Independent of the purpose, anesthesia principles are going to be fairly similar although anesthesia for non-obstetric surgery includes special considerations like teratogenicity of compounds used, prevention of premature labor, and avoidance of fetal asphyxia. These concerns make anesthesia for the gravid animal a unique and problematic situation for the veterinarian. The main objective is to provide the safest possible anesthetic to the mother while preserving fetus safety. This review focuses on fundamental maternal physiological principles, core to the adequate care of pregnant mothers and fetuses, and reviews the most recent literature on the subject to provide tips and recommendations for the veterinarian whenever this challenging clinical scenario arises.

Keywords: Anesthesia, pregnancy, fetal safety, cesarean, non-obstetric

Introduction

Anesthetic management of pregnant patients represents a big challenge for the veterinarian. Due to uncertain drug effects on fetal development and high maternal anesthetic risk, any unnecessary anesthesia during pregnancy should be postponed. However, on occasion anesthesia is required and the most sensible approach requires a good understanding of maternal and fetal physiology, altered drug pharmacology, and thorough risk analysis of the clinical situation. The most recent veterinary literature shows maternal mortalities of 9 to 16% in mares,1-4 19% in sheep and goats,5 and 1% in pregnant dogs6 presenting for cesarean section with or without dystocia. Although maternal mortality associated with cesarean section has decreased in recent years due to the introduction of improved anesthetic techniques and postoperative care, the risk associated with anesthesia for obstetric and non-obstetric procedures during pregnancy is still much higher in veterinary medicine than in human medicine.

If anesthesia is warranted for a pregnant patient, the main principles for the anesthetic management will be similar whether the surgery procedure is obstetric or not. They are summarized in the following points:

- Optimization and maintenance of normal maternal physiologic function
- Optimization and maintenance of utero-placental blood flow and oxygen delivery
- Avoidance of myometrium stimulation and use of known teratogenic drugs
- Avoidance of maternal stress
- Use of loco-regional anesthesia techniques as much as possible

Maternal safety: physiological adaptations to pregnancy

In general, pregnancy can be seen as a hypermetabolic state accompanied by many physiological changes to support that increased energy demand. Most of those changes happen under the influence of gestational hormones in order to ensure adequate supply of oxygen and nutrition to the fetus while other changes are a result of mechanical effect of the expanding gravid uterus. The following are the most clinically relevant changes from the anesthetic point of view.

Maternal cardiovascular changes

During pregnancy, the cardiovascular system undergoes substantial changes. Due to the rise in energy demand and oxygen requirements, the cardiovascular system is put under stress. The most relevant changes are a large plasma volume expansion, increased heart rate, and decreased overall systemic vascular resistance. All of these will increase cardiac output and maximize oxygen delivery to
more peripheral tissues like the uterus and placenta. In normal circumstances those changes will be compensated but in females already suffering from a cardiovascular disorder, pregnancy may worsen it and even put them into cardiac failure. There have been some reports in dogs and cats with pregnancy-associated congestive heart failure, so any clinical signs should be investigated. If that is the case, the patient must be considered as very critical and should be treated for cardiac failure or at least stabilized as much as possible before anesthesia. Preservation of cardiac function and minimal cardiovascular depression should be priorities in determining the anesthetic protocol in these cases.

The decrease in systemic vascular resistance due to the pregnancy hormones prostaglandins and progesterone will affect directly the blood pressure and will predispose the mother to hypotension while anesthetized. As the uterus lacks an independent auto-regulatory blood flow mechanism and depends directly on maternal blood pressure, hypotension is a severe problem that needs to be addressed promptly when detected. In addition it has been seen that pregnant animals have a dampened baroreflex response and their ability to compensate for hypotension due to hypovolemia and hemorrhage is reduced; one study corroborates this, showing that pregnant dogs took longer to restore blood pressure in a model of acute hemorrhage compared to non-pregnant dogs. Pregnant patients still preserved mechanisms of compensation like increase in heart rate, cortisol and vasopressin levels but to a lesser extent. Accordingly, excessive bleeding during surgery can be very dangerous not only for the loss of ability to compensate but because the mother is already anemic, as described below.

Dilution anemia is another of the clinically relevant changes due to an enlarged plasma volume as water and sodium retention increases. If the pregnant patient suffers an excessive hemorrhage during surgery, ideally a blood transfusion or a hemoglobin-based oxygen carrying solution should be administered. Attempts to replenish volume with crystalloids or colloids may be only a temporary solution to support maternal hemodynamics and may be associated with dubious effects on oxygen delivery to the fetus, as they may produce further hemodilution. Moon et al in their study compared fetal oxygenation restoration by hetastarch versus blood or polymerized bovine hemoglobin solution in the ovine model of acute hemorrhage. The results were that while all three products brought back maternal cardiovascular measurements to baseline, only blood or the hemoglobin-based solution could restore fetal oxygenation.

Another consideration for anesthesia during pregnancy is the position of the patient as it is associated with maternal hypotension. This is especially important during the last trimester since the gravid uterus will cause aorto-caval compression and decreased venous return whenever the patient is placed in dorsal recumbency. For that reason, the time the patient is in the dorsal position should be minimized by doing as much surgical preparation as possible while the animal is still awake and standing. Positioning the patient in a supine position with a left lateral tilt or oblique angle has been seen as a successful strategy to improve cardiovascular function in woman and most likely would be helpful for large animal species like equine as well. Nevertheless there are anatomical differences between species and a much greater collateral circulation which would explain why in veterinary species, positioning the pregnant patient on its back does not seem to be as problematic as in human medicine. Veterinary research has shown that in full term pregnant anesthetized dogs, dorsal positioning did not cause more hypotension compared to lateral positioning or at a 10° to 15° oblique angle. Even so, there is always potential for dramatic changes in hemodynamics caused by recumbency in anesthetized full-term pregnant animals; changing their positions slowly and thorough monitoring of cardiovascular parameters during and after positioning are recommended.

On the whole, maternal hypotension is very likely to occur under anesthesia and the treatment must be prompt and aggressive. Intravenous fluids, either colloids or crystalloids, can be very helpful to increase cardiac preload but inotrope or vasopressor agents may be more indicated especially when the patient is not hypovolemic. The use of the inotropes dobutamine and dopamine in gravid ewes has been studied; at high doses they both improved maternal cardiovascular parameters and increased the uterine vascular resistance. Dobutamine induced uterine vasculature constriction to a lesser extent than dopamine. From this study it can be concluded that high doses of either should be avoided and dobutamine is a better treatment for hypotension than dopamine considering a selective preference for
beta adrenergic receptors and consequently better uterine blood flow. Traditionally ephedrine has been recommended for the treatment of hypotension in obstetrics. Ephedrine is a mixed alpha and beta adrenergic agonist drug. It may preserve utero-placental blood flow better than other vasopressors due to a superior beta adrenergic affinity and nitric oxide release that counteracts the vasoconstriction of alpha-1 receptors.15 Nowadays, ephedrine use is controversial as some recent systematic reviews found more beneficial the use of other vasopressors like phenylephrine for the treatment of spinal anesthesia hypotension in parturient women. The results of those reviews were that the risk of fetal acidosis was decreased whenever phenylephrine was utilized16 and that ephedrine was associated with lower umbilical cord pH.17 Considering umbilical pH as an indirect measure of uterine blood flow, there is no support for the traditional recommendation of ephedrine treatment for spinal hypotension in parturient women. When it comes to veterinary species there is a lack of well-controlled studies performed on the subject and it is dangerous to extrapolate results and conclusions based on a human-specific model during labor. Recommendations to treat hypotension in pregnant anesthetized animals should be done cautiously and every case taken as an individual, keeping in mind the preservation of cardiac output, maintenance of adequate peripheral blood perfusion, and avoidance of excessive vasoconstriction that will increase arterial blood pressure but may compromise the fetus oxygenation.

Maternal respiratory changes

There are several important changes in the respiratory system during gestation. The pregnant patient is at a higher risk of hypoxia due to an increased metabolic oxygen demand that could be as high as 60%18 increase at term, relative anemia, and important changes in lung volume. There is some compensation from the cardiovascular system by an increase in cardiac output, but some adjustments in the respiratory system must occur, too, to meet this higher oxygen demand and avoid hypoxemia. The respiratory rate and tidal volume increase, resulting in overall minute ventilation up to 45% to 70% higher than non-pregnant patients at full term.18 This will increase oxygen to the required levels and will produce maternal hypocapnia (reduced carbon dioxide levels in blood) with slight respiratory alkalosis. That rise in maternal pH is limited by renal excretion of bicarbonate. Normal levels of arterial carbon dioxide (PaCO2) in pregnant animals can be as low as 3.9-4.3Kpa (30-33mmHg).19 It is necessary to keep PaCO2 at those levels without any further hypocapnia as that would displace the maternal oxygen hemoglobin dissociation to the left increasing maternal hemoglobin oxygen affinity with a reduced oxygen delivery to the fetus. In addition, hypocapnia could cause uterine blood flow decrease by uterine vasculature constriction. On the other hand, hypoventilation and hypercapnia (abnormally high levels of carbon dioxide in blood) are not much better as the increased maternal PaCO2 will limit the gradient for CO2 diffusion from fetal to maternal blood leading to fetal acidosis. It is very important to keep adequate levels of oxygen and carbon dioxide; that is why tight control and monitoring of maternal ventilation is needed. Sometimes artificial ventilation will be mandatory, especially during the last trimester as the weight of the gravid uterus will worsen the typical hypoventilation caused by the respiratory depression and muscle relaxation due to the anesthetics in the recumbent anesthetized patient.

Other respiratory changes include a diminution in lung volumes, specifically the functional residual capacity (FRC), due to cranial displacement of the diaphragm with the expanding gravid uterus. This implies a reduction of residual volume in the lungs which gets near to the closing volume. That makes the alveoli prone to collapse, produces atelectasis, and reduces ventilation capacity and gas exchange efficiency. During anesthesia it might be very helpful to keep the patient on artificial ventilation with the application of periodic alveoli recruitment maneuvers and positive end expiratory pressure, in order to counteract hypoxemia and hypercapnia.

The pregnant patient is at most risk of hypoxemia during induction of anesthesia. At that stage, apnea may develop after administration of induction drugs. During apnea, gas exchange continues in the lungs thanks to the reserve gas volume FRC, but that reserve is smaller in the pregnant patient. That factor, combined with the raised oxygen demand, increases the risk of maternal hemoglobin desaturation and hypoxemia. Pre-oxygenation with 100% oxygen at 3-5 liters per minute via face mask or flow by, for
at least five minutes before induction of anesthesia, is the best way to prevent hypoxemia and is highly recommended.

Maternal neurological changes
Circulating gestational hormones have important effects on the anesthetic. On one side, progesterone is well known for its sedative effects. On the other side, higher endorphin levels make pregnant patients more tolerant to surgical stimuli as their pain threshold is increased. These hormones are directly responsible for a decreased anesthetic requirement in pregnant patients, as well evidenced in the veterinary literature. Studies in pregnant sheep and women showed that the minimal alveolar inhalant concentration required to keep them at a surgical anesthesia plane is reduced by 25% for halothane and 40% for isoflurane compared to non-pregnant individuals.

The maternal neural tissue becomes more sensitive to local anesthetics so lower doses should be used in loco-regional anesthesia techniques like epidurals. It is important to remember too that the epidural space becomes smaller with pregnancy due to compression of the inferior venous cava by the gravid uterus, producing engorgement of the sinuses venous plexus in the spine canal. As a consequence, lower dose-volumes for drugs should be used. Otherwise they could spread cranially too fast and too far, causing adverse effects like respiratory paralysis or central nervous system toxicity.

The autonomic system seems to have a parasympathetic predominance during the first trimester of pregnancy although this changes towards the last trimester when there is less vagal tone and sympathetic system is more prevalent. It would be important to minimize maternal stress as much as possible as this could trigger sympathetic system over-activity with tachycardia and increased peripheral vascular resistance, compromising uterine blood flow and putting the life of the fetus at risk.

Maternal physiological changes in other systems
Progesterone and estrogens decrease the lower esophageal sphincter tone. During pregnancy there is also an increase in intra-abdominal pressure, in addition to an increased gastric acidity and slower gastric emptying. The combination of these factors increases the risk of regurgitation for the pregnant patient under anesthesia. Regurgitation can have fatal consequences like aspiration pneumonia, esophagitis, and esophageal stricture. Although regurgitation in pregnant woman is a real concern, the evidence for its occurrence in veterinary species is scarce. In one prospective study five out of nine pregnant dogs that died after cesarean section had evidence of pneumonia but no regurgitation or aspiration of gastric content could be documented. To date there are no veterinary studies looking specifically at increased risk of regurgitation under anesthesia during pregnancy. In any case, most anesthetists’ recommendations are to secure and seal the airway with an endotracheal tube as quickly as possible after induction of anesthesia to avoid aspiration pneumonia. Another recommendation is to pre-treat the patients with pro-kinetics, H2 receptor antagonists and/or proton pump inhibitors to increase gastrointestinal motility and make the gastric content less acidic.

Fetal safety
Avoidance of fetal asphyxia
Fetal asphyxia may occur as a consequence of maternal hypoxemia, decreased intrauterine flow, or by inefficient maternal oxygen transfer to the fetus. Maternal hypoxemia will cause utero-placental vasoconstriction and decreased perfusion, the fetus will become hypoxic and acidotic, and ultimately will die.

There is a very tight relationship between maternal and fetal PaCO2. High levels of CO2 in maternal blood will limit the gradient necessary for the gas exchange among uterine and umbilical vessels; therefore, the fetus will be unable to offload CO2 and will become acidotic. Fetal acidosis causes myocardial depression and may progress to fetal death. On the other hand, maternal hypocapnia will cause uterine vasoconstriction and reduced fetal hemoglobin oxygen upload. These have already been discussed as part of maternal respiratory changes.
Close monitoring of the maternal respiratory system is essential for fetal safety. Pulse oximetry can be very useful for detecting hypoxemia and capnography can be used to monitor maternal levels of expired carbon dioxide; alternatively, arterial blood samples can be taken regularly to measure arterial blood gases. Measure should be taken to ensure normal levels of oxygen and carbon dioxide in the pregnant patient. In most cases, artificial ventilation is the best way to maximize oxygenation and ensure normocapnia. One of the downsides of the mechanical ventilation is the possible detrimental effect on the cardiovascular system. Special attention must be paid to positive pressures applied during ventilation when maternal hemodynamics are not stable, since positive pressure in the thoracic cavity will decrease venous return to the heart and worsen arterial blood pressure further.

Utero-placental circulation is not auto-regulated and depends directly on maternal blood pressure and cardiac output. Maternal cardiovascular parameters must be monitored and maintained at acceptable levels. As cardiac output measurement for clinical veterinary anesthesia is not a realistic option, we rely on arterial blood pressure monitoring complemented with capillary refill times, mucous membrane color, heart rate and even end tidal carbon dioxide to provide more information on blood flow and adequacy of peripheral tissue perfusion. Maintenance of satisfactory maternal cardiovascular parameters is crucial to avoid fetal asphyxia; maternal hypotension must be detected and aggressively treated. The use of balanced anesthetic techniques, close anesthesia depth monitoring and careful anesthetic titration to effect, together with intravenous fluids and the use of inotropes and vasopressors as needed, are some of the techniques we can use to counteract hypotension. The use of some specific inotrope-vasopressor drugs like ephedrine for obstetrics has already been discussed.

Teratogenicity and anesthesia

Teratogenicity is induction of any functional or anatomical abnormality in the newborn caused by a prenatal treatment. Virtually every drug has teratogenic potential in certain species, if administered in sufficient amount, for a sufficient length of time during a particular gestational period. Most drugs used for anesthesia have ideal properties like low molecular weight, low ionization and high liposolubility. Those characteristics allow them to rapidly cross the brain-blood barrier and at the same time cross the blood-placenta barrier. Consequently, the teratogenic potential of these drugs will depend on the stage of fetal development. During conception and implantation of the embryo, it is an “all or nothing” situation and either an abortion occurs or the embryo survives intact after the drug exposure. Later in the first trimester or period for organogenesis is when the fetus is more vulnerable to teratogen exposure. As the tissues differentiate, anatomical and structural malformations might be induced. Anesthesia and sedation during the first trimester should be avoided if possible. Functional abnormalities and fetal and organ growth retardation are associated with drug exposure during late pregnancy.

In experimental studies teratogenicity in laboratory species when exposed to specific drugs was demonstrated as follows:

- Nitrous oxide inhibits methionine synthetase activity interfering with DNA formation and myelin deposition. It has been shown that prolonged exposure of nitrous oxide in rat embryos during peak organogenesis is teratogenic. It is important to remark that these studies are based on a single species exposed to nitrous oxide for at least 24 hours, an unusual situation that would never be seen in clinical practice. Therefore, extrapolation of the study results and clinical application are questionable. There is no proof of teratogenicity in other species or after short time exposures.

- Inhalants have been studied under laboratory conditions in pregnant mice with conflicting results. Halothane has shown teratogenicity when mice were exposed for more than 12 hours but other investigators could not corroborate those results under similar circumstances. Others have studied isoflurane and enflurane exposure in pregnant mice and shown an increased incidence of cleft palate without any other abnormalities, but again other studies comparing halothane, isoflurane, enflurane and a known teratogen did not show any major abnormality within the groups exposed to anesthetics. Sevoflurane and desflurane are considered the safest as they have not shown any teratogen effect in animal studies.
Chronic use of diazepam during pregnancy has been associated with cleft lip and palate in human neonates, but the latest studies have failed to validate these results. In animal studies, benzodiazepines have been associated with that malformation too, although the real danger of their use is unknown in different animal species as is the risk of a single dose for a single anesthetic or sedation episode.

Non-steroidal anti-inflammatory drugs (NSAIDs) should not be administered to pregnant animals. The teratogenic effect of these analgesic drugs when administered to the mother can be quite profound. These drugs inhibit cyclooxygenase (COX) production and decrease prostaglandin production; prostaglandins maintain patency of the ductus arteriosus and regulate pulmonary vasculature in the fetus. The use of NSAIDs could cause constriction or closure of the ductus and cause fetal pulmonary hypertension. Oro-facial clefts in the fetus have also been associated with NSAID administration. Fetal circulation disruption and even cessation of labor are other possible effects of these drugs because of the blockade of prostaglandins. More recent studies have shown an important role of COX-2 in fetal kidney maturation, so potential placental transfer of NSAID’s from the mother can stop nephrogenesis in the fetus. Non-steroidal anti-inflammatory drugs should be withheld in the pregnant veterinary patient until scientific studies can prove their safety.

Whenever possible, elective surgery should be delayed at least until after the first trimester to minimize the risk of fetal demise or malformations due to teratogenicity. Ideally the anesthesia should be delayed until after term.

Prevention of pre-term labor/abortion
Anesthesia and surgery during pregnancy increases the risk of spontaneous abortion or pre-term labor, especially if the surgery involves intra-abdominal procedures. When those are planned for the late pregnant patient, pre-term labor represents one of the main concerns for the anesthetist. The risk can be decreased by minimizing uterine manipulation and avoidance of anesthetic drugs that increase uterine tone or induce uterine muscle contraction.

The perioperative use of prophylactic tocolytic therapy in the pregnant animal to prevent premature labor or abortion has not been studied; in humans that technique has shown to be controversial due to the maternal side effects and uncertain efficacy during non-obstetric surgery. There is a published case report in which the tocolytic drug isoxsuprine was used as part of the perioperative anesthetic protocol in a late-term gravid cow undergoing general anesthesia for a metacarpal fracture repair. In this case the outcome was positive and not only did the cow recover well from surgery but a healthy calf was born at term. Although it is not possible to prove that the tocolytic helped in the successful outcome of the case, it is true that the anesthetic protocol contained two drugs known for causing increased uterine tone and decreased uterus blood flow. Those drugs are ketamine and xylazine which should be avoided as much as possible in the late pregnant patient. If there are no other choices, as in the case report, then a tocolytic might help to relax the uterus and counteract uterine muscle contractions.

Xylazine is an alpha-2 agonist sedative drug widely use in veterinary medicine. Alpha-2 agonists in general have potent side effects like reduction of cardiac output, which will impair fetal oxygen delivery. For that reason, these drugs should be used very cautiously for the pregnant patient or not used at all if possible. Additionally, they can increase uterine motility. Xylazine use has been related to early parturition when administered during the third trimester.

Ketamine is a dissociative anesthetic injectable agent used in all veterinary species. Its use is a bit controversial in obstetrics; on one hand, it has very favorable cardiovascular properties helping to maintain the maternal hemodynamics but on the other hand, there is an increase in uterine tone and it might cause uterine vasoconstriction. The safest way to use ketamine would be as part of a balanced anesthetic technique where other anesthetic drugs can counteract the negative effects of ketamine by providing muscle relaxation and some vasoconstriction to help uterine perfusion. Moreover, ketamine can be administered at small bolus doses and in small dose constant rate infusions so side-effects like tachycardia and hypertension are less likely to occur.
Maternal stress can cause spontaneous abortion and it is considered one of the major risks during the first trimester. In humans, there is clear association with increased maternal cortisol as a physiological measure for stress and spontaneous abortion during the first three weeks. It is very important to plan well for the procedure so stress on the mother is minimal. It is true that some drugs can jeopardize the life of the fetus and some clinicians attempt to perform minor procedures by administering light sedation to the mother. However, if the mother gets quite stressed that can be very detrimental for the fetus too. Sometimes the risks for sedating pregnant patients before anesthesia must be weighed against preparing the patient without sedatives and dealing with maternal stress. Emergency cesarean section would be one of those occasions where drug effects on the fetus could be more important to consider than maternal stress. Fetal life is already in danger and the fetus will have more chance of survival if it gets delivered with the least amount of anesthetic possible so it suffers less cardio-respiratory and neurological depression and rapidly becomes an independent newborn, vigorous and strong enough to nurse straight away.

**Putting everything together: general anesthetic recommendations**

The best recommendation is to use a balanced anesthetic technique, where multiple drugs induce anesthesia targeting unconsciousness, muscle relaxation, immobilization and analgesia.

**Pharmacological considerations**

Pharmacokinetics and pharmacodynamics are altered during pregnancy so careful titration of drugs is recommended. Moreover the anesthetic and analgesic maternal requirements are decreased due to the effect of gestational hormones on the central nervous system.

The increase in blood volume causes a physiological hypo-albuminemia that alters drug protein binding and leaves a relative higher fraction of unbound/free drug. That potentiates the drug effect and puts the patient at risk of overdose, especially when drugs that readily bind protein are used.

Most of the anesthetic drugs are not highly ionized and very lipophilic so they can readily cross the blood-brain barrier; unfortunately, they cross the placenta barrier with the same facility. The amount that gets transferred depends on the placental blood flow and maternal protein binding, while the amount that is available for the fetus will depend on fetal uptake, metabolism, and clearance. In humans, it is known that the fetal liver is active and able to perform some drug metabolism, whereas in dogs this is not the case at all and the fetus depends entirely on maternal circulation, metabolism, and elimination of drugs and metabolites. It is safe to assume that drugs will affect the dam and fetus similarly. Drugs with low ionization, like the opioids and local anesthetics that are weak bases, will transfer to the fetus under a gradient concentration until a maternal-to-fetal equilibrium is reached. If for any reason the fetus becomes acidotic, these weak bases tend to get ionized and trapped in the fetal circulation. Once ionized, those molecules cannot cross the placenta back to the maternal circulation. This well-known phenomenon, ion entrapment, will cause accumulation of drug in the fetal tissues.

**Premedication**

One of the main uses of premedication is to minimize patient stress and that is very important in the pregnant patient. The clinician might consider not sedating the patient if it is calm or is very depressed and sick. Otherwise, mild sedation with narcotics can be very beneficial and helps to decrease required doses of induction drugs. Opioids have been shown to be the safest analgesic drugs for mother and fetus. They should always be part of the anesthetic protocol as they are potent analgesics, provide sedation, and have great sparing effects on induction and maintenance anesthetic drugs. Their side effects are minimal and dose-dependent and most of them can be easily reversed by the antagonist naloxone. Opioids should be carefully chosen based on the circumstances of the case. For cesarean sections an opioid that has short duration and is easy to antagonize should be chosen to improve the neonates’ chances for survival.

The use of sedatives like alpha-2 agonists is not recommended due to their potent side-effects on the cardiovascular system and uterus. If the patient is very aggressive and represents a danger to itself or
to the veterinary team alpha-2s could be chosen as they are the best sedatives available. Detomidine for large animals and dexmedetomidine for small animals are a safer option for the fetus than xylazine but still the use of these drugs is a high risk as they can cause fetal asphyxia or premature labor. On a more positive note, alpha-2s are easily reversed. If they must be used, the best option would be to reverse them with atipamezole once the sedation is not needed any longer.

Acepromazine is a major tranquilizer heavily used in animals as part of the anesthesia or just for sedation. It produces a calming effect and decreases anxiety. The negative side is that it causes vasodilation and can potentiate maternal hypotension under anesthesia. Because this tranquilizer has a very long duration of action and has no antagonist, it is better not to use it for the pregnant patient if possible. It is not recommended for cesarean section.

Other tranquilizers like benzodiazepines can potentiate sedative effects of opioids and provide muscle relaxation with very minimal side effects and a wide safety margin. Their effects disappear with administration of the antagonist flumazenil. The only concern about this class of drugs is the potential for teratogenicity. The evidence is scarce and inconsistent and the references are vague, therefore the use of benzodiazepines as part of anesthesia during pregnancy is probably a low risk worth taking. The benefits of including these drugs in the anesthetic protocol outweigh the low risk of teratogenicity, especially if they are used at clinical doses during a single anesthetic episode, rather than a prolonged chronic maternal use. Whenever benzodiazepines are used in cesarean section, the antagonist flumazenil must be available for administration to the newborns so they are not too sedated to nurse and even to hypoventilate due to the muscle relaxation.

Induction of anesthesia

There is no standardized technique for anesthesia induction in the pregnant patient. Two min techniques, either inhalants or injectable, can be employed. Both of them have advantages and disadvantages.

The main focus during induction is speed. The anesthetist must be able to gain control of the patient’s airway as soon as possible, as the predisposition to hypoxemia and high risk of regurgitation are well known. It is essential to secure and seal the airway with an endotracheal tube to avoid aspiration of regurgitation, and to start the delivery of oxygen at 100% to counteract hypoxemia. Maternal ventilation can be gently supported if the induction drugs produce hypoventilation or apnea. Injectable anesthetic agents will provide the quickest induction, which is why the author prefers this technique over the use of inhalants. Probably the best injectable anesthetics are propofol and etomidate. Propofol provides a smooth, quick induction although it causes profound cardiovascular depression by producing hypotension after excessive vasodilation. This cardiorespiratory depression is dose-dependent and lasts a few minutes due to propofol’s rapid re-distribution; consequently, most pregnant patients tolerate it with no significant problems. Etomidate is a higher profile induction agent, much safer than propofol, with minimal effect on the cardiovascular system so it is advantageous if the mother’s health is critical or if she suffers from a cardiac disorder. On the other hand, etomidate induction is not as smooth as propofol and it is much more expensive. Both agents have been safely used in cesarean sections in small animals with high rates of neonatal survival and increased newborn vigor. In contrast, thiopental, thiamylal, and ketamine, when used as induction agents for dog cesarean section, have been associated with decreased puppy vigor.31 Other studies done in puppies born by cesarean support those results and show that puppies with the highest neurological depression were the ones born from dams anesthetized with ketamine, followed by the ones with thiopental and then by the ones with propofol.32

Inhalant induction is another possibility and probably the most advantageous for the fetus about to be delivered by cesarean section due to the rapid elimination in the lungs while breathing with almost no metabolism or accumulation. Due to the cardiorespiratory changes during pregnancy, inhalant induction via face mask or induction chamber is much quicker than in the normal patient, nevertheless this induction is still very slow compared to injectable drugs and is rarely smooth. The main risk factors to be considered for an inhalant induction are: slow and long induction, increased maternal stress, and the profound cardiovascular effects of the inhalants as they have to reach very high levels to produce
unconsciousness. If this is the preferred induction method, volatile agents that are the least pungent and have the best pharmacokinetic properties should be employed. At this time, the best agent available to induce anesthesia is sevoflurane. Isoflurane is more soluble than sevoflurane so the induction would take longer. Desflurane is less soluble than sevoflurane and induction would be quicker but the odor is very pungent and will be less acceptable to the patient, prolonging the induction and making it more stressful.

Anesthesia maintenance

Most volatile agents used nowadays in veterinary medicine are very safe for mother and fetus. Isoflurane, enflurane and halothane have shown teratogenicity in specific research performed with rat embryos but other research studies fail to reproduce those results and it was concluded that they were all safe. As the evidence is so inconsistent, those inhalants should be used for clinical anesthesia of the pregnant patient as they represent low teratogen risk if any at all. Neither sevoflurane or desflurane have been associated with teratogenicity so they are the inhalant of choice during pregnancy.

In contrast, nitrous oxide is a known teratogen therefore its use is not recommended in pregnant patients. It is commonly used for pain relief during labor in human medicine but it might exacerbate hypoxemia in the newborn due to diffusion hypoxia. This could happen in neonates during cesarean section so the author cannot recommend its use for cesarean because neonatal resuscitation is already very challenging.

There are studies using injectable techniques to maintain anesthesia for non-obstetric surgical procedures in pregnant pony mares, which concluded that intravenous anesthesia provides safer anesthesia than halothane with fewer cardiovascular depressant effects; data comparing other inhalant agents are not available. One of the studies used propofol as total intravenous anesthesia and demonstrated that propofol anesthesia was smooth with satisfactory cardiovascular function in the mare and fetus; the authors concluded that propofol is a suitable safe option for pregnant ponies. The other study involved the same species and very similar scenario but with a different total intravenous technique which consisted of a combination of ketamine, guaifenesin and detomidine; the results were equally satisfactory for both mare and fetus so the authors recommended this protocol as a good technique for anesthesia in pregnant equidae. The latter study seems to confirm that the use of detomidine is safer than xylazine if an alpha-2 agonist must be used, and that ketamine can be used as part of a balanced anesthetic protocol similar to the pregnant cow case report already discussed.

Although there is not that much information about injectable techniques for anesthesia maintenance in pregnant small animals, Moon et al concluded in retrospective studies that the use of propofol for induction and isoflurane for maintenance had a positive effect in vigor of puppies delivered by cesarean whereas the use of methoxyflurane and xylazine was associated with puppies born dead and the use of ketamine or barbiturates had a negative influence in puppy vigor.

Local anesthesia

Spinal anesthesia presents the least placental drug transfer for the degree of anesthesia received. This is especially important for the parturient patient undergoing cesarean for delivery because the less drug transferred to the fetus before delivery, the better the chances for the fetus to survive. In the prospective study by Luna et al puppies delivered by cesarean from sedated mothers that received local anesthesia by epidural injection were livelier and had higher respiratory rates than pups delivered from dams that got general anesthesia with three different protocols.

Epidural anesthesia is probably the best loco-regional technique for the pregnant patient. It is indicated for any orthopedic or soft tissue procedure involving hind limbs, abdomen, genito-urinary and perineal region. It is a fairly easy technique with outstanding analgesia and great anesthetic sparing effects. Owing to those sparing effects, both mother and fetus are exposed to a lower amount of drugs with less potential for fetal toxicity, teratogenicity and better maternal cardiorespiratory function, reducing the risk for fetal asphyxia and death. Two things must be kept in mind when epidurals are performed in the pregnant patient: they can be more challenging than in the normal patient because the epidural space is reduced so local anesthetics doses should be reduced accordingly to avoid an excessive...
cranial spread, and an epidural with local anesthesia might cause maternal hypotension due to sympathetic blockade. If that is the case it is important to recognize and aggressively counteract the hypotension as discussed above.

Any other loco-regional technique appropriate for the surgical procedure will be of benefit to the pregnant patient. When successful they reduce the overall anesthetic requirements and will provide stability to the anesthetic by blocking the sympathetic response to surgical stimulation. It is definitely worthwhile to administer local blocks, especially those that are familiar to the clinician. The supplies and drugs needed for local anesthetics are inexpensive and most times the morbidity associated with nerve blocks is very low. Clinicians must remember to reduce doses of local anesthetics to avoid toxicity as pregnant patients have been shown to have an increased pain threshold and a special sensitivity to local anesthetics in the neural tissue.

References