Anesthesia for non-obstetric surgery in the pregnant patient

M. VAN DE VELDE, F. DE BUCK

Department of Anesthesiolog, University Hospitals Gasthuisberg, Catholic University of Leuven, Leuven, Belgium

ABSTRACT

Surgery during pregnancy is relatively common. The present review of the literature will focus on relevant issues such as maternal safety during non-obstetric surgery in pregnancy, teratogenicity of anesthetic drugs, the avoidance of fetal asphyxia, the prevention of preterm labor, the safety of laparoscopy, the need to monitor the fetal heart rate and will finally give a practical approach to manage these patients.

Key words: Non-obstetric surgery - Pregnancy - Anesthesia - Teratogenicity - Fetal asphyxia.

Non-obstetric surgery during pregnancy is relatively common. Several older studies have found that between 0.15% and 2% of pregnant women underwent non-obstetric surgery.[1-3] The European Union has 380 million inhabitants. Assuming a birth rate of approximately 10/1 000, 3.8 million pregnancies enter the (European Union) EU statistics each year. This means that in the EU, each year between 5 700 and 76 000 pregnant women undergo non-obstetric surgery. This figure may be a serious underestimation as many women of childbearing age may present for surgery with an unrecognized pregnancy. Several studies suggest this occurs in 0.3% to 2.4% of women presenting for surgery.[4, 5] However, routine pregnancy testing in women of childbearing age is not routinely recommended, since many of these pregnancies might be identified following a detailed history.[6]

The most common indications for surgery during pregnancy are either pregnancy related or non-pregnancy related. Pregnancy related surgery includes interventions for cervical incompetence and surgery for ovarian cyst problems. Increasingly popular is also fetal surgery with an estimated 250 to 500 cases performed now each year in the EU.[7] The most common non-pregnancy related indications are acute abdominal problems (most commonly appendicitis and cholecystitis), maternal trauma and surgery for maternal malignancies.[8] Of course any type of emergent surgery may be carried out during pregnancy.

Surgery may be indicated during any stage of pregnancy. In a Swedish registry of 5 405 patients who had surgery during pregnancy, 42% had an intervention during the 1st trimester, 35% during the 2nd trimester and 23% during the 3rd trimester.[2]

When caring for pregnant women undergoing non-obstetric surgery, anesthetists must provide safe anesthesia for both mother and child. Maternal safety is related to the physiologic adaptations associated with pregnancy, which enforce anesthetists to adapt their standard anesthetic techniques. Fetal safety relates to teratogenicity, avoidance of fetal asphyxia and avoidance of preterm labor and delivery. Each of these issues will be discussed in this manuscript.

Maternal safety: maternal physiologic adaptations to pregnancy

The pregnant woman undergoes significant physiologic adaptations to pregnancy. Pregnancy induced changes pose hazards to mother and fetus during anesthesia and surgery. Most of these changes are due to the mechanical effects of the enlarging uterus, hormonal changes associated with pregnancy, increased metabolic demands and the low resistance placental circulation. The most important changes for the anesthetist are summarized below as well as their impact on anesthetic practice in this patient population.

Cardiovascular changes

Cardiac output increases gradually beginning at 8 weeks of gestation and reaching its maximal increase by the end of the 2nd trimester. Both heart rate and stroke volume are increased, resulting in a 50% increase of cardiac output by the end of the 2nd trimester.[9] Myocardial contractility remains unchanged, but systemic vascular resistance is decreased. This is primarily due to progesterone as well as the presence of the low resistance placenta.

Of concern to the anesthetist is aortocaval compression.[10, 11] Compression by the gravid uterus of the vena cava results in a reduced cardiac preload, reduced cardiac output and maternal hypotension. Aortocaval compression becomes apparent from the 2nd trimester onwards. It occurs when the patient is supine and can be relieved by assuming the lateral position. During surgery left lateral tilt should be used.

Mild cardiovascular signs, such as mild tricuspid regurgitation, mild pericardial effusion, left ventricular hypertrophy, accentuation of the first heart sound and electrocardiographic changes are perfectly normal during pregnancy.

Respiratory changes

Minute ventilation is increased up to 70% by term. This results in chronic respiratory alkalosis with a decreased $PaCO_2$ of 28 mmHg to 32 mmHg and a slight increase in pH to 7.44. This is obvious from the 1st trimester onwards. Bicarbonate is increasingly excreted by the kidneys. Oxygen consumption increases, but PaO_2 does not change.

Functional residual capacity is decreased by approximately 20% and even more in the supine position. The pregnant patient is, therefore, at increased risk for hypoxia when periods of apnea occur. Pregnancy also results in anatomical changes in the airway, making endotracheal intubation more difficult. This is further complicated by the increased vascularization resulting in more bleeding during intubation attempts. Also mask ventilation is sometimes much more difficult.

Gastro-intestinal changes

Although gastric emptying is normal during pregnancy, the risk of gastric content aspiration is increased in pregnancy, because of reduced barrier pressures at the level of the lower esophageal sphincter.[12, 13] This already is obvious from the 15th week onwards, especially in patients with heartburn.[13] This is further accentuated by distortion of the gastric and pyloric anatomy.

Other important changes

As a result of an increased plasma volume, anemia occurs, despite an increase in red blood cell volume. Pregnancy is also associated with a benign leukocytosis. Pregnancy also causes a hypercoagulable state with increases in most coagulation factors. Platelet turnover is enhanced as well as clotting and fibrinolysis. Pregnancy is, thus, a state of compensated intravascular coagulation. Thrombocytopenia can occur in up to 1% of pregnancies without signaling pre-eclampsia. The hypercoagulable state puts the pregnant patient at high risk for postoperative thromboembolic complications.

Glomerular filtration rate increases by 50% during pregnancy and as a result creatinine clearance is increased by 50% as well. Serum concentrations of creatinine are, therefore, reduced by almost 1/3.

Anesthetic requirements are significantly reduced for both inhalational and intravenous anesthetic agents. Pregnancy is associated with an increased sensitivity to inhalational anesthetics with minimum alveolar concentration reductions up to 40% being reported.[14-16] Similarly, the sensitivity to intravenous agents is also increased.[17] The reduced anesthetic requirements are most

likely due to a progesterone effect.[18] Less spinal or epidural anesthetics are required to produce a similar dermatomal spread in pregnancy as compared to non-pregnant patients. This is due to hormonal as well as mechanical effects of the enlarging uterus.[19, 20] Non-depolarizing muscle relaxants have a prolonged duration of action, while the duration of action of succhinylcholine is unaffected by pregnancy.[21, 22]

These physiologic changes of pregnancy enforce anesthetists to adapt their routine anesthetic technique. Acid aspiration prophylaxis (in my institution a combination of an H2-blocking agent, sodium citrate orally 30 mL 0.3 M and metoclopramide) is, therefore, recommended to reduce gastric content and increase gastric pH. This clearly results in a reduced morbidity and mortality when accidental aspiration occurs. Adequate positioning with left lateral displacement of the uterus (at least 20° left lateral tilt) is required to avoid the supine hypotensive syndrome. This should be performed from the 2nd trimester onwards. The pregnant patient is more prone to hypoxia because of decreased functional residual capacity and increased oxygen consumption. Careful denitrogenation prior to induction of general anesthesia is, therefore, recommended. A rapid sequence induction should be performed using cricoid pressure and a rapidly acting muscle relaxant. The drug of choice remains succhinylcholine. Rocuronium would be an alternative. However, it exerts a significantly prolonged duration of action which is difficult to reverse.[22, 23] Mild respiratory alkalosis (for non-pregnant women) should be maintained during artificial ventilation. Pregnant patients are more prone to thromboembolic complications and adequate prophylactic measures should be taken including prophylactic administration of low molecular weight heparines.

Teratogenicity of anesthetic drugs

Drugs should only be administered to pregnant patients if the benefits outweigh the risks. Anesthetic drugs affect intra- and intercellular signaling and have known effects on cellular mitosis and DNA synthesis.[24-26] Such intracellular systems are involved in cellular differentiation and organogenesis. Therefore, all anesthetic agents can be potentially teratogenic. The teratogenicity of a drug is determined by the dose administered, the route of administration, the timing of exposure to the fetus and the species which is exposed to the drug. Timing of exposure is of crucial importance. During the first 15 days of human gestation an all or nothing phenomenon occurs: the fetus is lost or the fetus is preserved fully intact. During the time of organogenesis (15-56 days) structural abnormalities may occur. After this period, functional changes can be observed, but structural abnormalities are rare.

Since prospective clinical studies are impractical, unethical and would require enormous numbers, most of our knowledge comes from animal studies, accidental exposure and reports from series of patients that underwent anesthesia whilst being pregnant.

Although most anesthetics are known teratogens in certain species, when a high enough dose is administered or when directly administered to the fetus, most agents are, however, perfectly safe in clinical circumstances. We now know that local anesthetics, volatile anesthetics, induction agents, muscle relaxants and opioids are not teratogenic when used in clinical concentrations and when normal maternal physiology is maintained. Indeed, derangements in maternal physiology are teratogenic themselves.

It is probably best to avoid nitrous oxide during pregnancy because it is not necessary to use this agent to provide safe and effective anesthesia. Nitrous oxide has known effects on DNA synthesis and has been shown to have teratogenic effects in animals.[27]

Avoidance of fetal asphyxia

The most important and serious risk to the fetus of maternal surgery during pregnancy is that of intrauterine asphyxia. The most challenging goal of the anesthetist is, therefore, to avoid fetal asphyxia by maintaining normal maternal oxygenation and hemodynamics. Maternal oxygenation, maternal carbon dioxide levels, maternal blood pressure and uterine tonus are all factors that need to be

controlled during surgery to avoid fetal asphyxia. It is extremely important to avoid hypoxia, hypercarbia, hypocarbia, maternal hypo-tension and uterine hypertonus during non-obstetric surgery. This is probably much more important than concerns about teratogenicity of different anaesthetic drugs.

Mild periods of hypoxemia of short duration are well tolerated.[28] However, prolonged or serious maternal hypoxemia causes utero-placental vasoconstriction and decreased utero-placental perfusion, resulting in fetal hypoxemia, acidosis and, ultimately, fetal death.[29] Hyperoxia is not dangerous, contrary to what previously was thought. It has been clearly demonstrated that hyperoxia does not result in an increased uterine vascular resistance nor does it decrease fetal oxygenation as measured by fetal scalp blood gas analysis.[30]

Maternal hypercarbia directly induces fetal respiratory acidosis. Severe fetal respiratory acidosis causes fetal myocardial depression. Hypercapnia also results in uterine artery vasoconstriction and reduced uterine blood flow.[31] Similarly, hypocapnia as well results in reduced uterine blood flow and ultimately fetal acidosis.

To treat maternal hypotension, ephedrine was long considered to be the first choice. However, recent data suggest that phenylephrine is equally efficacious to maintain normal maternal blood pressure and that phenylephrine produces a significantly better fetal acid base balance, at least in term pregnancies undergoing C-section under regional anesthesia.[32] Therefore, the current advice is to treat aggressively maternal hypotension with phenylephrine.

Several drugs used commonly in anesthesia, such as ketamine or IV local anesthetics, can cause uterine hyperactivity and should be avoided.

Prevention of preterm labor

Following surgery during pregnancy, the risk of preterm labor or abortion is increased, especially if surgery involves intra-abdominal procedures. Many studies have reported an increased incidence of spontaneous abortion, premature labor and preterm delivery.[2] Prophylactic tocolytic therapy is controversial, since tocolytic agents have considerable maternal side effects and efficacy during non-obstetric surgery has not been proven. Tocographic monitoring during the first hours or days postoperatively is probably wise to detect and treat preterm labor as early as possible.

Fetal heart rate monitoring during surgery

From 18-22 weeks fetal heart rate (FHR) monitoring is feasible and from 25 weeks heart rate variability can be observed. I would recommend using FHR monitoring routinely when feasible. It certainly is a very good indicator of inadequate utero-placental perfusion. Unfortunately, there is no evidence to show that using intraoperative FHR monitoring improves fetal outcome.[33] As a result some recommend not to use it. The issue remains controversial, but many obstetric textbooks do advice to monitor whenever feasible. Remember, however, that loss of variability is not always an indicator of fetal distress, but may also signal fetal anesthesia.

Laparoscopy

Many authors have raised concerns about fetal well being during laparoscopy. They fear direct uterine or fetal trauma and they also fear fetal acidosis from absorbed carbon dioxide. Finally, because of increased intra-abdominal pressure, maternal cardiac output and thus utero-placental perfusion might be reduced. Animal data have corroborated these concerns.[34-36] However, clinical experience, using a careful surgical and anesthetic technique, has been favorable. Reedy *et al.* compared laparotomy and laparoscopy performed in pregnancy in over 2 million pregnancies in Sweden during a 20-year period.[37] These authors included 2 181 laparoscopies and 1 522 laparotomies with a gestational age between 4 and 20 weeks. They compared 5 fetal parameters (birth weight, gestational duration, growth restriction, infant survival and fetal malformations) for each type of surgery with the overall outcome in the non-operated population. Premature delivery, growth restriction and low birth weight was more frequent in the operated groups as compared to the general

population. No differences between laparoscopy and laparotomy were identified.

Thus, the following guidelines were issued by the Society of American Gastrointestinal endoscopic surgeons regarding laparoscopic surgery during pregnancy. Whenever possible, surgery should be deferred to the 2nd trimester. One should obtain a preoperative obstetric consultation. Intermittent pneumatic compression devices to prevent thrombosis should be used. Fetal and uterine status should be monitored as well as end-tidal CO_2 and maternal arterial blood gases. To enter the abdomen an open technique should be used. Aortocaval compression should be avoided. Finally, low pneumoperitoneal pressures (<12 mmHg) should be used.

Practical approach

So how should we address practically the pregnant patient that needs surgery during pregnancy for non-obstetric reasons?

Ideally, surgery should be performed during the 2nd trimester. A laparoscopy is possible. Patients should always receive acid aspiration prophylaxis. Left lateral tilt is required to avoid aortocaval compression. The FHR should be measured continuously.

Whenever feasible, a regional technique should be used. However, if general anesthesia is mandatory a rapid sequence induction is required: adequate denitrogenation, cricoid pressure, a rapid acting neuromuscular blocking agent (preferably succhinylcholine), and endotracheal intubation. All anesthetic agents can be used. A volatile agent is useful to prevent premature uterine activity. It is wise to avoid nitrous oxide.

Hypoxemia, hypercarbia and hypocarbia should be avoided and hypotension must be managed aggressively using intravenous fluids and phenylephrine or ephedrine. We must provide good postoperative analgesia.

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Address reprint requests to: M. Van de Velde, MD, PhD, Director Obstetric Anesthesia and Extra Muros Anesthesia, Department of Anesthesiology, University Hospitals Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium. E-mail: marc.vandevelde@uz.kuleuven.ac.be