Ref: Ro Med J. 2022;69(Suppl2)
DOI: 10.37897/RMJ.2022.S2.19

Anesthesia during pregnancy

Silvius Negoita[1,2], Nicolae Gica[1,3], Anca Marina Ciobanu[1,3], Gheorghe Peltecu[1,3], Anca Maria Panaitescu[1,3]

[1] "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[2] Department of Anesthesiology, Elias Emergency University Hospital, Bucharest, Romania
[3] Filantropia Clinical Hospital, Bucharest, Romania

ABSTRACT

Surgery during pregnancy post additional concerns an represent a major stress factor for both anesthesiologist and gynecologists. Approximately 0.5-2% of all pregnant women undergo a least one nonobstetric surgery during their pregnancy, and the number is growing in recent years. Until present days, no anesthetic drug has been shown to be clearly dangerous to human fetus. Thus, a pregnant woman should never be delayed from surgery regardless of teratogenic effects at any gestational age. The choice of anesthetic technique, drugs and surgical procedure should be guided by mother safety and continuation of adequate uteroplacental perfusion. Regarding Cesarean Section, it is now the most common surgery performed in the United States, with over 1 million women delivered by cesarean every year. Due to medical and legal implication, anesthesia must be safe in order to improve maternal and fetal outcome. Ultimately, success of each case is granted by multidisciplinary team approach and adherence to the latest clinical practice guidelines.

Keywords: anesthesia, non-obstetric surgery, pregnancy, caesarean section

INTRODUCTION

For a practitioner working in an emergency hospital with an obstetric emergency department, the need for nonobstetric surgery can arise at any point during gestation. Urgent and emergency surgeries are not based on pregnancy, while elective procedures generally can be delayed until after delivery. This can cause special anesthetic management problems for both mother and fetus. The need for nonobstetric surgery and anesthesia occurs in about 0.5-2% (1). In pregnant women, appendicitis, ovarian disorders (torsion, neoplasm) and trauma have the highest frequency. The anesthesiologist should adjust and individualize the management of pregnant women admitted in ICU or those who require neurosurgery (2). The surgical and anesthesia teams generally tend to avoid performing elective procedures in the first and third trimester and it is widely understood that non-obstetric surgeries are safest if performed in the second trimester (3).

MATERIALS AND METHODS

We searched electronic medical databases, the PubMed, Cochrane and reference lists and bibliographies for potentially relevant studies. Studies were selected, quality assessed, and data extracted according to preset protocols. The publications used are mentioned in References section.

MAIN PHYSIOLOGIC CHANGES DURING PREGNANCY

Cardiovascular changes

Important rise in cardiac output (CO) is observed during normal pregnancy implying both components: heart rate (HR) and stroke volume (SV). The increase in CO begins early in pregnancy, with a resultant 35% increase by the end of the first trimester. CO output continues to increase after the first trimester, reaching a plateau of roughly 50% above baseline by the end of the second trimester until the

Corresponding author:
Silvius Negoita
E-mail: silvius.negoita@umfcd.ro

Article History:
Received: 26 December 2021
Accepted: 12 January 2022

delivery (4). Systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) are decreased. The enlarging uterus predisposes patients to aortocaval compression which can reduce preload and effective cardiac output resulting in hypotension. This is most pronounced when patients are in the supine position (5).

Pulmonary changes

Starting in the first trimester, resting minute ventilation increases, primarily due to an increase in tidal volume, and reaches nearly 50 percent above baseline at term. This change is thought to be driven by progesterone-induced stimulation of ventilation. Increased minute ventilation results in a partially compensated chronic respiratory alkalosis with a resultant pH of 7.42-7.46 and a PaCO2 of 26-32 mmHg. Decreased functional residual capacity (FRC) makes pregnant patients more prone to hypoxemia during periods of apnoea. The enlarging uterus causes upward displacement of the diaphragm resulting in the reduction in FRC and a in total lung capacity (TLC), especially in supine position (6,7).

Hematologic changes

In normal pregnancy, haemoglobin levels are lower than in non-parturient women (10.5 g/dl in the second trimester), because of a relatively greater increase in plasma volume compared with red cell mass. Pregnancy also alters the coagulation and fibrinolytic pathways, with a resultant hypercoagulable state. Clotting factors VII, VIII, IX, X, XII, and plasma levels of fibrinogen and von Willebrand factor rise during pregnancy (8).

Gastrointestinal changes

In pregnancy, gastric contents and acidity are higher (9). Decreased lower oesophageal sphincter (LES) tone in conjunction with increased gastric pressure predispose pregnant women to gastro-oesophageal reflux (GERD). During endotracheal intubation of pregnant patients, they may present an increased aspiration risk.

Renal changes

High increase in renal blood flow and glomerular filtration rate (GFR). GFR increases by roughly 50%, and as such, serum levels of creatinine and blood urea nitrogen (BUN) values decreases. This induces a considerable retention in water and sodium (~ 1 g) and an increase in total body water (TBW) of up to 6 l. These changes can affect medications that undergo renal metabolism (8).

TERATOGENIC EFFECTS OF ANESTHETIC AGENTS

When prescribed in an effective dose, less than 20 drugs have teratogenic effects (10), but in order to produce any fetal defect, these should be administered in a specific dose and time manner. Based on the published animal and clinical studies, as well as input from neurotoxicity investigators and stakeholders, in December 2016, the US Food and Drug Administration (FDA) made statements about potential harms of anesthetic drugs administration in parturients and children under the age of three regarding neurodevelopment. FDA is especially concerned about repeated anesthetic drugs exposure in the first trimester of pregnancy and long procedures (more than three hours) (11). The American College of Obstetricians and Gynecologists (ACOG) is in disagreement with FDA's concerns regarding anesthetic drugs in pregnancy (12). Placental transfer of drugs can be classified as it follows: type I – full drug transfer occurs through placenta and concentration equilibrium is reached between maternal and fetal blood (e.g. thiopental), type II – drug concentration is higher in fetal blood (e.g. ketamine), type III – placental crossing is minimal (e.g. succinylcholine) (2).

Inhalation anesthetics are volatile and have various cellular effects, but to date these (i.e cellular effects) were not associated with teratogenesis (13). Since most anesthetics are fat-soluble, it can easily to cross the placenta, and the effect of placental barrier on drug transport is therefore studied first (14). Most studies on the sevoflurane-induced neurotoxicity have focused on the change in the development of the hippocampus and incidence of cleft palate (15). Nowadays, nitrous oxide is not largely used given the wide range of general anesthetics available. DNA synthesis and myelin formation are altered by nitrous oxide (16) which induces vitamin B12 oxidation and subsequently, methionine synthetase inhibition. Anesthetics can be toxic to brain development, and the vulnerability mainly depends on three factors: the stage of brain development and the concentration and duration of the exposure. In human, maternal, and fetal procedures are usually performed in the second or early third trimester, a critical time for the proliferation and differentiation of the fetal brain. Despite these observations in rats, the aforementioned teratogenic effects were not observed in humans regardless of anesthetics wide use and this suggest a species-specific response (17).

Diazepam, as an induction agent, used in early pregnancy may be associated with cleft palate and cardiac abnormalities. More recent studies have failed to demonstrate this association or a definite risk of other anomalies. Benzodiazepines that are commonly used in the perioperative setting (e.g.,

midazolam) have never been associated with congenital malformations (18). In clinically effective doses, propofol, etomidate, thiopental or ketamine do not have teratogenic effects. Nevertheless, ketamine can cause oxytocic effects during early pregnancy and should be avoided (19).

Analgesics and neuromuscular blocking agents were extensively studied. Although the reported odds ratios for septal defects after NSAIDs intake were increased, a large prospective cohort study found there is no significant association for risk of selected bith defects and NSAIDs administered while in the first part of pregnancy (20). Because most muscle relaxants are highly ionized with low lipid solubility, there is minimal placental transfer. Vecuronium crosses the placenta in small amounts, but neonatal outcome does not appear to be affected (21). Sugammadex encapsulates progesterone and reduces free progesterone levels in pharmacologic simulation studies. This has prompted manufacturer to recommend barrier contraception for one week following sugammadex exposure on reproductive potential and is reported to be safe and effective in parturients (22).

The severity of the effects of a local anesthetic on a fetus is determined by the amount of local anesthetic delivered across the placenta. Increased systemic absorption of local anesthetics occurs during epidural or plexus anesthesia and thus, increased fetal exposure through placental crossing of local anesthetics by simple diffusion. In pregnancy, neural sensitivity is increased via progesterone mediation and a lower local anesthetic dose induces anesthesia on a specific dermatomal level. Drugs that are highly protein bound (e.g bupivacaine), given repeatedly, have an increased risk of fetal accumulation and subsequently, fetal unwanted effects. Given the high affinity of bupivacaine for fetal erythrocyte membrane, this could explain, in part, one of mechanisms implicated in the neonatal jaundice. Of all local anesthetics, lidocaine has the highest safety profile. Mepivacaine and bupivacaine used in certain doses appear to be safe (23,24).

FETAL PERSPECTIVE

Both the FDA and the American College of Obstetricians and Gynecologists (ACOG) advise that necessary surgery should not be avoided or delayed during pregnancy. Neurodevelopment alterations secondary to in utero exposure to anesthetic drugs is not supported by the available data and also, no effect was observed on animal models during exposures shorter than 3 hours. Some non-obstetric procedures in pregnant women present the risk of preterm delivery and corticosteroid therapy should be taken into account if the fetuses are viable at the given preterm age. One should constantly monitor these patients for possible signs and symptoms of preterm labour before and after surgery, therefore, these surgical procedures eventually will be done at an institution with neonatal and paediatric facilities. Postponement after delivery is recommended for elective surgery and thromboembolism risk should be assessed (25).

ANESTHESIA MANAGEMENT

Pregnant patients should be evaluated preoperatively in the same manner as nonpregnant patients. A medical and obstetric history and anesthesia-directed physical examination, including airway assessment, should be performed for all pregnant patients who undergo any type of anesthesia. Laboratory evaluation should be performed selectively, based on patient factors and the planned procedure. Additional testing is not indicated in an uncomplicated pregnancy. The anesthetist has the following goals: correct and preserve normal physiology of the mother; correct and preserve utero-placental blood flow and oxygen delivery; minimise fetal side effects of the drugs; prevent oxytocic effects; avoid awareness during general anesthesia; use regional anesthesia, if possible (26).

Based on the anatomic and hormonal changes that occur, pregnant patients may be at increased risk of aspiration during induction of (or emergence from) general anesthesia, especially in cases of difficult or failed intubation when mask ventilation may be required. Multiple large studies have failed to identify pregnancy as a risk factor for aspiration. Gastric emptying is not affected by pregnancy, and gastric acid secretion is unchanged or decreased in pregnant women. American Society of Anaesthesiologists (ASA), recommend that patients abstain from solid food for at least six hours (eight hours for fried or fatty foods) and from clear liquids for two hours, prior to surgery. Some experts routinely administer nonparticulate antacids, H2 receptor antagonists and/or metoclopramide for patients who are beyond 18 to 20 weeks gestation. Many pregnant patients prefer to avoid unnecessary sedatives. If anxiolysis is required, small doses of a sedative can safely be titrated to effect (e.g., midazolam 1 mg IV, repeated as necessary (27,28).

After 18-20 weeks of gestation, the parturient should be positioned for surgery to avoid aortocaval compression and resulting supine hypotension syndrome. Thus,15 degrees of left uterine displacement should be used, when possible, when the patient is supine. Placing a wedge under the right hip or tilting the operating table to the left accomplishes left uterine displacement. Blood pressure can be maintained with intravenous fluid or phar-

macologically with vasopressors if the surgery requires the parturient be supine (29).

Standard physiologic monitors are used for all patients during anesthesia; no additional patient monitors are required because of pregnancy. Advanced monitoring (e.g., intra-arterial continuous pressure monitoring) may be indicated based on the type of surgery or patient comorbidities. For all pregnant patients, the fetal heart rate (FHR) should be documented pre- and postoperatively. In some cases, intermittent or continuous FHR monitoring may be performed during surgery as well. Current ACOG recommendations are to continuously monitor electronic FHR and contractions in all viable fetuses greater than 23 weeks of gestation age throughout surgery. Blood pressure goals and the use of vasopressors in pregnancy have generally been studied in women undergoing caesarean delivery; the goals for physiologic parameters are also applicable for women having other types of surgery during pregnancy. While many of recommendations are to maintain systolic blood pressure at ≥ 100 mmHg and mean arterial pressure ≥ 65 mmHg or ≥ 80 percent of baseline, the optimal blood pressure goal has not been defined and there is likely to have individual variability. Anesthetic agents have minimal direct effects on uterine blood flow but can contribute to hypotension and uteroplacental hypoperfusion because of cardio depressant or vasodilatory effects (30).

Phenylephrine (direct-acting sympathomimetic amine that functions as an alpha-1 adrenergic agonist) and ephedrine (alpha and beta-adrenergic agonist) are reasonable choices to treat hypotension. Phenylephrine is generally preferred but can cause reflex bradycardia. Ephedrine increases maternal heart rate, but it has been associated with increased fetal metabolic activity and lower fetal pH values. Ephedrine crosses the placenta and can produce an increase in FHR variability and an increase in baseline FHR lasting several hours (31).

Peripheral nerve blocks or neuraxial anesthesia with or without sedation are options for surgery of the extremities. A common complication of neuraxial anesthesia is hypotension and decreased uteroplacental blood flow. Lower doses of spinal and epidural local anesthetics may be required during pregnancy due to mechanical and hormonal factors. Anesthesia-related mortality in the parturient is most often related to respiratory events. Airway changes are noted during pregnancy. The airway of a pregnant patient is 8 times more difficult that the airway in a non-pregnant female. As gestation advances, the oropharyngeal diameter becomes narrower from oedema (32).

Preoxygenation prior to induction of anesthesia is critical during any stage of pregnancy, and apneic oxygenation should also be considered (apnoeic oxygenation refers to administration of oxygen to achieve mass flow through the upper airways and into the alveoli in the absence of respiratory effort). Pregnant patients are more sensitive to IV and inhalational medications. Propofol seems to be the preferred induction medication for standard, routine induction in healthy pregnant patients. Studies suggest a reduction in the propofol dose required for loss of consciousness in pregnant women. The respiratory effects of pregnancy result in increased oxygen consumption and, therefore, a quicker rate of oxygen desaturation. Common best practice guideline to minimize desaturation on induction involves preoxygenate and ensuring that end tidal O2 is greater than 80% before induction is initiated. Pregnant women also seem to be more sensitive to neuromuscular blockers as well due to the reduction of pseudocholinesterase (33).

The proper strategy for airway management may depend on the gestational age at the time of the procedure, with increasing risk of passive regurgitation as pregnancy progresses. Some anesthetists will use a supraglottic airway for appropriate general anesthetics prior to 18 to 20 weeks of gestation and perform endotracheal intubation later in pregnancy to minimize the risk of aspiration.

Maintenance of anesthesia and mechanical ventilation – electroencephalography (e.g., bispectral index [BIS]), not mandatory for safety of the procedure are widely recommended. Mechanical ventilation should be adjusted to maintain the normal physiologic chronic respiratory alkalosis of pregnancy. Because carbon dioxide crosses the placenta relatively easily, the goal for EtCO2 during mechanical ventilation should be approximately 30 to 32 mmHg in the last half of pregnancy. Fetal oxygenation is critically for mother and fetus. Therefore, a fraction of inspired oxygen (FiO2) of at least 50 percent during anesthesia is highly recommended. Postoperative care should be focused on maternal monitoring, fetal assessment, and postoperative pain control.

SPECIAL CONSIDERATIONS REGARDING CAESAREAN SECTION

Place one 16-18-gauge intravenous (IV) catheter in preparation for routine elective cesarean delivery. It (e.g., 16 G) ensures a flow of ~180ml/min and is useful for rapid fluid replacement, rapid blood transfusion, etc. Central venous catheter is not routinely used and is role reserved for expected or sudden large amount of blood loss like placenta previa and/or accrete (34). American Society of Anesthesiologists monitors include pulse rate, blood pressure measurement, electrocardiography, oxygen satura-

tion via pulse oximetry, and temperature monitoring. If sedatives are administered, end-tidal carbon dioxide (EtCO2) should be monitored as well. For most patients who undergo cesarean delivery, is recommend using neuraxial anesthesia (NA) rather than general anesthesia (GA). NA is used for > 95 percent of CDs in the United States and Canada (35). A meta-analysis of 22 randomized studies including 1800 patients who underwent cesarean delivery reported no difference in neonatal outcome, umbilical artery, or vein pH during non-urgent cesarean delivery between patients with neuraxial versus general anesthesia (36). Combined spinal–epidural (CSE) anesthesia provides the rapid onset and other advantages of spinal anesthesia and in addition, the option to extend and prolong anesthesia with the epidural catheter. Bupivacaine is the most used local anesthetic (LA) for spinal anesthesia because of its duration of action, a low incidence of transient radicular irritation, low cost, and wide availability. Opioids may be added to the LA solution to improve intraoperative analgesia and for postoperative analgesia. The addition of an opioid is particularly helpful for blocking the discomfort of visceral manipulation (e.g., manipulation of the uterus). The need for intraoperative analgesia supplementation decreased from 24 to 4 percent with the addition of opioid to the LA (37). Patients should be positioned with left uterine displacement (LUD) for caesarean delivery, to minimize the chance of aortocaval compression. Most healthy parturients do not require supplemental oxygen during neuraxial anesthesia for uncomplicated caesarean delivery. But some doctors do so, especially regarding the fetus. Nausea with or without vomiting occurs commonly during caesarean delivery with neuraxial anesthesia. It is recommended to administer prophylaxis with ondansetron 4 mg IV or dexamethasone. Crystalloid solutions are used more commonly than colloid solutions for caesarean delivery because they are less expensive and more readily available. Limited available data do not indicate an absolute benefit of colloids over crystalloids (38). Administration of phenylephrine, rather than ephedrine, to prevent and treat neuraxial block-induced hypotension in the absence of maternal bradycardia is recommended (Grade 2B recommendation). Like other patients having surgical procedures, patients who undergo caesarean delivery are at risk for hypothermia due to prolonged skin exposure and fluid shifts. Routinely prevention and monitor of temperature is recommended. Uterine contraction is the main mechanism for reduction of uterine bleeding after delivery. The uterus is massaged, and oxytocin (protocol and drug may vary by institution) is administered as the first line uterotonic medication.

DISCUSSIONS

In current practice, laparoscopic procedures can be performed in a safe fashion regardless of pregnancy trimester and have the same indications as in non-parturient patients for acute abdominal conditions. The main advantage in pregnant women is represented by a lower fetal exposure to potentially toxic drugs. Smaller incisions lead to a decreased pain level perioperatively and subsequently, a decreased need for pain medication and faster recovery but these advantages are seen in all patients requiring laparoscopic surgery (37).

Women of child-bearing age should be asked about their last menstrual period, informed of potential risks, and pregnancy testing offered if their menstrual history is uncertain, or they request it to avoid elective procedures during early gestation.

Timing is a key factor in these surgeries and, if possible, surgery in the second trimester with perioperative fetal monitoring should be performed to reduce the risk of teratogenicity and fetal loss.

A postponement of six weeks after delivery is recommended for elective surgery.

CONCLUSIONS

The anesthetic plan for a pregnant patient must consider the type of surgery, patient factors, and effects of anesthesia on the fetus.

Abdominal surgery for nonobstetric conditions in pregnant women can be performed safely regardless of trimester, if it is indicated, without adverse obstetric events for either mother or fetus.

Development of the fetus can theoretically be jeopardized by various drugs depending on the dosage, exposure duration, timing, and route of administration. Until date, there is no anesthetic considered clearly harmful to the human fetus.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

1. Fanzago E. Anaesthesia for non obstetric surgery in pregnant patients. *Minerva Anestesiol.* 2003 May;69(5):416-27.
2. Upadya M, Saneesh PJ. Anaesthesia for non-obstetric surgery during pregnancy. *Indian J Anaesth.* 2016;60(4):234-241.
3. Ravindra GL, Madamangalam AS, Seetharamaiah S. Anaesthesia for non-obstetric surgery in obstetric patients. *Indian J Anaesth.* 2018 Sep;62(9):710-716.
4. Costantine MM. Physiologic and pharmacokinetic changes in pregnancy. *Front Pharmacol.* 2014 Apr 3;5:65.

5. Bamber JH, Dresner M. Aortocaval compression in pregnancy: the effect of changing the degree and direction of lateral tilt on maternal cardiac output. *Anesth Analg.* 2003 Jul;97(1):256-8.
6. Van De Velde M, De Buck F. Anesthesia for non-obstetric surgery in the pregnant patient. *Minerva Anestesiol.* 2007 Apr;73(4):235-40.
7. Hegewald MJ, Crapo RO. Respiratory physiology in pregnancy. *Clin Chest Med.* 2011 Mar;32(1):1-13.
8. Pacheco LD, Maged MC, Hankins GDV. Physiologic changes during pregnancy. *Clin Pharmacol Dur Pregnancy.* 2013:5-16.
9. Hong JY, Park JW, Oh JI. Comparison of preoperative gastric contents and serum gastrin concentrations in pregnant and nonpregnant women. *J Clin Anesth.* 2005 Sep;17(6):451-5.
10. Tsamantioti ES, Hashmi MF. Teratogenic Medications. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-.
11. FDA Drug Safety Communication: FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women.
12. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2016/12/fda-warnings-general-anesthetics-sedation-drugs-young-children-pregnant-women.
13. Goodman S. Anesthesia for nonobstetric surgery in the pregnant patient. *Semin Perinatol.* 2002 Apr;26(2):136-45.
14. Zheng H, Dong Y, Xu Z, Crosby G, Culley DJ, Zhang Y, Xie Z. Sevoflurane anesthesia in pregnant mice induces neurotoxicity in fetal and offspring mice. *Anesthesiology.* 2013 Mar;118(3):516-26.
15. Li X, Jiang X, Zhao P. Effects of Pregnancy Anesthesia on Fetal Nervous System. *Front Pharmacol.* 2021 Feb 1;11:523514.
16. Littleford J. Effects on the fetus and newborn of maternal analgesia and anesthesia: a review. *Can J Anaesth.* 2004 Jun-Jul;51(6):586-609.
17. Kunitz O, Rossaint R. Anesthesia during pregnancy. *Chirurg.* 2005 Aug;76(8):737-43.
18. Wikner BN, Stiller CO, Bergman U, Asker C, Källén B. Use of benzodiazepines and benzodiazepine receptor agonists during pregnancy: neonatal outcome and congenital malformations. *Pharmacoepidemiol Drug Saf.* 2007 Nov;16(11):1203-10.
19. Cheung HM, Yew DTW. Effects of Perinatal Exposure to Ketamine on the Developing Brain. *Front Neurosci.* 2019 Feb 22;13:138.
20. van Gelder MM, Roeleveld N, Nordeng H. Exposure to non-steroidal anti-inflammatory drugs during pregnancy and the risk of selected birth defects: a prospective cohort study. *PLoS One.* 2011;6(7):e22174.
21. Kaneko T, Iwama H, Tobishima S, Watanabe K, Komatsu T, Takeichi K, Tase C. Placental transfer of vecuronium administered with priming principle regimen in patients undergoing cesarean section. *Masui.* 1997 Jun;46(6):750-4.
22. Richardson MG, Raymond BL. Sugammadex Administration in Pregnant Women and in Women of Reproductive Potential: A Narrative Review. *Anesth Analg.* 2020 Jun;130(6):1628-1637.
23. Guillén-Dolores Y (July 14th 2019). Bupivacaine Pharmacokinetics in Pregnant Women, Topics in Local Anesthetics, IntechOpen, 2018.
24. Clark DA, Landaw SA. Bupivacaine alters red blood cell properties: a possible explanation for neonatal jaundice associated with maternal anesthesia. *Pediatr Res.* 1985 Apr;19(4):341-3.
25. Nonobstetric surgery during pregnancy. ACOG Committee Opinion No.775. American College of Obstetricians and Gynecologists. *Obstet Gynecol.* 2019;133:e285-6.
26. Walton NKD, Melachuri VK. Anaesthesia for non obstetric surgery during pregnancy. *Continuing Education in Anaesthesia Critical Care & Pain.* 2006;6(2):83-85.
27. D'Angelo R, Smiley RM, Riley ET, Segal S. Serious complications related to obstetric anesthesia: the serious complication repository project of the Society for Obstetric Anesthesia and Perinatology. *Anesthesiology.* 2014 Jun;120(6):1505-12.
28. Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration: Application to Healthy Patients Undergoing Elective Procedures: An Updated Report by the American Society of Anesthesiologists Task Force on Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration. *Anesthesiology.* 2017 Mar;126(3):376-393.
29. Okeagu CN, Anandi P, Gennuso S, Hyatali F, Stark CW, Prabhakar A, Cornett EM, Urman RD, Kaye AD. Clinical management of the pregnant patient undergoing non-obstetric surgery: Review of guidelines. *Best Pract Res Clin Anaesthesiol.* 2020 Jun;34(2):269-281.
30. Okutomi T, Whittington RA, Stein DJ, Morishima HO. Comparison of the effects of sevoflurane and isoflurane anesthesia on the maternal-fetal unit in sheep. *J Anesth*. 2009;23(3):392-8.
31. Wright RG, Shnider SM, Levinson G, Rolbin SH, Parer JT. The effect of maternal administration of ephedrine on fetal heart rate and variability. *Obstet Gynecol.* 1981;57(6):734.
32. Izci B, Vennelle M, Liston WA, Dundas KC, Calder AA, Douglas NJ. Sleep-disordered breathing and upper airway size in pregnancy and post-partum. *Eur Respir J.* 2006 Feb;27(2):321-7.
33. Baraka A, Jabbour S, Tabboush Z, et al. Onset of vecuronium neuromuscular block is more rapid in patients undergoing Caesarean section. *Can J Anaesth* 1992;39:135-8.
34. Li P, Liu X, Li X, Wei X, Liao J. Clinical outcomes and anesthetic management of pregnancies with placenta previa and suspicion for placenta accreta undergoing intraoperative abdominal aortic balloon occlusion during cesarean section. *BMC Anesthesiol.* 2020;20(1):133.
35. Bucklin BA, Hawkins JL, Anderson JR, Ullrich FA. Obstetric anesthesia workforce survey: twenty-year update. *Anesthesiology.* 2005 Sep;103(3):645-53.
36. Afolabi BB, Lesi FE. Regional versus general anaesthesia for caesarean section. *Cochrane Database Syst Rev.* 2012 Oct 17;10:CD004350.
37. Dahl JB, Jeppesen IS, Jørgensen H, Wetterslev J, Møiniche S. Intraoperative and postoperative analgesic efficacy and adverse effects of intrathecal opioids in patients undergoing cesarean section with spinal anesthesia: a qualitative and quantitative systematic review of randomized controlled trials. *Anesthesiology.* 1999 Dec;91(6):1919-27.
38. Tawfik MM, Tarbay AI, Elaidy AM, Awad KA, Ezz HM, Tolba MA. Combined Colloid Preload and Crystalloid Coload Versus Crystalloid Coload During Spinal Anesthesia for Cesarean Delivery: A Randomized Controlled Trial. *Anesth Analg.* 2019;128(2):304.