

## **Anesthetic drugs and their effects on fetuses**

**By:**

Komail wasel alamer  
Murtadha Abdulkarim ALrushaydan  
Khalid jawad alhaddad  
Qassem Habib bu sbih  
Muntathir khalifah alomayshi  
Abdullah saud alismail  
Abdulkareem Abdullah Abdullah alsubi  
Ahmed Naji AL Yousif  
Talal Eid Alanazi  
Mahdi abduallah al sultan  
Amnah ibrahim alrasheed

## Introduction:

Anesthesia, which is defined as a numbing of the body's sensations and/or a numbing of consciousness, can be effectively produced by a vast array of medications. The substances in question encompass a wide range of medicinal uses, from analgesics and sedatives (such as barbiturates and benzodiazepines) to anticonvulsants and skeletal muscle relaxants, as well as the more traditional drugs used for anesthesia (both general and local). All of these substances deliver their anesthetic effects by blocking the conduction of sensory neurons and, in some cases, motor neurons. The exact ways by which they do this are still up for debate. These days, many of these medications are standard operating procedure for helping patients through various medical and surgical operations. The drugs commonly referred to as "general" and "local" anesthetics will be the primary emphasis of this chapter (Maher, T. J., 2012).

All pregnancies present unique challenges for anesthesiologists and necessitate close interdisciplinary collaboration when administering anesthesia to pregnant women. Both the mother and the unborn child face a quantifiable risk as a result of the procedure being performed. It is feasible to anticipate and successfully avoid such problems with the use of qualified staff, specialized equipment, proficiency in administering different types of anesthetic, and thorough understanding of the effects of the medications utilized.

In the last fifteen years, research on animals has shown that sedatives and anaesthetics have the ability to induce neurodegenerative alterations in young mammals' brains, including neuroapoptosis (Sanders, R. D., et al., 2013). This worry has prompted a slew of research looking back at human infants and toddlers; among them, some have found a link between neonatal exposure to general anesthesia and neurobehavioral issues in later years (DiMaggio, C., et al., 2012).

The urgency of the indication determines whether surgery is necessary at any stage of pregnancy. Among the most extensive studies on the topic of prenatal anesthesia and surgery, 42% of these procedures took place in the first trimester, 35% in the second, and 23% in the third. It is imperative to ensure the safety of both the mother and the child while administering anesthesia to pregnant women having non-obstetric surgeries.

A comprehensive grasp of the physiological and pharmacological changes that occur during pregnancy is necessary to guarantee the safety of the mother. Ensuring fetal safety involves avoiding medicines that could be harmful during important stages of fetal development, making sure there is enough blood flow to the placenta throughout the pregnancy, and doing what is needed to prevent or treat premature birth (Van De Velde, M., & De Buck, F., 2007).

### **General aspects of anesthesia:**

#### **1) Before surgery (pre-medication):**

- ✓ Under the influence of diazepam, the patient undergoing surgery may experience amnesia and sedation; as a result, he or she may require reassurance that the procedure is straightforward and won't take too much time.
- ✓ Analgesia, achieved through the administration of pethidine or morphine, is crucial in cases of pre-existing pain or as a supplementary measure to enhance the effects of a less potent anesthetic drug. Analgesia is unnecessary in the absence of preexisting pain. However, if post-surgery pain is anticipated, an analgesic medication may be administered at the conclusion of the procedure, regardless of whether the patient has reported pain.
- ✓ Using ant muscarinic agents such as atropine or hyoscine can inhibit the para-sympathetic autonomic system. This inhibition leads to a reduction in bronchial secretion, salivary gland secretion, reflex bradycardia, and hypotension.

#### **2) During surgery:**

Primarily, the use of a single or combination of drugs to induce drowsiness, pain relief, and muscular relaxation is of paramount importance.

#### **3) After surgery:**

The anesthesiologist ensures that the analgesic, hypnotic, and muscle relaxant effects are adequate. No patient should ever be left alone without medical supervision while they are on the following medications: antibiotics, analgesics, tranquilizers, purgatives, enemas, agents for hypotension or hypertension, anticoagulant, steroids, diuretic, bronchodilator, etc (Arabia, S., 2022).

### **Pre-anaesthetic assessment:**

It is essential to have close communication with the obstetricians and to conduct fetal ultrasounds when a delivery is expected. In addition, neonatologists should be contacted. Heart murmurs, peripheral edema, dyspnea, and other symptoms typically seen in patients with cardiac illness are prevalent throughout a normal pregnancy. Pregnancy-related ECG abnormalities include a shifted left axis, irregular heartbeats, and alterations in the ST and T waves that are not specific to the waveforms. Radiation exposure to the fetus should be kept to a minimum during diagnostic imaging procedures. It is essential to have the results of pertinent blood tests readily available and to order cross matched blood before any major surgery.

If resuscitation is necessary, it should be administered vigorously according to the standard advanced life support (ALS) or advanced trauma life support (ATLS) protocols, with the addition of a left lateral tilt to prevent hypotension while the patient is unconscious (Upadya, M., & Nayak, M., 2019).

Aspiration prophylaxis, such as ranitidine, sodium citrate, and metoclopramide, should always be included in pre-medication. Analgesia should be administered when necessary to prevent the harmful impact of stress on both the mother and the fetus. Avoid using non-steroidal anti-inflammatory medicines due to the potential for premature closure of the ductus arteriosus. Nevertheless, the use of low-dose aspirin, even with regular intake, seems to be safe in this regard.

### **ANAESTHETIC DRUGS:**

The effects of drugs on rapidly dividing cells in the first trimester of pregnancy may be teratogenic and lead to severe disorders of organogenesis, including severe congenital abnormalities of the fetus, including pregnancy loss. We do not have randomized trials assessing the teratogenic effects of anaesthetic drugs on the fetus, but it seems that the doses of routinely used anaesthetic drugs for various anaesthetic techniques are safe. This is confirmed by the analysis of the material collected in the National Study of the Prevention of Birth Defects in the United States, which showed that general or regional anaesthesia to pregnant women for dermatological, dental or gynaecological procedures, mainly in the cervical area, regardless of the duration of pregnancy, was not associated with the occurrence of 25 analyzed congenital malformations assessed in the study (Reefhuis, J., et al., 2020).

Inducing general anesthesia requires the use of hypnotic medications such as thiopental, propofol, etomidate, and ketamine. The maternal haemodynamic alterations caused by propofol and thiopental are similar, and there is no significant difference in the Apgar score of the infant when both drugs are taken (Tumukunde, J., et al., 2015). Unlike thiopental, which is associated with a lower Apgar score at one and five minutes after birth, ketamine has a far greater rate of this problem (Khemlani, K. H., et al., 2018).

### **Anaesthesia and gestation:**

While a woman is pregnant, she should not have any elective surgeries done; instead, she should wait six weeks after giving birth to do any surgeries, such as tubal ligation, so that the body can adjust to the changes that pregnancy brings. No matter the gestational age, emergency surgery must be performed with the primary goal of preserving the mother's life. Reducing the risk of teratogenicity and miscarriage by delaying surgery until the second trimester is a common practice, even though there is no solid evidence to back this method.

### **Characteristics of Anesthesia During Pregnancy:**

The specifics of administering general anesthesia to a vulnerable group, like pregnant women, require extra care. When it comes to the transfer and distribution of medications in mothers and newborns, the placental barrier plays a significant role, unlike conventional general anesthesia. There is a lack of data on the fetal metabolism and pharmacodynamics of anesthetics because of technological constraints. Considering that the majority of anaesthetics are soluble in fat (Zheng, H., et al., 2013).

Because of its ease of passage over the placenta, research into how the barrier affects drug transport must begin with this organ. The levels of isoflurane in the brains of both the mother and the fetus were found to be significant after 6 hours of 1.3% isoflurane anesthesia (0.40 and 0.42 mmol/g, respectively) (Li, Y., et al., 2007).

Nevertheless, due to their limited placental penetration, the fetus is mostly unaffected by maternal use of muscle relaxants (Kampe, S., et al., 2003). Based on these findings, the pharmacokinetic model of anesthetic transshipment in the mother's and the fetus's bodies is complex. Clinical trials revealed that

after crossing the placenta, general anaesthetics produced an irregular fetal heart rhythm. Transparent anesthetic transport and metabolism in both the mother and the fetus are prerequisites for studying the anesthetic's direct effects on the fetus.

### **Physiological changes during pregnancy which are relevant to anaesthesia:**

It took a lot of fighting for anaesthetic to be used in human surgeries. Painful treatments performed under the influence of ether and nitrous oxide were on display on both sides of the Atlantic Ocean in the 1840s. People looked askance at successful demonstrations and made fun of those that failed. A surgeon's fame was proportional to the ease and rapidity with which he executed his "craft," which may explain why some were reluctant to acknowledge the necessity of anesthetic. Over time, the use of anaesthesia would cause patients to have different expectations of surgeons. There was also the belief that the faithful would persevere through adversity since God had entrusted us with it. The attitude of the male-only surgical team toward childbirth was a prime example of this.

### **Anaesthesia for conception and in the first trimester:**

A significant number of women undergo anesthesia and intravenous sedation for in vitro fertilization. An optimal anesthetic approach should not disrupt the process of fertilization or early embryo development and should lead to minimal occurrences of postoperative nausea, drowsiness, discomfort, and psychomotor impairment. Minor medical procedures typically require minimal amounts of midazolam and opioids. Continuous propofol sedation and patient-controlled sedation are increasingly gaining popularity. It is advisable to ensure that the administration of propofol is consistently overseen by an anesthesiologist. Certain surgeons administer local anesthesia to the vaginal wall, however the advantages of this procedure are up to debate. Spinal anesthesia has been employed for women seeking complete elimination of sensation during oocyte retrieval, and general anesthesia is also utilized. General anesthesia may also be necessary for laparoscopy in assisted reproductive procedures. Avoiding nitrous oxide is recommended due to animal research indicating its strong inhibitory effect on methionine synthase. Nevertheless, there is currently no empirical data in humans to indicate that this has any clinical relevance. Following 6–8 weeks of gestation, significant changes occur in cardiac, haemodynamic, respiratory,

metabolic, and pharmacological parameters. Pregnant women experience a faster onset of hypoxemia due to an increase in minute ventilation and oxygen consumption, as well as a decrease in oxygen reserve caused by reduced functional residual capacity and residual volume. During critical periods, it is essential to administer supplemental oxygen to ensure adequate oxygen levels. throughout pregnancy, hyperventilation typically leads to a decrease in the amount of carbon dioxide exhaled (32-34mm Hg). It is important to maintain this level throughout anesthesia.

### **Anaesthesia in the second trimester:**

From around the 20th week onwards (and perhaps earlier), aortocaval compression poses a significant risk; it reduces blood supply to the uterus and, in rare cases, causes supine hypotension in pregnant women. Regional or general anesthesia might worsen this effect by reducing or eliminating the body's natural compensating mechanisms. The lateral position is the only one that may successfully prevent aortocaval compression. Uterine displacement, whether by wedging or manual means, can alleviate this. The danger of intravascular injection during regional blocking is increased due to venacaval compression, which causes the epidural venous plexus to enlarge. Local anaesthetics tend to spread more easily during pregnancy, likely because to the diminished capacity of the epidural space. A hypercoagulable state is linked to pregnancy due to an increase in pro-coagulant factors. It is vital to practice thromboprophylaxis during pregnancy due to the fivefold increase in the incidence of thromboembolic events (Haggerty, E., & Daly, J., 2021).

### **Anaesthesia for the third trimester:**

By this point in the pregnancy, most doctors advise having a caesarean section before undergoing any significant surgery. If possible, wait 48 hours before surgery so fetal lung maturation can be improved with steroid medication. To save time and avoid complications during the final procedure, it may be best to use regional anesthesia to deliver the baby and then switch to general anesthesia. The use of volatile agents should be limited or eliminated altogether after giving birth in order to reduce the likelihood of uterine atony and hemorrhage. It is important to adjust the anesthesia post-delivery to the specific surgical needs.

Some medical procedures, including surgery, stress, and anesthesia, might temporarily reduce lactation. Radioactive chemicals, ergotamine, lithium, and psychiatric medicines are among the few that are completely contraindicated while nursing, however the majority of pharmaceuticals are excreted into breast milk. Informing the mother about the potential neonatal consequences of other medications, like sedatives and opioids, is important. In order to keep the baby from becoming too dependent on formula, it may be necessary to express milk (De Tina, A., & Palanisamy, A., 2017).

### **Avoidance of fetal asphyxia:**

Consultations with perioperative physicians typically result in a recommendation to prevent hypoxia and hypotension. While this command is a fundamental principle of anesthesia practice, it is especially crucial for the maternal-fetal unit during non-obstetric surgery. Short durations of mild oxygen deficiency are often well tolerated. However, if the mother experiences prolonged or severe oxygen deficiency, it can lead to the narrowing of blood vessels in the uterus and placenta, reducing blood flow and oxygen supply to the fetus. This can result in fetal oxygen deficiency, acidosis, and ultimately, death (Dilts Jr, P. V., et al., 1969).

Deficiency in maternal blood glucose levels causes respiratory acidosis in developing babies. Hypoxia of the heart muscle occurs in cases of severe foetal respiratory acidosis. Vasoconstriction of the uterine arteries and decreased uterine blood flow are additional effects of hypercapnia. The same holds true for hypocapnia; it reduces blood supply to the uterus, which can lead to foetal acidosis (Walker, A. M., et al., 1976). Due to the relative passivity of the uteroplacental circulation, it is critically important to maintain normal maternal systemic arterial pressure. The spiral arteries are at their widest point when everything is working as it should (Valdes, G., & Corthorn, J., 2011).

### **Anesthetic management:**

Patients who are pregnant have been productively undergoing nonobstetric surgery under both general and regional anesthesia. There has been no conclusive evidence that one method is better than the other in terms of infant outcome in the available research. One advantage of regional anesthetic is that it lessens



the likelihood of teratogen exposure while simultaneously minimizing the risk of unsuccessful intubation and aspiration. Strict adherence to steady maternal hemodynamic parameters and oxygenation throughout anesthesia and surgery is the gold standard for fetal well-being assurance. Extreme caution should be exercised when assessing foetal reactions for symptoms of distress (jyoti Borah, T., et al., 2017).

There are a number of reasons why premedication to alleviate anxiety might be considered during the preoperative evaluation. Starting at 16 weeks of gestation, no particulate antacids and H<sub>2</sub>-receptor antagonists should be given to prevent aspiration pneumonitis. Aortocaval compression and aspiration pneumonitis should be considered risks for individuals after that point. To make uterine displacement easier, the patient must be positioned with a 158 degree left lateral tilt. It is important to proceed gently while placing the mother in Trendelenburg's or reverse Trendelenburg's position while she is under anesthesia since changes in her position might have significant implications on her hemodynamics.

### **Conclusion:**

For pregnant patients undergoing nonobstetric surgery, successful outcomes following the administration of anesthesia are contingent upon a comprehensive preoperative assessment, meticulous attention to detail in relation to maternal and fetal physiology during the perioperative period, and ongoing supportive care during the postoperative period. Important considerations include ensuring that the mother remains stable, determining the best time to perform surgery, and selecting the most effective anesthetic procedures.

Despite the fact that maintaining uteroplacental perfusion is the primary objective of anesthetic management, the importance of a multidisciplinary team in the treatment of pregnant patients at high risk should not be overlooked. Successful outcomes during nonobstetric surgery in pregnant patients require meticulous attention to maternal and fetal factors, and anesthesiologists must consider newer surgical procedures accordingly. During the course of management, it is crucial to keep everyone in the loop, particularly on the surgery's scheduled time and the surgical methods employed.

## References:

- Arabia, S. (2022). 2nd IFSO-MENAC| 4th PASMBS| 7th GOSS| 5th SASMBS.
- De Tina, A., & Palanisamy, A. (2017). General anesthesia during the third trimester: any link to neurocognitive outcomes?. *Anesthesiology Clinics*, 35(1), 69-80.
- Dilts Jr, P. V., Brinkman III, C. R., Kirschbaum, T. H., & Assali, N. S. (1969). Uterine and systemic hemodynamic interrelationships and their response to hypoxia. *American Journal of Obstetrics and Gynecology*, 103(1), 138-157.
- DiMaggio, C., Sun, L. S., Ing, C., & Li, G. (2012). Pediatric anesthesia and neurodevelopmental impairments: a Bayesian meta-analysis. *Journal of neurosurgical anesthesiology*, 24(4), 376-381.
- Haggerty, E., & Daly, J. (2021). Anaesthesia and non-obstetric surgery in pregnancy. *BJA education*, 21(2), 42.
- vyoti Borah, T., Sonowal, J., Chanu, S. M., Dey, S., & Yunus, M. (2017). Anaesthetic Management of a Pregnant Patient with Intraspinial Schwannoma for Excision. *Annals of International Medical and Dental Research*, 3, 5.
- Kampe, S., Krombach, J. W., & Diefenbach, C. (2003). Muscle relaxants. *Best Practice & Research Clinical Anaesthesiology*, 17(1), 137-146.
- Khemlani, K. H., Weibel, S., Kranke, P., & Schreiber, J. U. (2018). Hypnotic agents for induction of general anesthesia in cesarean section patients: A systematic review and meta-analysis of randomized controlled trials. *Journal of Clinical Anesthesia*, 48, 73-80.
- Li, Y., Liang, G., Wang, S., Meng, Q., Wang, Q., & Wei, H. (2007). Effects of fetal exposure to isoflurane on postnatal memory and learning in rats. *Neuropharmacology*, 53(8), 942-950.
- Maher, T. J. (2012). Anesthetic agents: general and local anesthetics. *Foye's Princ. Med. Chem., 7th ed., Lippincott Williams & Wilkins*, 508-539.
- Reefhuis, J., Gilboa, S. M., Anderka, M., Browne, M. L., Feldkamp, M. L., Hobbs, C. A., ... & National Birth Defects Prevention Study. (2015). The national birth defects prevention study: a review of the methods. *Birth Defects Research Part A: Clinical and Molecular Teratology*, 103(8), 656-669.

- Sanders, R. D., Hassell, J., Davidson, A. J., Robertson, N. J., & Ma, D. (2013). Impact of anaesthetics and surgery on neurodevelopment: an update. *British journal of anaesthesia*, *110*(suppl\_1), i53-i72.
- Tumukunde, J., Lomangisi, D. D., Davidson, O., Kintu, A., Joseph, E., & Kwizera, A. (2015). Effects of propofol versus thiopental on Apgar scores in newborns and peri-operative outcomes of women undergoing emergency cesarean section: a randomized clinical trial. *BMC anaesthesiology*, *15*, 1-6.
- Upadya, M., & Nayak, M. (2019). Anaesthesia for non obstetric surgery during pregnancy. *Update in Anaesthesia*, *34*.
- Valdes, G., & Corthorn, J. (2011). The angiogenic and vasodilatory utero-placental network. *Placenta*, *32*, S170-S175.
- Van De Velde, M., & De Buck, F. (2007). Anesthesia for non-obstetric surgery in the pregnant patient. *Minerva anesthesiologica*, *73*(4), 235.
- Walker, A. M., Oakes, G. K., Ehrenkranz, R. I. C. H. A. R. D., McLaughlin, M. A. R. G. A. R. E. T., & Chez, R. A. (1976). Effects of hypercapnia on uterine and umbilical circulations in conscious pregnant sheep. *Journal of Applied Physiology*, *41*(5), 727-733.
- Zheng, H., Dong, Y., Xu, Z., Crosby, G., Culley, D. J., Zhang, Y., & Xie, Z. (2013). Sevoflurane anesthesia in pregnant mice induces neurotoxicity in fetal and offspring mice. *The Journal of the American Society of Anesthesiologists*, *118*(3), 516-526.