Anaesthesia for non-obstetric procedures during pregnancy

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FOR ANAESTHETISTS
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Martina Nejdlova MD
Trevor Johnson FRCA

Key points

Avoid or minimize aortocaval compression.

Perform surgery in the second trimester where possible. Avoid elective surgery until after delivery.

Regional anaesthesia is preferred to general anaesthesia where possible.

Maintain normal maternal physiology. Optimize uteroplacental perfusion and avoid fetal asphyxia.

Avoid unwanted drug effects on the fetus, but be aware that no anaesthetic agents have been shown to be teratogenic in the clinical use.

> The pregnant patient can have any disease that any other woman can have—except sterility
>
> Dr Frederick C. Irving[1]

Up to 2% of pregnant women undergo surgery for non-obstetric conditions each year.[2] The most common indications are acute appendicitis, cholecystitis, trauma, and surgery for maternal malignancies. The main risks of surgery during pregnancy are fetal loss, premature labour, and delivery, which can result from both the disease process itself and the intervention. Intra-abdominal procedures for inflammation immediately adjacent to the uterus are more likely to result in uterine irritability, and the risk of preterm labour or abortion is significantly higher. The anaesthetist must provide safe anaesthesia to the mother while minimizing the risks to the developing fetus.

Maternal considerations

It is important to understand the physiological changes of pregnancy and the effect of drugs on the mother. Maternal physiology changes rapidly from the first trimester, owing to the hormonal effect of increasing progesterone production by the placenta and increased metabolic demands, and, from the second trimester, the mechanical effects of an enlarging uterus. A summary of the major physiological changes and their anaesthetic implications is presented in Table 1.

Fetal considerations

The safety of the fetus is affected by the placental transfer of drugs and by factors predisposing to fetal asphyxia, preterm labour, and delivery. Teratogenicity should not be ignored (see the Anaesthetic drugs and teratogenicity section), but maintaining uteroplacental perfusion is likely to be the main challenge. Maternal hypoxaemia leads to uteroplacental vasoconstriction, reduced uteroplacental perfusion, fetal hypoxaemia, acidosis, and, ultimately, fetal death. Maternal hyperoxia is not harmful to the fetus. Maternal hypercapnia, which may occur during spontaneous ventilation and deep levels of anaesthesia, causes fetal respiratory acidosis, uterine vasoconstriction, and reduced uterine blood flow. Moderate elevations of fetal P_{CO_2} are probably well tolerated, but severe fetal acidosis may cause myocardial depression. Hypocapnia also causes uterine vasoconstriction and a shift in the maternal oxyhaemoglobin dissociation curve to the left, resulting in reduced oxygen release to the fetus. Excessive positive pressure ventilation leads to maternal hypocapnia, increased intrathoracic pressure, reduced venous return, and reduced uterine blood flow. Maternal hypotension of any cause should be treated immediately. Uterine hypertonus is associated with an increase in uterine vascular resistance and will decrease uterine blood flow.

Timing of surgery

Timing seems to be critical to fetal outcome, and a decision on proceeding with surgery should be made by a multidisciplinary team, involving surgeons, anaesthetists, and obstetricians. An overall miscarriage rate after surgery of 5.8% has been reported, increasing to 10.5% during the first trimester.[3] During the first 2 weeks of gestation, the fetus is either lost or preserved intact. During the period of organogenesis between the 3rd and 8th weeks, exposure to teratogens can cause major structural organ abnormalities. After this period, drug exposure can cause functional changes or fetal growth retardation, but structural abnormalities are rare.[4] In the advanced stages of pregnancy, the difficulties of manoeuvring around a large gravid uterus and the management of the maternal airway need to be considered. The more advanced the pregnancy, the greater the chance

Martina Nejdlova MD
Consultant Anaesthetist
Department of Anaesthesia
Heart of England NHS Foundation Trust
Birmingham Heartlands Hospital
Bordesley Green East
Birmingham B9 5SS
UK

Trevor Johnson FRCA
Consultant Anaesthetist
Department of Anaesthesia
Gloucestershire Hospitals NHS Foundation Trust
Cheltenham General Hospital
Sandford Road
Cheltenham GL53 7AN
UK
Tel: +44 1242 274143
Fax: +44 1242 273405
E-mail: trevor.johnson@glos.nhs.uk
(for correspondence)

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Table 1 Physiological changes in pregnancy. CO, cardiac output; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance; AP, arterial pressure; ERV, expiratory reserve volume; RV, residual volume; FRC, functional residual capacity; V/Q, ventilation/perfusion; MAC, minimum alveolar concentration; WCC, white cell count; GFR, glomerular filtration rate

System	Physiological change	Anaesthetic implications
Cardiovascular	↑ CO up to 50%	
	↑ Uterine perfusion to 10% of CO	Uterine perfusion not autoregulated
	↓ SVR, ↓ PVR, ↓ AP	Hypotension common under regional and general anaesthesia
	Aortocaval compression from 13 weeks	Supine hypotensive syndrome requires left lateral tilt
Respiratory	↑ Minute ventilation	Faster inhalation induction
	Respiratory alkalosis (Pa_{CO_2} 3.7–4.2 kPa)	Maintain Pa_{CO_2} at normal pregnancy levels
	↓ ERV, ↓RV, ↓ FRC	
	↑ V/Q mismatch	
	↑ Oxygen consumption	
	Upward displacement of diaphragm	Potential hypoxaemia in the supine and Trendelenburg positions
	↑ Thoracic diameter	Breathing more diaphragmatic than thoracic
	Mucosal oedema	Difficult laryngoscopy and intubation; bleeding during attempts
CNS	↑ Epidural vein engorgement	Bloody tap more common
	↓ Epidural space volume	More extensive local anaesthetic spread
	↑ Sensitivity to opioids and sedatives	
Haematological	↑ Red cell volume 30%, ↑ WCC	
	↑ Plasma volume 50%	Dilutional anaemia
	↑ Coagulation factors	Thromboembolic complications (DVT prophylaxis)
	↓ Albumin and colloid osmotic pressure	Oedema, decreased protein binding of drugs
Gastrointestinal	↑ Intragastric pressure	↑ Aspiration risk
	↓ Barrier pressure	Antacid prophylaxis, RSI after 18 weeks gestation
Renal	↑ Renal plasma flow, ↑ GFR	Normal urea and creatinine may mask impaired renal function
	↓ Reabsorptive capacity	Glycosuria and proteinuria

of uterine irritability and preterm labour. There is no evidence to suggest that any anaesthetic agent, dose, or technique influences this risk; it is more likely to result from the disease process itself and direct manipulation of the uterus during surgery. Lower abdominal and pelvic inflammatory conditions, such as acute appendicitis with peritonitis, are associated with a particularly high risk.

The second trimester is preferred for semi-elective surgery which cannot be deferred. Elective surgery should be postponed until at least 6 weeks postpartum, to allow resolution of physiological changes. However, urgent surgery should not be delayed as secondary complications may increase the risk to both mother and fetus.

Anaesthetic management

The choice of anaesthetic technique should be guided by the indications, nature, and site of the surgical procedure. Laparoscopic rather than open techniques may be preferred when abdominal surgery is undertaken.

Pre-anaesthetic visit and premedication

Verbal reassurance is usually preferred to pharmacological premedication. A standard preoperative assessment is carried out with careful attention to the airway. Gestational age should be noted, and the possibility of miscarriage and preterm labour should be discussed. The mother should be informed about the low risks of teratogenicity associated with anaesthetic agents in the current use (see the Anaesthetic drugs and teratogenicity section). The obstetric team should be involved, and also a paediatrician if preterm labour is anticipated. Antacid prophylaxis is recommended after 14 weeks of gestation, and deep venous theombosis prophylaxis should always be considered.

Choice of anaesthetic technique

Regional anaesthesia is preferred to general anaesthesia where feasible. This enables the mother to maintain her own airway, minimizes fetal drug exposure, and provides good postoperative analgesia. Nevertheless, evidence demonstrating superior safety is lacking, and general anaesthesia is frequently required.

Monitoring

In addition to the standard monitoring, cardiotocographic (CTG) monitoring may be considered after 24 weeks of gestation. This would only be warranted if continuous observation of the CTG monitor is possible in theatre and an obstetrician is available for immediate delivery if necessary. Before 24 weeks, confirmation of fetal well-being should be performed at an appropriate time in the postoperative period. The loss of fetal heart rate variability may be related to the administration of drugs rather than fetal distress.

Conduct of general anaesthesia

Avoid aortocaval compression from 20 weeks (or earlier with larger gravid uteri, e.g. polyhydramnios or multiple gestation) by adopting a lateral position when possible, or by maintaining uterine displacement manually or through tilt when supine. Head-up tilt may help increase functional residual capacity (FRC), reduce breast interference with intubation, and alleviate gastro-oesophageal reflux. Airway management, mask ventilation, laryngoscopy, and intubation may all be challenging due to weight gain, breast engorgement, and increased vascularization, which can predispose to bleeding during intubation attempts. A smaller tracheal tube may be required. Equipment for difficult intubation should be available. Preoxygenation with a close-fitting mask for at least 3 min is recommended, as hypoxia develops up to three times more quickly in pregnancy, due to reduced FRC and increased oxygen consumption. Pregnant women are at higher risk of regurgitation and aspiration during both induction and emergence.

Lower oesophageal sphincter tone is reduced from early gestation and intra-abdominal pressure increases from the second trimester, so rapid-sequence induction with cricoid pressure is recommended.

Once the airway is secured, ventilation should aim to keep the P_{CO_2} in the normal range for pregnancy. Care must be taken to avoid excessively raised intra-abdominal pressures during laparoscopy.[5] Pregnancy is associated with an increased sensitivity to volatile anaesthetic agents, with MAC values slightly reduced. All volatile agents up to an MAC of 1.5 dilate uterine arteries and increase uterine blood flow, but at higher concentrations, this is offset by decreases in maternal arterial pressure and cardiac output. Volatile agents also reduce uterine tone. Nitrous oxide is avoided during the first trimester (see the Anaesthetic drugs and teratogenicity section). Light anaesthesia and pain are avoided to prevent maternal catecholamine release and consequent reduced uteroplacental perfusion. Extubation should be done with the patient fully awake and, preferably, in the lateral position.

Regional anaesthesia

Regional anaesthesia is highly desirable, although there are particular considerations during pregnancy. Obesity and oedema can obscure anatomical landmarks. Interspinal ligaments are hormonally softened, causing difficulty with epidural loss of resistance techniques. The spread of the local anaesthetic within the epidural or spinal space is greater in pregnancy, and lower doses are required. This may be due to both the mechanical effect of the enlarging uterus and hormonal changes, increasing sensitivity to local anaesthetic agents. Albumin concentration is reduced, with lower plasma binding and a higher risk of local anaesthetic toxicity.

Sympathetic activity is increased in pregnancy, and the sympathetic block due to central neuraxial block can cause significant maternal hypotension in the presence of hypovolaemia. Hypotension needs to be treated promptly by a left lateral tilt and a vasoconstrictor such as phenylephrine, and by giving i.v. fluids in the presence of hypovolaemia. Physiological changes mask the early signs of blood loss and subclinical hypovolaemia will compromise placental perfusion. Hypotension may not be evident until 25–30% of blood volume is lost.

Tocolytic therapy

If premature labour occurs, tocolysis will be necessary to preserve the pregnancy. Prophylactic therapy can be considered in the third trimester in patients undergoing lower abdominal or pelvic surgery for inflammatory conditions, although its efficacy during non-obstetric surgery is unproven and its use is also controversial because of maternal side-effects. The use of volatile anaesthetic agents has been advocated as they relax the uterus, although high concentrations can cause undesirable hypotension. Other agents used include magnesium sulphate, β-mimetics (terbutaline), calcium-channel blockers (nifedipine), and vasodilators (GTN).[6] Prostaglandin synthetase inhibitors, such as indomethacin, are no longer recommended.

Anaesthetic drugs and teratogenicity

Almost all anaesthetic agents can be potentially teratogenic,[7] although teratogenicity may also be caused by infection, pyrexia, hypoxia, acidosis, radiation, or the pathological process itself. Teratogenicity depends on genetic predisposition, dose, route of administration, duration, and timing of exposure. Most of our knowledge is based on animal studies, which are difficult to extrapolate, and retrospective human surveys.

The use of nitrous oxide during pregnancy has long been controversial because it inhibits methionine synthetase. Exposure to concentrations >50% for prolonged periods has been proven to be teratogenic during the peak organogenic period in animal studies. However, no adverse reproductive outcome has been detected in women during short periods of exposure. A Swedish registry study involving 5405 women having anaesthesia and surgery during pregnancy failed to implicate nitrous oxide in adverse perinatal outcome.[8] It would seem prudent to use inhaled concentrations of 50%, to limit the duration of use to reasonable intervals, and to avoid it completely during the first trimester. Some retrospective studies have shown a link between sustained maternal diazepam use and cleft palate defects. A single dose of benzodiazepine has never been associated with teratogenicity. Drugs increasing uterine tone should be avoided, including ketamine and i.v. local anaesthetics. Endogenous or exogenous sympathomimetics can increase uterine vascular resistance, an effect seen in anxious patients or during light general anaesthesia.

All commonly used induction agents, opioids, neuromuscular blocking agents, and volatile anaesthetics can be used in pregnancy. They are not teratogenic when used in clinical concentrations and when maternal physiology is maintained. Thiopental is the most commonly used agent for rapid-sequence induction, although a lower dose may be required.[9] Propofol is increasingly used as an alternative, especially in early pregnancy, as it is not teratogenic in animal studies. Early pregnancy does not appear to decrease the concentration of propofol required for the loss of consciousness.[10] Neuromuscular blocking agents are generally ionized and cross the placenta in only very small amounts. Plasma cholinesterase concentration can be reduced by up to 35% in pregnancy, but recovery from succinylcholine is not usually prolonged, as an increased volume of distribution and relative resistance may offset the effect of lower concentration. The intensity of fasciculations and muscle pain after succinylcholine is generally less, reflecting hormonal changes.[11] Since the introduction of sugammadex, the use of rocuronium has been advocated as an alternative. Atropine may be preferred to glycopyrrolate to antagonize the muscarinic effects of neostigmine during reversal. Neostigmine crosses the placenta and fetal bradycardia can occur, while glycopyrrolate does not. Opioids are highly lipid-soluble and readily cross the placenta. Although brief exposure is safe, long-term exposure will

Table 2 Drugs, important side-effects, and anaesthetic implications in pregnancy

Drugs	Side-effects and anaesthetic implications
Inhalation anaesthetics	
Volatile agents	Decreased MAC, reduced uterine tone, hypotension
Nitrous oxide	Prolonged exposure may inhibit DNA synthesis; avoid in the first trimester
Neuromuscular blocking agents	
Succinylcholine	Reduced plasma cholinesterase, possible prolonged action
Non-depolarizing neuromuscular blocking agents	Quaternary ammonium compounds do not cross the placenta
Local anaesthetics	Reduced protein-binding, increased risk of toxicity; use lower intrathecal doses in late pregnancy
Opioids	Increased maternal sensitivity, fetal withdrawal, intrauterine growth restriction with chronic use
Non-steroidal anti-inflammatory drugs	Premature ductus arteriosus closure, avoid after 28 weeks; ketorolac contraindicated
Anticoagulants	
Warfarin	Teratogenic, crosses the placenta
Heparin	Does not cross the placenta
Anticholinergics	
Atropine	Fetal tachycardia, crosses the placenta
Glycopyrrolate	Quaternary ammonium compound, does not cross the placenta
Anticonvulsants	
Phenytoin, carbamazepine, sodium valproate	Congenital malformations (neural tube defects)
Magnesium sulphate	Muscle weakness, interaction with neuromuscular blocking agents
Antihypertensives	
ACE inhibitors	Intrauterine growth restriction, oligohydramnios, renal impairment
β-Blockers	Intrauterine growth restriction, neonatal hypoglycaemia, bradycardia
Diuretics	
Thiazides	Neonatal thrombocytopenia
Tocolytics	
β_2-agonists: ritodrine, terbutaline, salbutamol	Tachyarrhythmias, pulmonary oedema, hypokalaemia, hyperglycaemia
Oxytocin receptor antagonists: atosiban	Nausea, vomiting, fewer side-effects than β_2-agonists
Calcium-channel blockers: nifedipine	Hypotension, fewer side-effects than β_2-agonists

cause symptoms of withdrawal when the fetus is delivered. Non-steroidal anti-inflammatory drugs in early pregnancy may be associated with increasing fetal loss[12] and in the third trimester may cause the premature closure of the ductus arteriosus. Single doses are unlikely to be harmful. Table 2 summarizes the major side-effects and clinical considerations for anaesthetic agents and adjunctive drugs.

Summary

Despite the many concerns, safe anaesthesia and surgery has been demonstrated for a wide range of non-obstetric procedures during pregnancy. The indications for surgery and its timing are major determinants of maternal and fetal outcome.

Declaration of interest

None declared.

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Please see multiple choice questions 29–32.