Surgical anaesthesia for the pregnant patient

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In the U.S.A., approximately 50,000 women every year undergo anaesthesia and surgery at some time during gestation for indications which are unrelated to parturition itself.¹ Expressed in another way: 1.6–2.2 per cent of pregnant women are subjected to surgery sometime during pregnancy.^{2,3}

The particular hazards of surgical anaesthesia during gestation are related to the physiological changes in the mother and to possible adverse effects on the fetus. These are similar to those encountered in obstetric anaesthesia, with two important differences. Firstly, while one of the aims of obstetric anaesthesia is to avoid interfering with the course of labor, surgical anaesthesia should not stimulate uterine activity and precipitate premature labour. Secondly, obstetrical anaesthesia has to avoid central nervous system depression in the newborn lest it delay the establishment of spontaneous and sustained breathing, whereas in surgical anaesthesia, foeto-maternal gas exchange depends solely on the integrity of the uterine and umbilical circulations.

Physiologic changes associated with pregnancy

Major alterations in practically every organ system occur in association with pregnancy. The changes of greatest interest to anaesthetists are obviously those involving the cardiovascular and respiratory systems, acid-base balance, and the gastrointestinal tract.⁴

Cardiovascular system

BLOOD VOLUME AND CONSTITUENTS

Both the plasma volume and the red cell volume begin to increase between the sixth and twelfth week of pregnancy, resulting at term in a plasma volume increase of 40–50 per cent and a total blood volume increase of 25–40 per cent. Since the red cell volume only increases by approximately 20 per cent there is a decline in the red cell count, haemoglobin and haematocrit. The fibrinogen content increases throughout pregnancy both in absolute amounts and in relative concentrations, the latter from 250–300 mg · 100 ml⁻¹ to 450 mg · 100 ml⁻¹. There is also a marked increase in activity of several clotting factors, rendering the blood hypercoagulable and predisposing the pregnant woman to thromboembolic phenomena.

Pregnancy and the puerperium are associated with a

decline in serum cholinesterase activity. It amounts to approximately 21 per cent and takes place during the first trimester, remaining fairly stable during the remainder of pregnancy.⁵ It is not associated with any structural malformation of the enzyme molecule, as indicated by normal dibucaine, fluoride and chloride numbers.

HAEMODYNAMIC CHANGES

Cardiac output begins to rise during the eighth week of pregnancy, initially through an increase in the stroke volume, and reaches its peak of 30–50 per cent above normal at 30–34 weeks. Older studies, performed in the supine position, indicated that by the 39th to 40th week the cardiac output declines to the nonpregnant level. It was subsequently postulated that the low cardiac output seen in the supine position was due to compression of the inferior vena cava by the enlarged uterus since, when measured in the lateral decubitus, cardiac output during the last few weeks of pregnancy was no lower than that seen in the second trimester. Vena caval compression can begin to develop during the second trimester and becomes maximal at 36 to 38 weeks. It may decrease thereafter with the descent of the fetal head into the pelvis. A radiographic study revealed that complete obstruction of the inferior vena cava occurs in approximately 90 per cent of pregnant women at term, lying supine.⁷ Venous blood from the lower part of the body reaches the heart through the superior vena cava, after diversion via the intervertebral venous plexus and the azygous vein. In the supine position, the lower aorta may also be compressed. This phenomenon affects primarily the renal and uteroplacental blood flows. Thus, the supine position should be avoided during the second and third trimesters of pregnancy, even in the absence of maternal arterial hypotension.

Respiratory system

ANATOMICAL CHANGES

Capillary engorgement occurs in the majority of pregnant women throughout the respiratory tract. Swelling in the area of the nasopharynx makes nose breathing difficult for some women and increases the risk of bleeding following nasotracheal intubation.

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LUNG VOLUMES

Lung volumes undergo progressive changes beginning in the fifth month of pregnancy. There is a decrease in expiratory reserve volume, residual volume and functional residual capacity. There is a concomitant increase in inspiratory capacity and inspiratory reserve volume so that total lung capacity remains unchanged.

The closing volume of the lung is the pulmonary gas volume below which bronchiolar airways close off, trapping gas in pulmonary alveoli. These rapidly become atelectatic and augment the pulmonary shunt. Closing volumes in young, nonpregnant women are well below expiratory reserve volume. Measurements made during pregnancy indicate no changes in closing volume. However, a decrease in functional residual capacity as pregnancy progresses leads to airway closure during tidal breathing in more than 50 per cent of patients at term when in supine position, but not when seated.⁸

VENTILATION

Ventilation increases early in pregnancy, approaching maximum in the second or third month. At term, tidal volume is increased by 40 per cent and respiratory rate by 15 per cent, with a net minute ventilation of approximately 50 per cent above the nonpregnant level. As dead space does not change significantly, alveolar ventilation at term is approximately 70 per cent above that in the nonpregnant state.

Acid-base balance

Basal oxygen consumption increases during pregnancy but is offset by hyperventilation so that there is an increase in maternal PaO_2 to a mean of 106 mmHg and a decrease in the mean PaCO_2 to 32 mmHg. At the same time, the plasma buffer base decreases from an average of 47 mEq $\cdot$ L⁻¹ to 42 mEq $\cdot$ L⁻¹, and the pH remains practically unchanged. All these changes occur early in pregnancy.

Increased alveolar ventilation along with decreased FRC enhance maternal uptake and elimination of inhalation anaesthetics. On the other hand, decreased FRC and increased metabolic rate predispose the mother towards hypoxaemia, even during brief periods of airway obstruction or the apnoea of intubation.⁹

Gastrointestinal tract

During the course of pregnancy, the stomach and intestines are gradually pushed upward by the enlarging uterus. Eventually, the stomach assumes a horizontal position with the pylorus displaced upward and posteriorly, thus slowing the evacuation of gastric contents. It has been noted, indeed, that gastric retention of a watery meal is prolonged from the 34th week onward.¹⁰ Pain, anxiety,

administration of narcotics and belladonna alkaloids may further delay gastric emptying.

Effects of anaesthesia on the embryo and fetus

Direct effects

The idea that surgical anaesthesia, though deemed necessary for the patient, might have detrimental effects on the growth and development of the human fetus has led to a great deal of investigation, both *in vitro* and in experimental animals. These studies present difficulties in interpretation because the concentrations of anaesthetic and duration of exposure are frequently far in excess of what is clinically used, and also because most studies were performed in lower animals. The first test of embryotoxicity of an anaesthetic agent (nitrous oxide) was made in the chick embryo. Subsequent studies have been mostly on mammalian models, such as the rat, where pregnancy lasts for a few weeks, and organogenesis only for a few days.

Work in animals exposed to toxic substances and anaesthetics shows a dose-related response, the first observable change being decreased fertility and increased fetal death. With increasing dose, the number of surviving fetuses with anomalies begins to increase, the peak incidence of anomalies being at a dose which causes 50 per cent fetal death.¹¹ The variability of teratogenic effects between species, and also between animals of greater genetic susceptibility within the same species, are very marked. The stage of development is also important in teratogenic effects. There may be dramatic sensitivity to exposure during certain days of gestation, and little or no effect at a later time. While it is true that the most critical period of exposure is during organogenesis in the first trimester (15–56 days in humans), there may be a particular sensitivity of the central nervous system to external factors at a later time, during the period of myelination. This is chiefly due to the high metabolic stability of constituents of myelin sheaths. Extrapolation from animal data to man would place the vulnerable period of the human brain from the seventh intrauterine month to the first few months after birth.

Exposure to nitrous oxide leads to a decrease in activity of methionine synthetase, a vitamin B₁₂-containing enzyme, which is involved in DNA synthesis. It has been suggested that this effect of nitrous oxide may be responsible for congenital anomalies noted in animal experiments and some authorities have recommended that pregnant women should not be exposed to nitrous oxide during the first two trimesters.¹² However, a more recent study demonstrated no significant changes in plasma methionine concentrations following exposure to 60–70 per cent nitrous oxide for up to four hours.¹³ Furthermore,

administration of nitrous oxide during early human pregnancy was found to have no adverse fetal effects.¹⁴⁻¹⁶ In rats, the teratogenic effects of nitrous oxide were prevented by the concomitant administration of halothane.¹⁷

There are numerous other factors contributing to the potential teratogenicity of anaesthesia. The cytotoxicity of anaesthetic agents is closely associated with biodegradation, which, in turn, is influenced by oxygenation and hepatic blood flow. Thus, the complications associated with anaesthesia, such as maternal hypoxia, hypotension, administration of vasopressors, hypercarbia, hypocarbia, electrolyte disturbances, etc., may possibly be a greater cause for concern as regards teratogenesis than the use of the agents themselves. Certainly hypoxia is a well-documented teratogen in the incubating chick embryo. The role of maternal carbohydrate metabolism on embryonic development is also very important. For example, the effects of 48 hours of fasting and administration of insulin, to pregnant rats on days 7, 9 or 11 of gestation, have included a large number of skeletal deformities.

HUMAN IMPLICATIONS

Several studies have attempted to relate surgery and anaesthesia during pregnancy in the human to fetal outcome, as regards congenital anomalies, premature labour, or abortion.^{1-3,14-16,18} Neither correlated congenital anomalies with anaesthesia and surgical exposure. Mothers in the surgical group had a higher percentage of babies of birth weights under 2,500 grams than those in the control group.¹ When analysis was made according to type of operation and anaesthesia, it was found in one study that premature labour was more related to the surgical disease than to other factors, e.g., incidence was higher after appendectomy, or where there was pelvic surgery, than after other procedures. In another study, an increased rate of abortions accompanied general anaesthetic procedures during the first and second trimester.¹⁸

Indirect effects

The adequacy of the uteroplacental circulation, so vital to the well-being of the fetus, is easily affected by drugs and anaesthetic procedures.

Perfusion of the intervillous space of the placenta may be diminished consequent to maternal systemic hypotension, which, in turn, may be due to the use of epidural or spinal anaesthesia, to aortocaval compression in the supine position, or to haemorrhage.

Similarly, increased uterine activity may result in reduced placental perfusion. Thus the use of alpha-adrenergic drugs to correct maternal hypotension, and anaesthetics such as ketamine (in doses above $1 \text{ mg} \cdot \text{kg}^{-1}$)

may produce increased uterine tone sufficient to endanger the fetus.

Hyperventilation of the mother, if severe, may also reduce uterine blood flow. A study performed in pregnant sheep has established that placental hypoperfusion results from the mechanical effect of hyperventilation, since it could not be corrected by restoring PaCO_2 to normal, or above normal levels.

Finally, it has been shown in experimental animals that epinephrine and norepinephrine infusion results in a decrease in uterine blood flow, and deterioration of fetal condition. Maternal pain and apprehension may similarly affect the fetus.

Practical recommendations

It is generally agreed that only emergency surgery should be performed during pregnancy. Based on the already described maternal and fetal hazards of anaesthesia, the following rational approach to anaesthesia seems indicated:

- 1 Apprehension should be allayed as much as possible by personal reassurance and adequate premedication.
- 2 Pain should be relieved whenever present.
- 3 Administration of an antacid, 15-30 ml, approximately one hour prior to induction of anaesthesia, will usually raise the pH of gastric juice above the critical level.
- 4 Beginning in the second trimester, mothers should not be transported or placed on the operating table in the supine position. The lateral decubitus position or left uterine displacement will minimize the risk of vena caval compression.
- 5 Hypotension related to spinal or epidural anaesthesia should be prevented as much as possible by rapid intravenous infusion of at least one litre of a crystalloid solution prior to induction. Should maternal blood pressure fall despite this pretreatment, a beta-adrenergic vasopressor, such as ephedrine, should be promptly administered intravenously.
- 6 General anaesthesia should be preceded by careful denitrogenation to avoid maternal and fetal hypoxaemia during induction and intubation.
- 7 The risk of aspiration should be minimized by application of cricoid pressure and rapid tracheal intubation with a cuffed tube.
- 8 To reduce fetal hazard, particularly during the first trimester, it appears preferable to choose drugs with a history of safe usage over many years. These would include thiopentone, morphine, meperidine, succinylcholine, tubocurarine and low concentrations of nitrous oxide. It is controversial whether parenteral administration of folic acid affords protection against

the consequences of inhibition of methionine synthesis by nitrous oxide.^{17,19} Ketamine, 0.5–0.75 mg·kg⁻¹, might be preferable to thiopentone as an induction agent in the face of severe hypovolaemia. In these low doses, ketamine should have practically no effect on uterine tone. Halothane may offer a specific advantage of relaxing the uterus during procedures involving pelvic organs, particularly the uterus itself.

- 9 In order to avoid maternal hyperventilation, one should monitor arterial blood gases or end-expiratory PCO₂.
- 10 It is also advisable to monitor the fetal heart rate continuously throughout surgery and anaesthesia providing that placement of the transducer does not encroach upon the surgical field. Using the directional Doppler apparatus, this monitoring is technically feasible from the 16th week of pregnancy. Uterine tone may also be monitored with an external tocodynamometer if the uterus has grown enough to reach the umbilicus or above.
- 11 Special procedures, such as hypothermia and induced hypotension might be desirable to facilitate surgery. Successful fetal outcome following both procedures for intracranial operations has been reported.^{20,21}
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