
A review associated with the development of guidance for pre-procedure pregnancy testing in adolescent girls.**Background**

It is estimated that anaesthesia for non-obstetric surgery occurs in approximately 2% of pregnant women, although this figure may be considerably higher in the first trimester, when the pregnancy may not yet have been detected. Of these procedures, approximately 42% occur in the first trimester, 35% during the second and 23% during the third.¹ Many studies and literature reviews have been undertaken to try to determine the risks to mother, pregnancy and fetus associated with exposure to both the anaesthetic and the surgical procedure. It is generally accepted that elective surgery should be avoided during pregnancy, and that recommendations are required for the anaesthetic and surgical management of emergency situations in pregnant patients.

Pregnancy outcome in young women

Any examination of the risks of anaesthesia and surgery in pregnancy must take into consideration the background incidence of poor outcome of pregnancy in young women.

In a study of all births in Denmark from 1978 to 1992, the rates of miscarriage, ectopic pregnancy and stillbirth in women aged less than 20 years were 10.6%, 1.6% and 0.4% respectively.² Three studies looking at the incidence of congenital abnormalities, show that in babies born to women aged less than 20 years, the rates are 3.5%³, 2.8%⁴ and 3.7%⁵. The incidence of poor outcomes varies with age during pregnancy, but all are higher in teenage pregnancies than in women in their 20s. Poor pregnancy outcome then becomes more common with increasing maternal age. It has also been reported that 22% of pregnancies are lost before they have been detected clinically.⁶

Risks of anaesthesia and surgery during the first trimester of pregnancy

Knowledge regarding the safety of surgery and anaesthesia during pregnancy is based primarily on animal studies and retrospective human studies. However, it may not be appropriate to extrapolate the conclusions from animal studies to the human population, due to differences in drug doses, drug responses, time-scales of embryological development, etc. and retrospective human studies have a number of confounding variables which make their conclusions difficult to interpret. Women are generally given multiple anaesthetic agents and other drugs during surgery, and it is difficult to discern whether an adverse outcome is due to the operative procedure, the underlying maternal condition, maternal stress, fever, the anaesthetic agents or the altered physiological responses to anaesthesia during pregnancy.

In terms of undertaking anaesthesia and surgery in an adolescent girl with an undetected pregnancy, the outcomes of interest are the risk to the patient, the risk to the pregnancy and the risk to the

fetus. Several large studies of non-obstetric surgery in pregnancy have been reported⁷⁻¹⁰ including one systematic review of all English Language literature on the subject.¹¹

Risks to the patient

Maternal death is rare following non-obstetric surgical intervention. The incidence reported in the systematic review of 12452 patients in 54 studies is 0.006%, which refers to a single death due to abdominal haemorrhage in the 20th week of pregnancy in a patient who had undergone a laparoscopic cholecystectomy two weeks earlier.¹¹

Maternal physiology begins to adapt to the pregnancy after 6-8 weeks gestation, following which cardiac, haemodynamic, respiratory, metabolic and pharmacological parameters are considerably altered. With the increase in minute ventilation and oxygen consumption and a decrease in oxygen reserve (decreased functional residual capacity and residual volume), pregnant women become hypoxaemic more rapidly. Airway management may become more challenging, due to weight gain affecting the soft tissues of the neck and increased vascularity of the mucous membranes. The body's handling of drugs also alters due to changes in plasma proteins and volume of distribution. In an undetected or undisclosed pregnancy the adaptations required to anaesthetic technique and drug dosing will not be considered, and anaesthetic adverse events may be more common.

Risks to the pregnancy

Studies appear to show that there is an increased risk of spontaneous miscarriage in patients who have been exposed to anaesthesia and surgery during pregnancy. One study reported a rate of 7.1% fetal loss, compared with 6.5% in controls who had no surgery⁷, while the systematic review reported an incidence of 5.8% in all patients who underwent a surgical intervention in pregnancy, increased to 10.5% if the surgery occurred in the first trimester.¹¹ Several smaller studies have reported fetal death rates of 11.1% (no control group)¹², 8.5% loss of pregnancy where surgery was undertaken in the first trimester (control group 2.0%)¹³, and 9.6% (control group 5.1%).¹⁴ Although higher than the control groups, these rates are similar to the miscarriage rate quoted for pregnancies in women aged less than 20 years. Studies looking specifically at appendicectomy in pregnancy have reported miscarriage rates of 13.3% and 26% in patients whose operation took place during early pregnancy.⁹

Risks to the fetus: prematurity, low birth weight and infant death

There appears to be an increase in very-low- and low-birth-weight infants in the offspring of women having surgery during pregnancy, due both to premature birth and intrauterine growth retardation.^{8,10,15} The incidence of early infant death is also increased.⁸

Congenital malformations

An important question to answer is whether exposure to anaesthesia and surgery during pregnancy increases the risk of congenital malformations. The taking of medication during pregnancy is generally viewed with extreme caution, particularly during the first trimester, and many drugs have been shown to be associated with teratogenic effects. The teratogenic effects of medications vary depending on the time taken during pregnancy. The fetus's susceptibility to injury depends on its period of development. Different organs have different critical periods, though the span from gestational day 15 to day 60 is critical for many organs. The heart is most sensitive during the third and fourth weeks of gestation, whereas the external genitalia are most sensitive during the eighth and ninth weeks. The brain and skeleton are sensitive from the beginning of the third week to the end of pregnancy and into the

neonatal period. Confusion may arise when a congenital abnormality or syndrome, which may have been caused by medication taken during pregnancy, has similar characteristics to a spontaneously occurring genetic syndrome, e.g. fetal warfarin syndrome and Happle Syndrome (human X-linked dominant chondrodysplasia punctata).

Large studies of populations of pregnant women have shown no statistically significant difference in the rates of congenital abnormalities in babies of those who have had surgery during pregnancy compared with controls.^{7-11,15-16} Although two studies have suggested that there could be an association between anaesthesia in the first trimester and neural tube defects or the combination of hydrocephalus and eye defects in the fetus¹⁷, it is felt that this is as yet unproven.¹⁸ There has also been concern that chronic benzodiazepine use may be associated with an increased risk of cleft palate anomalies¹⁹, but this is not an association seen with use of benzodiazepines solely during anaesthesia. There is ongoing concern about the risk of increased neuronal apoptosis, with associated adverse effects on neurodevelopmental outcome, in babies exposed to anaesthetic agents in utero or during the neonatal period and infancy. It is felt that this effect is more likely to be of influence if anaesthesia occurs after 28 weeks gestation, but further work is awaited to determine if the results seen in rodent studies can be extrapolated into the human population.²⁰ At present, it appears that although many drugs have been identified that have teratogenic effects in pregnancy, especially in rodent models, anaesthetic medications, including induction drugs, barbiturates, opioids, muscle relaxants, volatile agents and local anaesthetics are associated with safe use in humans during pregnancy. Nitrous oxide remains controversial, because of effects on B12 metabolism, and its use in the first trimester is not recommended.²¹

Type of surgery

The risks associated with surgery during pregnancy did not seem to be associated with any particular type of surgery in a large study including patients having both abdominal and non-abdominal surgery,⁸ or in a case control study of reproductive outcome after exposure to surgery during pregnancy.¹⁰ No difference was found between five fetal outcome measures when patients having laparoscopy or laparotomy between 4 and 20 weeks gestation were compared.¹⁵ It is suggested that the incidence of appendicitis during pregnancy lies between 1 in 655 to 1 in 6635 pregnancies, but that it occurs more commonly in teenage women than in other age groups.⁹ Surgery for appendicitis during pregnancy is associated with a high rate of surgery-induced labour (4.6%). Fetal loss associated with appendicectomy is 2.6%, but this increases to 10.9% if peritonitis is present.¹¹

Summary

It does not appear that anaesthetic agents have teratogenic effects in humans. However anaesthesia and surgery during pregnancy are associated with an increased risk of miscarriage, premature birth, low birth weight infants and infant death.

Recommendations

- It would be prudent to aim to detect early pregnancies that may not yet have become clinically obvious, prior to exposing a patient to anaesthesia or surgery.
- Elective surgery ideally should not take place during pregnancy and particularly during the first trimester.
- Emergency surgery should proceed as indicated, with consideration of the anaesthetic implications of the altered physiology of pregnancy. Suitable anaesthetic regimes are detailed in a number of comprehensive review articles.^{1, 21-23}

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