Focused Reviews

CME Intraoperative Awareness During General Anesthesia for Cesarean Delivery

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Intraoperative awareness is defined as the spontaneous recall of an event occurring during general anesthesia. A move away from rigid anesthetic protocols, which were designed to limit drug transmission across the placenta, has reduced the incidence of awareness during cesarean delivery to approximately 0.26%. Nevertheless, it remains an undesirable complication with potential for the development of posttraumatic stress disorder. Assessing depth of anesthesia remains a challenge for the anesthesia provider as clinical signs are unreliable and there is no sensitive and specific monitor. Bispectral Index monitoring with the goal of scores <60 has been recommended to prevent awareness. Induction drugs vary in their ability to produce amnesia and the period of hypnotic effect is affected by the rate at which they are redistributed. After initiation of anesthesia, volatile anesthetics should be administered to a target of 0.7 minimum alveolar anesthetic concentration, which has been shown to consistently achieve mean Bispectral Index scores <60. Because of its rapid uptake, nitrous oxide remains an important adjunct to reduce the risk of awareness during emergency cesarean delivery. In the absence of fetal compromise, there is no rationale for an inspired oxygen concentration above 0.33. Deeper levels of anesthesia reduce the incidence of awareness; current evidence does not suggest an increased risk of tocolysis or fetal morbidity.
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THE DILEMMA OF OBSTETRIC ANESTHESIA

The objectives of general anesthesia for cesarean delivery are to keep mother and fetus adequately oxygenated, while limiting fetal drug transmission and maintaining maternal comfort. Crawford[1] called this conflict "the dilemma of obstetric anesthesia and analgesia" and said it epitomized the challenge and the attraction of the specialty. The balance of this conflict has changed over the years. Intraoperative recall during general anesthesia was unreported with the spontaneous breathing and ether of Mendelson's day, but this changed with the introduction of succinylcholine in the late 1950s when endotracheal intubation and muscle relaxation were popularized. Initially, anesthesia was provided largely by thiopental and nitrous oxide[2] and was associated with an incidence of awareness up to 26%.[3] A reluctance to load with a volatile anesthetic, and concern about lack of care for an anesthetized newborn from an undeveloped neonatal service, might have helped make this frequent incidence of recall seem an acceptable side effect.

The addition of halothane 0.5% (0.66 minimum alveolar anesthetic concentration [MAC]) to the anesthetic moved the balance further in the maternal direction, reducing awareness to around 1%,[4] and throughout the 1970s, this was widely regarded as an acceptable incidence. The balance shifted further toward maternal comfort when it was demonstrated that awareness at cesarean delivery could be reduced by more generous doses of thiopental and more liberal use of a volatile anesthetic.[5] This practice became more widely disseminated in the 1990s, a time in which access to neonatal resuscitation support became more widely available. Additionally, anesthesia providers were taking advantage of the electronic monitoring revolution (including measurement of end-tidal gas concentrations), which offered a dynamic alternative to the traditional recipe approach. Today, the incidence of awareness during anesthesia in the United States is believed to be between 0.1% and 0.2% of all patients undergoing general anesthesia, representing 20,000–40,000 cases per year.[6] The risk appears to be higher when muscle relaxants are used and during cesarean delivery.[7] In Australia and New Zealand, the Australian and New Zealand College of Anesthesia (ANZCA) Trial studied 1095 cesarean

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Table 1. Terminology of Awareness[37,44]

Consciousness	State in which information from patient's surroundings can be processed
Recall	Ability to retrieve stored memories
Amnesia	Absence of recall. Event not retained in long-term memory
Wakefulness/ responsiveness	Unequivocal communication with an anesthetized patient without subsequent recall
Explicit memory	Recall of specific intraoperative clinical events
Priming	Presentation of material to an anesthetized patient
Learning	Evidence of communication or detection of priming through postoperative tests but without recall
Implicit memory	Postoperative evidence of priming but without recall

deliveries and interviewed 763 women postoperatively; two women had recall giving an incidence of 0.26%.[8]

DEFINITIONS AND SCOPE

Awareness is defined as the spontaneous postoperative recall of an event that occurred during general anesthesia (Table 1).[9] One difficulty with explicit memory of perioperative events is distinguishing between recall of genuine intraoperative events and emergence phenomena, because voices, the baby crying, and wound pain are part of the postoperative experience. A wider definition of recall takes in a spectrum that ranges from dreams, through recall of specific events, to full consciousness with paralysis and pain. Dreaming is often thought to be indicative of light anesthesia but more likely occurs during emergence from anesthesia and recovery.[10] Crawford[1] took the view that unpleasant dreams did reflect awareness and that the two should always be linked. Anecdotal reports have shown that, even when the content can be linked to intraoperative events, dreams are not necessarily unpleasant.[5]

INDUCTION OF ANESTHESIA

Monitoring cerebral function to detect awareness has advanced considerably in recent years, but the perfect monitor has yet to be developed. The most widely studied brain function monitor, Bispectral Index (BIS) monitoring, is easy to initiate but even rapid application may delay delivery of the fetus in an emergency cesarean delivery. A BIS monitor was used in 32% of 1095 general anesthetics studied as part of the ANZCA trial. Of note, 30% of Category 1* and 37% of Category 4* cesarean deliveries were monitored.[8] Clearly, the limiting factor in the use of monitoring was not the urgency of the procedure. Another consideration is whether, within the context of an emergency cesarean delivery, a BIS score target <60 is attainable predelivery. When the target anesthetic concentration is 0.8 MAC or above, it seems that mean BIS scores <60 can be achieved,[11,12] but without a commitment to this level of volatile anesthetic delivery at the outset, the rationale for BIS monitoring is lost. Intraoperative brain function monitoring during cesarean delivery has yet to become a mandatory requirement by any governing or regulatory agency.

The risk of recall is increased with a rapid sequence induction of anesthesia as tracheal intubation and surgical incision follow in rapid sequence. There may be insufficient time to allow adequate uptake and distribution of volatile anesthetic to prevent awareness[12] before redistribution causes brain levels of the induction drug to decrease. The choice and dose of induction drug then becomes critical. Many regard thiopental as the drug of choice but a single induction dose is soon redistributed with rapid recovery of consciousness. Recommended doses range from 3 to 7 mg/kg; in the ANZCA Trial the mean dose was 4.9 mg/kg.[8,13–17] Not surprisingly, larger doses of hypnotic drug result in a lower incidence of recall.[5] The wide variation in recommended dose may reflect how anesthesiologists view their role in the conflict between fetal drug transmission and maternal comfort. There is general agreement that doses <4 mg/kg are unlikely to lead to fetal depression, and that doses in excess of 7 mg/kg are liable to do so.[1] The degree of concern for maternal awareness might be expected to decide where, between those limits, the choice lies. At low doses, thiopental is mildly amnesic[18] but it does not produce retrograde amnesia.[19]

Although thiopental remains the drug of choice, a new generation of anesthesiologists is largely untrained in its use. Propofol is now the most widely used IV drug in anesthesia but there are concerns over its capacity to produce neonatal depression and adequate depth of anesthesia. Celleno et al. examined the maternal electroencephalogram with either thiopental 5 mg/kg or propofol 2.4 mg/kg. Half of the propofol group had rapid low voltage (8–9 Hz) waves on their electroencephalogram suggestive of a light plane of anesthesia compared with 10% of the thiopental group.[20] Another disadvantage of propofol is its long effect-site equilibration time, which slightly prolongs the period from injection to hypnosis. Other studies have provided no evidence for the superiority of thiopental compared with propofol.[21] However, severe maternal bradycardia has been reported with propofol combined with succinylcholine.[22] Propofol has a greater amnesic effect than thiopental[23] through interference with long-term memory.[24] Although there are no data on which dose is best to avoid awareness, 2.5 mg/kg is commonly used.[25] Worldwide, there is little doubt that propofol is used for

*Category 1: emergency cesarean delivery indicated because of presence of condition which is of immediate threat to the life of the woman or fetus; Category 4: elective procedure, cesarean delivery can be scheduled to suit the woman and staff.

cesarean delivery despite these concerns and, to date, without the accumulation of adverse reports.[8,23]

Ketamine is used as an induction drug <2% of the time.[8] It is associated with less responsiveness and recall than thiopental when used at a dose of 1 mg/kg,[26] but the sympathomimetic effects limit its use in preeclampsia, and when there are concerns about hypertension. The associated hallucinations and emergence phenomena are another problem, although both are dose related and possibly occur less frequently in obstetric patients.[27] Ketamine may be of use to reduce hypotension at induction in the setting of hemodynamic instability.

Benzodiazepines are used infrequently as sole induction drugs, although they may be used occasionally to supplement an induction sequence.[8] Midazolam produces more profound amnesia than propofol,[28] impairing both explicit and implicit memory,[29] but the onset of hypnosis is slow and neonatal depression is slow to resolve. It does not produce retrograde amnesia.[28]

MAINTENANCE OF ANESTHESIA

The rapid redistribution of induction drugs underlines the importance of introducing an adequate volatile anesthetic as soon after induction as is practical. In some centers, the skin is prepared and the drapes applied before induction of anesthesia. Although this might be in the best interests of a fetus in need of immediate delivery, emergency surgery and inadequate uptake of the volatile anesthetic are known risk factors for awareness.[12] Depth of anesthesia can be considered in terms of the MAC that is required to achieve anesthesia in 50% of the patients. MAC may be reduced in pregnancy by 25%–40%, possibly because of increased pain thresholds or analgesia administered in labor. Lower BIS scores were observed for similar anesthetic concentrations in pregnant compared with nonpregnant patients.† A comparison between parturients with and without prior labor undergoing cesarean delivery found that prior labor was associated with lower intraoperative BIS values during sevoflurane/nitrous oxide general anesthesia.[30]

The rapid uptake of nitrous oxide makes it a useful adjunct despite being a weak anesthetic. The choice of concentration is secondary to that of the inspired oxygen requirement. The administration of 100% oxygen may improve 1-min Apgar scores[31] but oxygen-free radicals have been detected in newborns after maternal administration of high oxygen concentrations,[32] and resuscitation of neonates with oxygen was associated with poorer Apgar scores than air.[33] A common recommendation is that 50% oxygen should be given,[13,15–17] but 33% has been shown to result in similar outcome provided there is no fetal compromise.[34] Nitrous oxide has little influence on monitors of cerebral function[35,36] but a concentration of 70% contributes around 0.5 MAC and, if less is given, a corresponding increase in volatile anesthetic is needed to compensate.

Several textbooks recommend that the MAC of volatile drug administered predelivery should be approximately 0.5[1,15] despite evidence that this policy is associated with an incidence of awareness close to 1%.[5] This finding is consistent with predelivery BIS scores at 0.5 MAC in 50% nitrous oxide that range between 57 and 64.[12] In a small sample, anesthesia with 0.2% end-tidal isoflurane in 50% nitrous oxide gave BIS scores between 70 and 80 with evidence of learning but not spontaneous recall.[37] When MAC was increased to 0.8 in nonobstetric patients, BIS scores between 40 and 60 were achieved but the incidence of awareness was still 0.21%.[38] One point to consider is whether the target MAC should represent the MAC for the volatile drug alone or include the contribution of nitrous oxide. Because the effect of nitrous oxide on memory is uncertain, prudent advice would be to regard the target MAC as that of the volatile drug alone.[39] However, increasing the concentration of the volatile drug introduces a new conflict as all volatile drugs are tocolytic and uterine contractility and tone decrease in a dose-dependent manner. The uterus will contract in response to oxytocin, however, provided MAC is <0.8–1.0.[40] These operational limits should provide sufficient scope for adequate anesthesia without penalty.

In pregnancy, reduced functional residual capacity and increased minute ventilation increase the rate of equilibration of blood and inspired concentration of the volatile anesthetic, although the pregnancy-induced increase in cardiac output counteracts this to some degree. Equilibration between inspired and brain concentrations may take 4–12 min depending on the volatile anesthetic. Uptake of volatile anesthetic therefore needs to be accelerated. McCrirrick et al.[41] described an overpressure technique with initial vaporizer settings in excess of MAC to speed equilibration, but measurement of end-tidal vapor concentrations has offered a more dynamic approach. Indeed, investigators found no difference in the incidence of recall when noncesarean patients were randomized to adjustment of the vaporizer setting to deliver a target end-tidal concentration or BIS monitoring with a target BIS score <60.[38] Unfortunately, because this study was underpowered, equivalence between the two techniques cannot be assumed. Isoflurane and sevoflurane are favored because of rapid uptake; for the former, the target end-tidal concentration should be in excess of 0.7%,[11] and for the latter, an end-tidal concentration of 1.5% achieved mean predelivery BIS scores of <60.[12]

After delivery, the concentration of nitrous oxide may be increased and opioids may be administered. This will result in a reduction in reflex activity but not necessarily a reduction in the incidence of recall. The

†Gin T, Chan MTV. Pregnancy reduces the bispectral index during isoflurane anesthesia (abstract). Anesthesiology 1997; 87:A305.

Table 2. Techniques to Avoid Awareness

Beware drug and equipment errors
Brain function monitoring (e.g., Bispectral Index monitoring to achieve scores <60)
Thiopental dose 5–7 mg/kg
Target end-tidal volatile anesthetic monitoring to achieve concentration >0.8 MAC[a]
Highest concentration of nitrous oxide compatible with maternal and fetal oxygen requirements
Opioid analgesia after delivery
Consider benzodiazepines after delivery

[a] There is no evidence of fetal morbidity with increased depth of anesthesia.

volatile anesthetic should be continued until completion of the operation, but in the event of uterine atony, it can be reduced and a small dose of midazolam or ketamine substituted. Suggested techniques to reduce the risk of awareness during cesarean delivery are summarized in Table 2.

BRAIN FUNCTION MONITORING

Routine brain function monitoring of patients undergoing general anesthesia is controversial, although in one study, it was shown to result in an 82% reduction in the incidence of awareness in patients undergoing procedures considered at high risk for awareness, including cesarean delivery.[9] However, a low BIS score does not guarantee unconsciousness.[42] Whether routine monitoring of brain function in the specific setting of general anesthesia for cesarean delivery can reduce the incidence of awareness has not been studied.

THE FETUS

Catecholamine secretion during light anesthesia promotes uterine vasoconstriction and tocolysis. Depressant effects from transplacental drug transmission are usually responsible for a lower 1-min Apgar score in neonates after general anesthesia compared with neuraxial techniques, but by 5 min, differences have largely disappeared. Provided neonatal resuscitative support is available, the effects of general anesthesia are wholly reversible and the uterine incision to delivery time is more important than the induction to delivery time for good neonatal outcome. Evidence is lacking that an awareness avoidance approach to general anesthesia has untoward neonatal effects beyond the first few minutes of life.

AVOIDING LITIGATION

Intraoperative awareness is one of several major patient concerns when undergoing general anesthesia; Klafta and Roizen[43] showed that up to 54% of patients worry about the possibility of pain, paralysis, and mental distress during surgery. Current advice is that patients considered to be high risk should be informed of the possibility of awareness, when circumstances permit.[44] It may not be appropriate to do this before an emergency cesarean delivery when anxiety can be extreme. When possible, a preoperative discussion may help align expectation with experience and reduce the risk of litigation.[45]

When awareness occurs, a full account with precise details should be recorded in the medical record for future reference. An apology costs nothing and might avert legal proceedings; denial is unhelpful. Symptoms consistent with posttraumatic stress disorder, sleep disturbance, nightmares, irritability, and lack of concentration that can interfere with work, may follow. Counseling is recommended, but its efficacy is unknown. The anesthesiologist may also be distressed by the incident.[46]

Hull and Thorburn[47] believe that awareness cannot occur without negligence and equated light anesthesia with inadequate anesthesia. An analysis of 81 incidents of awareness found that 32 occurred because of avoidable drug and equipment errors.[46] The alternative view is that a low incidence of awareness during general anesthesia for cesarean delivery is unavoidable, but the difficulty of mounting a successful defense is acknowledged.[47]

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