IJOA 07293
Received October 2007
Accepted January 2008
Final Revision
Text

ORIGINAL ARTICLE

A prospective study of awareness and recall associated with general anaesthesia for caesarean section.

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Funding: This study was supported by a starting grant from the Australian and New Zealand College (ANZCA) Trials Group, followed by a 2006 project grant from ANZCA.

Short Title: Awareness associated with general anaesthesia for caesarean section

SUMMARY

Background: The obstetric population is considered at high risk of awareness and recall when undergoing general anaesthesia for caesarean section. In recent years the incidence may have been altered by developments in obstetric anaesthesia.

Methods: A prospective observational study of general anaesthesia for caesarean section was conducted during 2005 and 2006 in 13 maternity hospitals dealing with approximately 49,500 deliveries per annum in Australia and New Zealand. As a component of this study the frequency of recall of intraoperative events was examined using a structured postoperative interview on two occasions.

Results: There were 1095 general anaesthetics surveyed with 47% being performed for urgent fetal delivery. Thiopental was the most common induction agent (77%) with sevoflurane being used for maintenance in 63%. In 32% of cases a depth of anaesthesia monitor was used and 763 cases (70%) had at least one post operative interview for dreaming and awareness. There were two cases deemed to be consistent with awareness (incidence 0.26%, CI 0.03-0.9%, or 1 in 382) and three cases of possible awareness.

Conclusions: Awareness with recall of intraoperative events remains a significant complication of obstetric general anaesthesia but was potentially avoidable in all cases detected in this study.

Key words: anaesthesia, general, anaesthesia, caesarean section, awareness, recall

INTRODUCTION

General anaesthesia for caesarean section is traditionally considered a high risk procedure for awareness, despite the potency of volatile anaesthetic agents being enhanced by pregnancy. Awareness and recall of intraoperative events is highly likely to cause patient dissatisfaction and can result in prolonged psychological disturbance with anxiety, mood and sleep disturbance and phobic behaviour.[1-3] It is a prominent cause of litigation.[4] A higher risk of awareness in the obstetric population compared to the general surgical population is likely to be related to a number of factors. These include the physiological changes of pregnancy, particularly the high cardiac output of pregnancy, which results in a more rapid redistribution of intravenous anaesthetic agents as well as slowing the establishment of an adequate partial pressure of volatile anaesthetic agent. Coupled with this is the concern for the anaesthetist in regards to neonatal drug exposure just prior to delivery, the effect of volatile anaesthetics on uterine tone and the haemodynamic effects of anaesthetic agents in emergency situations.

In recent years there have been a number of developments in anaesthesia, particularly in anaesthetic pharmacology and technology, which have potentially changed obstetric anaesthesia practice. The impact and clinical application of these changes on the incidence of awareness and recall in this population is unclear. Examples of developments that may have altered this incidence include the widespread availability of depth of anaesthesia monitors; volatile anaesthetic agents with a more rapid onset of action such as sevoflurane and desflurane; an acceptance of higher levels of volatile anaesthetic agents; a declining use of nitrous oxide and the use of propofol for induction of anaesthesia.

Whilst the use of general anaesthesia for caesarean section (CS) appears to be in decline throughout the world there has been little recent research involving the review of techniques and practices pertaining to general anaesthesia for CS. We conducted a prospective observational study during 2005 and 2006 to assess the nature of contemporary practice in relation to general anaesthesia for CS. In this paper we present the information on the complication of awareness, as well as information on anaesthetic techniques and pharmacology relevant to this complication.

METHODS

A multi-centre prospective observational study of general anaesthesia for CS was conducted with the assistance of the Australian and New Zealand College of Anaesthetists (ANZCA) Trial Group across 13 hospitals in Australia and New Zealand between June 2005 and January 2007. Each centre had its own designated site coordinator who was responsible for

obtaining local institutional ethical approval; maximising capture of cases; collating data collection on a standardised case record form and for conducting an interview for recall and dreaming on days 1 and 4 post-operatively. Ethical approval was received from all sites to perform the data collection with two sites requiring individual patient consent. Women were considered eligible if they were aged 18 years and over and underwent CS under general anaesthesia.

The case record form requested information about patient demographics and caesarean characteristics (age, weight, American Society of Anesthesiologist's (ASA) classification, anaesthetic risk factors and co-morbidities, urgency of caesarean delivery rated as category 1-4,[5] reason for use of a general anaesthetic technique, and experience of the attending anaesthetist). In addition, data that were collected that were relevant to the complication of awareness included the anaesthetic induction and maintenance technique; the use of nitrous oxide; and the monitoring employed. Minimum alveolar concentration (MAC) values were the estimated median maintenance and lowest values, and values at the time of delivery and termination of anaesthesia.

After surgery, patients were interviewed using a structured, standardised questionnaire[2] on two scheduled occasions, the first 2-6 hours post operatively and the next at least 48 hours after surgery but prior to discharge from hospital. At both interviews patients were asked "What was the last thing you remember before going to sleep?" "What was the first thing you remember when you woke up?" "Can you recall anything in between?" "Did you have any dreams during your anaesthetic?" If there was any report of dreaming or suggestion of recall, a narrative report was collected from the patient at the time of the interview and recorded in the patient's own words. This narrative was assessed by an independent endpoint adjudication committee, consisting of three specialist anaesthetists experienced in evaluation of such narratives, each of whom independently coded each report as "awareness", "possible awareness" or "no awareness". Awareness was defined as postoperative recall of events occurring during the period of general anaesthesia. Confirmed awareness was defined as two or more members coding "awareness". "Possible awareness" was defined as one adjudicator only coding "awareness" or at least two adjudicators coding "possible awareness".

Data were analysed using STATA (Statacorp, 2005) and are presented as number or percentage; mean and standard deviation (SD) for normally distributed data and median and interquartile range (IQR) for non-parametric data, with 95% confidence intervals (CI). After

closure of the database further detailed information was obtained from the relevant sites for cases of potential awareness with recall.

RESULTS

In total 13 hospitals contributed to the data set, with contributions from centres ranging from 16 to 219 patients.[6] A total of 1095 cases were surveyed and of these, 763 had at least one postoperative interview for dreaming and recall. Of the 1095 cases surveyed, 47% were classified as emergency (Category 1) and 18% were elective (Category 4) (Table 1) A depth of anaesthesia monitor was applied in 32% of cases (30% of Category 1 cases, 27% of Category 2/3 cases and 37% of elective cases). Procedure and patient demographics, including possible patient factors for an increased risk of awareness, are shown in Table 1.

Thiopental was the most popular induction drug (83%, mean dose 4.9 [1.1] mg/kg), followed by propofol (15%, mean dose 2.4 [0.9] mg/kg) and ketamine (1.6%, 1.1 [1.2] mg/kg). The induction sequence included intravenous opioid in 18% and a benzodiazepine in 3.6%. Sevoflurane was the most commonly used drug for maintenance of anaesthesia (63%), followed by isoflurane (28%), desflurane (8.5%) and propofol (1.3%). Nitrous oxide was used in 69% of cases at some time and an inspired oxygen concentration of equal to or greater than 50% was used in 89% of cases prior to delivery. The highest mean MAC values were at the time of delivery (Table 2).

Twenty-five women reported dreaming (23 at the first interview, 19 again at the second interview and two at the second interview but not at the first). Only one had an unpleasant dream and only three had dream content that in any way related to the operating environment (Table 3). Examination of the intraoperative record did not suggest an inadequate depth of anaesthesia in these three cases. Two patients were deemed to have experienced awareness, giving an incidence of 0.26% (CI 0.03-0.9%, 1 in 382). There were also three cases deemed “possible awareness” (Table 4).

Case 1

An emergency caesarean was performed because of likely placental abruption and fetal compromise in a parturient with recently detected hypertension. The platelet count and coagulation tests were not available, so general anaesthesia was used. Depth of anaesthesia monitoring was not used. Awareness resulted from the unintentional administration of sterile water followed by suxamethonium. The sterile water had been drawn up into a 20 ml syringe in preparation for the reconstitution of thiopental but this reconstitution had not occurred.

The anaesthetic trainee was working alone after hours and recognised the error as a result of seeing the patient's hands moving prior to fasciculations. Gas induction using sevoflurane and 100% oxygen was commenced immediately and cricoid pressure applied. Verbal communication with the paralysed patient was maintained. The patient remained well oxygenated throughout and intubation was performed successfully at the time of a minimum alveolar concentration of 1.4. Boluses of propofol 100 mg and midazolam 2 mg were given after intubation.

The patient and her husband were counselled in the recovery room, following an otherwise uncomplicated procedure, in the presence of the obstetrician. In the first few days following surgery the patient was visited regularly by the pain service. She experienced episodes of anxiety, sleep disturbance and altered mood, so was prescribed a benzodiazepine at night and was referred to the hospital's Maternal Mental Health service. Over several further days her episodes of anxiety and sleep disturbance resolved, she reported improved mood and she had no problems with the care of her infant.

Case 2

An elective repeat caesarean section was scheduled and the attending anaesthetist agreed to a late request from the obstetrician that the woman receive a general anaesthetic, on the basis of his concern about the anterior placental location and an increased risk of haemorrhage. Awareness was discussed with the patient as a potential risk of general anaesthesia. Depth of anaesthesia monitoring was not used. Anaesthesia was induced, by a specialist and trainee, with remifentanil 50 mcg, thiopental 3.3 mg/kg and suxamethonium. Intubation required two brief attempts, the maternal inspired oxygen fraction was 0.9 and atracurium was required soon after intubation. Delivery of the baby was rapid and the end-tidal isoflurane concentration at that time was noted to be 0.2%. The specialist anaesthetist documented that the end-tidal concentration was "a bit low" at that point and increased the inspired concentration, as well as adding nitrous oxide 50% after delivery. Anaesthesia was maintained with a remifentanil infusion, morphine and isoflurane.

The patient mentioned awareness spontaneously on wakening. Memories included hearing conversation that included the words "Christmas holiday". She said she had also felt her delivery and the surgeon working on her, and that it was "not exactly painful but a little scary". She had tried to move and to talk but was unable to do so. After the baby was delivered the next thing she remembered was being in the recovery room where she heard her baby cry and was in pain. The anaesthetist recalled discussing the intubation and getting the

husband in to see the baby but did not recall any conversation about holidays. She was counselled over several days and offered postpartum follow-up.

DISCUSSION

In this study we found an incidence of awareness with recall of intraoperative events to be approximately 1 in 400 general anaesthetics for CS, although it is possible that the incidence was closer to 1 in 150 and the upper confidence interval, assuming only two cases, is 1 in 100. This is consistent with the incidence reported in 1991 by Lyons and Macdonald (0.4%)[7] and is higher than the incidence reported in the general surgical population (0.1-0.2%),[8] confirming that pregnant women remain at increased risk.

Both cases of recall detected in this study were avoidable. In the first case the pressure of performing an emergency general anaesthetic for a trainee working alone after hours is likely to have contributed to the medication error that occurred. Ensuring that the patient was unresponsive to verbal communication and assessing the eyelash response prior to the administration of the suxamethonium would also have prevented this episode of awareness. It is unclear whether the propofol and midazolam was administered post intubation to address a light level of anaesthesia or in the hope that retrograde amnesia might occur. Midazolam has not been shown to induce retrograde amnesia[9] and neither agent can be recommended for this indication**.**

In the second case the anaesthetic agents administered to the patient appear to be insufficient for sustained unconsciousness. A modest dose of thiopental was used- 3.3 mg/kg, compared with a mean dose of 4.9 mg/kg for the entire population in this study. With the dramatically increased cardiac output of pregnancy the intravenous induction agent is redistributed from the cerebral circulation rapidly, which potentially leaves a period of light anaesthesia as the volatile anaesthetic agent enters the effect site. This can be exacerbated if more than one attempt at intubation is required, as happened in this case. The use of an overpressure technique has been described[10] as a method of rapidly increasing the volatile anaesthetic concentration following intravenous induction of anaesthesia for CS. The uterus responds well to oxytocic drugs despite the tocolytic effect of volatile anaesthetics at 0.75 MAC.[11] The decision to perform general anaesthesia at the obstetrician's request for placenta praevia is not supported by current guidelines. The UK National Institute for Clinical Excellence guideline for Caesarean Section (2004) specifically recommends regional anaesthesia over general anaesthesia for cases of placenta praevia.[12] We consider that the anaesthetist, as part of a team approach, is the best person to decide on the most appropriate

method of anaesthesia for CS, with the obstetrician providing information on the maternal and fetal condition and a time-frame for delivery.

The incidence of dreaming in this study was low (3%) compared with that reported recently.[13] Dreaming is not related to the depth of anaesthesia and it appears that it probably occurs predominantly during recovery from anaesthesia. This study supports the findings of Leslie et al that unpleasant dreams are rare and that dream content is infrequently specific to the operating room environment.

It can be argued that conscious state monitoring, such as the Bispetral Index (BIS) Monitor (Aspect Medical Systems) or the Entropy monitor (GE Healthcare), may have prevented both cases of awareness and recall in this study. There has been little research into the use of these monitors in obstetric anaesthesia. Chin and Yeo showed that when sevoflurane is delivered at an end-tidal concentration of 1% (0.5 MAC) with 50% nitrous oxide following thiopental for CS, BIS values are within the range 60-70, whereas 1.5% maintains BIS values less than 50,[14] supporting the use of a higher concentration of volatile anaesthetic in this situation. In the B-Aware study[15] none of the patients having CS, half of whom were monitored with BIS, were aware, but the sample size was small (n=172). However, across a cohort of high-risk patients, BIS monitoring reduced the risk of awareness by 82%. These monitors take a minute or two to apply and activate, which may be a barrier to their use in emergency situations. In our institution, in the most urgent of cases, the monitor is applied by the anaesthetic assistant whilst the anaesthetist is pre-oxygenating the patient. Currently, with the lack of specific evidence of benefit provided by depth of anaesthesia monitors in the obstetric population, resources should be focused on providing adequate training in general anaesthesia for caesarean section in the first instance. Nevertheless, both the cases of awareness in this study could potentially have been avoided had a depth of anaesthesia monitor been applied and observed.

Compared with techniques used in the past, some practices noted in this study have the potential to decrease the risk of awareness, while others may increase risk. In 1991 Lyons and Macdonald showed a decrease in the incidence of awareness from 1.3% to 0.4% with the more generous administration of intravenous induction agent and volatile anaesthetic agent.[7] The majority of patients in our study received at least 1 MAC of volatile anaesthetic (either with or without nitrous oxide) with sevoflurane being the most commonly used volatile agent. Sevoflurane has been shown to have comparable intraoperative maternal and neonatal effects to isoflurane[16] and has attractive properties such as a lower blood gas partition coefficient than isoflurane and fewer sympathetic and airway related side effects when

compared with desflurane.[17-19] Whilst evidence is lacking, the introduction and routine use of end-tidal volatile anaesthetic monitoring may arguably have reduced the incidence of awareness and recall. It could be argued that this obstetric population was at an increased risk of awareness compared with that from past eras. Increasing obesity in the community and during pregnancy[20] favours higher initial dose requirements and more rapid drug redistribution. Propofol has been associated with lighter levels of anaesthesia.[21] The evidence supporting adverse effects from nitrous oxide or benefits from delivery of a high inspired oxygen concentrations increases[22, 23] and the decreased exposure and training opportunities with general anaesthesia for CS have been well documented.[24]

In summary, whilst a number of changes have occurred which have the potential to reduce the incidence of awareness and recall, the pregnant woman undergoing general anaesthesia for CS should still be considered at significant risk. Both cases of awareness detected in this study were potentially avoidable, highlighting the importance of appropriate training and experience in the provision of obstetric general anaesthesia.

Acknowledgements

We wish to thank our trial coordinators Mrs Desiree Cavill and Tracy Bingham. We also thank the awareness endpoint adjudicating committee, Drs Tim McCulloch, Tim Short and Andrew Davidson, for their evaluations of the patient interview narratives.

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Table 1 Patient and procedure characteristics

Age	30.4 [6.2]	n=1095	
Weight	76 [68-90]	n=1058	
ASA status		n=1083	
1	58%		
2	32%		
3	9%		
4/5	1%		
Patient awareness risk factors		n=1095	
Previous awareness			0.3%
Known or predicted difficult intubation			6%
Drug dependence			4%
Risk of intraoperative hypotension			15%
Category of caesarean section		n=1088	
1	47%		
2 or 3	35%		
4	18%		
Experience of attending anaesthetist		n=1066	
Trainee year 1 or 2		23%	
Trainee year 3,4 or 5		49%	
Specialist		23%	
General practitioner anaesthetist		5%	

ASA = American Society of Anesthesiologists (physical health status)

Table 2 Values of minimum alveolar concentration (MAC)

At delivery	1.15 [0.5]	CI 1.10–1.20	n=658
Median maintenance	1.1 [0.5]	CI 1.05–1.11	n=617
At end*	0.96 [0.43]	CI 0.93-0.99	n=650
Lowest	0.86 [0.41]	CI 0.83–0.89	n=648

* “end” refers to time of termination of anaesthetic gases. Values are mean [SD]. CI = 95% confidence interval

Table 3 Dreaming reports from postoperative interviews

Age (y)	Weight (kg)	Reported Experience
21	100	Remembered dreaming during her anaesthetic but unable to remember content, possibly related to being scared about the baby.
39	88	Had a positive dream about a man and two children.
36	76	Thought she heard some noises during the operation but unsure.
33	135	Had a very pleasant dream about being on an island.
26	60	Thought she was dreaming but no recall of content.
30	63	Had a pleasant dream but couldn't recall any content.
36	70	Thought she was dreaming just before she woke up but couldn't remember anything about the dream.
37	89	Dreamed of gardens with flowers and birds.
42	68	No report
30	90	Dreamed about her father. Not an unpleasant dream.
39	90	No report
40	75	* Described a group of doctors in light blue clothing talking to each other. No sound or perception of touch, movement, pain or paralysis. Did not believe this was related to the surgery.
28	55	* Had a memory of people in the theatre talking, with no detail of the conversation, between the time of the mask being held on her face and her next recall of seeing a clock three hours later.
26	68	* Dreamed that she woke up in theatre and felt cold down one side of her body.
28	80	Thought she dreamed during her surgery but unable to describe the dream.
32	80	Thought she dreamed during her surgery but unable to describe the dream.
38	53	Dreamed that she was having twins - the first twin had already been delivered naturally, but she had to have caesarean section to deliver the second. She was surprised because she knew she had a singleton pregnancy.
39	75	Vague memory of dreaming but unable to describe the dreams.

30	105	Had a weird drug induced dream of continuous motion, going round and round and a dream of lights, fast moving and vivid.
38	70	Pleasant dream that she was still at home in Tonga and her mother was next to her bed.
34	70	Dreamed she was having a baby. No unpleasant aspect.
28	75	No report.
36	78	Dreamed what sex the baby would be.
22	87	Dreamed about a baby and heard "The baby is great".
35	58	Vague recollection of a bad dream involving her children. This was a not uncommon dream for her because she was always worrying about her family.

* dream with content possibly related to the period after induction of anaesthesia

Table 4 Awareness and possible awareness reports from postoperative interviews

Cases deemed “awareness”

Age (y)	Weight (kg)	Reported Experience
41	77	First interview. Awake and paralysed. Aware of anaesthetist talking to her that she would breathe for her and that she was going to sleep with gas. Second interview not performed.
34	90	First interview. Remembered voices talking about Christmas holidays. Tried to move and talk but could not. Felt her baby come out. Second interview. Heard voices, especially a man’s voice, asking about the Christmas holiday. Tried to move her hands and feet and to talk but couldn't.

Cases deemed “possible awareness”

Age (y)	Weight (kg)	Reported Experience
34	83	First interview. No memories. Second interview. Thinks she heard some noises during the operation (or talking) but not sure what. Told the recovery nurse but was not distressed at all. Has put it all down to dreaming.
33	83	First interview. Woke up just for a few minutes in either operating theatre or recovery room and heard doctors saying "All is good". Second interview. Woke briefly and heard voices saying “It’s OK” and saw people then remembers being woken up in recovery room.
23	78	First interview. Heard people talking about holidays. Remembers feeling nauseous when she woke up. Second interview. After being told to take deep breaths and count down remembers hearing people talking about holidays, one voice being the same person who was speaking to her before she went to sleep. At the same time, remembers someone

		feeling her pulse and commenting "her pulse is good". No recall of feeling the operation or any pain. Unable to see anything but didn't feel paralysed.