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ORIGINAL RESEARCH **OBSTETRIC ANESTHESIA**

Awareness during general anesthesia for cesarean section: A prospective observational cohort study

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Abstract

Objective: The incidence of intra-operative awareness with explicit recall in the western world has been reported to be between 0.1% and 0.2% in the general surgical population and up to 1-2% of patients at high risk for this complication. There is paucity of literature of awareness in the Indian population undergoing cesarean section (CS), therefore we wanted to study the incidence of awareness in this high-risk group in Indian population.

Methodology: We have prospectively evaluated the incidence and characteristics of awareness during general anesthesia (GA) in pregnant patients undergoing cesarean section in a tertiary care hospital. Structured interviews were conducted in the post–anesthesia care unit, at 4 hours post extubation, at 24 hours and on postoperative day 3. The perceived quality of the awareness episode, intraoperative dreaming, and sequelae were investigated. The anesthetic records were reviewed to search for data that might explain the awareness episode.

Results: The study included 350 patients. Calculated incidence of intraoperative awareness was 1.4% (5 out of 350 patients). Out of which 1.1% patients (i.e. 4 out of 350) were considered to have 'definite awareness' and 0.3% patient (one patient) was categorized as 'possible awareness'.

Conclusions: Incidence of awareness during general anesthesia was found 1.4%. In spite of not using benzodiazepine, opioids and volatile anesthetics before baby delivery in sizeable number of patients, it is a reassuring to know that incidence of awareness is lesser than assumed (3%).

Key words: Cesarean section; Consciousness; Anesthesia, General; Intraoperative awareness; Obstetric Anesthesia; Post traumatic stress disorder

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1. Introduction

'Awareness' is the recall of intraoperative events by a patient operated under general anesthesia (GA), which is often associated with significant adverse psychological sequelae for the patients and medicolegal problems for the anesthesiologists.[1–5] In the western world, in all surgeries, the incidence of awareness with recall has been reported to be between 0.1% and 0.2%.[1, 6] Patients undergoing cesarean section (CS), cardiothoracic surgery or emergency surgery, patients with a difficult airway and those developing intraoperative hypotension,[7–9] are the patients who are considered to be at risk of awareness; the incidence in this group may be as high as 1-2%.[10, 11]

Awareness in the Indian pregnant women undergoing CS has never been studied; although this group of patients are at high risk of experiencing the awareness during the surgery.[3, 12, 13] The restrictions on administering benzodiazepines (BZD) and/or opioids, as well as the limitations in using full doses of induction agents to prevent the fetal respiratory depression are the main causes. Drugs like midazolam and opioids are routinely given after the delivery of the baby, predisposing these patients to recall of intraoperative events. In emergency CS due to the fetal distress or maternal compromise, as in bleeding, hypotension etc., may mandate 100% oxygen till delivery with or without volatile anesthetics (VA).

We evaluated the incidence of intraoperative awareness during GA in patients undergoing CS; the objective was to find out the association between awareness and different parameters, including CS category, patient's demographic data (age, ASA physical status, socioeconomic status, education), and the time of surgery, as well as the risk factors, monitoring methods, outcome and prevention of intraoperative awareness.

2. Methodology

We conducted a prospective, single arm observational non-comparative cohort study at a tertiary care hospital in India from January 2018 to October 2019. The institutional review board (IRB) approved the study vide No. IEC/29/17 dated 27/11/17. The study was registered in the National Clinical Trial Registry of India (www.ctri.nic.in), Reg No. CTRI/2018/04/013143. All the pregnant patients who had undergone CS under GA were included. We excluded those patients who didn't give consent, patients who were not extubated and were shifted on mechanical ventilator, patients with fetal demise either intraoperatively or postoperatively, GA given after failed spinal and GA supplementation given for inadequate spinal anesthesia. This was a pragmatic study with no change in routine clinical practice. The choice of anesthetic agents, muscle relaxants and perioperative analgesia was decided by the anesthesiologist conducting the case.

Routine anesthesia protocol in our setup is as follows. In all patients, general anesthesia is administered by modified rapid sequence induction (RSI) technique. All patients receive balanced anesthesia, which includes administration of an anti–sialagogue (glycopyrrolate 0.2 mg IV) with or without opioid (fentanyl 1 µg/kg IV), followed by propofol 2 mg/kg or thiopentone 5 mg/kg or etomidate 0.2 mg/kg or ketamine 2 mg/kg IV; or intravenous plus inhalational anesthesia, cricoid pressure, muscle relaxant (e.g., succinylcholine 1.5 mg/kg or rocuronium 1.2 mg/kg), endotracheal intubation and positive pressure ventilation. Patients are ventilated with either 100% oxygen or oxygen with VA till baby delivery. BZD, opioids and intravenous or volatile maintenance anesthetics are usually administered after baby delivery as per discretion of the attending anesthesiologist. Some cases like heart disease, Pregnancy induced hypertension may require opioid administration even before the baby is delivered. Mandatory intraoperative monitoring includes continuous electrocardiogram monitoring (ECG), pulse oximetry, capnography and noninvasive and manual blood pressure monitoring. After completion of the surgical procedure and return of consciousness, with adequate return of muscle tone, power and reflexes and patient obeying verbal commands, neuromuscular blockade is reversed, patient extubated and subsequently shifted to post–anesthetic care unit (PACU).

Postoperatively patients were visited by the anesthesiologists conducting the study, at 4 h, 24 h and on 3rd day; following details were noted from their anesthesia case record form.

1. The age, weight, level of education, SE status of the patient, ASA–PS grading, indication for CS, category of CS, time of surgery.
2. Difficulty in intubation (if any).
3. Drugs used with their dosages, gas mixtures used for ventilation, heart rate, mean arterial pressure, oxygen saturation was noted from the anesthesia record form at 5–min intervals (time 0 being the induction time) till baby delivery, and every 10 min thereafter.
4. Intraoperative events, e.g. sweating, lacrimation, bucking (violent expiratory muscle contraction of patient during general anesthesia), and body movements, (if any). These events were specifically noted down in the anesthesia case record form during prospective study period.

Subsequently all the included patients were interviewed for awareness in their own language using Modified Brice Questionnaire (Box 1).[14]

The interview was conducted on three occasions:

Box 1: Awareness Questionnaire: Modified Brice Questionnaire

- What was the last thing you remember before going to sleep?
- What was the very next thing did you remember after waking up?
- Do you remember anything between going to sleep and waking up?
- Did you dream during your procedure?
- What was the worst thing about your procedure?

In case of awareness, following details were sought.

1. **What did you perceive**? Touch / Auditory / Visual / Pain / Unable to breath /Feeling surgery without pain / Sensation of breathing tube
2. **Motor function**? Tried to move / Able to move
3. **Mental reaction**? Immediate understanding / Immediate anxiety / Delayed symptoms
4. **In case dreams are detected, were your dreams**? Pleasant / Disturbing / Indifferent

1. Immediate post-operative period (at 4 h post extubation), only if the consciousness level by Glasgow Coma scale (GCS) was 15/15 (E4M6V5). If GCS was less than 15, the interview was not conducted on that day and the same was noted and the patients were excluded from the analysis.
2. At 24 h and,
3. Again on 3rd day after surgery.

Evaluation of awareness was based upon these three interviews.

The primary outcome measure was the incidence of 'confirmed awareness', which was defined by the patient's recollection of intra-operative events during any of the interviews using the structured questionnaire.

Consent was taken postoperatively before the first interview (delayed consent).

Question 1 and 2 of the questionnaire, aimed to orient the patient for the subsequent questions and diagnosis of the awareness was not made on these replies.

For **question 3 and 4,** if the patient answered 'Yes' or 'Not sure', then the details of the same were sought. A probable diagnosis of awareness ('Yes' or 'Possible') was made and all such cases were assessed in detail by a senior investigator and cross confirmed and discussed with the concerned anesthesia team conducting the case, after which the final diagnosis was made.

For **question 5,** answer was relevant only if it was pertaining to intraoperative recall and was handled in the same manner as above. If the reply points to preoperative or postoperative events, the same was regarded as irrelevant for detecting awareness.

Patients were asked if they had any dreams under anesthesia. If the answer was in affirmative, the dreams were classified as pleasant, unpleasant or indifferent. Patients with dreams were not considered as cases of confirmed awareness.

After the questionnaire, patients were categorized into either having 'definite awareness' or not. In case awareness was detected, full details were sought to summarize the details of the events. Patients having awareness were offered counselling by the same seniors.

'Definite awareness' was considered as occurring when the patient was certain of having been aware at any time during the surgery. **'possible awareness'** was considered when patient was unable to recall any event which could definitely indicate awareness, but memories could be related to intraoperative events. **No awareness** was considered if patient giving history of peaceful sleep with no recall during surgery. This classification is similar to other studies done to assess intraoperative awareness.[6,15–17]

Statistical analysis

This study was designed to establish the incidence of intraoperative awareness. Assuming an incidence of no more than 3%, with 95% confidence interval and with 2% margin of error, a sample size of 279 participants was estimated; therefore, 350 participants were included to cater for the drop–outs.

Data was entered into Microsoft Excel (Windows 7; version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, and frequencies and percentages were calculated for categorical variables. Association between Variables was analyzed using Chi-square test for categorical variables. Level of significance was set at 0.05.

3. Results

In the period of January 2018 to October 2019, a total of 6412 patients underwent CS, 755 of these were done under GA, out of which 405 patients that were excluded; 62 refused consent, 115 were shifted on ventilatory support, 86 patients had fetal demise, 64 patients received GA after inadequate spinal anesthesia and 78 patients received GA after failed spinal anesthesia. 350 patients were included in the study.

Table 1 summarizes the characteristics and the demographic details of the included patients.

Within this population, sub-groups of patients, considered to have independent risk factors for awareness, such as age of patient, higher ASA–PS grade, education, SE status, and the time of surgery, did not

Table 1: Demographic data of the patients

Parameter		n (%)
Age (in Years)	≤ 20	29 (8.3)
	21-25	147(42)
	26-30	128(36.6)
	>30	46(13.1)
	Mean (SD)	25.99 (4.21)
ASA	2	274 (78.3)
	3	76 (21.7)
Education	Illiterate	34 (9.7)
	Primary	161 (46)
	Secondary	139 (39.7)
	Graduate	14 (4)
	Post Graduate	2 (0.6)
SE Status	Poor	210 (60)
	Middle	140 (40)

Table 2: Indications of LSCS. Data given as n (%)

Indications	Awareness Response			
	Yes	Possible	No	Total
▪ Fetal distress	1 (0.9)	-	108 (99.1)	109 (31.1)
▪ Seizure disorder	1 (9.1)	-	10 (90.9)	11 (3.1)
▪ Bleeding placenta previa	1 (2.4)	-	41 (97.6)	42 (12)
▪ Heart disease in labour	1 (7.7)	1 (7.7)	11 (84.6)	13 (3.7)
▪ PIH	-	-	67 (100)	67 (19.1)
▪ Abruptio placentae	-	-	25 (100)	25 (7.1)
▪ Previous LSCS with thinned out scar	-	-	5 (100)	5 (1.4)
▪ CPD in labour	-	-	6 (100)	6 (1.7)
▪ Abnormal presentation in labour	-	-	48 (100)	48 (13.7)
▪ Others	-	-	24 (100)	24 (6.9)

show any association with awareness. The indications for GA for CS are summarized in Table 2.

Out of the 350 patients, 4 patients had 'definite awareness' and 1 was categorized as 'possible awareness'. Hence the incidence of awareness was 1.4%. Table 4 summarizes the details of all the 5 patients with awareness during intraoperative period.

Among the 4 patients with 'definite awareness', 3 were induced with injection thiopentone and one with injection etomidate. One patient of 'possible awareness' was induced with injection etomidate. None of the patient who were induced with injection propofol and ketamine reported awareness. Succinylcholine was used during induction of 345 patients (3 cases of 'definite awareness', 1 case of 'possible awareness' and rest 341 patients of no awareness). While injection rocuronium was used for 5 (1 'definite awareness' plus 4 no awareness patients). Although it appears that 98.8% of patients in which succinylcholine was used, had not reported awareness while 20% of the patients in which rocuronium was used reported awareness; it cannot be considered significant because in our institute most commonly used induction agent and muscle relaxant are thiopentone and succinylcholine.

All patients positive for 'definite awareness', had not been given opioids before baby delivery while one patient of 'possible awareness' was premedicated with iv opioids before delivery of baby. After exclusion of these 5 patients among rest of the 345 patients, only 5 patients had been premedicated with opioid before baby delivery ($p < 0.001$)

Out of 4 cases of 'definite awareness', 2 were given 100% oxygen before baby delivery, while the remaining 2 received VA plus oxygen. The patient with 'possible awareness' also received oxygen plus VA before delivery. Among the rest 345 patients, 107 were given 100% oxygen and 238 patients were maintained on oxygen plus VA ($p = 0.571$).

Out of 312 patients in which nitrous oxide (N_2O) was started post–delivery, 3 reported awareness, while 309 had no intraoperative memory; and 38 patients in which N_2O was not given, one patient reported 'definite awareness', one patient 'possible awareness' and 36 patients had no awareness; ($p = 0.011$). Use or non-use of BZD after baby delivery did not show any association with awareness.

28 patients had episodes of intraoperative tachycardia, among which 4 patients had recalled intra operative events too ($p < 0.001$); 26 patients had hypertension ($p = 0.815$) and 3 patients had an episode of hypotension ($p = 0.907$) intraoperatively, but none of them were aware of intraoperative events. Intraoperatively 1 patient had sweating, 1 had lacrimation, and 2 patients had some movement of limbs out of 4 positive cases; none had bucking. The patient of 'possible awareness' was not associated with any of these events intraoperatively. Sweating was present in only one patient in our study and that patient reported recall of intraoperative events ($p < 0.001$). Similarly, 3 patients had movements of limb intraoperatively in which 2 patients had 'definite awareness' and 1 patient had no awareness ($p < 0.001$).

4. Discussion

By definition, GA is a state of unconsciousness accompanied by loss of sensation without interference with vital functions, whereas awareness is described as a state of alertness, sensitivity or perception which is incompatible with GA. The patient remains aware due to inadequate anesthesia.

In our study, in a target population of pregnant patients undergoing CS under GA, we found 1.1% incidence of 'definite awareness'. 'Definite awareness' plus 'possible awareness' cases were 1.4% of the total. This is similar to other studies conducted on high-risk population with reported incidence of intraoperative awareness around 1-2%.[10] Other studies conducted in the general surgical

population of western world, have found incidence of awareness in between 0.1% and 0.2%.[1, 6] Increased awareness incidence in our high-risk group in comparison to other studies could be due to nature of surgery involving two lives with some cases being of emergent nature, our limitations in administering opioids, BZD and N_2O prior to baby delivery to prevent fetal respiratory depression and usage of titrated doses of general anesthetic drugs to prevent maternal compromise. Some other studies have considered CS along with oncosurgery, cardiac surgery, trauma, one lung ventilation in thoracic surgery, emergency surgery and surgery associated with significant blood loss, as one of the most vulnerable surgery, where patients are more prone to recall intraoperative events.[7, 18] Ghoneim MM et al. found that the overall incidence was higher among obstetric and cardiac cases, 0.4% and 1.1-1.5% respectively.[19] In their study, on considering only obstetric patients, in comparison to general surgical population, the incidence seems to be high, but it is still lower than our findings. The difference could be due to use of different anesthetic and monitoring techniques. They induced patient with thiopentone + succinylcholine and started on VA+O2+N2O even before baby delivery. Along with that they used minimum alveolar concentration (MAC) and bispectral index (BIS) monitors throughout the procedure to maintain adequate depth of anesthesia. Similarly, Ambulkar et al. conducted a study in patients posted for major cancer surgeries in Indian population. Although cancer patients undergoing major surgeries may have many of the risk factors for intraoperative awareness, like difficult airway in head and neck cancer patients and radical surgeries with massive blood loss; they found very less incidence of awareness, less than 0.33%, in their study.[20] Above mentioned both studies used inhalational balanced anesthesia and respiratory gas monitor with end tidal anesthetic concentration monitoring throughout the procedure in most of the cases; this could be the reason of lower incidence of awareness even in high risk population.

Similarly a study conducted in Japan reported crude incidence of intraoperative awareness to be 0.028%, which was minimal compared with other studies.[21]

In our obstetric operating setup, MAC and EEG based monitors like entropy and BIS are not available. Therefore, the use of muscle relaxants in the lighter plane of anesthesia could result in recall. Several studies in the past have shown significant decrease in the incidence of awareness even in high-risk groups when BIS was used,[22–25] while other studies have failed to show any such improvement.[6, 16]

The timing of the postoperative interview with the patient is still unsettled. A single short postoperative visit by an anesthesiologist without use of a structured interview is unlikely to elicit many cases of awareness. Some recommend it to be just after regaining consciousness.[26] However, the majority of patients remain drowsy and may give an unreliable account. Others suggest that interview should be taken much later, so that patient may have more time to reflect upon the sequence of events. To overcome this hurdle we used a structured interview for our patients at three time points using Modified Brice Questionnaire[14] (the gold standard for postoperative awareness screening), used by similar studies designed to assess intraoperative awareness in the past.[1, 6, 14, 16, 27–29, 30] These interviews were conducted to define the nature of the episode if intraoperative awareness was reported, and to provide postoperative counselling or psychological support by senior anesthesiologists.

In this study, we have not found any influence of age, weight, education, SE status and ASA–PS on the incidence of awareness. Similarly Errando et al. did not notice any significant relationship between the incidence of awareness and weight, ASA–PS.[10] Some other studies, however, found positive correlation between ASA-PS and the incidence of awareness.[6, 31] Patients with higher ASA–PS may require a low depth of anesthesia, because of low physiologic reserves related to their comorbidities. In our setup for all the obstetric patients undergoing CS our plan of anesthesia management remained the same. Irrespective of ASA–PS grade; opioids, N_2O and VA were avoided prior to baby delivery to prevent fetal respiratory depression. This could be the reason of no apparent finding of positive association of ASA–PS and the incidence of awareness in our study. Regarding category of CS, we could not find any positive association between category of CS and intraoperative awareness. The reason could be the same as mentioned above.

5. Recommendations

However, it cannot be forgotten that for the cases who tested positive for awareness, it is a 100% experience which cannot be ignored. Therefore, various monitoring devices can be used to detect intraoperative anesthesia awareness to minimize the incidence of this potentially devastating complication. Future work should include research and development of precise reliable detection systems, systems for real-time delivery and monitoring of intravenous anesthetic drugs, the identification of the appropriate lower MAC limit and the development of new drugs that target consciousness and memory while minimizing adverse effects.

6. Limitations

Despite all precautions, our study had certain limitations. First, because of unavailability of BIS, MAC

monitor, entropy etc. we were not able to establish relationship between the depth of anesthesia and awareness. Second, as our study population was pregnant patients, none of the patient was premedicated with BZD, so we were not able to study effect of the sedatives on intraoperative awareness. Third, the method we used for assessment of intraoperative awareness was subjective, rather than objective indicators. Last, we have not evaluated the long-term psychological sequelae of patients who reported awareness.

7. Conclusion

We conclude that patients undergoing cesarean section under general anesthesia in our setup have chances of intraoperative awareness (1.4%), albeit lesser than the projected incidence of 3%. Despite not using BZD, opioids and VA before baby delivery in sizeable number of patients, it is reassuring to know that the incidence of awareness is lesser than assumed.

8. Conflict of interest

None declared by the authors.

9. Authors' contribution

SS: Concept, Design, Data collection, Analysis and interpretation, Literature review, Manuscript writing

VC: Design, Data collection, Analysis and interpretation, Manuscript writing

DP: Concept, Supervision, Data collection, Analysis and interpretation, Literature review, Critical review

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