Original Article

Awareness during general anesthesia: An Indian viewpoint

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Abstract

Background and Aims: 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. Awareness in the Indian population has never been studied; we therefore wanted to detect the incidence of awareness in patients who were at high risk of experiencing awareness during surgery in our population.

Material and Methods: We conducted a prospective single-center observational study at a 600-bedded tertiary cancer care referral hospital. We recruited adult patients posted for major cancer surgery who were considered to be at high risk for awareness. These patients were interviewed at three time-points using the structured modified Brice interview questionnaire. The primary outcome studied was the incidence of definite intra-operative awareness.

Results: A total of 934 patients were included in the final analysis of which none reported awareness. Using the rule of three (Hanley and Lippman-Hand) we conclude that the upper 95% confidence interval for the incidence of awareness in this population is <1 in 300 (0.33%).

Conclusion: Awareness under anesthesia is a distressing complication with a potential for long-term psychological consequences, and every effort should be undertaken to prevent it. It is reassuring though that our data in Indian cancer patients at high risk for intra-operative awareness suggests that it is an uncommon occurrence.

Key words: Anesthesia technique, awareness, depth of anesthesia, general anesthesia

Introduction

Awareness during general anesthesia is an infrequent but serious problem with potential long-term psychological consequences for the patient and medico-legal implications for the anesthetist.[1] The incidence of awareness has been reported to be between 0.1% and 0.2% in the general surgical population in the Western world.[2,3] Patients undergoing cesarean section, cardiothoracic surgery or emergency surgery, patients with a difficult airway and those developing intra-operative hypotension are among those considered to have increased chances of awareness and the incidence in this group may be as high as 1-2%.[4] Cancer patients undergoing major surgery may have many of these risk factors (for example, difficult airway in head and neck cancer patients and radical surgery with massive blood loss) predisposing them for awareness under anesthesia. The incidence of awareness may vary among patient population due to differences in genetic make-up and anesthesia technique.[5] Awareness in the Indian population has never been studied; hence, we prospectively evaluated the incidence of awareness in cancer patients population would be no higher than 3%, which is the reported incidence in the Western world.

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Material and Methods

We conducted a prospective single-center observational study at a 600-bedded tertiary cancer care referral hospital. The Institutional Review Board approved this study prior to commencement.

We recruited adult patients posted for major cancer surgery who were considered to be at high risk for awareness. These included patients receiving one lung ventilation (thoracic surgery, use of high oxygen concentrations), patients undergoing emergency surgery (hemodynamically unstable), receiving air/oxygen intra-operatively (avoiding

nitrous oxide), unanticipated difficult airway (difficulty in maintaining adequate depth of anesthesia), and intra-operative hypotension (requiring reduction of anesthetic depth).[3,6-8] In all the patients recruited in this study, an additional common and significant risk factor for accidental awareness under general anesthesia was the use of neuromuscular blockade.[9] Exclusion criteria for this study were refusal of consent, ongoing psychiatric medication, altered sensorium, and language barrier.

This was a pragmatic study with no change in routine clinical practice. The choice of anesthetic agents, muscle relaxants, and perioperative analgesia was left to the discretion of the theater anesthetist. Being a tertiary care cancer center, all the cases in our institution are managed by anesthesia residents in training supervised by qualified anesthesia consultants. All patients received balanced anesthesia (induction with induction agents, opioids and muscle relaxant with maintenance of anesthesia with opioids, muscle relaxants and halogenated agents) with or without regional technique depending on the surgery and the theatre anesthetist. Over the whole study period, anesthesia technique remained consistent. Mandatory intra-operative monitoring included continuous electrocardiogram monitoring, pulse oximetry, capnography and noninvasive blood pressure; in addition, invasive blood pressure monitoring was instituted where considered necessary. None of the patients had bispectral index (BIS) monitoring; however, respiratory gas monitors were available in most cases to measure end-tidal anesthetic concentration (ETAC). Based on the inclusion criteria, patients at high risk for awareness were identified at the end of the surgery by questioning theater anesthetists. These patients were interviewed by our project nurse at three time-points, immediate postoperative, at 24 h and on day 7 postoperative or on discharge (whichever was earlier) during their postoperative hospital stay using a simple structured questionnaire (modified from Brice *et al.* Appendix 1).[10] 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 at the 24-h interview (delayed consent), and any patient who refused consent was excluded, in the final analysis. All patients who were suspected to have awareness as per interview were to be re-interviewed by an independent reviewer to confirm the diagnosis of awareness. Definite awareness was defined as occurring when the patient was certain of having been aware at any time during the operation. Awareness was considered as possible in those cases where the patient thought he had been awake during surgery, but was not completely sure. These definitions were based on a previous study by Errando *et al.*[4] In case of awareness being detected, there was support arranged from in-hospital psychologist for counseling of affected patients.

Patients who were mechanically ventilated/died in the postoperative period which resulted in a missed interview were excluded in the final analysis.

Statistical considerations

The incidence of awareness in high-risk population has been reported to be between 1% and 2%.[4] A sample size of 850 would allow us to detect an incidence of 3% (with a 1.1% margin of error) with 95% confidence. To account for protocol deviations and losses to follow-up, we planned to accrue 1000 patients. Data were entered into statistical software (SPSS 18.0, SPSS Inc., Chicago, IL, USA) for analysis. Descriptive statistics was used to report results.

Results

Between March 2009 and September 2011, a total of 15,554 patients underwent surgeries of which 1030 patients were eligible to participate in this study. Of these, 934 patients were included in the final analysis. Of the 96 patients that were excluded, 63 refused consent, and 33 could not complete all the three interviews as they were either ventilated in the postoperative period or did not survive.

Figure 1 and Table 1 summarize the characteristics and the details of the included patients. None of the 934 patients reported awareness. Using the rule of three (Hanley and Lippman-Hand) we conclude that the upper 95% confidence

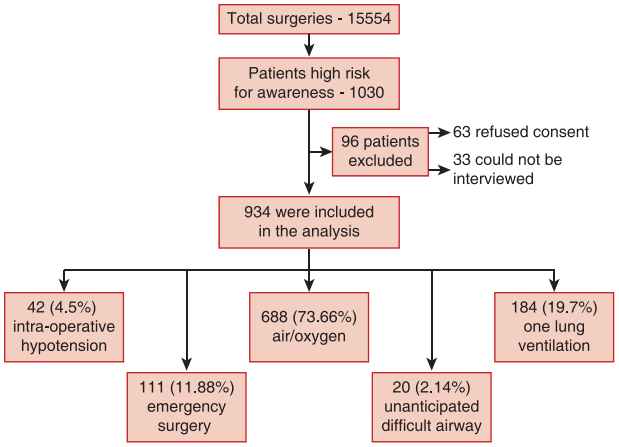

Figure 1: Study flow chart of included patients

Appendix 1: Awareness questionnaire

Questions to be asked:

1. What is the last thing you remember before surgery?
2. What is the very next thing that you remember?
3. Do you remember any dreams which you saw during the surgery?
4. Can you remember anything in between these two periods?

If the awareness is detected then

- What did you notice: Sound, touch, paralysis or pain?
- Have there been any consequences for you?

Perception			Motor function		Mental reaction			Assessment
Auditory	Visual	Pain	Tried to move	Able to move	Immediate understanding	Immediate anxiety	Delayed symptoms	Confirmed event
—	—	—	—	—	—	—	—	—

Time of asking these questions:

1. In recovery unit before discharge
2. 24 h after surgery
3. At the time of discharge from hospital

Table 1: Patient characteristics

Characteristics	Number (%)
Gender	
Male	507 (54.3)
Female	427 (45.7)
Age (years)	
≥18–40	271 (29)
41–60	486 (52)
≥60	177 (19)
ASA physical status	
ASA I	645 (69)
ASA II	277 (29.9)
ASA III	11 (1)
ASA IV	1 (0.1)
ASA V	Nil (0)

Data are presented as number (%). ASA = American Society of Anesthesiologists

interval for the incidence of awareness in this population is <1 in 300 (0.33%).[11] In statistical analysis, the rule of three (as proposed by Hanley) states that if a certain event did not occur in a sample with *n* subjects, 0-3/*n* is the 95% confidence interval for the rate of occurrences in the population. The accuracy of this estimation is more when the sample size (n) is more than 30.

Discussion

Awareness is caused by the administration of general anesthesia that is inadequate to maintain unconsciousness. This could be due to various factors, patient and surgical factors which necessitate a deliberate reduction in depth of anesthesia. Another contributory mechanism could be pharmacogenetic factors resulting in variability in anesthetic dose requirement among patients. Patients undergoing major surgery for cancer would be expected to have an increased incidence of awareness because of multiple predisposing factors such as extensive surgery with major blood loss, one-lung ventilation in thoracic surgery and unanticipated difficult airway in head and neck cancer.[4] However, our study failed to demonstrate awareness under general anesthesia in this patient group.

Within this population, sub-groups of patients who were considered to be having independent risk factors for awareness such as sicker patients (American Society of Anesthesiologists physical status III-V), female gender and younger patients (age <40 years) also did not report awareness.[4,12,13]

We found that the incidence of awareness in this group of patients is likely to be <0.33% and would therefore possibly be even lower in patients without these risk factors. Previous studies on awareness among Caucasian patients have determined the incidence to be between 1 and 2 in 1000 in the general population to as high as 1-2 in 100 patients in high risk for awareness.[2-4] One possible explanation for this difference between our study and the published data could be a variation in anesthetic techniques. All the patients in our study received inhalation-based balanced anesthesia and in most, respiratory gas monitor with ETAC measurement formed a close alternative measure of the pharmacodynamic effect of general anesthesia. The inter-patient variability with respect to adequate dose requirement might be less with the use of inhalational anesthetics with ETAC, when compared to total intravenous anesthesia (TIVA).[14] There is also evidence that TIVA may predispose patients to awareness compared to inhalational anesthetics with measurement of ETAC.[2,4,9,15,16] In addition, there has been speculation about the influence of genetics and ethnic differences on

anesthetic requirements; this may have also contributed to the low incidence of awareness in our study as compared to western population.[5,17]

One of the difficulties in identifying the true incidence of awareness is that it is a patient-reported outcome and, therefore, the detection of awareness can be subjective and also depends on the timing and structure of the interview. To minimize bias, we used a structured interview that has been utilized in prior studies to detect awareness.[2,4,10] We also planned for re-interviews of potential cases of awareness by an independent investigator. We chose three time-points for interviews as approximately 35% of cases are detected only at a delayed postoperative interview.[18] The strength of this study is that the study design involved no change in routine anesthetic care. This ensured that the results of the study would be applicable to day-to-day practice. An important consideration is that although some patients are able to report awareness immediately postsurgery, others may not realize that they were aware until days or even weeks after the event. One of the limitations of this study is that for logistic reasons, we were not able to follow patients beyond hospital discharge. In addition though ETAC measurement was available in most cases, their values (ETAC below the recommended levels) were not recorded in the case report form, as our aim was to determine only the incidence of awareness in our population. As this study was conducted in a highly selected group of cancer patients at a tertiary care cancer center, the results of this study cannot be extrapolated to all surgical patients.

Over the past years, techniques to monitor depth of anesthesia have evolved. Several brain-function monitors based on the processed electroencephalogram or evoked potentials have been developed to assess anesthetic depth. It has been recommended that BIS monitoring should be used in patients at increased risk of awareness undergoing general anesthesia with muscle relaxant to decrease the incidence of awareness.[3] A large randomized controlled trial conducted in over 20,000 unselected surgical patients demonstrated that BIS monitoring may decrease intra-operative awareness when compared with routine care.[19] In contrast, in the B-Unaware and the BAG-RECALL trials, the superiority of BIS over ETAC monitoring for the prevention of awareness was not established.[20,21]

We conclude that despite concerns among anesthetists about under-reporting of awareness, our data in Indian cancer patients at high risk for intra-operative awareness suggests that it is an uncommon occurrence.

References

1. Samuelsson P, Brudin L, Sandin RH. Late psychological symptoms after awareness among consecutively included surgical patients. Anesthesiology 2007;106:26-32.
2. Sebel PS, Bowdle TA, Ghoneim MM, Rampil IJ, Padilla RE, Gan TJ, *et al.* The incidence of awareness during anesthesia: A multicenter United States study. Anesth Analg 2004;99:833-9.
3. Myles PS, Leslie K, McNeil J, Forbes A, Chan MT. Bispectral index monitoring to prevent awareness during anaesthesia: The B-Aware randomised controlled trial. Lancet 2004;363:1757-63.
4. Errando CL, Sigl JC, Robles M, Calabuig E, García J, Arocas F, *et al.* Awareness with recall during general anaesthesia: A prospective observational evaluation of 4001 patients. Br J Anaesth 2008;101:178-85.
5. Ezri T, Sessler D, Weisenberg M, Muzikant G, Protianov M, Mascha E, *et al.* Association of ethnicity with the minimum alveolar concentration of sevoflurane. Anesthesiology 2007;107:9-14.
6. Tramèr M, Moore A, McQuay H. Omitting nitrous oxide in general anaesthesia: Meta-analysis of intraoperative awareness and postoperative emesis in randomized controlled trials. Br J Anaesth 1996;76:186-93.
7. Hardman JG, Aitkenhead AR. Awareness during anesthesia. Contin Educ Anesth Crit Care Pain 2005;5:183-6.
8. Mackay JH. AAGA in cardiothoracic anesthesia. In: Pandit JJ, Cook TM, editors. Accidental Awareness During General Anesthesia in the United Kingdom and Ireland. 5th National Audit Project of the Royal College of Anesthetists and the Association of Anesthetists of Great Britain and Ireland; 2014. p. 119-23.
9. Pandit JJ, Andrade J, Bogod DG, Hitchman JM, Jonker WR, Lucas N, *et al.* 5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: Summary of main findings and risk factors. Br J Anaesth 2014;113:549-59.
10. Brice DD, Hetherington RR, Utting JE. A simple study of awareness and dreaming during anaesthesia. Br J Anaesth 1970;42:535-42.
11. Hanley JA, Lippman-Hand A. If nothing goes wrong, is everything all right? Interpreting zero numerators. JAMA 1983;249:1743-5.
12. Pollard RJ, Coyle JP, Gilbert RL, Beck JE. Intraoperative awareness in a regional medical system: A review of 3 years' data. Anesthesiology 2007;106:269-74.
13. Ghoneim MM, Block RI, Haffarnan M, Mathews MJ. Awareness during anesthesia: Risk factors, causes and sequelae: A review of reported cases in the literature. Anesth Analg 2009;108:527-35.
14. Avidan MS, Mashour GA. Prevention of intraoperative awareness with explicit recall: Making sense of the evidence. Anesthesiology 2013;118:449-56.
15. Eger EI 2nd, Sonner JM. How likely is awareness during anesthesia? Anesth Analg 2005;100:1544.
16. Miller DR, Blew PG, Martineau RJ, Hull KA. Midazolam and awareness with recall during total intravenous anaesthesia. Can J Anaesth 1996;43:946-53.
17. Sonner JM. Ethnicity can affect anesthetic requirement. Anesthesiology 2007;107:4-5.
18. Sandin RH, Enlund G, Samuelsson P, Lennmarken C. Awareness during anaesthesia: A prospective case study. Lancet 2000;355:707-11.
19. Mashour GA, Shanks A, Tremper KK, Kheterpal S, Turner CR,

Ramachandran SK, *et al.* Prevention of intraoperative awareness with explicit recall in an unselected surgical population: A randomized comparative effectiveness trial. Anesthesiology 2012;117:717-25.
20. Avidan MS, Zhang L, Burnside BA, Finkel KJ, Searleman AC, Selvidge JA, *et al.* Anesthesia awareness and the bispectral index. N Engl J Med 2008;358:1097-108.
21. Avidan MS, Jacobsohn E, Glick D, Burnside BA, Zhang L, Villafranca A, *et al.* Prevention of intraoperative awareness in a high-risk surgical population. N Engl J Med 2011;365:591-600.

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CONFERENCE CALENDAR October-December 2016

Name of conference	Dates	Venue	Name of organising Secretary with contact details
20th Annual National Conference of Indian Association of Cardiovascular Thoracic Anaesthesiologists (IACTA)	February 16th-19th, 2017	JW MARIOTT, PUNE	Dr. Sandeep Mutha, Secretariat- IACTA 2017 Pune, A801 Rohan Tapovan patrakar nagar road, Gokhale nagar, Pune- 411 016, India
9th National Conference on Paediatric Anaesthesia	February 17th-19th, 2017	Scientific Convention Centre, KGMU, Lucknow	Prof. V. K. Bhatia Organizing Chairman Contact no. +919415195056 E-mail: shwetakashish@hotmail .com Prof. Anita Malik Organizing Secretary Contact no. +919936425729 E-mail: dranitamalik@yahoo.co.in Prof. Sanjay Chaubey Joint Organizing Secretary Mobile: +919621119747 E-mail: sanjay.chaubey@yahoo.com
18th Annual National Conference of the Indian Society of Neuroanaesthesiology and Critical Care and International Symposium on Aneurysmal SAH	February 24th-26th, 2017	Bhargava Auditorium, PGIMER, Chandigarh	Dr. Nidhi Panda Organizing- Secretary 07087009525 Dr. Hemant Bhagat, CO-Organizing- Secretary 09216387387 Department of Anaesthesia, 4th floor, Nehru Hospital, PGIMER, Chandigarh - 160 012, India E-mail: isnacc2017@gmail.com
Regional Anesthesiology and Acute Pain Medicine Meeting	April 6th-8th, 2017	Marriott Marquis San Francisco San Francisco, California	https://www.asra.com/page/284/regional-anesthesiology-and-acute-pain-medicine-meeting
The 2017 SOAP 49th Annual Meeting	May 10th-14th, 2017	Hyatt Regency Bellevue Bellevue, Washington	https://soap.org/future-meetings.php
14th Conference of Asian Society of Paediatric Anaesthesiologists" (ASPA 2017) with Preconference workshops	June 3rd-4th, 2017 June 2nd, 2017	Grand Hyatt, Mumbai, India. Surya Children Hospital, Mumbai, India	website: www.aspa2017.com Organising Secretary: Dr. Vrushali Ponde
7th National Conference of the Academy of Regional Anaesthesia India AORA 2017	September 8th-10th, 2017	Brilliant Convention Center, Indore, Madhya Pradesh, India	Dr. Javed Khan ED -59, Sector- D, Scheme NO.94, MR-9, Ring Road Square, Behind Siddhi Vinayak Marbe Shop, Indore -452 016, Madhya Pradesh, India Mobile: 09589755065, 9826955065 E-mail: javed1964khan@gmail.com, secretaryaora2017@gmail.com Website: www.aora2017.com