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INCIDENCE OF ACCIDENTAL AWARENESS DURING GENERAL ANESTHESIA – A TERTIARY CANCER CARE HOSPITAL EXPERIENCE

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ABSTRACT

Objective: To find out the incidence of accidental awareness during general anesthesia in a cohort of cancer patients in a tertiary care center in Pakistan.

Methodology: This was an observational study conducted on cancer patients undergoing surgery under general anesthesia in Shaukat Khanum Memorial Cancer Hospital and Reserach Center. A total of 1000 patients were interviewed by a registered nurse in the Post-Anesthesia Care Unit (PACU) using the modified Brice questionnaire. The outcome measured was the incidence of awareness and/or dreaming intraoperatively.

Results: Among the total 1000 patients, 516 patients were male and 484 were females. There were 356 patients under the age of 40, 462 between the ages of 41 and 60, and 182 above 60 years. Most of the patients were American Society of Anesthesiologists (ASA) Grade 2 (n = 834), while 14 were ASA Grade 1 and 152 were ASA Grade 3. The total intravenous anesthetic was used on 83 patients, whereas balanced anesthesia was used on 917. Elective surgery was performed on 968 individuals, while emergency surgery was performed on 32 others. Two patients had definitive awareness (n = 2) and two patients described dreaming during surgery (n = 2).

Conclusion: Our study found the incidence of awareness during general anesthesia in the adult cancer population to be at par, if not more than that reported worldwide.

Keywords: General Anesthesia; Accidental Awareness; Cancer Care

INTRODUCTION

Accidental awareness during general Anesthesia (AAGA) is defined as "consciousness and subsequent explicit recall of intra-operative events, whether the experience is spontaneously reported by the patient, or detected by direct questioning or prompting."[1] It may manifest as merely a vague memory of people talking during surgery, or it may even be as horrifying as feeling excruciating pain from the ongoing surgery while being unable to move or say anything. This is one of the uncommon complications of general anesthesia that is not only a medico-legal debacle for the anesthetist but can also be extremely distressing and psychologically traumatic to the patient.[2]

While it is a difficult side effect to report and recognize, previous literature[3, 4] has estimated an incidence of 1-2 in 1000 patients in general surgical population. However, the results of the more recently conducted 5th National Audit Project (NAP5)[5] indicated an incidence of merely 1:19,600, which is 20 times lesser in frequency than postulated earlier. Considering the possibility of underestimation of actual figures, the real incidence of awareness, therefore, remains controversial.

Suggested risk factors mentioned in the literature include patient factors such as female sex[6], higher ASA physical status[7], obesity[6], previous history of awareness[8], and certain types of surgeries like obstetric[6,9], cardiac[10], and emergency surgery.[11] Data suggests that even the pediatric population may develop intraoperative awareness.[12] In addition, patients may have a genetic propensity to develop awareness.[13] Studies have also suggested the influence of using neuromuscular blockade[6,14] as well as anesthetic technique (Total Intravenous Anesthesia vs. balanced anesthesia) on the incidence of awareness. A vast majority of patients have idiopathic cases of awareness[15] where no anesthetic or other risk factors are identified.

Numerous researches have been conducted to detect the occurrence of this phenomenon with electroencephalographic techniques but none of them proved to be reliable to identify and prevent intraoperative

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awareness. To establish awareness post-operatively, the Brice questionnaire[16] was developed initially and then was modified by Abouleish and Taylor[17] as the original did not distinguish awareness from dreaming.

This study was initiated to detect the incidence of AAGA and to identify the possible risk factors associated with its occurrence. This was particularly important due to a lack of data in this specific population subset in Pakistan.

METHODOLOGY

This was a cross-sectional study done at Department of Anesthesia Shaukat Khanum Memorial Cancer Hospital and Reserach Center Lahore - Pakistan. Based on the previously estimated[3,4] incidences of 0.1%, a sample size of 995 patients was calculated, assuming a precision of 0.02% and a 99% confidence interval. A total of 1000 patients were enrolled to account for missing data, drop-outs, and/or losses to follow-up.

We started including adult cancer patients undergoing elective or emergency surgery under general anesthesia from June 2021 and the enrollment continued until our sample size of 1000 patients was achieved i.e., until September, 2021.

Patients were excluded if they were under the age of 12 years, had ongoing psychiatric medication, or altered sensorium. Patients who died or required postoperative mechanical ventilation in the perioperative period were also excluded.

Intraoperatively, the conduct of general anesthesia was according to standard clinical practice. Monitoring included invasive or non-invasive blood pressure, pulse oximeter, ECG, end-tidal carbon dioxide concentration as well as end-tidal anesthetic concentration (ETAC) where required. Entropy or Bispectral index (using the BIS™ Complete 4-Channel Monitoring System) was used when Total Intravenous Anesthesia (TIVA) was employed.

Some patients received balanced anesthesia i.e. intravenous induction with or without muscle relaxant and maintenance with inhalational anesthetics. Others received TIVA with target-controlled infusion (TCI) of Propofol for induction as well as maintenance. Analgesia included Fentanyl, Paracetamol, and/or Morphine as required. Peripheral or central neuraxial blocks were used where warranted.

The choice of anesthetic modality and drugs was as per the patient's condition and the attending anesthetist's discretion. The opted plan was, however, mentioned on record.

Protocol for Detection and Follow-up of patients with AAGA

All the patients were interviewed postoperatively by a registered nurse at the time of discharge from the PACU using a simple structured questionnaire using a few questions from Brice et al.[16,17,18] They were asked if they had a history of awareness during any previous anesthetic and whether or not they had any disturbing dreams or recalled any intra-operative events during the current operation.

Those with the suspected occurrence of awareness during the primary interview then underwent a structured interview by the primary investigator 7 days after surgery using the Brice questionnaire to confirm the finding and to classify the incident as possible or definitive. Patients were requested to describe details of the episode including visual, auditory, movement, or pain perception. Moreover, they explained the possible cause(s) of the awareness and offered psychological support and treatment, as required.

Intraoperative anesthetic data recorded on our pre-designed study proforma was also analyzed for evaluating possible risk factors contributing to the occurrence of awareness.

The collected data were analyzed with Statistical Package for the Social Sciences® (SPSS Inc., Chicago, IL, USA.), version 23.0. Descriptive data, anesthetic modality, and type of surgery were described in numbers and percentages. Thereafter, patients were evaluated concerned knowing high risk factors (categorical variables) such as female gender, previous history of awareness, etc. Those with the incidence of awareness were compared with the remaining number of patients using the $\leq$ Fisher's exact test (two-sided). A p-value 0.05 was considered significant.

Table 1: Descriptive data of studied groups

Parameter		Number (%)
Gender	Male	516 (51.6%)
	Female	484 (48.4%)
Age	< 40 Years	356 (35.6%)
	41 – 60 Years	462 (46.2%)
	> 60 Years	182 (18.2%)
Grades as per the American Society of Anesthesiologists (ASA)	ASA 1	14 (1.4%)
	ASA 2	834 (83.4%)
	ASA 3	152 (15.2%)
	ASA 4	NIL
	ASA 5	NIL

Table 2: Anesthetic and surgery characteristics (n = 1000)

Parameter		Number (%)
Anesthetic technique	Total Intravenous Anesthesia	83 (8.3%)
	Balanced Anesthesia	917 (91.7%)
Modality	Elective	968 (96.8%)
	Emergency	32 (3.2%)
Type of Surgery	Breast	260 (26%)
	Gastrointestinal surgery	174 (17.4%)
	Gynecological surgery	40 (4%)
	Hepatobiliary surgery	27 (2.7 %)
	Maxillofacial/otolaryngology	67 (6.7%)
	Neurosurgery	38 (3.8%)
	Orthopedic	39 (3.9%)
	Thoracic surgery	14 (1.4%)
	Thyroid/Parathyroid	38 (3.8%)
	Urology	303 (30.3%)

Table 3: Key characteristics of two identified AAGA cases

Case #	1	2
Surgery	Right hip disarticulation (osteosarcoma)	Left breast lumpectomy + axillary lymph node dissection
Age (years)	12	39
American Society of Anesthesiologists	2	2
Pre-existing risk factors	NIL	Prior history of awareness
Premedication	NIL	NIL
Anesthetic	Propofol Total Intravenous Anesthesia	Propofol Total Intravenous Anesthesia
Neuromuscular block	Atracurium	Atracurium
BIS target reading	40 – 60	40 - 60
Surgery duration	4 hours, 30 minutes	1 hour, 40 minutes
Awareness report	On direct questioning, with agitation	Spontaneous
Perception	Conversations between surgical staff, tactile sensation, no pain	Pain, tactile sensation of incision, inability to move or breathe

Table 4: Analysis of different risk factors for developing AAGA, when compared to 2 patients who developed awareness

	Report (Proportion)	p-value
Female Gender	484 (48.4%)	0.17
Prior History of Awareness	2 (0.2%)	0.02*
Total Intravenous Anesthesia	25 (2.5%)	0.001*
Use of Benzodiazepines	383 (38.3%)	0.52
Use of Neuromuscular blockade	613 (61.3%)	0.26
Emergency Surgery	32 (3.2%)	1.0
Emergency Surgery	32 (3.2%)	1.0

* *P*-value ≤ 0.05. Analyzed using Fisher's exact test.

RESULTS

Descriptive statistics of the patients are briefed in Table 1 while Table 2 depicts the anesthetic technique and proportion of the types of surgeries.

From the available data, we identified two patients with definitive awareness i.e. an incidence of 0.2%. Their characteristics are summarized in Table 3. Both patients were debriefed about the incident postoperatively and offered psychological support but they refused and did not report any lasting emotional or psychological distress in subsequent interviews.

Patients that developed awareness were younger (mean age 26±18.3) compared to the rest of the population (mean age 46.9±14.4). However, this difference was not statistically significant (p-value = 0.41).

ASA status and type of surgery had no significant relationship with the incidence of awareness (p-value = 0.81 and 0.17 respectively).

Table 4 illustrates a detailed report and analysis of patients grouped in high-risk factor variables and their respective significance when compared to patients who developed awareness.

Furthermore, two patients (0.2%) reported unpleasant dreaming intraoperatively. Both were given balanced anesthesia: induction with Propofol, and maintenance with Sevoflurane and Atracurium for neuromuscular blockade. Interestingly, both were also pre-medicated with Midazolam. They could recall their dreams but not any intraoperative events. None of them agreed to receive any psychological assistance.

DISCUSSION

In the past, studies have estimated the in-

cidence of Accidental Awareness during General Anesthesia (AAGA) to be 1-2 in 1000 patients.[2,19] Other studies done in China, Spain, and Brazil have even reported incidences of definitive awareness as high as 0.41%, 1% and 2.5%, respectively.[15,20,21] In the literature review, several risk factors have been identified viz. female gender; young age; history of AAGA; rapid sequence induction; use of neuromuscular blockers; emergencies; and obstetric, cardiac or thoracic surgeries.[5, 22] According to some, extensive surgery in oncological patients may also make them more prone to develop awareness due to accumulation of multiple causative factors at once e.g. massive blood loss or one lung ventilation[15]. In some patients, it may even occur despite adequate anesthesia and in absence of any risk factors.

In our study population, the patients who reported AAGA (n = 2) had several of these independent risk factors i.e., both the patients were young (< 40-years old), females, and cancer patients. Both patients received neuromuscular blockade and Total Intravenous Anesthesia (TIVA), which are both known to cause awareness when compared with balanced anesthesia using halogenated anesthetics with ETAC measurement.[5, 15] Additionally, one of these patients had a history of awareness during a previous anesthetic. Of these, TIVA and a positive history of awareness showed a statistically significant relationship with the incidence of awareness during our analysis.

It is complicated to identify the occurrence of AAGA due to possible shortcomings in the anesthetic system not alarming the attending anesthetists of such an event. It may also be overlooked by the patient resulting in their failure to report it spontaneously. We used a structured interview for explicit recall of intraoperative events and detection of AAGA. This served as a strength of our study since such an interviewing scheme is a strongly preferred methodology for correctly estimating the incidence of awareness. This has been previously demonstrated by Mashour et al. who described a five-fold difference in the incidence of awareness while comparing two strategies of assessment: 0.1% in patients that underwent structured interviews with direct questions vs. 0.02% in routine quality assurance approach conducted on the first postoperative day, inquiring about any troubles during anesthesia.[23]

In addition, we used few questions from the Brice questionnaire[16] for the interviews that have formerly been used in various studies[4, 18, 24] to minimize any subjective bias. To further eliminate bias by anesthetists, our initial interviews were carried out by an RN that was not involved in the anesthetic management of the patient intraoperatively.

Another strength of our study is that we incorporated a delayed re-interview into our study design and this approach is also known to detect cases more efficiently.[9,24,25]

A potential limitation of our study was a deficit in data collection. In earlier literature, the use of a BIS monitoring system had been shown to reduce the risk of awareness by 82%.[25] While both our awareness cases involved TIVA with BIS monitoring, our pro forma did not include a record of intraoperative BIS readings since our main outcome to be measured was the incidence of accidental awareness. Our results were more consistent with those reported by Avidan et al. in their B-Unaware trial followed by the Bispectral Index or Anesthetic Gas to Reduce Explicit Recall (BAG-RECALL) trial, which invalidated the superiority of Bispectral Index (BIS) monitoring over end-tidal anesthetic concentration (ETAC) monitoring in preventing awareness.[26,27,28] Similar findings were outlined by Lewis et al. who noted no difference in the incidence of awareness between BIS or ETAC-guided anesthesia.[29] Our shortcoming may, therefore, be considered trivial since recent evidence to suggests that awareness may occur despite the maintenance of BIS and ETAC values.[30]

While on one hand, one may generalize our results into their everyday anesthetic practice considering that our study involved no change in routine clinical practice, on the other hand, the results may not be hypothesized for all surgical populations since the study took place specifically in the cancer population.

Nonetheless, we suggest that it is imperative to identify patients at high risk for developing this harrowing complication and subsequently, improve anesthetic preparation (e.g., equipment and drug checking) and apply appropriate strategies such as maintaining ETAC, neuromuscular monitoring, and anesthetic depth monitoring (with BIS or Entropy, etc.) to curb the incidence of intraoperative awareness thereby preventing serious psychological outcomes.

CONCLUSION

Our study found the incidence of awareness during general anesthesia in the adult cancer population to be at par, if not more than that reported worldwide.

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Author's Contribution

TA conceived the idea, finalized the study design, and collected the data. RSQ contributed to data analysis, data Interpretation, and writing the manuscript. MA collected the data and designed the questionnaire. AAK supervised and contributed to the revision of the manuscript. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.