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Awareness and Explicit Recall After Surgical Procedures in Intensive Care: Incidence and Risk Factors - CABIS Study

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Introduction

Awareness and Intra-operative Explicit Recall (IoER) are uncommon situations during general anesthesia; its incidence has been reported 0.1 to 0.01 percent and the risk to present IoER is deemed higher in severely ill unstable patients under total intra venous anesthesia (TIVA) [1] [2] [3] [4].
For the purpose of this work, we consider Awareness when the patient becomes conscious during a procedure under general anesthesia, while IoER is the patient's postoperative ability to retrieve memories stored during the procedure.
Awareness and IoER can lead to postoperative morbidity: post-traumatic stress disorder, sleep disturbances, nightmares, flashbacks and fear to further anesthesia and surgery [5] .
Diagnosis of awareness during general anesthesia is difficult, especially in severely ill patients in whom tachycardia, hemodynamic instability and chronic sedation is common. Processed EEG has been proposed as a tool for awareness recognition, but its used has not gained universal acceptance; when inhalational anesthesia is used End Tidal anesthesia gas concentration seems to perform similarly to EEG monitoring [6].
In our hospital, severely ill patients under mechanical ventilation and hemodynamic support are usually submitted to surgical procedures in their bed at the ICU. There is no inhalation anesthesia available in the ICU; so all patients receive TIVA at the anesthesiologist discretion. At the time, most anesthesiologists in our hospital did not use BIS monitoring routinely, although available. We had 2 anecdotic cases of IoER in our severely ill population, in whom memories of surgical procedures were difficult to differentiate from suffering during ICU stay associated with minor procedures not performed under general anesthesia (change dressing, nurse's procedures, physical and respiratory therapy).
The objective of this study is to establish the real incidence of IoER in our high-risk patients, to evaluate the risk factors for IoER in them and to evaluate a potential tool for awareness recognition and IoER prevention in our service.

Materials and Methods

After IRB approval (July 2011), all patients in ICU who were intubated, under mechanical ventilation, free of cerebral damage that could preclude postoperative evaluation and requiring surgical procedures in ICU were eligible.
Patients were evaluated for eligibility and a relative was asked to provide informed consent for the inclusion in this study. All patients received TIVA at the anesthesiologist discretion. BIS® monitoring (Covidien, Mansfield, MA) was started just before anesthesia; its display was concealed to the anesthesiologist. An independent physician registered vital signs, drugs used, BIS score and surgical events at intervals of 2.5 min during the procedure and postoperative period for up to 90 minutes in total. According to protocol, if the BIS score raised over 60 during surgery the anesthesiologist was informed. Severity of illness was assessed by means of APACHE II score at admission, SOFA score and ASA score at the day of procedure.
IoER was assessed by one of the investigators in structured postoperative interviews at 2-6 hours (immediate), 4-7 days (mediate) and 21-28 days (late) (Brice method adapted to Spanish by Luengo) [7] [8]. In the absence of sedation or disorientation (delirium) patient were asked 4 questions:
What is the last thing you remember before you went to sleep?
What is the first thing you remember on wakening?
Did you dream whilst you were asleep?
Do you remember any other thing between falling asleep and awakening?

Recruitment started in August 2011 for the pilot phase, and July 2013 for the main phase with the last patient recruited on January 2013.
Primary end-point was the incidence of IoER in any of the postoperative interviews.

Statistical Analysis. Categorical variables were described as absolute and relative frequencies, and continuous variables as median and Inter-quartile range (IQR). Comparisons between IoER status were assessed by Fisher's and Mann-Whitney's U tests, respectively. Local IRB approved the trial and informed consent was obtained from patient's relative.

Results

43 patients were included in the study (table 1) they had 49 procedures, 22 male and 21 female with a mean weight of 61 Kg, and a height of 160 cm. Their ASA physical status was 3 (27 cases, 62.8%) or 4 (16 cases, 37.2%), APACHE II score at admission was 21 (IQR 17 – 24), comorbidities were present in 36 (83.7%) cases.
Mortality occurred in 11 cases (25.6 %) no patient died during Anesthesia management (see table 1)
The day of the procedure all patients were under mechanical ventilation (oro-tracheal tube or tracheostomy). SOFA score was 6 (IQR 5 to 9). Sedation was used in 38 (69.4%) and RASS score was -1 (IQR -3 to 0). Hemodynamic stability was assured with vasoactive and inotropic support in 15 (30.6%) cases.
General anesthesia was administered at anesthesiologist's preferences with different drugs (see table 3), in 16 cases only Midazolam and Fentanyl were used, while 33 cases (67.3%) received other anesthetics in addition to the above. Neuromuscular blocking agents were used in 32 (65.3%) cases. Intra-operative hemodynamic instability led to increase or start vasopressor in 8 (16,3%) cases.
Intra-operative Explicit Recall IoER was diagnosed in 5 patients, after 6 procedures (see table 1) only one patient reported IoER in 2 interviews after one procedure, other 4 patients reported IoER in one of the visits with no recall in the other two visits (table 3); at late visit only 2 patients had memories of intraoperative events: one unpleasant (abdominal pain) and another neutral (OR personnel conversation).
Patient characteristics were not associated with to occurrence of IoER, not were the intra-operative hemodynamic data (arterial pressure and Heart rate) or the occurrence of intraoperative movements in non paralyzed patients (see table 2). Maximum BIS score, and the Occurrence of BIS score > 60 are the only factors with a significant association with IoER.
All patients with IoER had a BIS score > 60, and none of patients whose BIS was always < 60 had IoER (table 4). BIS score was > 60 at least once during surgery in 27 procedures (55.1%); it was not associated to any preoperative or intraoperative characteristic.

Table 1. Initial characteristics of 43 **patients** according to IoER status after 49 surgical procedures. Five patients reported IoER after 6 procedures.

	Total n=43 n (%)	No IoER n=38 (87.4) n(%)	IoER n=5 (11.6) n(%)	P value
Age (years)*	62 (36-75) *	59 (36-73) *	67 (64-81) *	0.4485
Sex (male)	22 (51.2)	20 (52.6)	2 (40)	0.664
ASA physical status				
3	27 (62.8)	26 (68.4)	1 (20)	0,056
4	16 (37.2)	12 (31.6)	4 (80)	
Apache II at ICU admission*	21 (17-24) *	21 (17-24) *	19 (18-22) *	0,789
Comorbidity	36 (83.7)	31 (81.6)	5 (100)	0.314
Previous IoER	1 (2.3)	1 (2.6)	-	
Previous Alcoholism	1 (2.3)	1 (2.6)	-	
Previous Drug abuse	2 (4.7)	2 (5.3)	-	
Psychiatric disorder				
Depression	1 (2.3)	1 (2.6)	-	
Other	2 (4.7)	2 (5.3)	-	

* Median (IQR)

Table 2. Characteristics of patients during 49 surgical procedures performed at ICU, under TIVA.

	Total n= 49	No IoER n=43 (87.8)	IoER n=6 (12.2)	P value
Surgical Procedure				
Re-Laparotomy **n(%)**	24 (49)	21 (48.8)	3 (50)	1
Mediastinal exploration **n(%)**	2 (4.1)	2 (4.7)	-	
Tracheostomy **n(%)**	22 (44.9)	19 (44.2)	3 (50)	1
Inguinal injury unpacking **n(%)**	1 (2)	1 (2.3)	-	
SOFA score ***Median (IQR)***	6 (5-9)	6 (5-9)	6 (5-8)	0.8415
Sedation previous 24 Hours **n(%)**	34 (69.4)	31 (72.1)	3 (50)	0.353
RASS score ***Median (IQR)***	-1 (-3 to 0)	-1 (-3 to0)	-2 (-0.5 to 0)	0.343
Previous Vasoactive or Inotropic support n(%)	15 (30.6)	14 (32.6)	1 (16.7)	0.652
Intraoperative medications				
Midazolam **n(%)**	48 (98)	43 (100)	5 (83.3)	0,122
Fentanyl **n(%)**	46 (93.9)	41 (95.3)	5 (83.3)	0.33
Other anesthetics ¶ **n(%)**	33 (67.3)	29 (67.4)	4 (66.7)	1
Neuromuscular blockers **n(%)**	32 (65.3)	29 (67.4)	3 (50)	0,4
Intra-operative movement **n(%)**	7 (14.3)	6 (14)	1 (16.7)	1.0
Mean Arterial Pressure (during procedure)				
Min **(mmHg)** ***Median (IQR)***	63 (54-70)	63 (54-71)	58.5 (48-66)	0.3517
Max **(mmHg)** ***Median (IQR)***	92 (79-104)	92 (79-103)	103 (79-115)	0.3067
Heart rate (during procedure)				
Min **(b/min)** ***Median (IQR)***	86 (69-106)	86 (69-106)	80.5 (65-93)	0.6363
Max **(b/min)** ***Median (IQR)***	102 (86-119)	102 (85-119)	101.5 (93-151)	0.8428
BIS score				
Min ***Median (IQR)***	33 (24-43)	33 (24-43)	34.5 (24-53)	0.8189
Max ***Median (IQR)***	61 (49-79)	61 (48-76)	86.5 (71-93)	0.005
BIS > 60 **n(%)**	27 (55.1)	21 (48.8)	6 (100)	0.027

¶ use of Ketamine, Thiopental, Propofol or Remifentanyl

Table 3. Postoperative visits and findings

	Early visit (2 – 6 hours)	Intermediate visit (4 – 7 days)	Late visit (21 – 28 days)
n (%)	48 (98)	44 (91.8)	35 (71.4)
Still sedated	33 (67.3)	9 (18.4)	0
Dreams	3 (6.1)	3 (6.1)	3 (6.1)
Probable recall	2 (4)	1 (2)	1 (2)
IoER	2 (4)	0	1 (2)

Discussion

This is a small cohort of very ill patients in whom awareness is difficult to identify; we found an extremely high incidence of IoER in this population. We choose this group because we had to deal with this specific patient population. Our group performed similar to Spanish report in which the sub-group of mixed anesthesia (N2O based) with no or little amnesic agent had a incidence of 5% of awareness with recall [1].
Usual risk factors do not emerge as related to IoER in our work, but the small numbers preclude any further analysis of regression in order to better categorize this issue. Other groups found risk factors to be: younger cases, female gender, obstetric or cardiac procedures, receiving fewer anesthetic drugs and showed more episodes of tachycardia or hypertension during the procedure [4] higher ASA status and TIVA [9] low doses of anesthetics [10]
Clinical clues used by anesthesiologist during the surgical procedure did not allowed them to identify the risk of postoperative IoER.
Interestingly, the report of IoER can vary through time, patients seems to forgot events they had been able to recall early in postoperative period, or to recall later events related to the surgical experience. We choose the short Brice protocol of structured interview because of its low potential of pseudo-memory generation [11] and it is validated in Spanish by a Chilean group [8]. Structured interview has been shown to have a higher sensibility than standard quality assurance reports [12] or spontaneous complaints
Weaknesses: Small cohort study. Lack of association with known risk factors can be due to beta error. Same investigator registered intraoperative events and performed postoperative interviews. Attitude of anesthesiologist was not consistent over time. Drugs used in the anesthesia management were not standard. Neither doses
External validity of this finding is restricted to very ill patients, chronically sedated, under mechanical ventilation and hemodynamic support; such population frequently need surgical procedures and constitutes a major challenge for the anesthesiologist. We need to develop better tools to identify awareness and to prevent IoER.

Founding
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References

1. Errando, C.L., et al., *Awareness with recall during general anaesthesia: a prospective observational evaluation of 4001 patients*, in *Br J Anaesth*2008. p. 178-85.
2. Sebel, P.S., et al., *The incidence of awareness during anesthesia: a multicenter United States study*, in *Anesthesia and analgesia*2004. p. 833-9, table of contents.
3. Xu, L., A.-S. Wu, and Y. Yue, *The incidence of intra-operative awareness during general anesthesia in China: a multi-center observational study*, in *Acta Anaesthesiologica Scandinavica*2009. p. 873-82.
4. Ghoneim, M.M., et al., *Awareness during anesthesia: risk factors, causes and sequelae: a review of reported cases in the literature*, in *Anesthesia and analgesia*2009. p. 527-35.
5. Leslie, K., et al., *Posttraumatic stress disorder in aware patients from the B-aware trial*, in *Anesthesia and analgesia*2010. p. 823-8.
6. Avidan, M.S., et al., *Prevention of intraoperative awareness in a high-risk surgical population*, in *N Engl J Med*2011. p. 591-600.
7. Brice, D.D., R.R. Hetherington, and J.E. Utting, *A simple study of awareness and dreaming during anaesthesia*, in *Br J Anaesth*1970. p. 535-42.
8. Luengo J, V., et al., *[Anesthesia awareness]*, in *Rev Med Chil*2010. p. 352-7.
9. Wang, E., et al., *Incidence and risk factors of intraoperative awareness during general anesthesia*, in *Zhong Nan Da Xue Xue Bao Yi Xue Ban*2011. p. 671-5.
10. Ranta, S.O., et al., *Awareness with recall during general anesthesia: incidence and risk factors*, in *Anesthesia and analgesia*1998. p. 1084-9.
11. Enlund, M. and H.G. Hassan, *Intraoperative awareness: detected by the structured Brice interview?*, in *Acta Anaesthesiologica Scandinavica*2002. p. 345-9.
12. Mashour, G.A., et al., *Brief report: assessment of intraoperative awareness with explicit recall: a comparison of 2 methods*, in *Anesthesia and analgesia*2013. p. 889-91.