

Update on post-traumatic stress syndrome after anesthesia

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Abstract. – **BACKGROUND:** Between 0.5% and 2% of surgical patients undergoing general anesthesia may experience awareness with explicit recall. These patients are at a risk for developing anxiety symptoms which may be transient or can lead to post-traumatic stress disorder (PTSD).

AIM: The aim of this review was to assess the prevalence of PTSD after intraoperative awareness episodes and analyze patients' complaints, type and timing of assessment used.

METHODS: PubMed, MEDLINE and The Cochrane Library were searched up until October 2012. Prospective and retrospective studies on human adult subjects describing prevalence of PTSD and/or psychological sequelae after awareness episodes were included.

RESULTS: Seven studies were identified. Prevalence of PTSD ranged from 0 to 71%. Acute emotions such as fear, panic, inability to communicate and feeling of helplessness were the only patients' complaints that were significantly correlated to psychological sequelae including PTSD. There were cases that reported psychological symptoms after 2-6 hours from awakening (%) or 30 days after (%). Previous studies used psychological scales lacking of dissociation assessment.

CONCLUSIONS: Whenever an awareness episode is suspected, a psychological assessment with at least three interviews at 2-6 h, 2-36 h and 30 days must be performed in order to collect symptoms associated with both early and delayed retrieval of traumatic event. As a dissociative state could hide the expression of reactive symptoms after intraoperative awareness, future studies should be focused on detecting dissociative symptoms in order to carry out a prompt and appropriate treatment aimed at avoiding long-term psychological disability.

Key Words:

Post-traumatic stress syndrome, Anaesthesia, Awareness, Recall.

anaesthesia are at increased risk of developing post-traumatic stress syndrome (PTSD) that causes a clinically evident hardship or severe changes in working, social and emotional life¹. The prevalence of awareness with explicit recall under anaesthesia has been reported to be 0.5-2%²⁻⁴. Patients experiencing awareness episode describe it with auditory perceptions, sensation of paralysis, anxiety and panic^{4,5}.

Awareness is often missed and dismissed by medical staff as it is a retrospective diagnosis. It has been found that 65% of patients who experienced awareness during general anaesthesia did not inform their anaesthetist about what had happened⁶. Patients, in fact, may not voluntarily report their experiences without being asked directly. Sandin et al⁷ prospectively interviewed 11,785 patients who had undergone general anaesthesia. They were interviewed for awareness on 3 occasions: in the post-*anaesthesia* care unit (PACU), again at 1 to 3 days, and lastly at 7 to 14 days. Of the 18 patients who reported awareness, 7 (39%) recalled it in the PACU interview; 6 (33%) recalled awareness for the first time at the second interview; and 5 (28%) recalled it at the third. For anaesthetists to understand the true appearance of awareness in their practice, they need to interview patients postoperatively in a detailed and extensive manner to "jog" their memories for intra-operative experiences. Patients should be asked about the last thing they remember before going to sleep for the operation; the first thing they remember when they woke up; anything in between these two periods, including sounds, dreams, imagination and finally about the worst thing they remember about their operation). Inspection of records of awareness cases for relevant parameters such as heart rate, blood pressure and anaesthetic technique has not been helpful in retrospectively explaining why awareness occurred⁶. Bispectral index is the only one of neuromonitoring devices available for assessing

Introduction

There is increasing evidence that patients experiencing awareness with recall during general

depth of anesthesia for which substantial data exists about awareness during anesthesia. Ekman et al⁹ demonstrated a 77% reduction in the occurrence of awareness when BIS-guided anesthesia was used (compared with a historical cohort). A prospective randomized blinded trial was conducted in 2,500 high-risk patients and BIS-guided anesthesia was found to be associated with an 82% reduction in the prevalence of awareness⁹. Episodes of awareness are usually associated with one of following conditions: selection of inadequate anaesthetic dose (70%); resistance to the anaesthetics of some patients (22.5%); machine malfunction or misuse resulting in an inadequate delivery of anaesthetics (2.5%)⁹.

Bergman et al¹⁰ reviewed 81 cases of awareness reported to the Anaesthetic Incident Monitoring Study. Where the cause could be determined, awareness was mainly caused by drug error resulting in inadvertent paralysis in awake patients (n=32) and failure of volatile anaesthetics delivery (n=16) due to the equipment malfunction; vaporiser problems were the most frequently reported (13/16) followed by breathing circuit problems (3/16). Hypotension or cardiovascular instability necessitating a reduction in the inspired volatile concentration caused 4 awareness incidents. Prolonged attempts at tracheal intubation contributed to 5 cases of awareness. Less common causes included muscle relaxant apnoea with inadequate administration of hypnotic (n=3) and deliberate withdrawal of volatile anaesthetics (n=4).

Practical strategies have been suggested for minimizing the occurrence of awareness, including premedication with amnesic drugs, such as benzodiazepines impairing acquisition of new information¹¹. Nitrous oxide and opioids should be supplemented with halogenated anaesthetic agents with end-tidal concentrations of 0.6 minimum alveolar concentration (MAC) or more¹¹. When halogenated anaesthetics are used alone, at least 1 MAC should be administered, bearing in mind that the end-tidal, not the inspired concentration of volatile agents should be used¹². Actually, informing the patient about the possibility of awareness should be restricted to cases in which such a risk is relatively high (e.g. open-heart surgery, trauma surgery, cesarean section). It would also be prudent for the operating theatre team to avoid discussion about the patient or the prognosis as patients are most likely to recall emotionally threatening remarks⁶.

In case of intraoperative awareness, a percentage of patients ranging from 0 to 71% (Table I)

may develop PTSD -after surgery- that commonly appears with sleep disturbances and recurrent nightmares, diurnal flashbacks of the event, anxiety and preoccupation with death. The syndrome persists for longer than one month and even years and causes clinically significant discomfort or impairment in social functioning, problems in the working area and in life needs. In some cases, patients may require long term medical and psychological treatment^{13,14}. Severity and duration of the traumatic event are the most important factors influencing the subsequent development of PTSD¹⁵. It seems that intraoperative awareness is followed by recall only if it has lasted more than two minutes^{8,16}. The symptoms of PTSD follow the exposure to such abnormal traumatic factor such as the feeling of a death threat. Characteristic symptoms of PTSD involve re-experiencing the event, persistent avoidance of stimuli associated to the trauma, numbing of general responsiveness or increased arousal. Sometimes patients can show a dissociative state of variable duration. When the subject is exposed to trigger events, which resemble the traumatic one, often he/she perceives an intense psychological discomfort. As a consequence, the subject tries to avoid all of the stimuli related to a traumatic event such as thoughts, emotions or conversations. This behaviour can cause amnesia for a part of the event. Frequently, immediately after the traumatic event, a reduction of reactivity towards external environment, known as "psychic paralysis" or "emotional anaesthesia" may appear. The subject may complain of a strongly decreased involvement in pleasant activities: he/she feels like an outsider towards other people, feels a marked decrease of ability to perceive emotions and shows a lowered interest in future projects. Moreover, patients can manifest persistent symptoms of anxiety or increased arousal, which had been absent before the trauma and may include exaggerated alertness or strong response of alarm, difficulty in falling asleep and in having an uninterrupted sleep due to frequent nightmares. Some patients report irritability or flaring up of anger and difficulty in concentration or in performing simple tasks.

The aim of this review was to assess the prevalence of psychological sequelae including PTSD after an awareness episode occurring during general anaesthesia and analyze type and timing of assessment used and patients' complaints. Further discussion then focused on relationship between implicit memory/dream recall, awareness and PTSD, and legal implications.

Table 1. Clinical studies on psychological consequences of awareness during anaesthesia.

| Authors | Year | Study design | Patients with awareness* | Type of assessment | Timing of assessment** | Patients with psychological sequelae (N) | PTSD prevalence, N (%) | Complaints during awareness episodes | Described psychological sequelae other than PTSDs |
|-----------------|------|---|--------------------------|---|--|--|------------------------|---|--|
| Schwender et al | 1998 | Consecutive referrals and advertisement | 45 | "Awareness anaesthesia" questionnaire 0.1-30 years) | 9,6 years during (range: 2 and 6 months) | 22 | 3 (6.6) | Hearing voices and conversation, visual perception, feeling being touched, helplessness, paralysis, fear, anxiety, severe panic, moderate-severe pain | Daytime anxiety, nightmares, fear about future operation |
| Ranta et al | 1998 | Prospective, cross-sectional | 5 | SCID-NP; SCID-II; Impact of the event scale | 2 weeks-2 and 6 months | 1 | 0 (0) | Heard voices, pain, felt the tube in his throat, fear | Sleep disturbances |
| Domino et al | 1999 | Observational Retrospective Closed claims | 61 | NS | NS | 61 | 6 (10) | Hearing conversations and sounds, feeling surgery with and without pain, paralysis, tracheal intubation, severe panic | Temporary emotional distress, recurrent nightmares, need for psychotherapy |
| Osterman et al | 2001 | Referrals and advertisements | 16 | CAPS; SEQ 17.9 years | Mean: | NS | 9 (56) | Inability to communicate, feeling of helplessness, terror and pain | Postoperative distress |
| Lenmarken et al | 2002 | Prospective | 9 | A1-F criteria according to DSM-IV | 27 months (range: 20-35) | 7 | 4 (44) | Fear and feeling of helplessness | Transient anxiety and sleep disturbance |

Table continued

Table 1 (Continued). Clinical studies on psychological consequences of awareness during anaesthesia.

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|------------------|------|--|--------------------------|-----------------------|------------------------|--|------------------------|--|---|
| Samuelsson et al | 2007 | Retrospective | 46 | Structured Interview | NS | 15 | 1 (2) | Pain, acute emotional reactions, flashbacks, indifference, loneliness, and lack of confidence in future life | Schizophrenia, anxiety, chronic fear, nightmares, |
| Leslie et al | 2010 | Prospectively planned matched cohort study | 7 | CAPS (range, 4.3-5.7) | 5.3 years | 7 | 5 (71) | Pain, inability to move, terror, hearing talking, inability to move | NS |

*Who underwent psychological assessment (N); **time from awareness episode. NS = not stated; SCID-NP = Structured Clinical Interview for DSM-III-R Non patient edition; SCID-II = Structured Clinical Interview for DSM-III-R Personality Disorders; CAPS = Clinician administered PTSD Scale; SEQ = Surgical Experience Questionnaire.

Methods

The literature search was conducted using computerized databases including PUBMED, The Cochrane Library, and MEDLINE in order to identify the relevant articles that have been published until October 2012. Articles were retrieved using the following keywords: “awareness” AND “anaesthesia” AND “post-traumatic stress disorder”, and “intra-operative awareness” AND “psychological sequelae”. Abstracts were read thoroughly before complete articles were obtained and the references from the relevant publications were manually explored to ascertain further potential articles. The search was restricted to studies that were published in English. Inclusion criteria were: human adult subjects, prevalence of PTSD and/or psychological sequelae. Observational studies and retrospective analysis were not eliminated. Case reports/ case series and review were not considered.

Results

Based on the initial search results, 55 titles and abstract were examined. One additional publication were retrieved by hand search of the references. 11 reports were rejected because they were not relevant to our study focus. Of the remaining 44 articles, 37 did not meet the inclusion criteria (16 review article, 4 editorial, 6 case report, 1 non-human study, 5 non-adult studies, 5 for lack of PTSD or psychological sequelae description). In the end, 7 publications were reviewed.

Outcome After Awareness: Psychological sequelae and PTSD

Late psychological symptoms after awareness were described in 1961¹⁷. Since then, PTSD has been defined and identified as a complication of awareness. With the exclusion of case reports and case series, more than half of the available studies on patients suffering from PTSD due to awareness are retrospective, and potential selection bias in the investigated cohorts should be considered.

Prevalence and manifestation of PTSD in patients who have experienced awareness during anaesthesia were examined in 7 studies (Table 1). Among 45 patients who had suffered from awareness, Schwender et al¹⁸ identified 3 of them who had developed PTSD resulting in the need for medical treatment. 19 patients had other psychiatric symptoms after having been awake during operation. Nearly all of the 49% who had ex-

perienced anxiety and fear while awake during surgery described their reaction as severe panic. Pain, which in most of the cases was severe, was reported by 25%.

Nine out of 16 patients with awareness suffered from PTSD (56%), with a mean duration of 18 years (range, 3 months to 30 years) in the study conducted by Osterman et al¹⁹. Most of the patients complained of inability to communicate, a feeling of helplessness, terror and pain.

Domino et al¹⁷, by studying 4,183 malpractice claims, entered into the ASA Closed Claims Project between 1961 and 1995, identified 79 cases related to awareness. The majority of awareness claims occurred in women younger than 60 years of age ASA physical class I-II undergoing elective surgery. Female gender was significantly overrepresented and constituted 77% of the claims. 21% of the patients had experienced pain, and 11% reported panic. Postoperative, temporary emotional distress was reported by 84%, and 10% had been assigned a diagnosis of PTSD¹⁷.

Many patients who become aware during surgery report a variety of complaints. In a recent study by Samuelsson et al²⁰, auditory and tactile perceptions were the most common (70% and 72% respectively), followed by feelings of helplessness, acute fear, panic and pain (56%, 58%, 43% and 46% respectively). Acute emotions such as fear, panic and helplessness were the only factors during awareness that were significantly related to late psychological symptoms. Therefore, although awareness seems to occur most frequently in patients undergoing painful procedures requiring light anaesthesia such as cardiac surgery (1.1-1.5), major trauma (11-43%) or caesarean section (0.4%)⁷, the most determinant for late psychiatric symptoms after awareness seemed not to be pain perception. Indeed, the fractions of patients reporting pain and panic were lower in the Domino et al study compared to the Schwender et al¹⁸ and Osterman et al¹⁹, while the risk for psychiatric symptoms after awareness was higher. The Lennmarken et al report²¹ was based on a previous cohort study in which 18 awareness cases had been identified among 11,785 consecutive patients given general anaesthesia. All 18 patients had been offered repeated information and supportive counseling immediately after their awareness episodes, and all of them stated that their psychiatric problems had resolved within 3 weeks. The patients were asked to take part in an interview, on average 27 months after the unfortunate anaesthetic. One pa-

tient had died, 2 patients could not be located, and 6 patients declined to participate. Among the 9 patients (50% of the original cohort) who consented to the follow-up interview, four had PTSD that did not tend to decrease with time, and two of those required medical therapy. Another 3 patients had some psychiatric problems that had become less severe with time and were able to cope with daily life.

Interestingly, in the report of Samuelsson et al²⁰, 2 female patients experienced serious mental illness after awareness episode. The first had a diagnosis of PTSD. She had been exposed to extreme mental stress earlier in her life. The second had a diagnosis of schizophrenia. The personality was not investigated before anaesthesia but the finding was not explained by any mental symptoms that the authors were able to identify post-hoc. Eventually, the Authors stated that, in both cases, it is far from clear that their psychiatric diagnoses can be attributed to awareness episodes. The criticism to this study could be considered the lack of a validated instrument for psychiatric assessment. Not by accident, the investigations using not-standardized questionnaires were those with lesser percentage of PTSD diagnosis (Table I). However, in the work of Ranta et al¹⁴, neither PTSD nor other severe psychological *sequelae* were found although all diagnoses were carried out according to strict Diagnostic and Statistical Manual²² criteria by using the Structured Clinical Interview for DSM-III-R (SCID-I and SCID-II)^{23,24}. The Symptom Checklist 90-Revised was used to make the diagnostic structured interview complete. Patients were also asked to complete the Impact of Event Scale, a measure that indexes symptoms which characterize posttraumatic stress disorder (PTSD). The interview was done immediately after operation or two weeks later (first interview) and the patients were re-interviewed at 2 and 6 months after surgery. Three of the five patients with awareness had a history of major depression and also had preoperative symptoms of depression and anxiety. The mental state of two depressive patients did not significantly change after the operation, but one patient was treated with antidepressant medication and recovered. It is very difficult to establish if awareness episode could have worsened their depressive state¹⁴. Furthermore, patients with certain psychological profiles might be more prone to experiencing awareness during general anaesthesia. Further studies are needed to evaluate these issues.

Lastly, in the recent paper of Leslie et al²⁵, in which 5 of 7 awareness patients (71%) met criteria for a diagnosis of PTSD, the Authors underline the need to investigate post-traumatic dissociation as it is to be expected that dissociative symptoms, not formally assessed in their cohort, could play a significant role in determining long-term psychological disability. Two of five patients who developed PTSD reported their experience only at 30-day interview²⁵.

Relationship Between Implicit Memory/ Dream Recall, Awareness and PTSD

Implicit memory (processing of auditory information which conscious recall strategies are not able to retrieve) can be demonstrated by letting subjects do the actions which facilitate access to unconscious memory traces. This facilitation of task performance is known as priming²⁶. Priming effect and its neural correlated has been studied during anaesthesia^{27,28}.

Cognitive processing during anaesthesia includes any psychologically mediated response which occurs during or after surgery and which seems to be elicited by an intra-operative event. For example, intra-operative suggestion may cause specific behavioural responses. Intra-operative events may also be remembered implicitly through “dream-like process” which has been described as a subconscious state of awareness characterized by vivid thoughts and images, usually with a strong affective component, related to the external stimuli²⁹.

Care should also be made to pinpoint dreams which had occurred outside the general anaesthetic period such as those which happened in the recovery room; many anaesthetised patients have a distorted appreciation of time and place. This might be called “pseudo-awareness”¹⁶.

In the report of Ranta et al¹⁴, two of the eight patients with unpleasant intraoperative dreams had possible awareness. None of the patients developed PTSD. To date, there are no dates supporting the hypothesis that dream-like processes could be implicated in PTSD occurrence. The characteristics of the dream did not seem to be relevant. However, a 40 year female patient, who subsequently developed PTSD, described her intraoperative awareness episode such as a sensation of suffocation, paralysis and severe abdominal pain. Its desperation to escape after hearing “gossip” and laughter and its belief she was dying were being intermittently interrupted by a pleasant dream¹³.

How to Prevent PTSD After Intraoperative awareness

If a patient complains of awareness, a detailed interview of the experiences should be obtained. The “gold standard” for diagnosing PTSD, as suggested by Leslie et al²⁵, is a structured clinical interview which should be performed by a psychiatrist or clinical psychologist experienced in the assessment and treatment of PTSD²². The Clinician-Administered PTSD Scale has been developed and validated to be used by experienced clinicians and thoroughly trained paraprofessionals. It has the advantage of providing a continuous severity measure for individual symptoms.

Patients should be reassured that the anaesthesiologist believes their account and sympathizes with their suffering. Patient should be reassured about non repetition of the same mishap with future anaesthetics because the details will be in the medical chart and will guide the anaesthesiologist managing subsequent anaesthetics. Patients should be offered early psychological or psychiatric support to reduce the probability for them to suffer from PTSD. It is also necessary to notify surgeon, nurse, and hospital lawyer or physician’s insurer about the incident. Moreover, patients should be visited daily during the hospital stay to look for and treat psychological sequelae. After patients’ discharge frequent phone contacts should be made to ensure the patients are fully recovered.

Legal Implications

Cases of awareness represent between 1.9% (ASA Closed Claims Analysis) to 12.2% (British data) of claims against anesthesiologists for both transient and late psychological symptoms. Domino et al¹⁷ analysed claims from the ASA Closed Claims Project Claims for awareness during anaesthesia accounted for 2% of all claims. This percentage was similar to rates of claims for familiar complication after anaesthesia such as aspiration pneumonia and myocardial infarction. The amount of compensation in these cases was \$18,000, although the highest was \$600,000¹⁷. It is noteworthy that what are generally considered to be the classic cues for light anaesthesia were absent in most cases: hypertension occurring in 15% of recall cases and tachycardia occurring in 7%. It is clear that awareness during anaesthesia can occur when an apparently adequate anaesthetic has been administered. In order to sustain a case for malpractice against anaesthesia personnel, it is necessary to demonstrate that the anes-

thetic given deviated from the normal standard of care and that the adverse consequences were a result of that deviation.

Another important aspect to bear in mind is that patients could simulate PTSD symptoms in a dispute policy. For these reasons, the diagnosis of PTSD should always be confirmed by a psychiatrist, able to rule out other pre-existing conditions and establish the real existence of the disease.

Conclusions

The frequency and severity of psychological sequelae following awareness during anaesthesia are key. There are cases that report anxious symptoms only after two or three interviews. It could be associated with a reaction of dissociation of some patients who, after recalling the awareness episode, involuntarily masked their hyper-arousal symptoms. Whenever an awareness episode is suspected, a psychological assessment with at least three interviews at 2-6 h, 2-36 h and 30 days must be performed in order to collect both early and delayed retrieval of traumatic event. A dissociative state, due to awareness episode, could hide the expression of reactive symptoms. Previous studies used psychological scales that lacked of assessment of dissociation. Investigating grading of dissociative state in future studies is important, both for research purposes and clinical intervention. Early detection of clinical symptoms would allow psychiatrists to choose a precocious intervention in order to increase the efficacy of the psychotherapeutic or medical treatment.

Conflict of Interest

None.

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