Awareness during anaesthesia
- A review of current literature -

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Introduction
The introduction of anaesthesia has changed modern medicine like few other things. Interestingly the demonstration of ether by Morton in 1846 was not only the first anaesthesia, it was also the first case of awareness during anaesthesia. Morton's patient felt no pain during the procedure but had recall from the surgery.[1] About 54% of patients planned for surgery worry about the possibility of pain, paralysis and mental distress under their operation.[2] Even though awareness happens quite seldom it is of significant concern to patients and besides PONV and pain the most important factor for patient dissatisfaction with anaesthesia care.[3]

Definition
Memory is not a single entity. Current classifications distinguish between two types. Explicit memory refers to the conscious recollection of previous experiences. Implicit memory by contrast refers to changes in performance or behaviour that are produced by previous experiences but without any conscious recollection of those experiences.[4] In this review the term “awareness” is used to describe explicit memory of events during general anaesthesia.

Incidence
Since the first publication of a study on awareness during surgery in 1960 the incidence has steadily decreased from 1,2% to 0,1 – 0,2% today.[5] These incidences were found when a structured interview was used in patients not undergoing cardiac or obstetric surgery.[4] An Australian study from 2009 showed an increased incidence of awareness associated with GA for caesarean section.[6] Investigations on awareness during cardiac surgery in the last ten years have shown an incidence between 0,3 and 0,5%.[5] Paediatric surgery has with 0,8% a even higher incidence of awareness cases.[7, 8]

Detection of awareness
Clinical signs
Clinical signs like heart rate and blood pressure are routinely used by anaesthetists to monitor anaesthetic depth. It has been shown that these methods are unreliable, meaning that these parameters are not bound to indicate anaesthesia depth correctly.[9, 10]
When Ghoneim and colleagues reviewed 271 reported cases of awareness from 1950 through 2005 they only found tachycardia and hypertension associated with awareness in one of five cases. 80% of the awareness patients had shown no symptoms whatsoever.[11] In a closed claims analysis by Domino and colleagues it was shown that only 15% of the patients with intraoperative recall had hypertension and only 7% tachycardia.[12] This means that a stable blood pressure or heart rate can not be taken as a guarantee for deeply anaesthetized patients but of course it seems logically that a high heart rate and/or blood pressure might indicate an awake patient.

Credibility
In order to establish credibility of awareness reports it is essential to confirm the patients statement by questioning op-staff whether the recall is authentic.
Furthermore it is common in current awareness studies to have a blinded board of “controllers” to analyze every detected case of awareness in order to determine the authenticity of the reports.

**Postoperative detection**

Detecting awareness is not simple. In his review article Ghoneim states that over the years the “Brice questionnaire” introduced by Brice and colleagues in 1970 and modified by Lin and colleagues 1991, has proven to be a reliable and efficient method to detect intraoperative recall. The interview comprehends four questions:

- What was the last thing you remember before you went to sleep?
- What was the first thing you remember when you woke up?
- Can you remember anything in between these periods?
- Did you dream during your operation?

These questions are less likely to suggest answers than others. A structured interview is also necessary because some patients, even if they have suffered from awareness might not report their experience spontaneously due to different reasons. They don’t want to appear ungrateful, they fear to be described as insane, they fear to be treated poorly because of their report or they just prefer to ignore and forget their experience.[5] Timing of the interview is essential. Directly after operation in the “post anaesthesia care unit” (PACU) it is difficult to gain the patients attention while he or she is very focused on more obvious symptoms like pain, PONV or simply fatigue. Recent studies found that only 50% of the awareness cases are detected in the PACU. Sometimes recall is delayed by several days, maybe even weeks.[2, 4] The technique might not be perfect, but even critics to the “Brice questionnaire” state that it is probably the least “bad” method of detecting awareness to date.[13]

**Risk factors**

The low incidence of awareness during anaesthesia makes it difficult to assess risk factors and even current prospective cohort studies have problems identifying exact causes. Yet reviewing current literature helps to find significant factors.[5]

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M. Ghoneim Incidence and risk factors for awareness during anaesthesia, 2007
Risk related to light anaesthesia/type of surgery
Due to several reasons a so called “light anaesthesia” might be required for some kinds of surgery. In cardiac surgery, to maintain myocardial contractility haemodynamic stability the anaesthesiologist is often forced to use a more opioid based regiment and reduce the application of hypnotic agents due to negative cardiovascular effects. Opioids have little amnesic power and so the risk for awareness during cardiac surgery is higher compared with other surgical disciplines.[5] Similar to cardiac surgery, anaesthesia for caesarean section has a traditionally high risk for awareness.[6, 11, 14] Pregnant women have an extremely high cardiac output which accelerates redistribution of intravenously applied drugs and slows down the establishment of an adequate partial pressure of volatile anaesthetic agents. Added to this is the concern about neonatal drug exposure, the effect of volatile anaesthetics on uterine tone and the haemodynamic depression due to anaesthetics in emergency situations. These circumstances potentially leave a period of light anaesthesia before the volatile anaesthetic fully reaches the effect site, especially in a case of prolonged intubation.[6] Emergency patients often receive light anaesthesia due to the same reasons as cardiac surgery patients do. With hypovolaemia or exsiccosis they are more likely to become haemodynamically instable.[5] Errando and colleagues found that night time surgery also has a higher risk for awareness.[14]

Risk related to muscle relaxation
The only dependable clinical signs of inadequate anaesthesia are patient movement and breathing pattern. Muscle relaxation (NMR) is a risk factor because these signs are lost then.[15] Sandin and colleagues showed in their prospective case study, that patients with NMR suffered from awareness in 0,18% of the investigated cases, patients who were not relaxed had an awareness incidence of only 0,1%. Furthermore eleven of the 14 NMR patients who suffered from awareness had unpleasant effects from their experience and four patients showed delayed symptoms. No patient from the non-NMR group felt anxiety during his phase of awareness neither had one of them delayed symptoms.[2]

Risk related to increased anaesthesia requirements
A history of awareness is to be classified as an important risk factor and higher doses of anaesthetic agents should be considered. Patients taking significant doses of sedatives or analgesics might also be in need of increased anaesthetic dosages.[15, 16]

Risk related to demographic data
Concerning demographic data like sex, age or weight it is difficult to determine whether one of them classifies as a risk factor as the studies reviewed differ a lot in their findings. Sebel and colleagues found no association between sex or age and the incidence of awareness during anaesthesia in a study on adult patients.[11] When Ghoneim and colleagues analyzed 271 case reports of awareness and compared them with two other studies, they found that females were overrepresented compared to study no.1, compared to study no.2 they were not. Ghoneim also concluded that weight had no effect on the incidence of awareness.[11] In their prospective case study Sandin and colleagues found a similar
incidence for men and women, too.[2] Studies analysing intraoperative awareness in children have shown a much higher incidence than in adults.[7, 8]

Risk related to human error or technical difficulties
Errando and colleagues showed that night time surgery had a higher incidence for awareness even when high risk patients were excluded. This could be related to staff fatigue.[14] The fact that errors like syringe swap, inadvertent under dosage and technical problems with syringe pumps or anaesthesia machines are impossible to avoid makes it clear, that awareness always will be possible.[15]

Consequences of awareness

Medico legal consequences
A study analyzing the claims of the ASA closed claims project showed that 2% of all claims were related to awareness during anaesthesia. This rate is similar to those for aspiration or myocardial infarction. The median payment for compensation after awareness during anaesthesia in the closed claims project was $18.000.-.[12]

Psychological consequences
Frequent complaints from patients who have experienced an episode of awareness during surgery were the ability to hear events and conversations, the sensation of paralysis, weakness, helplessness, anxiety, panic and impending death. Some patients are tormented by doubts whether what they experienced really happened or whether there is something wrong with their minds. The after-effects of intraoperative recall can be temporary and include nightmares, sleep disorders and daytime anxiety. In worst cases awareness under anaesthesia leads to post traumatic stress syndrome (PTSD) with repetitive nightmares, irritability and a preoccupation with death.[4] A long term follow up by Lennmarken and colleagues showed that four of nine patients who had experienced awareness developed severe symptoms of PTSD, another three of these nine patients had milder symptoms, but nevertheless still suffered from their experience. All of those patients had three weeks after their unsuccessful anaesthesia claimed that no further help was necessary. Those numbers might be higher as six patients declined to be questioned two years after the incident and denial is a symptom of PTSD. [17]

Prevention

Preoperative prevention
The first step in order to prevent intraoperative recall should be to identify those patients bearing a greater risk for awareness than others beforehand. This includes patients scheduled for cardiac surgery or cesarian section under general anaesthesia, rigid bronchoscopy, surgery known for significant blood loss. Further, patients who take significant doses of sedatives, analgesic or neuroleptic drugs and patients with a history of awareness have a higher risk for recall.[15] Premedication with benzodiazepines is common in modern anaesthesia management. The primary goal is, of course, to relieve preoperative anxiety, but as these drugs are also associated with anterograde amnesia it can be assumed that the prevention of awareness is also a goal, unfortunately there is no evidence to prove this effect.[17]

Intraoperative prevention
Even though avoidance of muscle relaxants is no guarantee for avoiding awareness [2, 10] should their administration be kept to a minimum as the only reliable signs indicating a not sufficiently anaesthetized patient are patient movement and breathing patterns.[15] Sandin
and colleagues found that of the awareness patients in their study only those who received muscle relaxants reported unpleasant effects of their awareness experience. The decision which anaesthesia regimen to choose in order to minimize the risk for intraoperative awareness is not easy. In my personal development in anaesthesia I have often been told that total intravenous anaesthesia (TIVA) bears a higher risk for intraoperative recall than balanced anaesthesia with volatile anaesthetic agents. This has never been proven, furthermore two studies indicate that the incidence is the same or lower. The problem regularly mentioned is the impossibility to measure patient side concentrations of i.v. anaesthetics in contrast to inhaled agents. It is therefore very interesting that Sandin and colleagues showed in their large prospective study including over 11,000 patients that measuring end tidal anaesthesia gas concentration (ETAGC) had no influence on the incidence of awareness. One point most authors agree on, no matter if they favour TIVA or gas, is that a device which can reliably measure the depth of anaesthesia is needed. Depth of anaesthesia monitors (DOAM) collect EEG signals and display parameters which are to help guiding general anaesthesia. Three different models are available to date. The BIS-Monitor by Aspect Medical, Norwood, MA, USA, the Narcotrend-Monitor by Schiller, Baar, Switzerland and the M-entropy-module by GE Healthcare, Helsinki, Finland. The three monitors provide the raw EEG, a dimensionless variable between 0 and 100 called BIS-Index, Narcotrend-Index and SE & RE respectively. They show also a trend of the variable, a signal quality index and the burst suppression ratio. The most important question is: Can DOAM prevent awareness? This is difficult to answer. Two recent studies indicate that they in fact can. Ekman and colleagues compared 4945 patients undergoing surgery in relaxant general anaesthesia with a DOAM with 7826 patients from a previous study without DOAM and found a reduction by 77% in the incidence of awareness. Myles and colleagues found an even higher reduction by 82% when they analyzed 2643 patients randomly assigned to a DOAM or non-DOAM group. In contrast to that, Avidan and colleagues showed in their study that it made no difference whether an anaesthesia was guided by a DOAM-protocol or a ETAGC-protocol when they assessed 1941 patients at high risk for intraoperative awareness. Avidans conclusion was that DOAM might be helpful to monitor TIVA since the regimen lacks other monitoring possibilities. It seems as further studies are needed to decide whether DOAM should become a standard in daily anaesthesia monitoring. For example in case of the BIS-Monitor, the most common DOAM today, this would imply $360,000,000,- only in disposable electrodes. As long as experts have not agreed upon the value of this technique, these costs can hardly be justified.

Management of awareness cases

If intraoperative awareness occurs it is important to gather as much information as possible. In most cases is it possible to verify the patients statement. The patient should be assured that his or her claims are taken seriously and if possible an explanation for the happenings should be provided. As already stated a thorough follow up is essential. The patient must be offered psychological support during hospital stay as well as afterwards. Longterm sequelae with PTSD as the worst case are likely to happen.
**Practise points and research agenda**

**Practise points**

Anaesthesia Training
- Physiology and pharmacology
- Equipment and clinical measurement
- Preoperative assessment and communication skills
- Work practices (vigilance, fatigue, seeking advice)

Pre-operative Assessment
- Identify patients at risk
- Inform, consent, reassure

Intraoperative management
- Pre-case equipment checks
- Adequate hypnotic administration, especially at times of increased noxious stimulation (intubation, sternotomy)
- Minimize use of muscle relaxants if possible
- Rapid response to suspected inadequate anaesthesia
- Modulate operating room behaviour
- Special care when aiming for rapid case turnover
- Consider using an EEG-based monitor of anaesthetic depth

Postoperative interview
- Conduct a post-operative interview about memories of anaesthesia
- Provide follow-up for aware patients
- Discuss awareness cases in quality assurance meetings

[15]

**Research agenda**

- Further large scale randomized trials are warranted to evaluate each of the Depth of anaesthesia monitors
- The cost-effectiveness of Depth of anaesthesia monitoring has yet to be clearly elucidated
- Unwanted artefact can result in misleading output from Depth of anaesthesia monitors; improved artefact suppression algorithms are needed
- Monitored parameters that reflect intra operative nociception would be a valuable addition to intraoperative monitoring

[15]