Intraoperative awareness — recommendations of the Committee on Quality and Safety in Anaesthesia, Polish Society of Anaesthesiology and Intensive Therapy

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Modern general anaesthesia is complex and reversible. It involves a temporary loss of consciousness, analgesia, a decrease in muscle tension or complete muscle relaxation, suppressed reactions of the autonomic nervous system, and the provision of amnesia of events after its completion. General anaesthesia is induced using agents of differing actions and various pharmacodynamic and pharmacokinetic properties. Given a suitable choice of agents and dosages, the procedure is safe and the incidence of procedure-related complications and adverse side effects is low. Additionally, the safety of anaesthesia is enhanced by appropriate intraoperative monitoring of individual vital functions and of the entire anaesthesia, based on continuous observation of patients and assessment of their clinical conditions. Such management, which has been obvious since the dawn of anaesthesiology and is still valid, occurs irrespective of advances in medicine.

The quality of anaesthesia is determined by its depth and reflects the suppression of activities of the central and peripheral nervous system. The assessment of anaesthesia depth resulting from subjective analysis of clinical parameters is increasingly being based on objective data obtained using modern devices that monitor the individual constituents of anaesthesia, including the degree of unawareness (pharmacological sleep).

The induction of sleep is one of the fundamental tasks of widely used general anaesthesia. If it is lacking or inadequate, this indicates a poor assessment of the depth of anaesthesia and leads to patient suffering during and after anaesthetic procedures.

Intraoperative awareness is a rare phenomenon (0.1–0.2% of all general anaesthesias) [1, 2], yet it is considered to be a serious anaesthetic event. It increases patient fears before any future anaesthetic and surgical procedures and often results in severe psychological and mental problems [3]. Awareness-related compensation claims have led to legal proceedings against anaesthesiologists [4]. The evaluation of this phenomenon is associated with serious difficulties resulting from nomenclatural, methodological and statistical problems [5]. For these reasons, the majority of available reports are casuistic. In future, substantial advances in comprehensive understanding of the problem should be achievable thanks to the electronic monitoring system recording intraoperative awareness cases, the system open in its nature and addressed to those who experienced such episodes [6].

NEUROBIOLOGICAL BASIS

Anaesthetics act primarily on the central nervous system, but a standardised way of assessing their effects on cerebral function has yet to be designed.

Inhalation anaesthetics, and most intravenous anaesthetics, appear to act as agonists of gamma-aminobutyric acid, thus exerting predictable changes in the EEG recording. Recent findings, however, have suggested that the influence of individual anaesthetics on the brain varies [7].

The agents used to induce general anaesthesia are likely to have preferential effects on the subcortical sleep-regulatory centres [8, 9]. Although physiological sleep is substantially different from general anaesthesia, the mechanism involved is the same, as are some features. The cycle of sleep and awareness is regulated by the nuclei located in the pons, mesencephalon and hypothalamus [10]. The likely effects of anaesthetics on sensations involve the inhibition of cortico-hypothalamic and cortico-cortical feedback loops. On the other hand, their impact on so-called explicit memory is associated with effects on the hippocampus, its

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gyrus, temporal lobe, and occasionally on the prefrontal and new cortex [11].

**CLINICAL PICTURE**

Awareness, irrespective of the circumstances in which it is described, is the term characterising certain mental activities, e.g. correct orientation to oneself, place and environment. It reflects the processes and/or reactions of an individual, of which he/she is aware. The basis of awareness is active use of the memory. The condition is often equated with consciousness; yet the terms are not synonymous, as consciousness is merely the presence of responses to external mental stimulation, e.g. visual, auditory or sensory.

The condition of sleep, including pharmacological coma, is characterised by temporary loss of consciousness and awareness.

Intraoperative awareness is the subjective feeling of the patient experienced ex post as the recall of anaesthesia-related memories, usually unpleasant. Memory can be explicit — spontaneously reported by the patient — or implicit, retrieved using specialist psychological tests adjusted to the patient’s age. The majority of anaesthetics, in doses markedly lower than those necessary to provide unawareness, cause amnesia. Amnesia can also be achieved with benzodiazepines [12, 13].

It is believed that intraoperative awareness is a serious critical event during general anaesthesia. This condition is diagnosed when postoperative memory of events is explicit, regards the entire surgery or parts of it, and is associated with pain sensations. The scale used to standardise and classify the sensations is the five-degree Michigan Awareness Classification Instrument [9], where:

- 0 — anaesthesia without intraoperative awareness,
- 1 — isolated auditory perceptions,
- 2 — tactile perceptions (e.g. surgical manipulations, presence of an endotracheal tube),
- 3 — pain,
- 4 — paralysis (inability to move, speak, breathe),
- 5 — paralysis and pain.

Additionally, the symbol D (distress) serves to identify patients who experience fear, anxiety, suffocation, sense of dying or of impending death, etc.

Hearing is the last perception to be lost during anaesthesia induction, and the first to be restored after recovery. Therefore it is the most commonly reported form of intraoperative sensation, occurring in 48-100% of intraoperative awareness cases [14].

Other sensations reported by patients include weakness or paralysis, an inability to move or breathe, a feeling of dyspnoea (48%), fear, panic, and a sense of impending death.

Pain during surgery is the most dramatic experience in this context. It is reported by 10–28% of patients who experienced intraoperative awareness [14, 15, 16, 17]; in the majority of cases, the reported pain was localisable. Contrary to common fears, the perception of pain during intraoperative awareness appears to be rarer when various, synergistic methods of analgesia are used.

**DELAYED CONSEQUENCES**

The sequels of intraoperative awareness may be transient, and include irritability, anxiety, depression, fear or sleep disorders (insomnia, nightmares) [18]. In most cases, they subside with time; nevertheless, fears associated with future anaesthetic procedures and the perceived risk of other episodes of awareness can be long-lasting. Moreover, confusion, disorientation and fears regarding the patient’s own mental condition are also observed, caused by doubts as to whether the recalled intraoperative sensations were real [19].

The most severe form of disturbance is post-traumatic stress disorder (PTSD), which develops after a period of latency ranging from several weeks to several months. Its course is variable, yet in most cases, the symptoms are expected to remit. The incidence of PTSD is estimated at 4–40% of intraoperative awareness cases [3].

The clinical picture of PTSD mainly involves anxiety, irritability, sleep disorders, nightmares, depressive disorders, occasional suicidal thoughts and the re-experiencing of traumatic events. Left undiagnosed and untreated, PTSD can lead to permanent personality changes over the longer term (i.e. years). Early therapeutic intervention after the detection of intraoperative awareness can reduce the risk of PTSD [20].

**INCIDENCE**

Fear of intraoperative awareness occurs in over 50% of patients undergoing surgery, and is the leading source of anxiety related to the procedures planned [15]. Fortunately, the actual incidence of awareness is much lower. Intraoperative awareness is more common (in 2% of cases) when anaesthesia is maintained with nitrous oxide alone [21]; the additional use of opioids in single doses does not change this percentage [22]. Premedication with benzodiazepines reduces the risk of intraoperative awareness [23].

The assessment of awareness incidence is significantly hindered by the fact that patients do not on their own initiative describe their intraoperative perceptions immediately after procedures. Those who experienced such sensations sometimes recall them one or two weeks after surgery. The presence of unintended intraoperative awareness can be most accurately assessed using standard postoperative questionnaires.

The incidence of intraoperative awareness episodes in children seems to be slightly higher than in adult po-
pulations, reaching 0.8% [24, 25], which could result from methodological difficulties in this group of patients.

It is essential to differentiate between intraoperative awareness and still maintained (during anaesthesia induction) or regained (during recovery) consciousness.

RISK GROUPS
In each case, a past episode of awareness is a significant risk factor for its recurrence.

The following three groups of patients at risk of intraoperative awareness have been identified: 1 — patients with genetic or acquired resistance to anaesthetics; 2 — those with intolerance to large anaesthetic doses due to poor cardiac reserve, etc.; and 3 — those undergoing procedures that tend to reduce the doses of anaesthetics.

Traditionally, the high-risk groups include women subjected to Caesarean section, haemodynamically unstable patients, and patients who have experienced multiple organ failure or who have undergone cardiac surgery with extracorporeal circulation. A relevant risk factor is intraoperative hypotension [26, 27]. Moreover, procedures performed at night appear to be associated with a higher incidence of awareness [23]. It has been demonstrated that individuals below the age of 60 (89%), assessed as ASA class I and II (68%), undergoing emergent procedures (87%) and women (77%) predominate among patients reporting episodes of intraoperative awareness [4].

Resistance to anaesthetics, considered to be a risk factor, can be pharmacokinetic (increased metabolism related to alcohol abuse, use of opioids, amphetamine, etc.) or pharmacodynamic (altered receptor susceptibility of likely genetic origin, e.g. increased demand for inhalation agents in redheaded patients with melanocortin-1 receptor mutations) [28].

RISK FACTORS
DEPTH OF ANAESTHESIA INSUFFICIENT FOR SURGICAL NEEDS
Too shallow anaesthesia resulting from a lack of required anaesthetic care can occur during any surgical procedure. Awareness is more often associated with mistakes in labelling and the supply of agents (94%) rather than with errors in medical management (43%); it is also more common with opioids, relaxants, nitrous oxide and when the anaesthetic gases do not contain halogenated inhalational agents [23].

TOTAL INTRAVENOUS ANAESTHESIA (TIVA)
This is associated with a potentially higher incidence of awareness (as much as 4.4 times higher compared to inhalation anaesthesia combined with low doses of opioids) [29], probably due to a lack of monitoring of serum concentrations of agents and inter-patient variability in responses to propofol. In preventing intraoperative awareness episodes, target-controlled infusion (TCI) is more valuable than manually-controlled infusion (MCI). Although there is no direct evidence confirming a reduced risk of awareness when using TCI, the method is preferable as it is based on mathematical models which take into account effector concentrations of the selected agents and their numerous pharmacokinetic and pharmacodynamic parameters. Nevertheless, it is not as direct a measurement as analysis of end-expiratory anaesthetic concentration.

GENERAL ANAESTHESIA WITH MUSCLE RELAXANTS
This is the commonest cause of intraoperative awareness, featuring overly light anaesthesia, which is not signalled by the patient’s movements. Maintained muscle relaxation in a conscious or regaining consciousness patient ought to be regarded as a serious anaesthetic incident. Such situations occur particularly often during difficult, prolonged intubations (recorded in about 4% of cases) [23].

EQUIPMENT FAILURE
Malfunction of the equipment and medical devices supplying anaesthetics, e.g. malfunction of a vaporiser or its emptying, failures of medical gas pipelines (nitrous oxide), failures of infusion pumps or disconnection of the vascular line system, all contribute to such complications. Ninety four per cent of cases of intraoperative awareness are believed to result from human error and/or equipment failure [4].

Under certain circumstances, and in the patients mentioned earlier (high-risk groups), it is impossible to avoid intraoperative awareness episodes, which sometimes can be the price that must be paid for achieving relevant clinical goals [30].

ASSESSMENT METHODS
Analysis of brain activity suppression based on recordings of its electrical activity is a recognised means of assessing the depth of anaesthetic sleep. To confirm retrospectively intraoperative awareness, postoperative questionnaires are used.

INSTRUMENTAL METHODS (INTRAOPERATIVE)
Monitoring of the brain function in patients can be carried out using:
— analysis of its spontaneous bioelectrical activity based on [31]:
  - bispectral index (BIS) [32],
  - entropy [33],
  - narcotrend index [34],
  - patient state index (PSI) [35],
  - analysis of fractal dimension [36];
— analysis of evoked bioelectrical brain activity using:
  - auditory evoked potentials (AEP) [37, 38].
The modern devices used to assess bioelectrical brain activity during anaesthesia convert the EEG recording into a simple numerical index, which is the empirically determined equivalent of the standard of suppression of EEG cortical recording in the frontal region. Anaesthetics suppress not only the cerebral cortex, but also subcortical regions together with the reticular system and medulla oblongata, i.e. the areas which are not instrumentally evaluated. Moreover, the empirically determined standards of brain activity suppression were designed for some selected anaesthetics (propofol, thiopental, sevoflurane, desflurane, isoflurane) and do not relate to nitrous oxide, ketamine or xenon.

The monitoring method based on analysis of low-voltage EEG recordings is highly vulnerable to interference, particularly that induced by electronic devices in the operating room and generated by bioelectrical muscle activity (EMG); this diminishes the importance of EEG analysis, especially in the elderly. Additionally, in elderly patients, the optimal value of BIS is considered to be 50–60 and not 45 as in younger patients [39, 40]. It should be noted that intraoperative awareness may occur also at BIS < 60; therefore, reduced concentrations of inhalation anaesthetics based solely on BIS < 60 are not recommended [41].

In many cases, the variability of EEG recordings is conditioned genetically, which also limits the reliability of instrumental methods. Intraoperative awareness episodes have been observed even at BIS values suitably tailored to the circumstances [4, 42].

There is no explicit evidence that EEG-based monitoring of brain activity reduces the incidence of intraoperative awareness. Some publications have suggested such a correlation [32, 41], whereas others have not [42]. Moreover, BIS monitoring has not been proved to be superior to evaluation of anaesthesia quality using the method of maintaining suitable end-expiratory concentrations of inhalational anaesthetics [43].

NON-INSTRUMENTAL METHODS (POSTOPERATIVE)

Since intraoperative awareness episodes are identified after the completion of anaesthesia, their assessment is retrospective. Specialist questionnaires should be used, characterised by diverse episode detection and patient involvement in their filling out. There is no standard questionnaire; therefore, the majority of questionnaires currently used are specifically designed. All of them cover the same hospitalisation period and course of events, which is best illustrated by the Brice questionnaire consisting of five questions [44, 45]:

1. What was the last thing you remembered before going to sleep?
2. What was the first thing you remembered happening on waking?
3. Do you remember anything between going to sleep and waking?
4. Did you dream while you were asleep?
5. What was the worst thing about your surgery and anaesthesia?

RECOMMENDATIONS

To limit the number of intraoperative awareness episodes, the following pre-, intra- and postoperative measures are recommended.

— Preoperative period:
  • determination of increased risk based on:
    • history: previous awareness incidents, difficult intubation, chronic pain treated with opioids;
    • medicines (benzodiazepines, antidepressant, psychotropic, antiepileptic drugs) and substances (alcohol, amphetamine, cocaine, other drugs) taken;
    • patient’s general state (ASA IV or V, particularly with low cardio-vascular reserves);
    • type of anaesthesia (e.g. rapid induction of anaesthesia, relaxants necessary during anaesthesia maintenance, TIVA, anaesthesia based on nitrous oxide and opioids);
    • type of surgery (e.g. cardiac, Caesarean section, trauma);
  • patient examination and determination of severity of patient anxiety;
  • informing high-risk patients of possible intraoperative awareness during anaesthesia (studies on the effects of such information on anaesthesia are lacking).

— Immediate pre-anaesthesia period:
  • checklist of anaesthetic procedures:
    • anaesthetic machines;
    • anaesthetic devices;
    • agents used (type, dose);
  • routine premedication adjusted to the patient’s needs.

— Intraoperative management:
  • continuous clinical evaluation of the patient’s general condition. The traditional methods of assessing anaesthesia depth still form an indispensable part of intraoperative awareness prevention. This rule is reflected in the national regulations on standards of medical management in anaesthesiology and intensive therapy, which assume the presence of an anaesthesiologist in the immediate vicinity of the patient throughout the anaesthetic procedure [46]. Work overload and working time standards permitting additional jobs are likely to result in exhaustion, which increases the risk of negligence. Clinical evaluation of insufficient anaesthesia
primarily involves the detection of spontaneous and/or evoked motor reactions and commonly known autonomic reflex reactions. In cases involving artificial airways, it should be remembered that difficult and prolonged endotracheal intubation increases the risk of insufficient anaesthesia.

General anaesthesia combined with muscle relaxants favours intraoperative awareness episodes. The use of relaxants should be limited only to necessary cases:

- conventional monitoring of basic vital functions. This is obligatory and clinically valuable yet shows poor specificity for anaesthesia depth evaluation based on the degree of sympathetic system tension and stress reaction. There are no documented studies confirming the effectiveness of this monitoring in decreasing the incidence of awareness. Episodes of awareness have been demonstrated to occur when tachycardia or hypertension were absent [4];

- continuous analysis of end-expiratory concentrations of inhalation anaesthetics, a part of obligatory monitoring, is related to the depth of anaesthesia and has been proven to be as valuable as CNS monitoring methods. To maintain the appropriate depth of pharmacological sleep, concentrations of volatile anaesthetics should not be lower than 0.8–1.2 MAC (varies according to patient age and type of respiratory gas mixture). No equally efficient method of assessing the depth of intravenous anaesthesia has yet been developed;

- maintenance of proper anaesthetic supply during anaesthesia reduces the risk of awareness.

In cases of haemodynamic instability, the interventions undertaken should primarily be aimed at optimising the circulatory system, if possible. The lightening of anaesthesia should be a last resort combined with simultaneous administration of amnestic agents (benzodiazepines) and analgesics (opioids). Due to the potential risk of intraoperative auditory sensations, the operating room team ought to pay special attention to any words spoken, particularly with high-risk patients. Having music playing during surgery is likely to be beneficial for patients.

Postoperative care:

- early — once the symptoms suggestive of intraoperative awareness have been detected in the early postoperative period, the episode has to be evaluated using a questionnaire specifying the type of sensation; based on its results, the circumstances of the incident should be explained. In difficult cases, the short-term assistance of a clinical psychologist will be necessary. The suspicion or diagnosis of an episode ought to be described in the patient’s medical records;

- late — traumatic experiences can cause characteristic mental symptoms, as previously described; if prolonged, they are defined as post-traumatic stress disorder. Generally, its symptoms include dysregulation of affective stimulation, awareness and concentration disorders, somatisation and personality changes. Uncontrollable, intrusive recall of memories and visions of traumatic situations is of particular importance in cases of intraoperative awareness. Recovery requires specialist psychological and psychiatric aid, and depends on properly applied psychotherapy (e.g. cognitive-behavioural) and psychopharmacology (e.g. selective serotonin re-uptake inhibitors), which may be time-consuming and arduous. For these reasons, the importance of preventing this rare complication cannot be underestimated.

CONFLICT OF INTEREST

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References:
6. Awareness awareness registry. www.awaredb.org
46. Rozporządzenie MZiOS w sprawie standardów postępowania oraz procedur medycznych przy udzielaniu świadczeń zdrowotnych z zakresu anestesiologii i intensywnej terapii w zakładach opieki zdrowotnej. Dz. Ustaw 1997, Nr 37, poz. 215.