

## Emergence from anaesthesia: a winding way back

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Sir,

Accidental awareness with recall during general anaesthesia (AAWR) is a rare complication of general anaesthesia with an overall incidence of ~1:19,000 anaesthetics [1]. About 20% of AAWR cases occur at the emergence from anaesthesia, while 90% of these events are potentially preventable, especially through the use of neuromuscular monitoring [1]. The remaining AAWR emergence episodes could be attributed to an error in anaesthesia management, such as inappropriate anaesthetic administration due to device malfunction or human error [2, 3]. In very rare cases, there is no readily identifiable cause. This letter chronicles the clinical presentation of an AAWR episode manifesting itself at the emergence from anaesthesia, in order to provide a picture of this rare complication (Table 1), and to underline how the pharmacodynamic and operating mechanism of general anaesthetics, and the relationships between consciousness and anaesthesia, pose a puzzle still too difficult to solve.

A 58-year-old Caucasian man (86 kg, 178 cm) affected by colon cancer was selected for elective laparoscopic left hemicolectomy. Before the beginning of the surgery, midazolam 2 mg and fentanyl 100 µg were administered as premedication. Anaesthesia was induced with intravenous propofol, titrated (total dose 140 mg) until loss of consciousness (LOC), along with fentanyl 100 µg. Anaesthesia maintenance was obtained through end-tidal concentrations (ETAG) of desflurane (in 40% oxygen) with a minimum alveolar concentration (MAC) of 0.9. The ETAG-guide was achieved through a nomogram to estimate age, gender, weight, and height related MAC (Draeger Fabius® apparatus).

Manually controlled remifentanyl infusion was titrated on the patient's response. In addition, haemodynamic variations were managed through the guidance of the non-invasive cardiac output monitoring (NICOM®) system. Neuromuscular blockade was obtained with cisatracurium 15 mg. The monitoring of the neuromuscular blockade was performed (NMT Trident Drager Infinity®) allowing the maintenance of the depth of anaesthesia (DoA) status (ETAG 0.9) until full reversal of the neuromuscular blockade. The operative course was uneventful and according to our standard anaesthetic approach, the ETAG value was maintained for the entire duration of the operation (2 hours and 15 minutes). At the end of surgery, remifentanyl infusion was interrupted and extubation performed under recovery of the neuromuscular blockade (sugammadex 100 mg) with spontaneous breathing and the swallowing reflex. Moreover, we usually perform extubation under only a partial recovery of consciousness, usually corresponding to a MAC of about 0.2–0.3 with an anaesthetic expiration concentration ranging from 2 to 4%, in the case of desflurane.

Although the recovery of consciousness at emergence was sudden, the patient immediately reported to the anaesthesiologist detailed conversations which had taken place between several professionals in the theatre. The report was so impressive as it described a conversation between two non-Italian visiting medical students speaking in English. The patient provided specific information about the duration of symptoms which lasted an estimated 3 to 5 minutes at the phase of awakening from anaesthesia.

The patient did not experience paralysis and the AAWR episode did not cause him concern and distress. Moreover, conversational psychodiagnostic interviews, at 1 and 6 months, demonstrated that the patient had no psychiatric sequelae.

The misuse of neuromuscular monitoring is a major risk factor for AAWR during emergence from anaesthesia [1], especially in case of butyrylcholinesterase deficiency [4]. However, a root cause analysis showed that the patient had

**Table 1.** Features of AAWR at the emergence from anaesthesia

Incidence	About 20% of AAWR cases
Clinical Presentation	Paralysis and distress often reported
Causes	BChE deficiency (for succinylcholine and mivacurium) Inadequate anaesthetic management (missed use of neuromuscular monitoring, awake extubation) Equipment malfunction or human errors Pharmacodynamic mechanisms (e.g., due to tobacco smoking, alcohol consumption, and centrally acting drugs) Genetic resistance to anaesthetics
Psychological sequelae	Common (depending on the distress, and AAWR duration)
Avoidance strategies	Use of neuromuscular monitoring Maintenance of DoA until full reversal of neuromuscular blockade and avoid awake extubation, when possible
Treatment	Professional psychological interventions

AAWR: accidental awareness with recall during general anaesthesia; BChE: butyrylcholinesterase; DoA: depth of anaesthesia

no risk factors for AAWR, and had never undergone surgery. No equipment malfunction or human errors were detected, and neuromuscular monitoring was used. Moreover, a reversal agent (sugammadex) was administered.

On the other hand, in 16% of cases, the AAWR phenomenon has no easily recognizable cause [5]. Apart certain conditions, such as tobacco smoking, heavy alcohol consumption, and centrally acting drugs responsible for the so-called 'physiological resistance' to anaesthetic agents, probably through a pharmacodynamic mechanism, an innate or genetic resistance could be also possible. This is a fascinating and poorly understood pharmacodynamic phenomenon. For instance, preclinical experimental data, obtained from mutant analysis in *Drosophila*, demonstrated that a wide range of genes (e.g. encoding for second-messengers, memory formation substrates, ion channels, synaptic proteins) and related isoforms are implicated in the normal response to anaesthetics [6].

However, the matter seems to be more complex. Indeed, emergence from anaesthesia is not simply the reverse process of induction as it is subjected to the control of different neural pathways [7] while, probably, several EEG patterns characterize the recovery of consciousness from DoA status [8].

Regarding the postoperative AAWR sequelae, a longer duration (> 3–5 minutes) of awakening has been associated with a higher incidence of psychological consequences, including posttraumatic stress disorder (PTSD) [1]. Probably, our patient did not present sequelae as he did neither manifested intraoperative distress nor discomfort in the immediate postoperative period. Furthermore, the psychological postoperative assessment helped to resolve any potential psychological consequence [2].

Could the complication be avoidable? Probably, the above-described AAWR episode was inevitable. Although the use of a DoA monitor (e.g., bispectral index, BIS) could have provided some help, compared with ETAG-guided anaesthesia, the use of BIS monitoring has not been associated with a reduced incidence of AAWR [9], while this complication has been reported even when BIS values [10] and ETAG concentrations were suggestive of a proper DoA status [9]. Moreover, the literature does not support routine BIS monitoring as part of standard practice [3] whereas, on the contrary, a recent large-sized clinical trial confirmed the results of previous studies [11] and showed that the use of ETAG-guided anaesthesia with a MAC ranging at 0.7–1.3 decreased the incidence of AAWR [12]. In conclusion, perhaps compared to the emergence phase, the induction and maintenance phases offer most opportunities for AAWR prevention, including the use of benzodiazepines (e.g., midazolam) as a premedication [13]. However, not all

the AAWR events can be prevented, especially at emergence from anaesthesia which represents a very complex process with many dark sides still to be explained.

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