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"I would have everie man write what he knowes and no more."–Montaigne

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Editorial

Awareness and anaesthesia: think dose, think data

Two recent reviews of risk factors for awareness during anaesthesia emphasize the role of underdosing of drugs. Ghoneim and colleagues[1] concluded that the most common cause of awareness was '. . . overly light anaesthesia at the time of the episode'. Their study compared 271 cases of awareness with 19 504 patients who did not experience awareness, and found that awareness was particularly associated with reduced drug dosage, being younger, and with non-volatile anaesthetic techniques. The prospective study by Xu and colleagues,[2] which reviewed 11 101 patients and found 46 cases of definite awareness and 47 of possible awareness, reached a similar conclusion.

That inadvertent awareness due to underdosing occurs at all is both alarming and surprising given the drugs, monitoring equipment, and techniques available.[3–5] But unfortunately this is not a new observation.[6–9] Indeed, it has long been recognized that most instances of awareness arise from faults in dosage for one reason or another.[10 11] While underdosing is typically associated with a clearly avoidable system failure [e.g. failing to give an induction agent before a relaxant, or failing to respond to a low end-tidal anaesthetic agent (ETAG) concentration], it can be more subtle (i.e. failure to correct the ETAG concentration for age and temperature). Less obvious is the awareness associated with the so-called high-risk cases, due to strategic underdosing in the face of hypotension or low cardiac output[7 12 13]—avoidable with adequate cardiovascular support.

Of course, we need to keep an open mind[14] regarding the occasional reports of awareness associated with seemingly adequate dosage. However, there is currently no robust evidence for such cases, since, in our opinion, there are no known convincingly documented cases of awareness which are not associated with possible underdosing.

New paradigm

In view of these issues and the seemingly intractable problem of inadvertent awareness, we suggest that the time has come to reformulate the concept and adopt a new and pragmatic working premise, namely, *that all cases of awareness are due to underdosing unless there is convincing verifiable information to the contrary.*

This 'Occams razor' approach has a number of significant benefits. First, it clarifies the problem of awareness by defining it in a scientifically useful way. Secondly, it requires us to establish what is a truly adequate dose for a large majority of patients—we suggest the age-corrected EC_{95} as a starting point.[15] Thirdly, it places the onus on anaesthetists to show that an adequate dose is achieved at all times during an operation. Fourthly, it places the onus on authors of 'awareness' case-reports to present convincing and verifiable evidence of resistance to an adequate dose—such extraordinary claims will require extraordinary evidence.[16] Fifthly, it directs us to explore the shortcomings of current drug delivery and monitoring systems, and to question the culture of poor compliance with cerebral monitoring and ETAG-guided protocols.[17]

We, the anaesthetists, must confront the problem of underdosing by putting in place systems in which we can have confidence that they deliver an adequate dose, and by implementing the use of the latest alarms,[18] algorithms,[19] and corrections for age,[20–22] temperature[22] and so forth, as they come available. Emphasis should be directed towards equipment which can be calibrated. If other plausible causes of awareness do exist, then these are unlikely to be established unequivocally without recourse to a much more rigorous and comprehensive data-gathering strategy.

Data gathering

Data from patients known to have experienced awareness are an extremely important and sparse resource,[23] but journal articles describing such cases are often rendered uninterpretable by, for example, omitting key BIS data,[12] failing to define the MAC used in terms of ETAG

concentration, or even whether it was corrected for age and temperature.[17] Similarly, accounts of awareness where it is impossible to exclude underdosing with a high degree of confidence owing to a paucity of convincing data[24 25] are not useful, as has been pointed out.[26] Being casual with such important data hampers research.

Establishing dosage thresholds above which we can have confidence that awareness does not occur requires comprehensive data from anaesthesia monitors, ETAG, and total i.v. anaesthesia devices, including a continuous electronic data stream from induction to emergence, typically captured by automated anaesthesia record keepers (AARK). However, despite a large number of prospective trials, such data from operations of patients known to have suffered awareness are, with few exceptions,[17 27] non-existent.

This is unfortunate, since it is only with robust, verifiable, and convincing high-resolution real-time data that we can exclude underdosing, and hence recognize those few cases which may suggest either that the accepted dosage threshold should be raised or, perhaps, a significant pharmacogenetic difference. To this end, device manufacturers must be encouraged to facilitate free access to raw data in convenient and open formats; after all AARK technology has been available for two decades.[28] Since independent analysis is important in securing scientific confidence, we suggest that all sufficiently robust, comprehensive, and high-resolution awareness-related data should be collected, archived, and made available as an open-access database, perhaps overseen by a suitable task force.

To use an aviation metaphor, trials must stop simply counting crashes; flight-recorders need to be installed and the data analysed.

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