Editorial

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/0019-5049.108549

Quick response code

Emergence from anaesthesia: Have we got it all smoothened out?

Emergence from general anaesthesia implies liberation of the patient from the state of anaesthesia. The indication for anaesthetic state no longer exists at the end of surgery; the patient should ideally be free from effects of anaesthetics and only analgesia needs to be continued. The emergence should happen in a short-time, smooth and free from undesirable effects, a consequence of residual effects of anaesthesia and altered physiology related to airway, respiration, autonomic, metabolic and endocrine functions. Along with the advent of newer anaesthetic agents, reversal agents/antidotes and monitoring devices, there have been improved understanding of arousal pathways in the nervous system contributing to faster and smoother emergence from anaesthesia. Variability in patient population and pathology however, still poses challenges to the Anaesthesiologist who has to juggle with the available agents, and longer emergence times are still encountered. Attempts at early recovery may be associated with autonomic stimulation and precipitation of airway spasm and hence special care must be taken in patients with cardiac disease, hyper reactive airways and those undergoing brain surgeries.

The site of action and the mechanism of general anaesthesia are still not clear, long after Morton first used ether in 1846 and Lundy and Waters used Thiopentone in 1934. The goals of rapid but smooth awakening can be achieved provided the basic mechanisms of general anaesthetic action at the molecular, cellular and neural levels are clearly understood. Sonner *et al.* in an exhaustive review have postulated the mechanisms of inhalational Anaesthetics' action based on molecular modelling, genetic engineering, neurophysiology/pharmacology and whole animal model evidences.[1] Better understanding about the functioning and effects of various neurotransmitter receptors/channels (glycine, N-methyl-d-aspartate, sodium, γ aminobutyric acid, acetylcholine, potassium, 5-hydroxytryptamine-3, opioids and α 2-adrenergic) have helped in redefining their roles in immobility and anaesthesia. Each anaesthetic agent is said to have action at specific receptors, allowing for better understanding of its effects. Brown *et al*. have attempted neuro-science analysis to unravel the altered state of arousal induced by five classes of intravenous anaesthetic agents (Propofol, Etomidate, Thiopental, Methohexital and Ketamine), opioids, α2 adrenergic agonists and droperidol and suggested that they have multiple sites of action, producing behavioural and physiological effects acting at molecular targets in specific neural circuits.[2]

Post ether and halothane era, propofol, isoflurane, sevoflurane and desflurane have revolutionized anaesthesia management as they allow rapid titration of depth of anaesthesia. Interest in faster and smoother recovery was in a way related to growing numbers of day care surgeries with the aim of early ambulation. In a systemic review of 58 investigations of ambulatory anaesthesia wherein propofol, isoflurane, sevoflurane or desflurane were used as anaesthetic agents, Gupta *et al*. observed that early recovery was faster with desflurane and sevoflurane as compared to isoflurane and propofol. Post-operative nausea and vomiting was significantly less in the propofol group, a benefit during emergence.[3] In a study on emergence agitation in adults, Kim *et al*. found propofol infusion was associated with lower emergence agitation as compared to sevoflurane.[4]

Opioids have been studied for their beneficial effects in smoothening and reducing emergence time.

How to cite this article: Bhaskar SB. Emergence from anaesthesia: Have we got it all smoothened out?. Indian J Anaesth 2013;57:1-3.

Cough during emergence is seen when desflurane is used; short acting opioids such as alfentanil and sufentanil have been found to suppress the cough when used as a bolus dose at the end of surgery.[5,6] With a pleasant smell, sevoflurane has been a very useful agent for induction in paediatric population but emergence agitation is more when compared to other agents.[7,8] Various drugs have been used to reduce this incidence including propofol, α2-adrenoceptor agonists, midazolam and ketamine. Propofol at 1 mg/kg, given after discontinuation of sevoflurane at the end of surgery was found to reduce the incidence of emergence agitation, without delaying discharge from post-anaesthesia care unit in a prospective, randomized, double-blind study in children posted for strabismus surgery.[9] Dexmedetomidine has also been reported to provide smoother and faster emergence with sevoflurane in paediatric anaesthesia.[10,11]

Recovery from desflurane is faster as compared to isoflurane even after prolonged anaesthesia in children.[8] In a meta-analysis of 58 clinical trials for preventing emergence agitation in paediatric patients, it was found that propofol, ketamine, fentanyl, and pre-operative analgesia were effective and midazolam premedication was surprisingly, ineffective.[12]

Female population emerge faster compared to males, and this could also contribute to higher incidence of awareness in this group.[13] Gender differences in pharmacokinetics has been suggested as the reason for early recovery after propofol in female patients as compared to males.[14]

Buchanan *et al*. conducted a multi-centric prospective matched cohort study in 500 patients which involved intravenous and inhalational anaesthesia, posted for elective surgery. Women had higher bispectral index scores at similar anaesthetic concentrations and had faster emergence as compared to men. This could be related to the modulatory effects of progesterone and oestrogen on the excitability of neural circuitry within the brain and spinal cord. Their overall recovery rate was slower, with more pain, post-operative nausea and vomiting and reduced quality of recovery. Recovery rates were faster in premenopausal women as compared to post-menopausal women.[15]

Xenon, an inert and environment friendly gas with low blood gas solubility (0.14) has been found to hasten emergence when used in combination with isoflurane and sevoflurane as compared to nitrous oxide. Its prohibitive price prevents its routine use.[16]

Sugammadex, a synthetic γ cyclodextrin has revolutionized the reversal of neuromuscular blockade produced by steroidal non-depolarizing agents.[17] It has allowed use of high-dose rocuronium for obtaining intubating conditions as good as succinylcholine and allowing for rapid recovery when necessary. Its cost is a concern for routine use but may be used when need for rapid restoration of neuromuscular function arises.[18]

Electroencephalography based monitors such as bispectral index monitoring (BIS™), Narcotrend™, Spectral Entropy™, Patient State Analyser, the Patient State Index and others used over the past decade have contributed to assessment of level of consciousness during and at the end of surgery. Despite limitations, they have been usefully correlated with emergence and contributed to significant reduction in recovery times.[19,20]

While sugammadex can be considered as a revolutionary drug for steroid neuromuscular blockade reversal, search is on for an agent that can reverse anaesthesia and promote early emergence. In a dose response study in rats by Solt *et al*., early arousal and increased minute ventilation at the end of the surgery was observed with intravenous Methylphenidate. This was attributed to activation of dopaminergic and adrenergic arousal circuits by Methylphenidate and may have future clinical applications to reverse unconsciousness and respiratory depression at the end of surgery.[21]

Newer agents of different classes with good pharmacokinetic profile such as remifentanil, propofol, isoflurane, deflurane, dexmedetomidine and sugammadex have overall helped in a paradigmal shift in the way patients are managed allowing for early and smooth recovery after general anaesthesia. Modification of arousal pathways in the brain with respect to gender, age, and disease conditions however may add an element of inevitability to emergence problems in these patient groups. A balanced anaesthesia technique customized to the specific patient is still the sine-qua-non for a faster and smoother emergence by choosing the right agent or combination of agents aided by a suitable depth of anaesthesia monitor.

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