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EMERGENCE AGITATION IN PATIENTS WITH POSTTRAUMATIC STRESS DISORDER - LITERATURE REVIEW

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ABSTRACT

Emergence agitation (EA) is an acute condition, characterised by confusion, and restlessness, occurring in the early recovery phase from general anaesthesia. EA can have significant clinical impact, including patient distress, injury, increased morbidity, and increased healthcare costs, as well as possible long-term consequences. Though the pathophysiology of emergence agitation remains unknown, it is believed to involve a multifactorial mechanism, including heightened sympathetic nervous system activation, and psychological factors such as posttraumatic stress disorder (PTSD). PTSD, a psychiatric disorder resulting from exposure to trauma, may predispose individuals to emergence agitation.

This literature review aims to examine the relationship between EA and PTSD, highlighting possible mechanisms, prevalence and risk factors involved, as well as discuss possible prevention methods and pharmacological interventions. A comprehensive understanding of the pathophysiology and risk factors of emergence agitation in PTSD patients is critical for developing suitable prevention and anaesthesia management strategies.

KEYWORDS

Emergence Agitation, Emergence Delirium, PTSD, Posttraumatic Stress, General Anaesthesia

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Introduction.

Emergence agitation is an acute state of confusion, disorientation, and restlessness that occurs during the recovery phase from anesthesia (S.-J. Lee & Sung, 2020). While EA is most commonly observed in pediatric patients, it is also prevalent in adult populations (S.-J. Lee & Sung, 2020) with an incidence of approximately 19% (Card et al., 2015). Emergence agitation can have a significant clinical impact on patients, leading to distress, injury, and increased pain (Lepousé et al., 2006) as well as be potentially harmful to healthcare workers (Tolly, Waly, et al., 2021) causing challenges for recovery and need for interventions.

Although the pathophysiology of EA is not yet known, it is theorised that its mechanism may involve heightened activation of the sympathetic nervous system in reaction to internal factors (such as flashbacks, and anxiety) or external factors (such as surgical pain) as the patient emerges from anesthesia (Tolly, Waly, et al., 2021).

Potential psychological risk factors for EA include posttraumatic stress disorder, anxiety, and depression (McGuire, 2012). Posttraumatic stress disorder, which stems from exposure to trauma, is characterised by symptoms such as intrusive thoughts, hyperarousal, flashbacks, nightmares and sleep disturbances (Du et al., 2022). These symptoms can make patients more vulnerable to certain psychological responses like emergency agitation (McGuire, 2012). Therefore, understanding the relationship between EA and PTSD is critical, as it can significantly influence patient outcomes and the recovery process.

Methodology

A systematic literature search was conducted in PubMed and Google Scholar databases for articles providing clinical information on PTSD and emergence agitation. The search was performed using the following combined keywords: "emergence agitation", "emergence delirium", "PTSD", "posttraumatic stress", "general anaesthesia". Inclusion criteria focused on systemic reviews, meta-analyses, observational studies, and case studies published in English. References lists were cross-checked for additional studies to include. The selected publications were analysed and synthesised to identify common themes, mechanisms and risk factors related to emergence agitation in PTSD patients.

Discussion

DEFINITIONS

Emergence agitation is an acute altered mental state during early post-anaesthesia recovery. It is characterised by changes in the level of consciousness, attention, and disorganised thinking (Card et al., 2015) along with thrashing and non-purposeful movement occurring as the patient regains consciousness (S.-J. Lee & Sung, 2020). Emergence agitation differs from emergence delirium (ED), which is an acute state of confusion that may present with hypoactive or hyperactive symptoms, even though these terms are often used interchangeably. (Fields et al., 2018). Both emergence agitation and emergence delirium should be distinguished from postoperative delirium (PD) (S.-J. Lee & Sung, 2020). EA episodes are self-limiting, due to the rapid metabolism of most anaesthetic agents used nowadays. Emergence has a defined time frame, occurring within two minutes of the cessation of the inhalational anaesthetic or five minutes after extubation (Tolly, Waly, et al., 2021). Emergence agitation is characterised by its short duration, with studies reporting it lasts from 2 minutes (Choi et al., 2015) up to 15 minutes (Scott & Gold, 2006).

Posttraumatic stress disorder is a psychiatric disorder that occurs after exposure to a traumatic event, such as actual or threatened death, serious injury, or sexual violence. PTSD symptoms include reliving the traumatic event, avoidance of trauma reminders, emotional numbing, nightmares, arousal, and mood alterations (Radow et al., 2025), as well as changes in memory and concentration (Bremner, 2006). It is hypothesised that these symptoms reflect the behavioural manifestation of stress-induced changes in the brain, affecting the amygdala, hippocampus and prefrontal cortex, as well as its function, causing dysregulation of norepinephrine and cortisol systems (Bremner, 2006).

There is no specific, valid tool for the assessment of emergence agitation in the adult population (S.-J. Lee & Sung, 2020). In the majority of the reviewed literature, the Riker Sedation-Agitation Scale (RSAS), Richmond Agitation-Sedation Scale (RASS), and Aono's 4-point scale are most utilised for the diagnosis of emergence agitation (Tolly, Waly, et al., 2021). However, they only assess the severity of agitation and do not take into consideration other components of EA such as cognitive function (Hernandez et al., 2017). There is a diagnostic scale for children, the Paediatric Anaesthesia Emergence Delirium (PAED) scale, developed in 2004 by Sikich and Lerman, that evaluates eye contact with the caregiver, purposefulness of the child's actions, awareness of the surroundings, restlessness and inconsolability (Sikich & Lerman, 2004). It is commonly used in paediatric EA studies; however, it has been criticised for its subjectivity and low interrater reliability (S.-J. Lee & Sung, 2020).

Emergence agitation can cause injuries to both the affected patient and medical staff, surgical site disruption, accidental removal of catheters, and unintended self-extubation (Scott & Gold, 2006). EA is a strong predictor of postoperative delirium, which is associated with increased morbidity and mortality, as well as increased medical care costs (S.-J. Lee & Sung, 2020). The long-term consequences of emergence agitation have not been fully researched, however, several studies have reported a correlation between postoperative delirium and cognitive decline (Sauër et al., 2017; Sprung et al., 2017).

MECHANISMS

General anaesthesia induces sedation by activating the hypothalamus and produces analgesia through the central amygdala, which plays a key role not only in pain modulation, but also in behaviour selection, emotion regulation, and fear conditioning (McCall et al., 2020).

The pathophysiology of emergence agitation is not yet fully discovered; it is theorised that it is a multifactorial mechanism. Studies have shown that anaesthetics alter brain function, with their effects changing depending on the dose. Higher-order networks that are involved in mental processes are affected first. Lower-order sensory networks are preserved, even at concentrations of anaesthetic that suppress responsiveness. Therefore, during the emergence from general anaesthesia, the delayed recovery of impaired subcortical thalamoregulatory systems may slow down the cortical integration of information and lead to agitation (Bonhomme et al., 2012). Research has demontrated that increased amygdala activity at rest is exhibited in patients with clinical features of PTSD (Semple et al., 2000), confirming the role of the amygdala in PTSD, as well as the hippocampus and prefrontal cortex (Bremner, 2006). During general anaesthesia, the altered brain function in PTSD patients, especially the amygdalocentric neurocircuitry, is further affected by anaesthetic agents, making them more susceptible to emergence agitation. One of the theories suggests that during the emergence from anaesthesia, as normal brain function is regained, audition and locomotion recover first, with cognitive functions following (S.-J. Lee & Sung, 2020). Auditory and noxious stimuli increase the

activity of the amygdala, which, in patients with PTSD, is uninhibited by the medial prefrontal cortex and hippocampus. That leads to overstimulation of the hypothalamus resulting in increased excitatory activity, both motor and behavioural, in the patient and, ultimately, emergence agitation (McLott et al., 2013).

PREVALENCE

Since there is no appropriate tool designed to assess emergence agitation in the adult population, it is challenging to accurately determine its true incidence. The inconsistent use of available agitation scales has resulted in a wide range of reported EA incidence, ranging from 2.5% to 90.5% (Tolly, Waly, et al., 2021). In one prospective observational study investigating 400 adult patients in the post-anaesthesia care unit (PACU), using the RASS scale, the reported incidence rate of emergence agitation was 19% (Card et al., 2015). Another study researching the incidence of EA in the military combat veteran population reported that it occurred in 20% of the sample. Patients who were previously diagnosed with a psychological disorder had a rate of EA of 50% compared to 17.5% amongst those who did not, suggesting a positive correlation between emergence agitation and anxiety, PTSD symptoms, and depression (McGuire, 2012). Therefore, the prevalence of posttraumatic stress disorder in both the civilian population, ranging from 3.4% to 26.9%, and military veterans, ranging from 7.7% to 17.0%, contributes to a higher incidence of emergence agitation, as PTSD has been identified as a risk factor for EA (Huang et al., 2023).

RISK FACTORS

The aetiology of EA is usually multifactorial. Studies have found that potential risk factors are young age, male sex, obesity, African ethnicity, pre-existing mental health conditions, and cognitive impairment, history of alcohol and substance dependence, method of anaesthesia, duration and type of surgery, emergency procedure, postoperative pain (S.-J. Lee & Sung, 2020).

Post-traumatic stress disorder is a risk factor for emergence agitation (McGuire, 2012) and may be linked to comorbid risk factors that must be carefully considered when the patient is undergoing procedures requiring general anaesthesia.

Research indicates a strong association between PTSD and alcohol and/or drug use disorder (Back et al., 2024), as well as an elevated prevalence of high-risk opioid use behaviours, such as concurrent use of multiple opioids and sedative-hypnotic medications (Seal et al., 2012). Acute withdrawal from these substances, inadequately managed pain and potential drug interferences, may result in emergence agitation (Tolly, Waly, et al., 2021).

PREVENTION

It is important to identify patients who might be predisposed to emergence agitation to eliminate correctable risk factors and to plan appropriate preoperative and postoperative management and interventions.

Prevention often requires a multidisciplinary approach and includes building rapport (Tolly, Waly, et al., 2021), preventing preoperative anxiety (which relies on both premedication and psychological approaches), appropriate analgesia (regional or systematic, multimodal), and maintaining an optimal level of sedation (Dahmani et al., 2014).

Patients with PTSD present high levels of neuroendocrine activation, inflammation and oxidative stress. Posttraumatic stress disorder is also associated with higher than in general population rates of traumatic brain injury (TBI), chronic pain, and alcohol and substance abuse (Tolly, Erbes, et al., 2021) which all are relevant to the anaesthesia team as they may influence management strategy, especially regarding the increased probability of emergence agitation in these patients (McGuire, 2012). Since the pharmacological management of post-traumatic stress disorder symptoms often requires drugs such as selective serotonin reuptake inhibitors, tricyclic antidepressants, benzodiazepines, and trazodone, (Tolly, Waly, et al., 2021) it is crucial to consider the potential medication interactions, such as QT interval prolongation or altered drug metabolism due to hepatic drug-metabolising enzyme induction. (Huang et al., 2023)

There are no universal protocols for the prevention of emergence agitation in patients with posttraumatic stress disorder. Current research suggests that pharmaceutical agents such as dexmedetomidine (DEX) and ketamine might be effective in preventing and managing emergence agitation (Huang et al., 2023).

Dexmedetomidine is a highly selective α -2 adrenoreceptor agonist that produces sedation and anxiolysis while persevering muscle tone, ventilation, and responsiveness to external stimuli. A study comparing dexmedetomidine and midazolam found that the dexmedetomidine group experienced a reduced prevalence and duration of delirium (Scott-Warren & Sebastian, 2016). Another study reported that DEX was an effective

rescue treatment for patients with PTSD who experienced an episode of emergence agitation (Read et al., 2017). However, it was observed that the use of dexmedetomidine may increase the risk of perioperative delirium and adverse outcomes in certain populations (Pal et al., 2021).

Ketamine is a noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist, which has sedative, analgesic, and amnestic properties. Research suggests that ketamine reduced the incidence of emergence agitation, without causing any notable side effects or delays in recovery (Y. S. Lee et al., 2010). By contrast, a multicentre clinical trial concluded that subanaesthetic doses of ketamine fail to prevent postoperative delirium, but they may raise the incidence of postoperative hallucinations and nightmares (Avidan et al., 2017) potentially exacerbating symptoms in patients with PTSD.

MANAGEMENT

When a patient presents signs of emergence agitation, staff must adapt a calm demeanour to ensure safety and help prevent the escalation of the episode for the patient (Lovestrand et al., 2017). Since unfamiliar environments have been recognised as potential triggers for PTSD flashbacks, it is recommended to create a familiar and quiet setting in the post-anaesthesia care unit, as well as reassure and reorient the patient (Huang et al., 2023). Emergence agitation is self-limiting; therefore, the main principle of emergence agitation management is identification of potential physiological causes that may lead to agitation such as increased intracranial pressure, hypo- and hyperglycaemia (S.-J. Lee & Sung, 2020), airway obstruction, hypoxemia, electrolyte imbalance, arrhythmias, uncontrolled pain, and noxious stimuli (intubation, catheters) and addressing them accordingly (Lovestrand et al., 2017). In patients with post-traumatic stress disorder serotonin syndrome should be considered, due to selective serotonin reuptake inhibitors being a common drug used in the management of PTSD (Huang et al., 2023). Pharmacological treatment should be initiated when the patient is experiencing an episode of emergence agitation with a risk of self-injury or harm to caregivers (Dahmani et al., 2014). Sedatives such as propofol and midazolam, and opioids such as morphine and fentanyl are reported to be the preferred pharmacological agents in the general population (S.-J. Lee & Sung, 2020).

Conclusions

Emergence agitation is a significant concern in anaesthesia and perioperative care, with potential implications for patient safety and outcomes. Recent advancements have highlighted the potential of dexmedetomidine, which has demonstrated promising results in reducing the incidence and duration of emergence agitation. Further research is necessary to identify the mechanisms underlying emergence agitation, as it is crucial for the development of standardised diagnostic tools, as well as effective prevention and treatment protocols. Specifically, exploring the relationship between emergence agitation and mental health conditions such as posttraumatic stress disorder is essential for establishing anaesthetic considerations for this particularly vulnerable population.

Disclosures

Author's contribution

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Conflict of Interest Statement

The authors reported no potential conflict of interest.

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