POSTOPERATIVE DELIRIUM: WHAT HAPPENS AND HOW CAN THE ANESTHESIOLOGISTS PREVENT IT?

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Abstract

Perioperative neurological complications pose a significant challenge in modern anesthesiology, as they represent a major source of morbidity, affecting quality of life, threatening patients' long-term survival, and increasing healthcare resource utilization. A perioperative neurological complication is any new injury or damage to the nervous system that occurs during anesthesia or surgery, including symptoms such as stroke, confusion, or nerve damage. Perioperative cognitive disorders like delirium and postoperative cognitive dysfunction (POCD) are important; however, toften go unnoticed. Routine monitoring during the perioperative period is not standard practice in general, except for specific procedures. Prevention, early detection, and multidisciplinary management are crucial for effectively reducing the incidence of these complications and improving patient outcomes.

Key Words: *confusion, delirium, perioperative neurological complications.*

Introduction

Delirium is one of the most significant neurological complications that occur after surgery and anesthesia, because it is common and affects up to 70% of patients over 60 who undergo major hospital surgeries. Delirium is associated with adverse outcomes such as an increased risk of death, ongoing cognitive decline, longer stays in intensive care unit, extended hospitalizations, and a higher likelihood of institutionalization. Postoperative delirium (POD) can occur in patients of any age, from children to the elderly. Older patients are considered at greater risk due to factors such as pre- existing cognitive impairment, additional health conditions, multiple medications, sensory deficits, malnutrition, reduced functional status, and frailty, which tend to accumulate and overlap with aging (1-6). Postoperative delirium is an acute neurocognitive disorder that usually occurs within the first few days after surgery and anesthesia. It is characterized by impaired attention, disorganized thinking, and altered consciousness with a fluctuating course (7,8). POD typically develops 24 to 72 hours after surgery in the hospital ward; it can occur immediately after anesthesia in the recovery room, or may be present upon admission to the intensive care unit. Agitation refers to delirium that occurs immediately following anesthesia. Clinically, delirium can manifest as hyperactive (agitated, aggressive, and combative), hypoactive (decreased alertness and motor activity, with anhedonia), or mixed (showing both hyperactive and hypoactive symptoms). Among these subtypes, hypoactive delirium may be associated with a worse prognosis (9). The 2024 update of the European Society of Anaesthesiology and

Intensive Care (ESAIC) guidelines includes significant advances in understanding, preventing, and managing POD (10). The essential skills for physicians involved in perioperative patient care include identifying high-risk patients, promptly diagnosing postoperative delirium (POD), and effectively managing patients with POD. Delirium as an indicator of healthcare quality for geriatric patients has been incorporated into the patient safety agenda (11,12,13).

Risk Factors and Pathophysiology

The multifactorial model of delirium explains how patients with an underlying susceptibility or vulnerability are exposed to one or more precipitating factors, including perioperative injuries that can lead to delirium. Risk factors are varied and include patients aged 60 years and older (since older patients are at higher risk as predisposing factors accumulate and overlap with aging), the presence of multiple comorbidities (such as anemia, low ejection fraction, carotid artery stenosis, or high serum creatinine levels), functional disability, and pre-existing cognitive impairment. During the perioperative period, the precipitating factors include the surgical procedure itself (considering duration, complexity, and invasiveness) and anesthesia; however, it is unclear whether the choice of anesthetic significantly impacts the development of delirium. Other perioperative precipitating factors include exposure to sedatives, especially benzodiazepines, poorly managed postoperative pain, prolonged stays in the intensive care unit, and postoperative complications (14,15).

The pathogenesis of POD is not fully understood; however, numerous studies offer evidence on the underlying processes of this complex clinical syndrome. Potential mechanisms can be categorized into two groups: neuroinflammation and oxidative stress, which likely interact by promoting neurotransmitter imbalance and neuronal network dysfunction. Several harmful stimuli, such as surgical stress and/or infection, activate the inflammatory cascade, leading to the rapid release of inflammatory mediators into the bloodstream. Inflammation and other factors can weaken the blood-brain barrier, allowing inflammatory mediators and other harmful substances to enter the brain, thereby inducing the activation of brain parenchymal cells (microglia and astrocytes) and the production of proinflammatory cytokines and mediators. These neuroinflammatory changes cause neuronal and synaptic dysfunction, leading to the emergence of neurobehavioral and cognitive symptoms (16,17,18). The oxidative stress hypothesis suggests that during surgery and anesthesia, especially during periods of impaired perfusion and reperfusion, reactive oxygen species (ROS) are rapidly generated. These molecules cause excitotoxicity, apoptosis, and local inflammation. Acetylcholine deficiency is widely recognized as a mechanism, as its synthesis is sensitive to low oxygen levels resulting from systemic inflammation and microcirculatory dysfunction. Dopamine and other neurotransmitter systems are also impacted by the inflammatory process (16,19,20).

Genetic Predisposition

Individual genetic factors may also influence susceptibility to postoperative delirium. Polymorphisms in genes encoding for cytokines, neurotransmitter receptors, and other molecules involved in the inflammatory response and neuronal function may predispose certain individuals to develop delirium. The association between postoperative delirium and polymorphisms in apolipoprotein genes has been an area of research in recent years. Apolipoprotein E (ApoE) is a protein that supports recovery in the central nervous system (CNS) after injury. It is essential for maintaining normal neuronal function by facilitating cholesterol transport and promoting cell repair. Three ApoE isoforms—E2, E3, and E4—result from different variants of the apolipoprotein E gene. Among them, ApoE4 is more prone to degradation, which limits the mobilization of lipids needed for tissue repair (21,22). The ε4 allele of the apolipoprotein E gene has been hypothesized as a genetic risk factor for delirium (23,24). The results of our study "Does the apolipoprotein E genotype increase the risk of postoperative delirium in adult patients?" indicate an association between the apolipoprotein E gene polymorphism containing the minor allele e4 and postoperative delirium in this group of adult patients. To reach more valid conclusions a larger patient group is necessary (25).

Screening and Diagnosis

For the preoperative assessment of cognitive function, tools such as the Mini-Mental State Examination (MMSE), the MoCA, and the Mini-Cog are commonly used (26). The Mini-Cog is comprised of two parts: remembering three words (e.g., apple, table, money) and drawing a clock. The patient is asked to draw a clock showing a specific time (e.g., 11:10), then repeat the three words. If they correctly recall the words and draw the clock accurately, the cognitive function is considered normal. If they have difficulties, then mild cognitive impairment or dementia may be present (additional tests are needed). The test takes 3–5 minutes and is commonly administered to older adults. Unfortunately, daily POD screening is not yet routinely performed for all surgical patients, likely due to misconceptions that it is difficult and time-consuming (27).

The diagnosis of delirium relies on history, physical examination, laboratory tests, and imaging studies. Use validated tools such as CAM and Nu-DESC daily for first three postoperative days, beginning in the recovery room. The most commonly used tool for non-psychiatric staff to identify delirium is the Confusion Assessment Method (CAM), which was developed based on criteria adapted from DSM-V. The CAM has higher specificity (89%) and sensitivity (94%) than assessments by geriatric psychiatrists (28,29). It includes 10 items: fluctuating course, inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, psychomotor agitation, psychomotor retardation, and sleep-wake disturbances, each scored as 0 (absent), 1 (present or mild), or 2 (severe).

Prevention and Treatment

There is not enough evidence to recommend a specific anesthetic, including whether to use general anesthesia, conscious sedation, or regional anesthesia. It is also unclear whether neuraxial anesthesia reduces the risk of delirium compared to general anesthesia. The BIS monitor helps guide the adjustment of anesthetic drugs. A target value between 40 and 60 for general anesthesia is considered ideal, helping to prevent excessively deep anesthesia. Benzodiazepines have been associated with the development of delirium, with midazolam exposure identified as a risk factor for delirium in surgical and ICU patients. Routine use of benzodiazepine premedication should be discouraged, except in cases of prior severe anxiety or withdrawal from benzodiazepines or alcohol. Prophylactically administered subanesthetic doses of ketamine and dexmedetomidine have shown benefits in reducing delirium. Appropriate multimodal pain management should be implemented, and prolonged fasting and dehydration should be avoided (10).

Non-pharmacological strategies to reduce postoperative delirium include providing orientation (e.g., with a clock or communication), using visual and auditory aids, minimizing noise and promoting sleep, avoiding unnecessary catheterization, encouraging early mobilization, and supporting early feeding. In addition to staff care, family members or close friends can play a vital role in managing a patient's symptoms.

Pharmacological treatment should only be initiated to improve patient safety if non-pharmacological measures fail. The use of low-dose haloperidol or low-dose atypical neuroleptics is recommended for treating POD. Low-dose haloperidol usually starts at 0.25 mg and is gradually increased to a maximum of 3.5 mg. Doses exceeding 6 mg per day should be avoided. Careful patient monitoring is essential, not only to assess effectiveness, but also to detect side effects. Haloperidol is linked to an increased risk of Q-T interval prolongation, so ECG monitoring is advised. Regarding the use of antipsychotics for treating delirium, current guidelines recommend using the "lowest effective dose" for the shortest necessary duration and only after non-pharmacological interventions have failed (10,30).

Conclusion

Postoperative delirium can only be prevented through proactive, patient-specific, multidisciplinary interventions. Clinicians must prioritize early screening, create personalized care plans, and establish effective team communication to reduce the incidence of POD and improve surgical outcomes. The anesthesiologist plays a crucial role. Our responsibility does not end with a successful surgery. A positive outcome depends on compassionate care, effective communication with the family, early detection of risk, and active prevention and treatment of delirium. The way we care for our most vulnerable patients demonstrates the true value of our profession and health system maturity.

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