A Comprehensive Review of the Depth of Anesthesia and Its Impact on Postoperative Delirium Development

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Abstract: Postoperative delirium is a frequent surgical patient complication, particularly the elderly, which is always associated with more risk of extended hospital stays, heightened healthcare expenses, and elevated mortality rates. Although numerous factors contribute to postoperative delirium, recent research has emphasized the potential significance of anesthesia depth during surgery. In addition, while certain mechanisms behind the disease are still not clear, the impact of depth of anesthesia on the incidence of postoperative delirium is contradictory. This article first explores the pathophysiology, recognition and diagnosis of postoperative delirium, analyzing correlative risk factors of the cognitive disorder. As one of the conventional technologies monitoring the depth of anesthesia, the measurement method and principle of bispectrality analysis of electroencephalogram are listed. Ultimately, the link between anesthesia depth and POD incidence is examined, exploring the underlying causes. The analytical approach employed in this article may serve as a reference for investigating similar risk factors or cognitive disorders. Also, suggestions on clinical practice could be offered by the result of the study. However, whether deeper anesthesia would contribute to higher risk of postoperative delirium is still unclear. In addition, the certain mechanism of postoperative delirium could be focused in further studies.

Keywords: Depth of Anesthesia, postoperative delirium, perioperative protection.

1. Introduction

Postoperative delirium (POD), an acute central nervous system complication, is a disorder of attention and cognition in patients, characterized by abnormal levels of consciousness, declines of concentration and disruption of the sleep-wake cycle after anesthesia and surgery. What is worth mentioning is that it has become the most common psychiatric syndrome in normal hospital settings, of which the prevalence is more than the other better known psychiatric diseases like postoperative depression [1].

The incidence of delirium climbs significantly with the increasing ages of patients. To be more specific, delirium complicates approximately 50% of hospitalized seniors [1], bringing a higher mortality rate of 29% to delirium patients, while the figure for the other is 9% [2]. Despite a shorter time of survival, the costs for patients with delirium are more than two and a half times higher for those non-delirium individuals, ranging from \$60,516 to \$64,421, which will definitely add to the healthcare burden for both families and government expenditures. In addition, patients suffering from delirium might develop a permanent cognitive decline as well [2]. Accordingly, with a rocketing number of seniors undergoing surgery and anesthesia in recent days, reducing the incidence of patients developing delirium after anesthesia is of great necessity. However, limited by the lack of research on the precise mechanism of postoperative delirium, up to 80% of clinicians fail to recognize, prevent and address delirium after surgery [3].

In the surgical population, several validated researches indicate that patients with potential factors such as advanced age (>70-75 years), functional disability and the surgical procedure itself as well as anesthesia in perioperative setting are more likely to become delirious [3]. The bispectral index (BIS) monitor is pivotal in ensuring the anesthesia is not too light [4], which may cause potential long-term postoperative neurologic complications such as anxiety and delirium. Studies have shown that there is a significant correlation between anesthesia depth and postoperative delirium, while BIS monitor helps reduce anesthetic exposure and decrease the risk of POD after surgery [5,6]. However, some other researchers have also suggested that anesthesia guided by BIS monitoring has no obvious guiding effect on reducing the occurrence of perioperative cognitive impairment such as delirium [7,8]. Thus, the relationship between the anesthesia depth and the incidence of delirium is still controversial. This article aims to explore the progress of understanding the specific relationship between anesthesia depth and delirium, which would probably provide assistance for clinical treatment and provide prospects for the improvement of future treatment plans.

2. Postoperative delirium

Postoperative Delirium, a severe disease of nervous system characterized by acute episodes of attention and other cognitive disorders happening right after the surgery, might develop into other much more serious postoperative cognitive dysfunction or Alzheimer's disease without timely intervention [9].

2.1. Pathophysiology of postoperative delirium

As a multifactorial disease, each individual episode in the patient probably could be attributed to a unique set of component contributors [1]. So, to a large extent, the single pathogenesis or cause for postoperative delirium is yet remains unclear. However, as one of the cognitive disorders, it is widely acknowledged that neurotransmitter imbalance, acetylcholine deficiency, ischemia and global stressors might be responsible, all of which have strong correlations with the depth of anesthesia.

2.2. Recognition and diagnosis of postoperative delirium

As postoperative delirium is commonly hypoactive, it is likely to be ignored, although it may emerge on either the first or second day following surgery and anesthesia. In particular, spotting postoperative delirium in ICU patients can be harder, given that they're usually intubated and can't respond verbally based on standard assessments. Thus, the analysis of convenient and effective approaches during and after the surgery and anesthesia to monitor and minimize the morbidity of postoperative delirium is of great necessity.

There are three subtypes of Postoperative delirium patients, which are hypoactive, hyperactive, and mixed [10]. Clinically, the diagnosis of postoperative delirium could be divided into two steps. The first stage involves assessing the patient's attention and arousal level at the bedside. The second stage entails evaluation through family members, medical staff, and records [11]. Among over 50 kinds of diagnostic scales, one of the most widely used methods is the Confusion Assessment Method (CAM) scale [12], though it is relatively insensitive. The CAM algorithm is largely based on the appearance of certain acute symptoms or fluctuations such as inattention, logical disorganization, changing level of consciousness and so on [13] Both delirium rating scale (DRS) and delirium rating scale-revised-98 (DRS-R98) take into account dependability and availability [13]. The Delirium

Observation Screening (DOS) scale is a widely utilized tool primarily for nurses to promptly detect brain metabolism impairments, boasting sensitivity and specificity rates of 90% and 92%, respectively. [14].

2.3. Risk factors of postoperative delirium

The morbidity of postoperative delirium might be influenced by a wide range of factors. So approaches simply handling with only one or two pieces of contributing factors are unlikely to greatly decrease the risk for the patients to get rid of delirium; they are supposed to be addressed at the same time if possible. Dementia, cognitive decline, functional and vision impairments, alcohol abuse history, and being over 70 are key risk factors for postoperative delirium in both medical and non-cardiac surgery patients. Also, the development of certain comorbidities like stroke and depression or the severity of them would be associated with morbidity in all patient populations as well. Furthermore, the more frequent and severe manifestation could be triggered by the medication used during the perioperative period, including atropine volatile anesthetics [15,16], antihistamines, glucocorticosteroids, benzodiazepines, propofol and opioids. In such cases, reducing the target dose of the medicine might help [17].

The effects of predisposing factors mentioned above on different kinds of patient populations can be diverse. Specifically, abnormal laboratory values pose an additional risk factor, elevating the risk by a range of 40% to 500%. For medical patients, the primary contributors to delirium are polypharmacy, the use of psychoactive medications, and physical restraints, which elevate the risk by 4.5 times compared to other patients [1].

In conclusion, the inherent susceptibility, certain medications and related medical history of the patient population might all be attributed to higher morbidity of postoperative delirium. So timely preoperative evaluation and medication planning during anesthesia of patients are of great importance, which would be conducive to predicting and improving the postoperative delirium.

3. Conventional monitoring methods in depth of Anesthesia

In recent years, the advancement of modern general anaesthesia has greatly promoted the progress of complex surgery and perioperative protection, especially for those patients in serious conditions. The medication of anesthesia and sedation mainly interact with neurotransmitters and resolve neuronal integration between various brain regions to affect the central nervous system [17], reducing certain responses of body to specific external stimulation. Presently commonly used anesthetics exert sedative and analgesic effects chiefly through two mechanisms, either lowering the excitation via N-methyl-d-asparate (NMDA) receptors or enhancing inhibition through γ-aminobutyric acid (GABA) receptors. Increasing evidence has shown that neuronal degeneration and apoptosis would be brought about by excessive suppression of the neurons [18, 19].

About 90 years ago, Gibbs, Gibbs, and Lennox proved that with the increase of ether or pentobarbital dosage, the electroencephalogram and the level of consciousness of the patient would undergo certain systematic changes. They reckoned that the practical application of electroencephalogram could be utilized as an approach to measure the depth of anesthesia, according to these observations [20]. Through the bispectral analysis of electroencephalogram, a parameter called BIS could be obtained. Initially, the mix of fast and slow frequencies in a patient's brain waves determines their pattern. A non-invasive method to monitor anesthesia depth during surgery involves calculating a dimensionless anesthetic depth number, reflecting brain electrical activity. This is achieved by placing a specific sensor on the patient's forehead. The Bispectral Index (BIS) ranges from 0, indicating no EEG activity, to 100, representing normal EEG activity in awake patients.

Generally, an adequate anaesthetic depth for surgical intervention refers to BIS levels from 40 to 60. In order to reduce the potential risk of certain neurological complications, a BIS level of below 40 should be prevented, while over 60 would be unsafe, due to the danger of intraoperative awakening [21,22].

However, there are various influencing factors that may disturb the monitoring of BIS index. For example, deep muscular relaxation should be maintained, as the beta wave recognized could mistakenly be seen as brain activity, leading to elevated monitor reading. As for the anesthetics, the continuous infusion of propofol is supposed to be excluded, because of the beta waves produced, causing a falsely high value of BIS. Also, the use of dexmedetomidine should be excluded due to the delta waves brought, which might lead to unreliable values of anaesthetic depth [23].

4. Relationship between postoperative delirium and depth of anesthesia

4.1. Mechanisms underlying the relationship

So far, the exact mechanisms of how anesthesia depth affects postoperative delirium are not fully clear. However, several hypotheses have been proposed, which might be useful to explain the hidden relationship.

For example, one of the hypotheses suggested that deep anesthesia is associated with reduced cerebral blood flow and increased cerebral metabolic suppression, which may impair cerebral oxygenation and lead to neuronal injury. After that, an inflammatory response would be triggered, which is a risk factor for developing postoperative delirium. In addition, another hypothesis is that inadequate anesthesia depth might result in intraoperative awareness, which is a state in when patients are able to perceive their surroundings during surgery despite being anesthetized. Thus, it could lead to significant psychological distress, further contributing to the development of delirium in the postoperative period.

4.2. Implications for clinical practice

In the past two decades, electroencephalography-guided monitoring technology was regarded as one of effective ways to predict and decrease the incidence of postoperative delirium, which offers obvious indexes to evaluate the depth of anesthesia, preventing excessive general anesthesia during surgery. Luo et al. included randomized clinical trials (RCTs) and compared the incidence of developing postoperative delirium or other long-term cognitive disorders whether interventions like BIS or auditory evoked potential (AEP) were used, based on the 2,868 statistics collected in the databases. The outcome suggested that the incidence of postoperative delirium and long-term cognitive dysfunction could be declined by the BIS- and AEP-guided anaesthesia, as they might be helpful in monitoring and adjust the specific dose of anesthesia medication intraoperatively. Meanwhile, the different influence of the two monitoring technologies was not observed [24, 25]. Similarly, Li et al. Have discovered that the risk of postoperative delirium could be declined by light anesthesia, compared to the deep one, though the effects on postoperative cognitive dysfunction were not prominent [26]. Interestingly, according to another meta-analysis by Wang and his colleagues, lighter depth of anesthesia did not contribute to a lower prevalence rate of postoperative delirium. Also, in long term, mortality and further cognitive disorders did not decline obviously [27]. These contradictory effects of light anesthesia on the incidence of postoperative delirium might be caused by the different design of the studies. To be more specific, a index representing deep anesthesia in one research might be regarded as in the light anesthesia group in another.

5. Conclusion

In summary, this paper suggests that light anesthesia is more beneficial to reducing the incidence of cognitive disorders like postoperative delirium than deep anesthesia, improving postoperative neurocognitive function. This study carefully analyzed the risk factors of the disease and compared them with specific monitoring techniques, which provides reference and inspiration for subsequent research on postoperative delirium. However, according to the research, the classification standards between light anesthesia and the deep should be unified, which would be conducive to further exploring the relationship. Despite significant advancements in anesthesia depth monitoring and clinical practice, our understanding and management of long-term cognitive issues, notably postoperative delirium, are still limited. Progress in fundamental and applied anesthesia research will be crucial for achieving the objective of alleviating pain and neuro-related distress.

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