



Post-operative cognitive dysfunction – A brief review

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Abstract

Postoperative cognitive dysfunction (POCD) can be referred to as a mild but possibly long-lasting altered intellectual function occurring after surgery, which is more common in old age. It may last from a few hours to some months or may be permanent. Up to half of patients, young and old, have POCD within the first week after surgery. Three months later, 10 to 15 percent of patients still have POCD. It's still unknown whether POCD results from some neurotoxic effect of anesthetic agents, or it simply reflects a preexisting cognitive (intellectual) problem in older adults. It has also been suggested that cognitive after-effects of surgery may result from an inflammatory process. The nature of the relationship is unclear; as multiple factors may be involved. As the exact reasons are still not known, further research is needed to identify the patients and procedures that are at highest risk of POCD, and what steps can be taken to reduce that risk. Anesthesiologists should play a more active role in screening for reducing cognitive dysfunction before surgery.

Keywords: cognitive dysfunction; general anesthesia; post-operative; opioids; mini mental state examination

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Received 17 October 2015; Revised 5 December 2015; Accepted 17 December 2015; Published 26 December 2015

Citation: Patki J, Ravinutala S. Post-operative cognitive dysfunction – A brief review. J Med Sci Res. 2016; 4(1):31-34. DOI: <http://dx.doi.org/10.17727/JMSR.2016/4-010>

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Introduction

The statement 'Granddad was never the same after his operation' is occasionally heard. This lay person's worry actually represents post-operative cognitive dysfunction (POCD). Postoperative cognitive dysfunction (POCD) can be usefully defined as a long term, possibly permanent, disabling deterioration in cognitive function following surgery.

Anaesthetic medications, comprising mostly of central nervous system (CNS) depressants, result in impairment of memory and other higher functions of brain in the immediate postoperative period lasting usually for a few minutes to several hours. But if memory and concentration are impaired for more than 24 hours or beyond the effective period of sedative medications then this can be considered as cognitive dysfunction. POCD lasts from a few days to

a few weeks after surgery. In rare cases, this disorder may persist for several months after major surgery [1]. POCD has a major impact on physical recovery, cooperation with postoperative therapy, and length of hospital stay. It is observed that risk of death in the first year after surgery is more in these patients.

It is important to assess the severity of cognitive disturbance. Few tests such as mini-mental state examination (MMSE) (Table 1), verbal learning test, Stroop's color word test, trail making test, symbol digit modality test are used for the assessment of POCD. The MMSE is a test for global cognitive functions that can be performed at the bedside. It consists of a series of questions on orientation and simple commands to assess comprehension.

Table 1: Aspects of cognitive function tested by the mini mental state examination (MMSE).

<ul style="list-style-type: none"> • Orientation in time • Orientation in place • Repetition of named objects • Repetition of simple phrase • Ability to undertake simple arithmetic • Recall of objects named earlier in the interview • Naming of objects shown by examiner • Execution of simple tasks by written and spoken command • Writing a simple sentence, Copying a simple design

Etiology

The etiopathogenesis of POCD is unclear. More has been described regarding risk factors and associations for POCD than the mechanism itself. Age, duration of anaesthesia, intraoperative complications, and postoperative infections were found to be associated with POCD [2]. It occurs most commonly in older patients and those with pre-existing cognitive impairment [1]. A low-grade baseline state of systemic and neuronal inflammation is likely in groups of patients at risk of POCD, such as the elderly and those affected by neurodegenerative disease or atherosclerosis. It

has been proposed that systemic inflammation may contribute to postoperative cognitive deficits and there could be a relationship between interleukin response and impaired postoperative cognition. It may be mediated by the body's inflammatory response to surgery [3]. Elevated C-reactive protein is associated with impaired mental status in elderly patients with hip fracture [4].

It is found to be associated with alcohol intake, drug abuse and low education status. Other factors include history of stroke, dementia, higher ASA grading, major surgeries, heart operations etc. One of the concepts behind day care surgery is to avoid hospital admission, as recent evidence suggests it as a risk factor for POCD (Table 2).

Table 2: Predisposing factors for POCD.

<p>Early POCD</p> <ul style="list-style-type: none"> • Increasing age • Preexisting cognitive impairment • General rather than regional anaesthesia • Increasing duration of anaesthesia • Respiratory complication • Lower level of education • Re-operation • Postoperative infection • Immobility • Intensive care unit admission <p>Prolonged POCD (months postoperatively)</p> <ul style="list-style-type: none"> • Increasing age • Sensory impairment (auditory, visual) • Poor nutritional status
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Anaesthesia and POCD

Various studies have evaluated anesthetic techniques and anesthetic drugs used, as causative factors for POCD. Regional anaesthesia does not appear to be superior to general anaesthesia in preventing prolonged POCD [5]. A randomised study of regional versus general anaesthesia in 438 elderly patients found that there is no significant difference in the incidence of cognitive dysfunction 3 months after either general or regional anaesthesia.

Accordingly, there is no evidence to suggest any causative relationship between general anaesthesia and long-term POCD [5].

ISPOCD- 1 study concluded that increasing age and duration of anaesthesia, little education, a second operation, postoperative infections, and respiratory complications were risk factors for early postoperative cognitive dysfunction, but only age was a risk factor for late postoperative cognitive dysfunction. Hypoxaemia and hypotension were not significant risk factors at any time [2]. Some studies found no causal relationship between cerebral hypoxia and low blood pressure and POCD.

Patients who are taking drugs to support their cognitive function, including the anticholinesterase drugs such as donepezil, should not have them stopped perioperatively. There are grounds to believe that sudden stopping of anticholinesterases may precipitate cognitive failure that may be difficult to reverse [6]. Inflammatory response and opioids are two risk factors for development of POCD. One study indicates that Auditory Evoked Potential guided anesthesia allows dose reduction of anesthetic agents including opioids leading to better cardiovascular stability and less early POCD. Anesthesia depth did not influence the inflammatory response to surgery [6].

Fentanyl is associated with delirium, but there seems to be no clear relationship between fentanyl dosage and the incidence of POCD 3 or 12 months postoperatively [7]. There is no convincing evidence that anaesthetic agents cause inflammation resulting in POCD; indeed, control animals in recent studies that received isoflurane or neurolept anaesthesia, but no surgical procedures, showed neither cytokine activation, damage associated molecular pattern molecule elevation, nor behavioural changes associated with POCD [8, 9].

There is evidence, albeit controversial, that volatile agents may enhance the susceptibility of neurons to apoptosis, and may enhance neurodegenerative processes [10, 11]. Nevertheless, there is no evidence that volatile agents are associated with

POCD. Indeed, some studies investigating the effect of depth of inhalational anaesthesia on POCD have shown the opposite. In mice, high doses of isoflurane (2%) are associated with better cognitive performance after anaesthesia than lower isoflurane doses (1%) suggesting some beneficial effects of isoflurane [12]. In humans, deeper isoflurane anaesthesia titrated to the bispectral index (BIS) also results in better postoperative information processing [13]. Furthermore, two recent studies comparing propofol with sevoflurane and desflurane found a higher incidence of cognitive dysfunction in patients after propofol-based anaesthesia. These results suggest that there might even be a protective effect of inhalational anaesthesia, possibly mediated by so-called anaesthetic pre- and post-ischaemic conditioning [14]. Exposure to N2O in clinically relevant concentrations did not result in an increased incidence of postoperative delirium. These results suggest that N2O may be safely used in a balanced technique in geriatric surgical patients, without postoperative delirium [15].

A study comparing desflurane and sevoflurane noted that subjects in desflurane group performed slightly better than the subjects in sevoflurane group in most of the neurocognitive tests. Comparison of these scores showed no statistically significant differences between the study groups. A statistically significant difference was seen in comparison of pre-surgery and post-surgery scores only in the desflurane group [16].

POCD, while classically associated with cardiac surgery, is present in 30-40% of all adult patients regardless of age [16]. In patients over 60 years old it can persist for up to 3 months. This was not shown to be associated with length or procedure or anesthetic type. Instead, inflammation caused by the stress of surgery was implicated as the cause of cognitive decline.

Conclusion

Cognitive dysfunction is common in adult patients of all ages at hospital discharge after major surgery, but only the elderly (aged 60 year or older) are at significant risk for long-term cognitive problems.

POCD, while established as a diagnostic entity, requires more research to understand its aetiology. Extensive research conducted in this field led to an observation that the main pathophysiology behind POCD is systemic and neuronal inflammation following surgery. POCD is neither related to the type of anaesthesia nor the anaesthetic agents. The choice of anaesthetic, when several options exist, should be based on an open discussion of patients' preference, general postoperative complications, and the experience of the anaesthetist. The essence of good basic care is identification of the at-risk individual, awareness of common perioperative aggravating factors, simple preventive interventions, recognition of the disease state when it occurs, and basic treatments for patients with severe hyperactive manifestations. Ongoing studies of clinical cohorts may help us understand the risks of cognitive dysfunction after non-cardiac surgery. Future research may help us understand underlying biochemical or physical insults which may lead us to better prophylactic treatment and prevention.

Acknowledgements

Acknowledgements are due to the Department of Anaesthesiology and Critical Care, Krishna Institute of Medical Sciences, Secunderabad.

Conflict of interest

Authors declare no conflict of interest.

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