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Postoperative cognitive dysfunction in elderly patients: a frequent complication

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Abbreviations: POCD, postoperative cognitive dysfunction; CAM, confusion assessment method; ISPOCD, international study of postoperative cognitive dysfunction; CPB, cardio-pulmonary bypass; CRP, C-reaction protein

Introduction

The surgical and anesthesiological progresses that have characterized the last centuries have made it possible the increase of the number of elderly patients with coexisting diseases safely undergoing surgery. Despite advanced medical technologies have permitted to successfully manage cardiac and respiratory adverse effects, however prevention of postoperative central neurological complications is still a challenge for the anesthesiologists.[1] In particular, postoperative cognitive dysfunction (POCD) is a significant social and financial problem occurring in a high percentage of cases in peoples over 60years old. POCD has been defined as an impairment of thought processes such as memory, attention, concentration and that can be present also weeks or months after surgery and not always recognized in the early postoperative period because its recognition need the employment of neurological and psychological tests.[2] POCD must be distinguished by delirium that is present early in postoperative period and is characterized by an acute change of attention and thought. It can be diagnosed utilizing confusion assessment method (CAM).[3] The reported incidence of POCD varies from 7 to 71% at seven-eight postoperative days and 6 to 56% at an interval of 42-84 days.[4] The exact incidence is not known because POCD is not always recognized in the postoperative period since diagnosis requires many sensitive neuropsychological tests and these tests can be difficult to administer in clinical trials in which the sample of the patients may be elevated. Tests are different for the cognitive domain that they study. The working group ISPOCD (International Study of Postoperative Cognitive Dysfunction) has conducted several studies in this field and has also created some recommendations. It was found that in the diagnosis of POCD it should be used a battery of tests to investigate the different domains involved in cognitive functions such as memory, attention, speed motion sensory and flexibility cognitive; moreover, these tests should be sensitive to allow the diagnosis of mild deficits such as those characteristic of POCD. The assessment of cognitive function in the postoperative period is based on the results of pre-and post-operative tests. Often, to correct the "practice effect" that is often present when performing neuropsychological tests repeated over time it is used a control group.[5]

Moreover, the incidence of POCD varies in the studies examined because there are many risk factors promoting POCD related to patient, to surgery, to anesthesia and the incidence varies according the population studied. With regard to patient-related factors, the so-called predisposing factors, the last studies mentioned old age and low level of education,[6,7] the presence of preoperative cognitive impairment, the chronic use of narcotics and/or benzodiazepines, the number of comorbid conditions, the cerebrovascular and the occurrence of postoperative delirium;[8] role of genetic predisposition is not yet clear as the results available are conflicting. Regarding to surgery related factors, some studies have shown that POCD is more frequent after cardiac surgery than after non-cardiac surgery and the use of cardio-pulmonary bypass (CPB) has been described as a major contributor to the high incidence of POCD in this situation. Moreover, reoperation, infections and postoperative pulmonary complications increase the risk of occurrence of POCD.[9] If the anesthesia has a role in the development of POCD is still subject of debate. In the past, several studies have been performed to assess if regional anesthesia is not associated with cognitive impairment compared to general anesthesia. Silbert BS et al.,[10,11] in a recent randomized controlled trial studied elderly patients undergoing extracorporeal shock wave lithotripsy with general anesthesia or spinal anesthesia and have found no significant difference in the rates of POCD when comparing general anaesthesia with spinal anaesthesia, suggesting that the surgical or procedural process itself may contribute to the development of POCD. Furthermore, regional anesthesia does not offer any apparent direct physiologic benefit on cognitive function. However, animal studies indicate that volatile anaesthetics may affect amyloid-beta processing involved in the progression of Alzheimer's disease, but their clinical relevance remains inconclusive. Prospective randomized clinical trials are underway to address the clinical significance of these findings.

In the last years several studies have attempted to assess the effects of systemic inflammation following a surgical insult on neuroinflammation, neurogenesis and cognitive function postoperatively. In particular, systemic responses induced by surgery might trigger neuroinflammation and POCD.[12] It was demonstrated a strong association between inflammatory cytokines and development of POCD in patients undergoing cardiac surgery with cardio pulmonary bypass.[13] A recent clinical study by Wang T et al.[14] has reported an association between inflammatory cytokines like C-reactionprotein (CRP) and POCD. A relationship was seen also among patients who had higher values of IL-6 and IL-8 and postoperative delirium.[15]

The inflammatory response appears to be more evident in older mice, in agreement with the higher incidence of POCD that occurs in people of advanced age. However, surgery may not be the only responsible for the neuro-inflammatory response as increased levels of TNF-α, IL-6 and IL-1β have also been reported after single administration of isoflurane.[16] Zhang J et al.[17] investigated whether the type of anaesthetic (intravenous vs. volatile anesthetics) affects cognitive impairment and neuroinflammation in elderly rat. The authors have shown that surgery and anesthesia increased IL-1β and ionized calcium binding adaptor molecule (1Iba-1) in the cerebral cortex and hippocampus but there was no difference in the surgery-induced increase of the plasma IL-1β and TNFα levels under these two types of anesthesia.

Conclusion

The authors concluded that surgery under general anesthesia induces neuroinflammation and cognitive impairment without differences between intravenous and volatile anesthetics.[17] To know the pathogenetic mechanisms and the risk factors associated to POCD is very important because it was demonstrated a significant correlations between cognitive function and quality of life. Newman et al.[18] observed that patients with lower cognitive function scores after cardiac surgery in their 5 year follow up had a lower general health and a less productive working status. Moreover, the presence of POCD is associated with additional costs due to hospital stays and increased need for institutionalization, rehabilitation, and home care. Therefore, a correct treatment is mandatory since deterioration in cognitive function compromises quality of life with adverse social consequences.

The prevention seems to be the best treatment. It is based on adequate risk stratification, on anaesthetic and surgical management able to reduce operative risk choosing the most suitable anaesthetic and surgical techniques to allow patients to have a early functional rehabilitation. Adequate postoperative pain might be associated with lower incidence of POCD. Wang et al.[19] in their clinical study have reported that older patients who received oral postoperative analgesia were at significantly lower risk for the development of POCD. Surgical technique can affect the cognitive status of patients, and it was shown that patients with short surgical technique have lower risk to develop POCD compared to patients with long surgical technique and it is due to decreased inflammatory response.[4] In the last years it was seen that the use of anti-inflammatory strategies such as dexmedetomidine before the beginning of anesthesia, may reduce incidence of POCD.[20] Moreover, a normal nutritional status and hydration, a short period of fasting before surgery, physiological day-night rhythm, social contacts, frequent visits by family and friends aftersurgery, and early discharge from hospital are associated with reduced incidence of POCD.[4]

Since many factors are involved in the development of postoperative cognitive dysfunction, for the prevention and management of POCD it should be applied routinely in the clinical practice a multimodal approach involving the anesthesiologist, surgeon, geriatricians, and family members that togheter should promote early rehabilitation and avoidloss of independence in high risk patients.

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Conflicts of interest

Authors declare that there is no conflict of interest.

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