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Peri-operative brain dysfunction and damage in the elderly

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An increasing number of elderly patients are undergoing surgical procedures. Age is a very important risk factor for severe post-operative neurological complications such as stroke but also for the less obvious types of peri-operative brain dysfunction. It is, therefore, essential that anaesthesiologists are aware of the risk and possible pathophysiology of peri-operative brain dysfunction and damage in elderly patients.

Neurological complications with deficits like aphasia and hemiparesis are uncommon after non-cardiac surgery. In contrast, brain dysfunction is commonly observed in elderly patients after surgery. Occasionally, patients recognise the deterioration in their brain function, but in other cases it is only detected by the nursing staff or relatives. The usual complaints and findings are problems with memory, attention, organisation, and speed of information processing. These are signs of cognitive dysfunction and it is necessary to distinguish between delirium and the more subtle and long-lasting postoperative cognitive dysfunction (POCD).

Delirium

Delirium is an acute disturbance that may occur at emergence after anaesthesia [1]. This condition can be detected by a clinical examination, for instance by the Confusion Assessment Method (CAM) [2]. It consists of four features: 1. acute and fluctuating change in mental status; 2. inattention; 3. disorganised or incoherent thinking, and 4. altered level of consciousness. A patient will be diagnosed with delirium according to this method when features 1, 2 and either 3 or 4 are present.

The incidence of delirium is between 10 and 30% in hospitalised patients, but the risk is probably doubled in the elderly. The type of surgery and pre-existing brain disease (such as dementia) are other well-known risk factors. A number of eliciting factors for delirium have been described, and delirious patients should be carefully examined because the condition may be related to infection, a withdrawal state, dehydration, or the side-effects of drugs.

Postoperative cognitive dysfunction

POCD is much more difficult to detect than delirium and there is no agreement on the diagnostic criteria. Numerous definitions have been used, but in most studies POCD has been defined as a postoperative deterioration in the performance of a battery of neuropsychological tests. It is a significant problem that the available studies have used very different methods, for example the composition of the test battery, the timing of tests, the definition of deficits, and the statistical analysis used [3]. Questionnaires should not be used as they reflect patient expectations, anxiety, and mood rather than the actual performance. POCD is characterised by long-lasting cognitive deficits that are typically not apparent until the patient is discharged from hospital. As opposed to delirium, the level of consciousness is not affected and the condition can last weeks or months. It has been recognised for many years that POCD can occur after cardiac surgery - where the incidence is approximately 50% at discharge [4]. Traditionally, it has been assumed that POCD was caused by brain hypoperfusion or embolism related to the use of cardiopulmonary bypass but that assumption has recently been challenged after data from randomised studies comparing off-pump and on-pump coronary artery bypass showed no major difference. Some small studies suggested that the incidence of POCD after coronary artery bypass grafting could be reduced by off-pump surgery but subsequent major studies, even in high-risk patients, could not confirm this [5, 6].

Within the last 10 years POCD has been recognised after non-cardiac procedures. Previous research used less sensitive tests or did not take into account the practice effect associated with neuropsychological testing thereby under-reporting the condition. Careful selection of tests and comparison with appropriate age-matched control groups has provided a new approach. The incidence of POCD after non-cardiac procedures is probably around 25% at one week after major surgery in patients above 60 years of age and

approximately 10% at three months [7, 8]. POCD is less common in middle-aged patients and after minor surgery [9, 10]. It must be realised, however, that the available information about POCD has been based on data collected in patients undergoing elective surgery and, consequently, patients with pre-existing cognitive impairment have not been studied. In addition, some patients will refuse follow-up examination after surgery. All these limitations probably lead to an underestimation of the true incidence of POCD.

Stroke

Clinical neurological complications occur infrequently after surgery. The most common of these is stroke, which is seen in 0.1 to 1% of patients after major surgery [11]. Age and type of surgery are, again, very important risk factors, and certain types of vascular and cardiac procedures carry a risk that may be ten times higher. Most strokes are of an embolic origin and 50% occur after the first postoperative day [12]. The prognosis is most often poor although the symptoms and clinical findings may vary according to the site and extent of the infarction. Brain imaging should be carried out as soon as possible to establish if an infarct or a haemorrhage can be detected.

Mechanisms of brain dysfunction and damage

Hypoperfusion and hypoxaemia

Anaesthesia and surgery can be associated with large fluctuations in blood pressure and oxygenation, not only during the procedure, but also in the postoperative phase, such as that demonstrated by nocturnal desaturation after laparotomy. Brain hypoperfusion and hypoxia may, therefore, result. However, scientific studies conducted to date have not been able to verify a relationship between POCD and hypoxaemia or hypotensive episodes [7]. One possible explanation is that the detected hypoxaemia has been rather modest and there is no easy way to assess brain perfusion or oxygenation in the clinical setting.

Thrombosis and embolism

Patients receiving anti-thrombotic medication are at increased risk of bleeding and, therefore, it is common practice to reduce the dose or withhold therapy at the time of major surgery. Unfortunately, this increases the risk of peri-operative thrombosis and a stroke may result, for example in patients with heart valve prostheses or atrial fibrillation.

Cardiopulmonary bypass is associated with a substantial risk of embolism with air, lipid or atheromas reaching the brain. Macroemboli are defined as > 200 microns and may cause stroke, whereas microemboli may be a factor in the aetiology of delirium or POCD. The available data are, however, not entirely conclusive regarding their importance for POCD or delirium. As an example, arterial line filtration can reduce the number of emboli detected but the incidence of POCD may be unchanged. One problem could be that there are limitations associated with the methods for counting emboli. Careful examination of the aorta, preferably by ultrasound, may reveal plaques that should be avoided during cannulation and this does seem to improve outcome.

Embolism may also occur in connection with non-cardiac procedures and these may reach the brain in some situations, for example if there is a patent foramen ovale. Embolism after non-cardiac procedures is most likely during major orthopaedic surgery such as hip or knee replacement, but air may enter the circulation during any procedure where the operative field is above heart level – such as in the prone position.

Neurotoxicity of anaesthetic drugs

Animal studies have detected brain damage after general anaesthesia using various techniques with signs of apoptosis, altered protein synthesis, and abnormal behaviour [13, 14]. A large number of drugs are given to surgical patients and one could speculate if general anaesthetics could cause a long-lasting disturbance in neuronal function, for example related to cholinergic or glutaminergic receptors. This is an interesting hypothesis but does not seem to be supported by the numerous randomised trials comparing general and regional anaesthesia. In fact, none of the 17 available studies on this issue have found a significantly better cognitive outcome after regional anaesthesia beyond the first postoperative week [15, 16]. One explanation could be that the most fragile patients have not been studied. Another aspect is that regional anaesthesia is not always effective and intravenous sedatives or opioids may be given as well.

Cortisol secretion pattern and inflammation

Glucocorticoids and inflammatory mediators can alter cognitive function, as seen with trauma and sepsis. Surgery induces an activation of a metabolic stress response with high cortisol levels and flattening of the normal circadian secretion pattern [17]. Cytokines are also known to have profound effects on brain function and the blood levels of some cytokines have been shown to correlate with POCD after cardiac procedures [18].

Hospital environment

Hospitalisation itself may adversely affect cognitive function. Elderly patients are very sensitive and delirium can occur as a consequence of sleep deprivation, starvation, unfamiliar surroundings, etc. POCD also seems to be more common in surgical patients with postoperative sleep disturbances but it can be difficult to establish which came first [19]. Elderly patients may benefit from early discharge and it seems logical that many institutions no longer have an upper age-limit for ambulatory surgery.

Key Learning Points

- Age is a very important risk factor for peri-operative cerebral complications.
- Delirium occurs frequently in hospitalised elderly and is a condition characterised by acute onset, fluctuating course with inattention. Level of consciousness may be changed.
- Postoperative cognitive dysfunction is deterioration in brain function that lasts for weeks or months. Neuropsychological testing can verify this subtle condition.
- Peri-operative stroke is uncommon but has a poor prognosis. Most strokes are of an embolic origin.

References

1. Dodds C, Allison J. Postoperative cognitive deficit in the elderly surgical patient. *British Journal of Anaesthesia* 1998; 81: 449-62.
2. Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: The Confusion Assessment Method. *Annals of Internal Medicine* 1990; 113: 941-8.
3. Rasmussen LS, Larsen K, Houx P, et al. The assessment of postoperative cognitive function. *Acta Anaesthesiologica Scandinavica* 2001; 45: 275-89.
4. Newman MF, Kirchner JL, Phillips-Bute B, et al. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. *New England Journal of Medicine* 2001; 344: 395-402.
5. van Dijk D, Jansen EW, Hijman R, et al. Cognitive outcome after off-pump and on-pump coronary artery bypass graft surgery: a randomized trial. *Journal of the American Medical Association* 2002; 287: 1405-12.
6. Ostergaard Jensen B, Hughes P, Rasmussen LS, Pedersen PU, Steinbrüchel D. Cognitive outcomes in elderly high-risk patients after off-pump versus conventional coronary artery bypass grafting. *Circulation* 2006; 113: 2790-5.
7. Moller JT, Cluitmans P, Rasmussen LS, et al. Long-term postoperative cognitive dysfunction in the elderly: ISPOCD1 study. *Lancet* 1998; 351: 857-61.
8. Monk TG, Weldon BC, Garvan CW, et al. Predictors of cognitive dysfunction after major noncardiac surgery. *Anesthesiology* 2008; 108:18-30.
9. Johnson T, Monk T, Rasmussen LS, et al. Postoperative cognitive dysfunction in middle-aged patients. *Anesthesiology* 2002; 96: 1351-7.
10. Canet J, Raeder J, Rasmussen LS, et al. Cognitive dysfunction after minor surgery in the elderly. *Acta Anaesthesiologica Scandinavica* 2003; 47: 1204-10.
11. Kam PCA, Calcroft RM. Peri-operative stroke in general surgical patients. *Anaesthesia* 1997; 52: 879-83.
12. Selim M. Perioperative stroke. *New England Journal of Medicine* 2007; 356: 706-13.
13. Jevtovic-Todorovic V, Hartman RE, Izumi Y, et al. Early exposure to common anesthetic agents causes widespread neurodegeneration in the developing rat brain and persistent learning deficits. *Journal of Neuroscience* 2003; 23: 876-82.
14. Xie Z, Dong Y, Maeda U, et al. The common inhalation anesthetic isoflurane induces apoptosis and increases amyloid beta protein levels. *Anesthesiology* 2006; 104: 988-94.
15. Rasmussen LS. Postoperative cognitive dysfunction: incidence and prevention. *Best Practice and Research Clinical Anaesthesiology* 2006; 20: 315-30.
16. Wu CL, Hsu W, Richman JM, Raja SN. Postoperative cognitive function as an outcome of regional anesthesia and analgesia. *Regional Anesthesia and Pain Medicine* 2004; 29: 257-68.

17. Rasmussen LS, O'Brien JT, Silverstein JH, et al. Is perioperative cortisol secretion related to postoperative cognitive dysfunction? *Acta Anaesthesiologica Scandinavica* 2005; 49: 1225-31.
18. Ramlawi B, Rudolph JL, Mieno S, et al. C-Reactive protein and inflammatory response associated to neurocognitive decline following cardiac surgery. *Surgery* 2006; 140: 221-6.
19. Gögenur I, Middleton B, Burgdorf S, et al. Impact of sleep and circadian disturbances in urinary 6-sulfatoxymelatonin levels on cognitive function after major surgery. *Journal of Pineal Research* 2007; 43: 179-84.