Postoperative cognitive decline, dementia and anaesthesia

The potential for older people to develop cognitive impairment as a consequence of major surgery with anaesthesia has been increasingly recognized over the last 10 years. This article reviews the evidence regarding the incidence, outcome and potential mechanisms of cognitive impairment and considers the specific implications for people with dementia.

The experiences of older people undergoing anaesthesia and clinicians have long suggested that cognitive function may worsen after major surgical interventions. It is only over the last decade, however, that systematic studies have investigated the problem, coining the term postoperative cognitive decline. This work has highlighted the frequency and importance of postoperative cognitive decline, which has become increasingly recognized as a common and potentially handicapping outcome after a broad range of major surgical procedures.

Although there is some variability between reports, probably reflecting the individual study definitions of postoperative cognitive decline and the differing age range of participants, the mean reported incidence rates are 25% (range 7–40%) 1 week postoperatively and 10% (range 7–15%) 3 months postoperatively for non-cardiac procedures. This mean is likely to be significantly higher in patients undergoing cardiac surgery because of the increased likelihood of major surgery being hypoxic and the potential need for a cardiopulmonary bypass to be performed in some types of surgery (Selwood and Orrell, 2004; Hanning, 2005). These findings clearly indicate that postoperative cognitive decline is a frequent and often persistent syndrome at all ages.

The first major multi-centre international study of long-term postoperative cognitive decline specifically in people aged 60 years and over (ISPOCD1 study; Moller et al, 1998) reported an incidence of postoperative cognitive decline of 25% 1 week after surgery and 10% after 3 months, despite excluding people with any pre-existing level of cognitive impairment from the trial. Importantly, the degree of postoperative cognitive decline identified was of sufficient magnitude to interfere with day-to-day activities, emphasizing the clinical significance of the problem. Furthermore, patients aged 70 years and over had twice the incidence of postoperative cognitive decline at 3 months (14%) than those aged 60–69 years (7%).

However, there are still very few studies of individuals of 70 years of age or older, who are probably the highest risk group, and only a handful of studies with follow-up periods longer than 3 months. Some level of cognitive impairment is extremely frequent after major surgical procedures, especially in the oldest age groups. Surprisingly, despite the high incidence rates, awareness is low among the medical community and among surgical patients, and people are rarely informed of the risk of postoperative cognitive decline preoperatively as part of the consent procedure (Casati et al, 2005).

Postoperative cognitive decline and persistent cognitive decline

Postoperative cognitive decline is a major and potentially preventable cause of persistent cognitive decline, which often goes unrecognized. Many key questions regarding the full significance of the syndrome remain unanswered. For example the proportion of people with persistent cognitive impairment has not been determined and it is unclear whether the magnitude of impairment is of sufficient severity to meet criteria for clinically significant syndromes such as mild cognitive impairment.

Perhaps most importantly, it has not been determined whether postoperative cognitive decline leads to an increased risk of incident dementia. This is a challenging question as the expected annual risk of incident dementia in people in their 60s and 70s is very small, hence even a doubling or tripling of risk could not be identified in this time period. Longer term follow up and studies focussing on individuals at higher risk of dementia, such as those over 80 years of age and people with mild cognitive impairment, are needed to address this key issue.

Possible causes

Several reviews have reiterated the magnitude of the problem but have been unable to offer any insights into the mechanisms or underlying causes (Mackensen and Gelb, 2004; Selwood and Orrell, 2004). For example, in the ISPOCD1 study trial neither hypoxaemia nor hypotension were identified as significant risk factors, even with continuing measurements for up to 3 days post surgery (Moller et al, 1998), although more detailed evaluation of the impact of altered regional cerebral oxygen saturation is still needed.

Another key perioperative factor pertains to the type and dose of the anaesthetic agents, muscle relaxants and analgesics used. Most anaesthetic agents may be toxic, in both the developing and the aged rat brain (Olney, 2002), with cognitive dysfunction persisting for several weeks in rodent studies. Anaesthetic agents exert a potent anticholinergic effect, which has been postulated to be a key factor in the development of postoperative cognitive decline. These impressions are supported in cell culture and rodent studies demonstrating loss of nicotinic cholinergic receptors after anaesthesia with sodium pentobarbital (Hanning et al, 2003). In addition, the 'anticholinergic hypothesis' has good face validity in the context of the profound cholinergic deficits that occur in people with Alzheimer's disease and synucleinopathies, and the detrimental impact of anticholinergic agents upon cognition in volunteer studies.

There are, however, a number of other credible potential mechanisms, which may not be mutually exclusive. For example, in rodent studies altered gene expression involving key pathways related to inflammation and amyloid processing have been demonstrated, which persist for several weeks after anaesthesia. Major surgery itself

is associated with widespread physiological changes and an inflammatory process. In the context of emerging work highlighting the potential of inflammation to accelerate cognitive decline, the surgery may also act as a possible adjunct to the development of postoperative cognitive decline.

Based upon the postulated mechanisms of postoperative cognitive decline, it is therefore an important clinical hypothesis that the quantity (duration times concentration) of anaesthetic agents used, especially during major surgery for older people, may be an important determinant of cognitive impairment. There may also be important differences between agents, and it is possible that agents such as remifentanil, which enable a reduced depth of anaesthesia, may help minimize the toxicity of the anaesthetic (Albertin et al, 2004). Evaluating the impact of the type and depth of anaesthesia is a key area for current research.

Postoperative cognitive decline and dementia

Beyond anecdotal experience there are few studies specifically evaluating the development of dementia after surgery or surgical outcome in people with established dementia. The more systematic evidence is predominantly limited to several reports suggest a significant increase in dementia clinically and pathologically after cardiac surgery. It is, however, a concern that the anticholinergic, pro-inflammatory and pro-amyloidogenic impact of anaesthesia and/or surgery is likely to have an impact on the dementia process, and individuals with vascular dementia or microvascular lesions associated with Alzheimer's disease may be at particular risk from reduced regional oxygen saturation. This is a priority area for further work to provide an evidence base to inform clinical practice.

Conclusions

For the future there are a number of urgent questions that need to be addressed. We need to better understand the mechanisms of postoperative cognitive decline, the long-term impact of postoperative cognitive decline on cognitive function, the risks of anaesthesia in people with dementia and whether the risks of postoperative cognitive decline or a detrimental outcome in people with dementia can be ameliorated with altered anaesthetic practice. While these are all key issues, we do know that postoperative cognitive decline occurs in more than 25% of people over the age of 70 years, and persists for at least 3 months in half of these individuals. This is therefore a frequent and important adverse event, and surely should be routinely explained to people over 70 years of age having major surgery as part of obtaining meaningful informed consent. BJHM

KEY POINTS

- Postoperative cognitive decline, the consequence of anaesthetic use in major surgery, occurs in more than 25% of people over 70 years of age after major surgery and persists for at least 3 months in half of these individuals.
- Little is known about the underlying mechanisms, although a correlation may exist between the severity of postoperative cognitive decline and the depth and/or type of anaesthetic used.
- The anticholinergic, pro-inflammatory and pro-amyloidogenic impact of anaesthetic and/or surgery is likely to have an impact on postoperative cognitive decline.
- More research into postoperative cognitive decline is urgently needed to better inform the use of anaesthetic in major surgery, particularly its use with older patients and those at risk from the reduced oxygen saturation associated with vascular dementia and microvascular lesions of Alzheimer's disease.

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