Might hyperoxia during surgical anaesthesia contribute to older patients’ higher dementia risk?

Chen et al present data showing that patients aged 50 and over have an earlier onset and higher hazard ratios for dementia following surgery and anaesthesia than controls, irrespective of the type of anaesthesia used – intravenous or intramuscular, regional or general. This finding begs the question: what common denominators exist among anaesthetics that produce increased dementia risks?

One factor common to all anaesthesia types is supplemental oxygen used to sustain or raise arterial oxygen saturation levels as a ‘safety hedge’ during respiratory depressant drug use. During anaesthesia, arterial oxygen saturation data from pulse oximeters are proxies for tissue oxygen partial pressure values. Notably, normal ageing produces progressive decreases in tissue oxygen partial pressure values. Notably, normal ageing produces progressive decreases in oxygen saturation values that do not require treatment, especially under circumstances where oxygen consumption is diminished by both age and anaesthetisation. Rather, when ventilation and tissue perfusion are maintained, mitochondrial oxygen consumption occurs at physiochemical rates determined by local respiratory complex reactions governed by mitochondrial oxygen partial pressure needs and adenosine triphosphate levels that cannot be increased through super-maximal oxygen tissue tensions. In fact, interference with normal cell signalling functions occurs when hyperoxia dominates the internal milieu. Herein resides one of the dangers of oxygen over-supplementation, especially relevant to dementia studies, given that tau hyperphosphorylation can occur in the presence of oxidative stress without anaesthesia.

Anaesthesia is but one clinical circumstance where iatrogenic hyperoxia can ‘trip’ the pro-oxidant/antioxidant ratio switch at the subcellular and mitochondrial level towards excessive reactive oxygen and nitrogen species formation, but it is an important one. In the USA, in 2010, over 51 million in-patient surgical anaesthetisations occurred. This figure excludes out-patient procedures, so the total surgical anaesthesia hyperoxia exposure remains elusive, the perioperative events contributing to oxidative stress after anaesthesia and surgery might contribute to the hazard risk of dementia development. Although the exact mechanism of oxidative stress remains elusive, the perioperative events contributing to oxidative stress include ischaemia-reperfusion damage, surgical trauma, and also iatrogenic hyperoxia during anaesthesia, as Professor Kopp elaborated. However, further studies need to be conducted to demonstrate the exact mechanism of oxidative stress due to anaesthesia and surgery in humans, and to demonstrate the effect of antioxidant agents to prevent the potential detrimental effect on cognitive function following anaesthesia and surgery.

We agree with Professor Kopp that hyperoxia during surgical anaesthesia might contribute to the higher risk of dementia following anaesthesia and surgery. Growing evidence has demonstrated that oxidative stress may augment the production and aggregation of amyloid-beta and facilitate the progression of Alzheimer’s disease. Animal and human studies have also demonstrated increased oxidative stress following anaesthesia and surgery.

Might hyperoxia during surgical anaesthesia contribute to older patients’ higher dementia risk?


Vincent J. Kopp, Department of Anesthesiology, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, NC 27599-7010, USA.

Email: vkopp@aims.unc.edu

doi: 10.1192/bjp.bp.204.2.163

Authors’ reply: We agree with Professor Kopp that hyperoxia during surgical anaesthesia might contribute to the higher risk of dementia following anaesthesia and surgery. Growing evidence has demonstrated that oxidative stress may augment the production and aggregation of amyloid-beta and facilitate the progression of Alzheimer’s disease. Animal and human studies have also demonstrated increased oxidative stress following anaesthesia and surgery. Furthermore, Kalimeris et al showed that propofol, which has antioxidant effects, seemed to improve cognitive performance after carotid endarterectomy, compared with sevoflurane. Therefore, oxidative stress after anaesthesia and surgery might contribute to the hazard risk of dementia development. Although the exact mechanism of oxidative stress remains elusive, the perioperative events contributing to oxidative stress include ischaemia-reperfusion damage, surgical trauma, and also iatrogenic hyperoxia during anaesthesia, as Professor Kopp elaborated. However, further studies need to be conducted to demonstrate the exact mechanism of oxidative stress due to anaesthesia and surgery in humans, and to demonstrate the effect of antioxidant agents to prevent the potential detrimental effect on cognitive function following anaesthesia and surgery.