

Is postoperative delirium a relevant outcome?

Moritoki Egi¹

Received: 3 May 2015 / Accepted: 8 May 2015 / Published online: 23 May 2015
© Japanese Society of Anesthesiologists 2015

Delirium is characterized by the acute onset of mental status or a fluctuating course and inattention and disorganized thinking or an altered level of consciousness [1], which is common in critically ill patients [2]. Recently, the diagnosis of delirium is recommended by using the Confusion Assessment Method for the intensive care unit (CAM-ICU) [3].

Postoperative delirium (POD) was defined as so because it occurs postoperatively. Although operation, anesthetics, and analgesics can contribute to POD, it is not just associated with emergence from anesthesia, but often occurs between postoperative days 1 and 3. Although POD is commonly recovered from within a short period of time [4], patients with POD are more likely to die or develop dementia and require institutionalization [5].

A number of risk factors are reported for POD, including older age, preoperative cognitive or functional impairment, decreased postoperative hemoglobin, markedly abnormal sodium potassium and glucose, the presence of alcohol abuse, noncardiac thoracic surgery, aortic aneurysm surgery, history of delirium, preoperative use of narcotics, low postoperative oxygen saturation, history of cerebrovascular disease, and untreated pain [6, 7].

In a recent prospective observational study conducted by Saporito and Sturini [8], they excluded patients with any known preexisting predisposing factor for POD; types of surgery, preoperative dementia, sensory deficits, requirement of psychotropic drugs, and alcoholism etc., and other

potentially confounding neurological dysfunctions. In their study with 100 postoperative patients without a known risk factor of POD, the incidence of POD diagnosed using CAM was 28 %. Their result suggested that the incidence of POD was common in patients after major surgery even without known risk factors. Major surgery might evoke a strong stress response. Recent studies provided the hypothesis that it may introduce postoperative delirium or cognitive dysfunction [9, 10]. As the authors have pointed out, prior studies have commonly been conducted in postoperative patients with known risk factors; their study is relevant and novel.

Another finding was a significant association of the use of thiopental with the risk of POD compared with propofol. Thiopental, a barbiturate class of drug, has effects on the gamma-aminobutyric acid (GABA) receptor [11] and propofol is also considered to act through potentiation of GABA receptor activity. Although their finding on thiopental may be skewed by the bias of patient characteristics and conditions which may cause anesthesiologists to choose thiopental rather than propofol, the potential action of thiopental on non-GABA-ergic ligand-gated ion channels, including the neuronal nicotinic acetylcholine receptor channels, may contribute to its association [12].

Although there are potential hypotheses for the etiology and pathophysiology of POD including cholinergic inhabitation, serotonin deficiency, dopamine activation [13], GABA activity [14], and melatonin activity [15], they are not fully understood [16]. This is one of the reasons why there are still just a few strategies for preventing POD [17]; the use of dexmedetomidine in post-cardiac surgery patients [18], multicomponent interventions, and antipsychotics. In this regard, further study should be warranted to develop a detailed understanding and preventive strategy for these postoperative complications.

✉ Moritoki Egi
moriori@tg8.so-net.ne.jp

¹ Department of Anesthesiology, Kobe University
Medical School, 7-5-2 Kusunoki-cho, Chuo-ku, Hyogo,
Kobe 650-0017, Japan

The known risk factors were defined at least a decade ago, and the patients' characteristics, types of operations, anesthetics, and analgesics were altered within this decade. According to this fact, and the finding reported by Saporito and Sturini [8], a more comprehensive study including with and without "known risk factors" might be required as future study.

To concern the high incidence, the significant association with short- and long-term outcomes, the uncertainty of its etiology and pathophysiology and developing knowledge for its prevention and treatments, it is difficult to doubt that post-operative delirium is relevant outcome for perioperative patients from both clinical and research point of views.

References

- Gleason OC. Delirium. *Am Fam Physician*. 2003;67:1027–34.
- Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. *Br J Anaesth*. 2009;103(Suppl 1):i41–6.
- Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The Confusion Assessment Method: a systematic review of current usage. *J Am Geriatr Soc*. 2008;56:823–30.
- Brauer C, Morrison RS, Silberzweig SB, Siu AL. The cause of delirium in patients with hip fracture. *Arch Intern Med*. 2000;160:1856–60.
- Bickel H, Grading R, Kochs E, Forstl H. High risk of cognitive and functional decline after postoperative delirium. A three-year prospective study. *Dement Geriatr Cogn Disord*. 2008;26:26–31.
- Marcantonio ER, Goldman L, Mangione CM, Ludwig LE, Muraca B, Haslauer CM, Donaldson MC, Whittlemore AD, Sugarbaker DJ, Poss R, Haas S, Cook EF, Orav EJ, Lee TH. A clinical prediction rule for delirium after elective noncardiac surgery. *JAMA*. 1994;271:134–9.
- Kalisvaart KJ, Vreeswijk R, de Jonghe JF, van der Ploeg T, van Gool WA, Eikelenboom P. Risk factors and prediction of postoperative delirium in elderly hip-surgery patients: implementation and validation of a medical risk factor model. *J Am Geriatr Soc*. 2006;54:817–22.
- Saporito A, Sturini E. Incidence of postoperative delirium is high even in a population without known risk factors. *J Anesth*. 2014;28:198–201.
- Hudetz JA, Gandhi SD, Iqbal Z, Patterson KM, Pagel PS. Elevated postoperative inflammatory biomarkers are associated with short- and medium-term cognitive dysfunction after coronary artery surgery. *J Anesth*. 2010;25:1–9.
- Cerejeira J, Batista P, Nogueira V, Vaz-Serra A, Mukaetova-Ladinska EB. The stress response to surgery and postoperative delirium: evidence of hypothalamic-pituitary-adrenal axis hyperresponsiveness and decreased suppression of the GH/IGF-1 Axis. *J Geriatr Psychiatry Neurol*. 2013;26:185–94.
- Orser BA, McAdam LC, Roder S, MacDonald JF. General anaesthetics and their effects on GABA(A) receptor desensitization. *Toxicol Lett*. 1998;100–101:217–24.
- Downie DL, Franks NP, Lieb WR. Effects of thiopental and its optical isomers on nicotinic acetylcholine receptors. *Anesthesiology*. 2000;93:774–83.
- Marcantonio ER, Rudolph JL, Culley D, Crosby G, Alsop D, Inouye SK. Serum biomarkers for delirium. *J Gerontol A Biol Sci Med Sci*. 2006;61:1281–6.
- Yoshitaka S, Egi M, Kanazawa T, Toda Y, Morita K. The association of plasma gamma-aminobutyric acid concentration with postoperative delirium in critically ill patients. *Crit Care Resusc*. 2014;16:269–73.
- Yoshitaka S, Egi M, Morimatsu H, Kanazawa T, Toda Y, Morita K. Perioperative plasma melatonin concentration in postoperative critically ill patients: its association with delirium. *J Crit Care*. 2013;28:236–42.
- Flacker JM, Lipsitz LA. Neural mechanisms of delirium: current hypotheses and evolving concepts. *J Gerontol A Biol Sci Med Sci*. 1999;54:B239–46.
- Zhang H, Lu Y, Liu M, Zou Z, Wang L, Xu FY, Shi XY. Strategies for prevention of postoperative delirium: a systematic review and meta-analysis of randomized trials. *Crit Care*. 2013;17:R47.
- Zhang X, Zhao X, Wang Y. Dexmedetomidine: a review of applications for cardiac surgery during perioperative period. *J Anesth*. 2014;29:102–11.