Original Article

Effect of Oxygen Content on Postoperative Cognitive Dysfunction in Patients Undergoing Open-Heart Surgery

Ratna Farida Soenarto, Aditya Arbi

Department of Anesthesiology and Intensive Care, Cipto Mangunkusumo General Hospital, Universitas Indonesia, Jakarta, Indonesia

Abstract

Introduction: Brain's decreased oxygen delivery is proposed as a risk factor for postoperative cognitive dysfunction (POCD). This study's objective was to investigate the effect of arterial oxygen content (CaO_2) on POCD in patients undergoing open-heart surgery. **Subjects and Methods:** Adult patients listed for elective open-heart surgery at Cipto Mangunkusumo General Hospital were enrolled. The patients' cognitive function was tested using the Rey Auditory Verbal Learning Test, trail-making test, and digit span test (forward–backward) before and 5 days after surgery. The hemoglobin level, arterial saturation (SaO_2), and arterial oxygen partial pressure (PaO_2) were measured at the following five time points: before induction, 10 min after the commencement of cardiopulmonary bypass (CPB), 10 min after the cessation of CPB, 6 h postoperatively, and 1 day postoperatively. The CaO_2 was calculated as follows: $CaO_2 = 1.36 \times \text{hemoglobin} \times SaO_2 + 0.003 \times PaO_2$. Data were compared using Student's *t*-test or the Mann–Whitney test with SPSS software version 20.0 (IBM Corp., Armonk, NY, USA). **Results:** POCD was found in nine patients (47.4%). The CaO was significantly lower in patients with POCD than those without POCD at 10 min after the cessation of CPB (12.1 ± 2.6 vs. 14.5 ± 1.7, respectively; $P = 0.03$). The hemoglobin level appeared to be the cause of the decreased CaO_2 in the POCD group (8.5 ± 2.3 vs. 10.2 ± 1.2, $P = 0.06$). Decreased oxygen content after CPB cessation may impair brain tissue oxygenation that causes POCD. **Conclusion:** Hemoglobin level may play an important role in POCD development after open-heart surgery.

Keywords: Hemoglobin, oxygen delivery, PaO_2, postoperative cognitive dysfunction, SaO_2

Introduction

Postoperative cognitive dysfunction (POCD) is defined as a decrease in cognitive function after surgery. It is a reversible condition but may become permanent in patients aged ≥65 years. The clinical interest in POCD is increasing because it has been recognized to disturb patients' social life. According to the International Study of POCD,[1] the incidence of POCD in patients of advanced age undergoing noncardiac surgery is 25.8% in the 1st week postoperatively and 9.9% at 3 months postoperatively. The incidence is higher (40%) for patients undergoing cardiac surgery.[1-5]

Although several studies have been performed to investigate factors that contribute to POCD, many questions about POCD remain unanswered. Tissue hypoxia is suspected to be the cause of POCD. Several factors can affect oxygen delivery during cardiac surgery with cardiopulmonary bypass (CPB). Assuming that good cardiac output is maintained during CPB, the outcomes with respect to cognitive function vary. The present study was performed to investigate the effect of oxygen content on POCD in patients undergoing open-heart surgery.[1,3,6]

Subjects and Methods

This was a prospective cohort study. The study population comprised adult patients who were listed for elective open-heart surgery in Cipto Mangunkusumo General Hospital [Table 1]. All the enrolled patients were mentally healthy as assessed by the Mini–Mental State Examination.[7] Patients with neuropsychiatric dysfunction, consumption of psychotropic drugs, or an inability to speak and write in Bahasa Indonesia were excluded from the study. CPB was used in all surgeries. Patients who did not fulfill the clinical pathway

Access this article online

Quick Response Code:

Website: www.jnsbm.org

DOI: 10.4103/jnsbm.JNSBM_28_19

Address for correspondence: Dr. Ratna Farida Soenarto, Cipto Mangunkusumo General Hospital, Diponegoro Street 71, Jakarta 10430, Indonesia.
E-mail: fida.soenarto@gmail.com

How to cite this article: Soenarto RF, Arbi A. Effect of oxygen content on postoperative cognitive dysfunction in patients undergoing open-heart surgery. J Nat Sc Biol Med 2019;10:S7-10.

(i.e., were ready to be discharged from the hospital on postoperative day 5) were excluded from the study.

One day before the surgery, the patients underwent testing with several neurocognitive instruments: the Rey Auditory Verbal Learning Test (immediate and delayed), trail-making test (A and B), and digit span test (forward–backward).[7-9] These tests, validated by the Department of Psychiatry at Cipto Mangunkusumo General Hospital, were used to assess the patients' cognitive function, especially attention, memory, and executive function. All the tests were conducted in Bahasa Indonesia. The patients were tested alone, unaccompanied by any relative. These cognitive tests were repeated on postoperative day 5. Cognitive dysfunction was defined as a ≥20% decrease in the cognitive score for at least two tests.

On the day of surgery, approximately 1–2 cc blood samples were taken at the following five time points: before induction, 10 min after the commencement of CPB, 10 min after the cessation of CPB, 6 h after surgery, and 1 day after surgery. Data derived from the blood samples were the hemoglobin level, arterial oxygen saturation (SaO_2), and partial pressure of oxygen (PaO_2). The oxygen content (CaO_2) was calculated by the following formula: $CaO_2 = 1.36 \times \text{hemoglobin} \times SaO_2 + 0.003 \times PaO_2$.

Data were analyzed using SPSS software version 20.0 (IBM Corp., Armonk, NY, USA). Statistical analysis was performed by Student's *t*-test or the Mann–Whitney nonparametric test. $P < 0.05$ was considered statistically significant. Ethical clearance for this study was obtained from the Ethical Committee of the Faculty of Medicine, Universitas Indonesia (0364/UN2.F1/ETIK/2018).

Results

This study involved 19 patients, of which nine (47.4%) developed POCD. The CaO2 was statistically significantly lower in patients with POCD than those without POCD at 10 min after the cessation of CPB (12.1 ± 2.6 vs. 14.5 ± 1.7, respectively; $P = 0.03$ [Figure 1]) [Table 2]. All patients had good and stable PaO_2 and SaO_2 levels during the surgery. The hemoglobin level was lower in the POCD group compared to non-POCD group, but not statistically significantly (8.5 ± 2.3 vs. 10.2 ± 1.2, respectively; $P = 0.06$) as described in Table 2.

With respect to the type of surgery, most patients with POCD had undergone coronary artery bypass graft alone ($n = 7$). No patients who underwent isolated valve surgery developed POCD in this study. We found that the duration of CPB was slightly longer in patients with POCD than those without POCD (136.9 ± 28.2 vs. 128.5 ± 31.0 min, respectively) [Table 2].

The statistical analysis showed that the only variable that was statistically significantly different between the POCD and non-POCD groups was the CaO_2 at 10 min after CPB (12.1 ± 2.6 vs. 14.5 ± 1.7, respectively; $P = 0.03$). At the same measurement time point, the hemoglobin level showed that there was no statistical significance between the two groups ($P = 0.06$). The hemoglobin level was also not statistically significantly different between the two groups

Table 1: Preoperative and intraoperative characteristics

Characteristics	POCD	Non-POCD
Age (years)	52.1±16.0	53.5±8.3
Sex, *n* (%)		
Male	7 (46.7)	8 (53.3)
Female	2 (50.0)	2 (50.0)
Comorbidities, *n* (%)		
Hypertension	5 (55.6)	7 (70.0)
Diabetes mellitus	6 (66.7)	3 (30.0)
CKD	2 (22.2)	3 (30.0)
CVD	0	1 (10.0)
Type of surgery, *n* (%)		
CABG	7 (77.8)	6 (60.0)
Valve	0	4 (40.0)
CABG + valve	1 (11.1)	0
Other procedure	1 (11.1)	0
Euro score	4.0 (0-6)	3.5 (2-5)
CPB duration (min)	136.9±28.2	128.5±31.0
AoX duration (min)	92.2±12.6	97.1±21.1

POCD: Postoperative cognitive dysfunction, CPB: Cardiopulmonary bypass, CABG: Coronary artery bypass graft, AoX: Aortic Cross Clamping Time, CKD: Chronickidney disease, CVD: Cardiovascular disease

Table 2: Analysis of oxygen content variables between postoperative cognitive dysfunction and non- postoperative cognitive dysfunction groups

Variables	POCD	Non-POCD	*P*
Hemoglobin (g/dl)			
Baseline	12.4±2.2	12.7±1.7	0.74
During CPB	7.6±2.2	8.7±1.5	0.20
Post-CPB	8.5±2.3	10.2±1.2	0.06
6 h postoperatively	8.9 (6.1-11.9)	9.8 (8.6-13.7)	0.08
1 day postoperatively	9.0±0.8	9.7±1.4	0.27
PaO_2 (mmHg)			
Baseline	198.2±119.2	191.7±75.4	0.88
During CPB	289 (194-330)	280.5 (141-356)	0.72
Post-CPB	255.0±118.3	253.7±114.6	0.98
6 h postoperatively	146.0±33.9	140.2±41.1	0.74
1 day postoperatively	152.6±57.4	131.52±21.0	0.29
SaO_2 (%)			
Baseline	99.0 (96-100)	99.0 (98-99)	0.45
During CPB	99.0 (94-100)	99.0 (99-99)	0.72
Post-CPB	99.0 (91-100)	99.0 (98-99)	0.64
6 h postoperatively	99.0 (98-100)	98.0 (94-100)	0.11
1 day postoperatively	99.0 (98-99)	99.0 (96-99)	0.36
CaO_2 (mlO_2/dl)			
Baseline	16.3±2.8	16.8±2.3	0.68
During CPB	10.9±2.9	12.6±2.0	0.18
Post-CPB	12.1±2.6	14.4±1.7	0.03*
6 h postoperatively	12.5±1.9	13.8±2.2	0.15
1 day postoperatively	12.6±1.2	13.4±1.9	0.32

*$P < 0.05$; significant, POCD: Postoperative cognitive dysfunction, CPB: Cardiopulmonary bypass

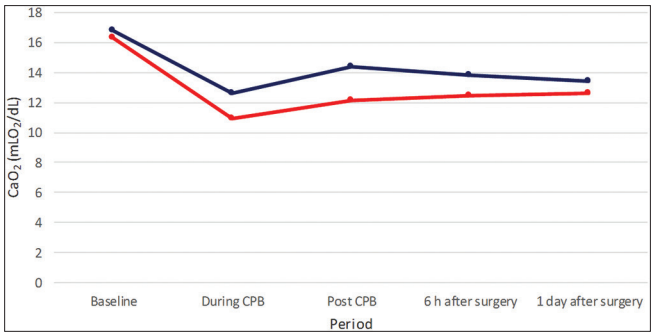

Figure 1: CaO_2 between POCD and non-POCD groups. The CaO_2 was similar at all time points except post-CPB, at which time it was lower in the POCD group. CaO_2: oxygen content, POCD: Postoperative cognitive dysfunction, CPB: Cardiopulmonary bypass

at 6 h after surgery (P = 0.08). The PaO_2 and SaO_2 were not significantly different between the two groups at any time point. The CaO_2 was statistically significantly lower in patients with POCD than those without POCD at 10 min after the cessation of CPB (12.1 ± 2.6 vs. 14.5 ± 1.7, respectively; P = 0.03). Based on these findings, the hemoglobin level was apparently found to be the cause of the lower CaO_2 in the POCD group when compared to non-POCD group (8.5 ± 2.3 vs. 10.2 ± 1.2, respectively; P = 0.06). However, lack of statistical significance was probably due to the small sample size.

Discussion

POCD refers to temporarily impaired cognitive function associated with surgery. This dysfunction can occur in patients of any age, but most cases occur in patients of advanced age.[10] However, this problem is less common than postoperative cardiopulmonary complications, pain, and nausea and vomiting.[1,2,11] This study revealed that the incidence of POCD after open-heart surgery was 47.4%. Hypoxia was assumed to be the cause of POCD after open-heart surgery. Hypoxia may be caused by cerebral hypoperfusion, low brain oxygen saturation, bleeding, or hemodilution that lowers the hematocrit to <30%. Low oxygenation due to poor oxygen delivery was not considered to be the cause of POCD in this study. During the entire period of surgery, oxygen saturation was closely monitored which remained adequate, as shown by the PaO_2, SaO_2, and peripheral capillary oxygen saturation. The PaO_2 and SaO_2 remained adequate in both groups.[1,6] No massive bleeding that could have led to decreased oxygen delivery to the brain occurred in this study.

The CaO_2 was slightly lower in the POCD group when compared to non-POCD group at all the five time points, but the only measurement that was statistically significantly different between the two groups was the CaO_2 10 min after CPB (P = 0.03). CaO_2 is determined by the PaO_2, SaO_2, and hemoglobin level. SaO_2 and PaO_2 should remain high throughout CPB regardless of the patient's preoperative condition because these parameters are totally controlled by the perfusionist. In the present study, because the PaO_2 and SaO_2 were adequate in all patients, hemoglobin may have played a significant role in determining the difference between the two study groups. The hemoglobin level fluctuates during CPB. After commencing CPB, the hemoglobin level usually drops as hemodilution begins. Although the amount of priming solution was the same for all patients in this study, the hemoglobin level was lower in the POCD group when compared to non-POCD group. The amount of intravenous fluid given by the anesthesiologist was not recorded, which is considered a limitation of this study.

The early period after completion of CPB seems to be the most critical time for oxygen delivery. During this period, the circulatory system is in transition from extracorporeal circulation to physiologic circulation. Hemoglobin and hematocrit are usually low due to hemodilution during CPB. Efforts to correct the hemoglobin level are often postponed until objective findings are available. This study showed that care must be taken in the critical time after CPB. The hemoglobin level should be determined before CPB completion so that any correction needed can be initiated early. Another important time point is 6 h postoperatively. Early postoperative care for patients who have undergone cardiac surgery is often focused on their hemodynamic state, especially in patients with potentially life-threatening conditions. Correction of electrolyte and hemoglobin imbalances is often delayed because they are not displayed on the bedside monitor. This study indicates that the 6-h postoperative hemoglobin level could contribute to POCD. Another modality used to measure the hemoglobin level immediately after surgery should be available so that a low hemoglobin level can be corrected as soon as possible. This study has three main limitations. First, we did not test the correlation between the hemoglobin level and the incidence of POCD. Second, we did not analyze the flow rate during CPB. Alston *et al*.[12] found that CaO_2 may be associated with the flow rate during CPB. Finally, the sample size was relatively small. A larger sample size is needed for further study of the relationship between CaO_2 and POCD. To conclude, CaO_2 may play an important role in the development of POCD after open-heart surgery. As PaO_2 and SaO_2 were both adequately maintained in this study, we can infer that the factor which influence the development of POCD in our study was hemoglobin level.

Conclusion

Hemoglobin level may play an important role in POCD development after open-heart surgery. Clinicians should provide efforts to maintain hemoglobin level during open-heart surgery.

Financial support and sponsorship

The 3rd ICE on IMERI (International Conference and Exhibition on Indonesia Medical Education and Research Institute) committee supported the peer review and manuscript preparation of this article. This study has been supported in

part by grant PITTA UI (Publikasi Internasional Terindeks untuk Tugas Akhir Mahasiswa Universitas Indonesia [2043/UN2.R3.1/HKP.05.00/2018]).

Conflicts of interest

There are no conflicts of interest.

References

1. Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. Br J Anaesth 2009;103 Suppl 1:i41-6.
2. Terrando N, Brzezinski M, Degos V, Eriksson LI, Kramer JH, Leung JM, *et al.* Perioperative cognitive decline in the aging population. Mayo Clin Proc 2011;86:885-93.
3. Gao L, Taha R, Gauvin D, Othmen LB, Wang Y, Blaise G. Postoperative cognitive dysfunction after cardiac surgery. Chest 2005;128:3664-70.
4. Khalil S, Roussel J, Schubert A, Emory L. Postoperative Cognitive Dysfunction: An Updated Review J Neurol Neurophysiol 2015;6:2.
5. Tsai TL, Sands LP, Leung JM. An update on postoperative cognitive dysfunction. Adv Anesth 2010;28:269-84.
6. Brown WR, Moody DM, Challa VR, Stump DA, Hammon JW. Longer duration of cardiopulmonary bypass is associated with greater numbers of cerebral microemboli. Stroke 2000;31:707-13.
7. Aprianti M. Influence of Age, Diabetes Mellitus, Duration of CPB, and Duration of Cross Clamping to Cognitive Function Decline Following Open Heart Surgery in Cipto Mangunkusumo Hospital [Thesis]. Jakarta: University of Indonesia; 2017.
8. Wulansari S. Profile of Cognitive Dysfunction of Patients with HIV with and without Anti Retroviral [Thesis]. Jakarta: University of Indonesia; 2017.
9. Ronawulan E. Validation and Normal Values in Neurocognitive Tests [Thesis]. Jakarta: University of Indonesia; 2004.
10. Chen CW, Lin CC, Chen KB, Kuo YC, Li CY, Chung CJ. Increased risk of dementia in people with previous exposure to general anesthesia: A nationwide population-based case-control study. Alzheimers Dement 2014;10:196-204.
11. Rundshagen I. Postoperative cognitive dysfunction. Dtsch Arztebl Int 2014;111:119-25.
12. Alston RP, Singh M, McLaren AD. Systemic oxygen uptake during hypothermic cardiopulmonary bypass. Effects of flow rate, flow character, and arterial pH. J Thorac Cardiovasc Surg 1989;98:757-68.