J Anesth (1996) 10:221–224

Journal of
Anesthesia

Continuous, noninvasive measurement of cytochrome oxidase in cerebral cortex by near-infrared spectrophotometry during aortic arch surgery

YASUYUKI KAKIHANA, AKIRA MATSUNAGA, HARUHIKO YAMADA, HIROSHI DOHGOMORI, TOSHIYUKI ODA, and NOZOMU YOSHIMURA

Department of Anesthesiology and Critical Care Medicine, Kagoshima University School of Medicine, 8-35-1 Sakuragaoka, Kagoshima, Japan

Kew words: Thoracic aortic aneurysm, Cytochrome oxidase, Near-infrared spectrophotometry

Introduction

The incidence of neurological dysfunction after cardiac surgery or thoracic aortic surgery with cardiopulmonary bypass (CPB) is much higher than after general surgery [1,2]. To prevent neurological complications, it is important to detect any deterioration in cerebral function and oxygenation as early as possible in the perioperative period. Accordingly, we noninvasively and continuously monitored changes in hemoglobin oxygenation and in the redox state of cytochrome oxidase (Cyt.aa_3) in the cerebral cortex by near-infrared spectrophotometry (NIRS) during aortic arch surgery, and evaluated whether or not the level of reduced Cyt.aa_3 could be used as a real-time indicator of any neurological prognosis.

Methods

A spectrophotometer (OM110 NIRS, Shimadzu, Kyoto, Japan) was used, following previously published analytical procedures [3–5]. After induction of anesthesia, but before any surgical procedure, two probes (light source and detector) were placed 4 cm apart on the lateral forehead. This enabled us continuous measurement by NIRS in the brain cortex of relative changes in the concentration of oxygenated hemoglobin (Oxy-Hb) and deoxygenated hemoglobin (Deoxy-Hb) and of the redox state of cytochrome oxidase (Cyt.aa_3).

Deep body temperature of the forehead was continuously monitored by a deep body temperature monitor (Coretemp, CTM-204, Terumo, Tokyo, Japan) placed on the forehead.

Case reports

Two patients, a 67-year-old man and a 63-year-old woman, underwent aortic dissection (DeBakey type I). The transverse aortic arch was repaired following cardiopulmonary bypass (CPB) and separate cerebral perfusion (SCP) under profound hypothermia. Anesthesia was induced and maintained with isoflurane and fentanyl in both cases. Figure 1 shows the relative changes in Oxy-Hb, Deoxy-Hb, and the redox state of Cyt.aa_3 at the initiation of CPB and SCP in case 1. The immediate decrease in Oxy-Hb at the beginning of CPB corresponded with an acute hemodilution (hematocrit decreased from 37% to 22%) but, at this time, the redox state of Cyt.aa_3 did not change. After the carotid artery was clamped, Oxy-Hb decreased further, and oxidized Cyt.aa_3 decreased rapidly. Following the start of SCP (blood temperature was maintained at 14°C), Oxy-Hb and oxidized Cyt.aa_3 started to increase, while Deoxy-Hb was gradually decreased. After gradual rewarming, the rectal temperature reached 32°C, but the blood temperature in the SCP still remained at around 20°C. The relative changes in Oxy-Hb, Deoxy-Hb and Cyt.aa_3 after termination of SCP in cases 1 and 2 are shown in Figs. 2 and 3. Oxy-Hb and oxidized Cyt.aa_3 fell rapidly after SCP was replaced by systemic perfusion but, in case 1, Cyt.aa_3 gradually reverted to the baseline value within 2 h (Fig. 2). This patient emerged from anesthesia uneventfully. On the other hand, in case 2, the hematocrit value was increased from 20% to 26%, Oxy-Hb reverted to its baseline level, Deoxy-Hb was gradually

Address correspondence to: Y. Kakihana
Received for publication on June 27, 1995; accepted on February 19, 1996

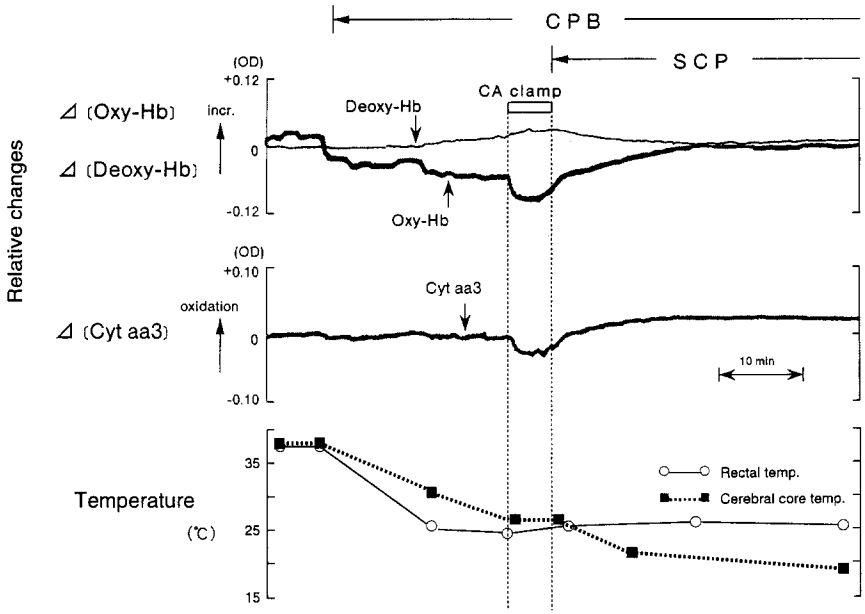

Fig. 1. Changes in Oxy-Hb, Deoxy-Hb, Cyt.aa$_3$, rectal temperature, and deep body temperature of the forehead at the initiation of CPB and SCP, and during CA clamp in case 1. *Oxy-Hb*, oxygenated hemoglobin; *Deoxy-Hb*, deoxygenated hemoglobin; *Cyt.aa$_3$*, cytochrome oxidase; *CPB*, cardiopulmonary bypass; *SCP*, separate cerebral perfusion; *CA*, carotid artery; *OD*, optical density. *Upward deflections* indicate: in Oxy-Hb and Deoxy-Hb, an increase in relative concentration; in Cyt.aa$_3$, an increase in oxidation form

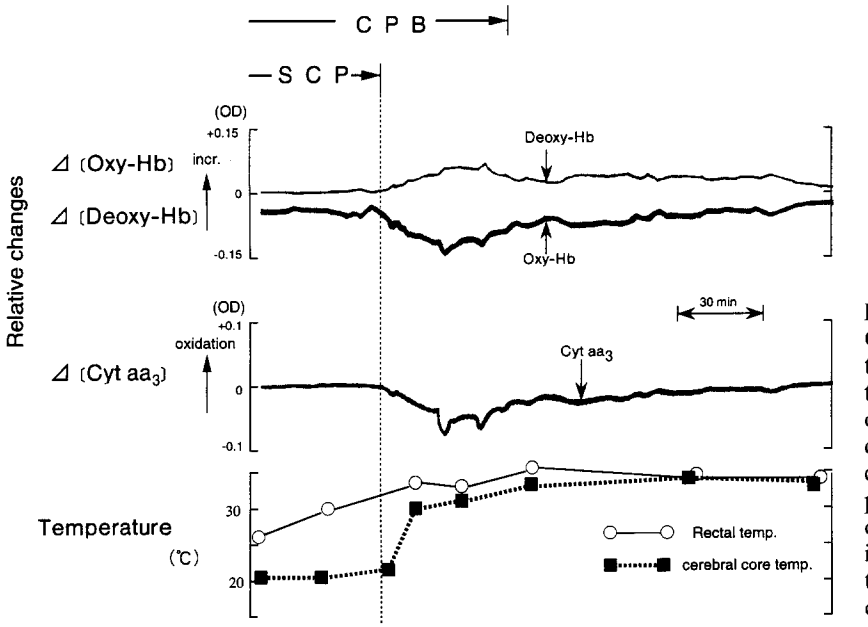

Fig. 2. Changes in Oxy-Hb, Deoxy-Hb, Cyt.aa$_3$, rectal temperature, and deep body temperature of the forehead after termination of SCP and CPB in case 1. *Oxy-Hb*, oxygenated hemoglobin; *Deoxy-Hb*, deoxygenated hemoglobin; *Cyt.aa$_3$*, cytochrome oxidase; *CPB*, cardiopulmonary bypass; *SCP*, separate cerebral perfusion; *OD*, optical density. *Upward deflections* indicate: in Oxy-Hb and Deoxy-Hb, an increase in relative concentration; in Cyt.aa$_3$, an increase in oxidation form

increased, and the hemodynamic state was stable, while oxidized Cyt.aa$_3$ continued to fall and never recovered (Fig. 3). This patient suffered from severe brain damage after surgery.

Discussion

Despite the many improvements in cardiopulmonary bypass technology and in surgical and anesthetic methods, it remains likely that all patients undergoing cardiac or thoracic aortic surgery suffer some degree of injury to the nervous system. The incidence of brain damage after repair of the transverse aortic arch has remained relatively high, a major cause of morbidity after such surgery being brain damage due to cerebral ischemia and hypoxia [6,7]. Therefore, maintaining adequate flow, pressure, and temperature in the CPB or SCP are the most important factors in preventing neurological complications. NIRS was recently proposed for the continuous and noninvasive monitoring of changes in hemoglobin oxygen saturation and the redox state of Cyt.aa$_3$ in the cerebral cortex [8]. Both hemoglobin and Cyt.aa$_3$ have a broad absorption band in the near-infrared region [9,10] and light in this region easily penetrates biological tissues. Cyt.aa$_3$ is a terminal

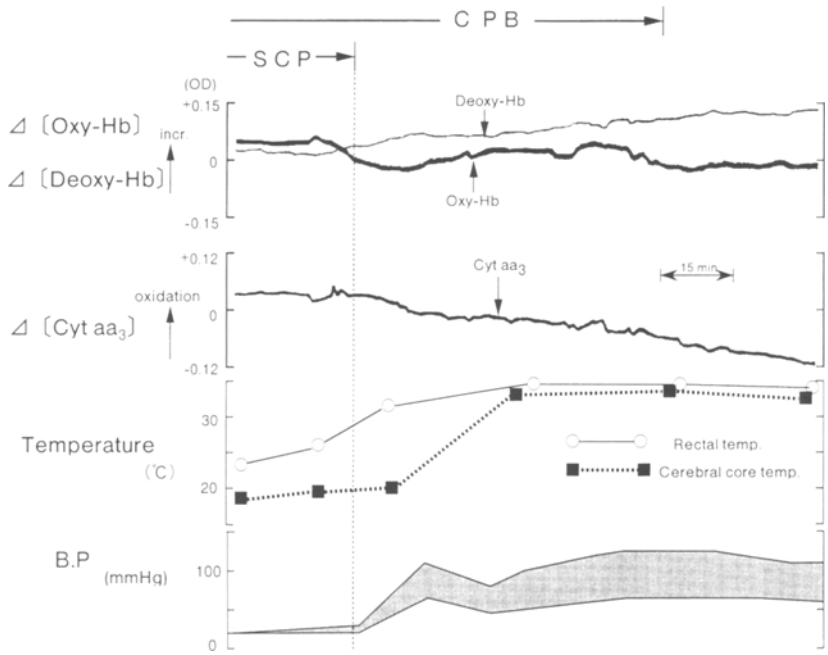

Fig. 3. Changes in Oxy-Hb, Deoxy-Hb, Cyt.aa$_3$, rectal temperature, deep body temperature of the forehead, and systemic blood pressure after termination of SCP and CPB in case 2. *Oxy-Hb*, oxygenated hemoglobin; *Deoxy-Hb*, deoxygenated hemoglobin; *Cyt.aa$_3$*, cytochrome oxidase; *CPB*, cardiopulmonary bypass; *SCP*, separate cerebral perfusion; *BP*, systemic blood pressure; *OD*, optical density. *Upward deflections* indicate: in Oxy-Hb and Deoxy-Hb, an increase in relative concentration; in *Cyt.aa$_3$*, an increase in oxidation form

enzyme of the respiratory chain which catalyzes approximately 95% of all O_2 utilization. Furthermore, as reported by Tamura et al. [11], Pcr/Pi measured by NMR simultaneously decreases with the reduction of Cyt.aa$_3$ measured by NIRS under hypoxic conditions. For this reason, monitoring of the oxidation-reduction state of Cyt.aa$_3$ provides information about the cerebral oxygen metabolism and energy storage. However, the accuracy of the measurement of the redox state of Cyt.aa$_3$ remains controversial because of many remaining problems with the methods, especially any algorithm containing a constant value for the absorption coefficient of Cyt.aa$_3$, which is not constant but varies with the energy levels [12]. We used new methods to measure the redox state of Cyt.aa$_3$, thus overcoming several technological problems in the measurement of Cyt.aa$_3$ during hematocrit values from 5% to 45% [4]. In our two cases, hemodilution (hematocrit values 15%–35%) during initiation of CPB caused a reduction in the cerebral hemoglobin concentration because of the decrease in the total hemoglobin concentration, which results in changes in the summation of Oxy-Hb and Deoxy-Hb. On the other hand, the redox state of Cyt.aa$_3$ did not change, presumably because there was sufficient oxygen in the brain tissues. When the carotid artery was clamped during insertion or extraction of the cerebral perfusion tube, oxidized Cyt.aa$_3$ decreased rapidly because of the occurrence of severe cerebral ischemia under the cessation of cerebral blood flow. Cyt.aa$_3$ was also reduced during the warming period, especially after SCP replaced by systemic perfusion, because of a huge increase in cerebral oxygen consumption (Figs. 2, 3). However, while the Cyt.aa$_3$ level recovered in patient 1, a gradual and persistent reduction was observed in patient 2, who eventually suffered from severe brain damage. From our observations, it appears that, while the hemoglobin oxygen saturation is an early indicator of cerebral hypoxia-ischemia and reflects a change in O_2 supply-O_2 demand, its level does not tell us whether or not the cerebral oxygenation is sufficient. On the other hand, the redox state of Cyt.aa$_3$ is a critical indicator of cerebral tissue oxygenation and energy store and, therefore, monitoring the redox state of Cyt.aa$_3$ can serve as an alarm of critical levels.

In summary, in these two cases, changes in the redox state of Cyt.aa$_3$ were measured with NIRS during aortic arch surgery. A reduction in Cyt.aa$_3$ indicated severe cerebral hypoxia or ischemia. These data suggest that the level of reduced Cyt.aa$_3$ could be used as a real-time indicator of critical conditions in cerebral tissues.

References

1. Brennan RW, Patterson RH, Kessler J (1971) Cerebral blood flow and metabolism during cardiopulmonary bypass: Evidence of microembolic encephalopathy. Neurology 21:665–672
2. Smith PLC, Treasure T, Newman SP, Joseph P, Ell PJ, Schneidau A, Harrison MJG (1986) Cerebral consequences of cardiopulmonary bypass. Lancet 1:823–825
3. Hazeki O, Tamura M (1988) Quantitative analysis of hemoglobin oxygenation state of rat brain in situ by near-infrared spectrophotometry. J Appl Physiol 64:796–802
4. Hazeki O, Tamura M (1989) Near-infrared quadruple wavelength spectrophotometry of rat head. Adv Exp Med Biol 248:63–69

5. Hoshi Y, Tamura M (1993) Dynamic changes in cerebral oxygenation in chemically induced seizures in rats: study by near-infrared spectrophotometry. Brain Res 603:215–221
6. Blauth C, Arnold J, Kohner EM, Taylor KM (1986) Retinal microembolism during cardiopulmonary bypass demonstrated by fluorescein angiography. Lancet 2:837–839
7. Stockard JJ, Bickford RG, Chir B, Schauble JF (1973) Pressure dependent cerebral ischemia during cardiopulmonary bypass. Neurology 23:521–529
8. Jobsis FF (1977) Noninvasive, infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters. Science 198:1264–1267
9. Takatani S, Cheung PW, Ernst EA (1980) A noninvasive tissue reflectance oxymeter. An instrument for measurement of tissue hemoglobin oxygen saturation in vivo. Ann Biochem Eng 8:1–15
10. Wharton DC, Tzagoloff A (1964) Studies on the electron transfer system. LV2. The near-infrared absorption band of cytochrome oxidase. J Biol Chem 239:2036–2041
11. Tamura M, Hazeki O, Nioka S, Chance B, Smith DS (1987) The simultaneous measurements of tissue oxygen concentration and energy state by near-infrared and nuclear magnetic resonance spectroscopy. Adv Exp Med Biol 22:359–363
12. Hoshi Y, Hazeki O, Tamura M (1993) Oxygen dependence of redox state of copper in cytochrome oxidase in vitro. J Appl Physiol 74:1622–1627