Changes in Arterial Blood PO_2, PCO_2, and pH during Deep Hypothermic Circulatory Arrest in Adults

Safe limits of time and temperature during deep hypothermic circulatory arrest (DHCA) still remain controversial. Furthermore, continuous changes of PaO_2, $PaCO_2$, and pH have never been measured during DHCA in humans. Continuous intraarterial blood gas (CIABG) monitoring is a new technology allowing us to study chronological changes occurring due to metabolism during DHCA. When the patients' temperature reached 18~20℃ following establishment of cardiopulmonary bypass (CPB), circulatory arrest was initiated. After a 20-minute period of DHCA, reperfusion commenced with 18℃ blood. We continuously monitored PaO_2, $PaCO_2$, and pH immediately before, during and following DHCA. Data was analyzed by Student's t-test. PaO_2, $PaCO_2$, and pH of pre- and 5 minutes post DHCA were not significantly different from each other. However, during DHCA, the PaO_2 was significantly decreased from 229±34 to 30±23 mmHg at 20-minute intervals. But the $PaCO_2$ increased significantly after 20 minutes of circulatory arrest from 34±5 to 42±6 mmHg. However, the pH did not change significantly over the 20-minute period. The PaO_2 level after 20 minutes is much lower than before DHCA, it would be well tolerated in normothermic adults. The PO_2 level in the brain may be even lower given its high metabolic rate. So measuring arterial PO_2 continuously during DHCA may provide a surrogate method for determining maximum safe time under DHCA for adults.

(JKMS 1997; 12: 199~203)

Key Words : *Induced heart arrest, Induced hypothermia, Brain metabolism, Blood gas monitoring*

Tae Sung Kim, M.D., Byeong Seong Kang, M.D., Hyun Soo Kim, M.D., Kwang Min Kim, M.D.

Department of Anesthesiology,
Hallym University Medical Center,
Seoul, Korea

Received : November 25, 1996
Accepted : March 18, 1997

Address for correspondence
Tae Sung Kim, M.D.,
Department of Anesthesiology,
Hangang Sacred Heart Hospital,
94-200 Yeoungdeungpo-Dong,
Yeoungdeungpo-Ku, Seoul 150-020, Korea
Tel : (02) 639-5503, Fax : (02) 631-4387

INTRODUCTION

Since the introduction of deep hypothermic circulatory arrest (DHCA) in the early 1960s, it has been increasingly used in centers with expertise in open-heart surgery for infants, children, and adults. The use of this technique is based on the premise that there is a safe duration of total circulatory arrest that is inversely related to body temperatures (1). The organ with the shortest safe circulatory arrest time is the brain. Conflicting reports of transient cerebral dysfunction and late neurologic adverse effects after DHCA have generated considerable controversy about its use. Furthermore, PaO_2, $PaCO_2$, and pH can not be measured during DHCA in humans because of sampling problems. Specifically, withdrawing blood from a patient during DHCA may cause severe neurologic deficit due to air embolism. It has recently become possible to continuously monitor intraarterial blood before, during, and after DHCA due to technological advancement (2). The continuous intra-arterial blood gas (CIABG) monitoring system (PB3300, Puritan-Bennett Corporation, Carlsbad, California, USA) continuously measures and displays arterial blood values for PaO_2, $PaCO_2$, and pH. The system consists of a sterile, disposable, fluorescent-based, 3-meter fiberoptic sensor (with a 10-cm invasive portion), and a microprocessor-controlled monitor with a self-contained calibration unit and detatchable display and control panel. The design of the sensing element is based on fluorescent dyes that interact with the desired analytes (PaO_2, $PaCO_2$, pH) at the tip of the optic fibers. Light of specific wavelengths is transmitted from the monitor via the sensor's fiber optic cable to the sensor tip. Return light from the tip is processed by the monitor and displayed as the patient's values. We hypothesized that there would not be any significant changes in PaO_2, $PaCO_2$, and pH during 20-minute DHCA at 18℃ because our patients have been tolerating circulatory arrest at this temperature and for this duration without significant neurologic injuries.

MATERIALS AND METHODS

After institutional review board approval and informed consent, six adult patients undergoing pulmonary arterial thromboendarterectomy (PTE) with the use of DHCA were studied. Ages ranged from 18 years to 65 years.

Anesthetic management was identical in all patients and consisted of fentanyl (100 μg/kg), 100% oxygen, pipecuronium, midazolam (0.1 mg/kg) and controlled ventilation with tidal volume 10~15 ml/kg and respiratory rate to maintain a 40 mmHg of $PaCO_2$. Prior to induction, a 20-gauge, 3.8 cm cannula was inserted into the radial artery of each patient for continuous arterial blood gas monitoring. Pressure waveform tracings were recorded before and after sensor placement to ensure that pressure monitoring was not altered. Patients were simultaneously monitored with femoral and pulmonary arterial catheters. Temperature was monitored by probes placed in nasopharynx, bladder, rectum, and via a Swan-Ganz catheter. Following median sternotomy, cardiopulmonary bypass was established with ascending aortic and two caval cannulation to improve venous return and allow for more rapid cooling.

During CPB, nonpulsatile pump flow with a membrane oxygenator was maintained at rate of 2.4 L/min/m^2 throughout the cooling phase to maximize cooling to the organs. All patients were cooled by maintaining a 10℃ gradient between arterial blood and bladder/rectal temperature. As the core temperature decreased, venous saturation increased, typically achieving mixed venous saturation of 80% at 25℃ and 90% at 20℃ (3). Blood gases were regulated according to the alpha-stat method (maintaining a constant buffering capacity of the alpha imidazole ring of the histidine amino acid moiety of hemoglobin during hypothermic condition) (4). Once the bladder/rectal and nasopharyngeal temperature were 18 ℃, Suritol was administered up to 7 mg/kg until the EEG became isoelectric. All monitoring line stopcocks toward the patient were turned off to eliminate the possibility of entraining air into the patient's circulation during exsanguination. The arterial pump was turned off and arterial cannula from the CPB pump clamped. The venous cannulae remained open to exsanguinate the patient's blood into the venous reservoir. Circulatory arrest times were limited to 20-minute periods. After 20 minutes the patients were reperfused at a low flow rate (0.7 L/min/m^2) with 18℃ blood until their venous saturation returned to 90% (- this took 6~15 minutes). This operation typically requires two to five periods of circulatory arrest of varying length. Data were compared between patients during 1st 20-minute period of DHCA only. Data of later periods were not comparable because of a markedly inconsistent time period for 2nd and subsequent periods of circulatory arrest. We continuously monitored PaO_2, $PaCO_2$, and pH using a PB 3300 CIABG monitoring system (Puritan-Bennett, Calsbad, CA, USA). Although formal psychometric studies were not performed, neurologic function of patients was evaluated grossly after recovering from the operation and prior to discharge from the surgical intensive care unit on post-op day 2 or 3. These evaluations included level of consciousness, Glasgow coma scale (GCS), and motor and sensory functions. Motor functions were classified into six categories as 0 ; no contraction, 1 ; able to contract extremity but not move muscle, 2 ; able to move muscle and extremity but not against gravity, 3 ; able to move muscle and extremity against gravity, 4 ; intermediate strength, 5 ; full strength. Data were analyzed by Student's t-test. Significance was assigned when $p<0.05$.

RESULTS

PaO_2, $PaCO_2$, and pH of pre DHCA and 5 minutes post DHCA were not significantly different from each other. Changes of Mean PaO_2, $PaCO_2$, and pH are shown in Table 1.

PaO_2 : Pre DHCA, mean PaO_2 was 229±34 mmHg. Following initiation of DHCA, PaO_2 declined sharply and continuously. The PaO_2 at 5, 10, 15, 20 minutes of DHCA were 121±47, 58±36, 37±29, 30±23 mmHg, respectively. These values were all statistically significant decreases compared to the PaO_2 of pre DHCA. Following re-institution of CPB the PaO_2 quickly returned to the pre DHCA value (Fig. 1).

$PaCO_2$: Pre DHCA, mean $PaCO_2$ was 34±5

Table 1. PaO_2, $PaCO_2$, and pH just before, during, and following DHCA

	Pre-DHCA	During DHCA				After DHCA 5 min.
PaO_2(mmHg)	229±34	121±47*	58±36*	37±29*	30±23*	253±39
$PaCO_2$(mmHg)	34±5	37±6	40±6	41±6*	42±6	37±6
pH	7.40±0.1	7.35±0.1	7.34±0.1	7.34±0.1	7.33±0.1	7.36±0.1

Values shown are Mean±SD for the various time periods. * = Statistically significant ($p<0.05$) compared to pre DHCA

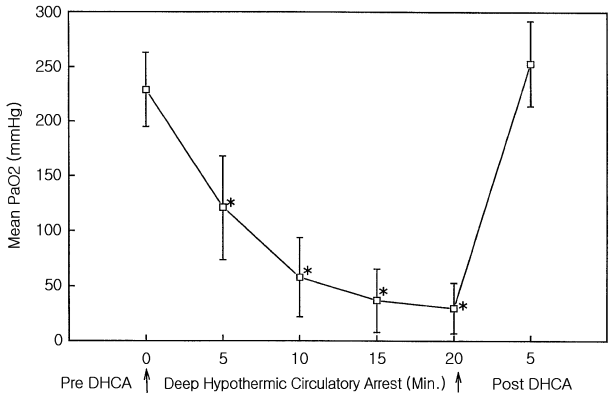

Fig. 1. PaO_2 just before, during, and 5 minutes following DHCA.
*= Statistically significant ($p<0.05$) compared to pre DHCA.
DHCA: Deep Hypothermic Circulatory Arrest.

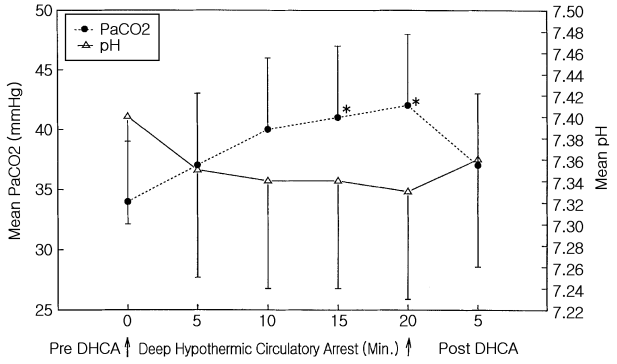

Fig. 2. $PaCO_2$ and pH just before, during, and 5 minutes following DHCA.
*= Statistically significant ($p<0.05$) compared to pre DHCA.
DHCA: Deep Hypothermic Circulatory Arrest.

mmHg. The $PaCO_2$ increased to 37 ± 6, 40 ± 6, 41 ± 4, 42 ± 6 mmHg at 5, 10, 15, 20 minutes during DHCA, respectively. However the statistical significance was only noted at the 15 and 20 minutes after DHCA compared to the $PaCO_2$ value of pre DHCA. Following re-institution of CPB, the $PaCO_2$ quickly returned to the pre DHCA value (Fig. 2).

pH: During DHCA, the pH decreased gradually but not significantly, compared to pre DHCA. Following DHCA, the pH increased toward the pre DHCA value (Fig. 2).

Neurologic outcome: Neurologic function of all of the patients assessed on the postoperative 2~3 days was grossly normal. All patients were oriented to time, place, and person with normal gross motor and sensory examinations (Table 2).

Table 2. Neurologic outcome after DHCA

LOC	Level of Consciousness Mentation			A&O×3 Normal
SPEECH	Speech			Clear
PUPILS	Size(mm)		R L	3 3
	Shape		R L	Round Round
	Reaction		R L	Brisk Brisk
GCS	Eye Opening Best Verbal Response Best Motor Response Total GCS Score			4 5 6 15
MOTOR	Left Arm	Motor	Response Strength	Follows Commands 5
	Left Leg	Motor	Response Strength	Follows Commands 5
	Right Arm	Motor	Response Strength	Follows Commands 5
	Right Leg	Motor	Response Strength	Follows Commands 5

Neurologic examinations were performed by physicians and nurses in Surgical Intensive Care Unit on Post Operative Day 2 or 3. LOC= level of consciousness. A&O ×3 = awake, oriented to person, place, time. GCS = Glasgow coma scale.
Motor examination; 0 = No contraction, 1 = Able to contract, but not move muscle, 2 = Able to move muscle and extremity but not against gravity, 3 = Able to move muscle and extremity against gravity, 4 = Intermediate strength, 5 = Full strenth.

DISCUSSION

Safe periods of DHCA remain controversial because of conflicting results from previous investigations. The variable results stem from studying disparate populations (adult vs pediatric) and physiologic end points (5~10).

The collection of arterial blood from patients during DHCA would be difficult with danger due to the likelihood of entraining air or administering flush solution which is warm and with low oxygen carrying capacity (saline) into the cardiovascular system and possibly into the brain. Following recent development of optical technologies, continuous arterial blood gas monitoring has been possible and indeed commercially available (2, 11~13). This technology is not only useful for continuous measuring arterial blood gas changes during CPB but also suitable for measuring changes when extraction of blood from patients is not allowed as in DHCA. We describe here the changes in arterial PO_2, PCO_2, and pH during DHCA as a surrogate of changes occurring in the brain.

In this study, the PaO_2 fell from a mean of 230 mmHg prior to DHCA to a mean of near 30 mmHg after 20 minutes of DHCA. During the same interval, the $PaCO_2$ increased from a mean of 34 mmHg to 42 mmHg. These abrupt and continuous falling of PaO_2 and significant increasing of $PaCO_2$ after DHCA suggest that oxygen consumption and CO_2 production occurred to a significant extent despite a markedly decreased temperature (18℃) during DHCA. Because the organ with the shortest safe circulatory arrest time is the brain (1, 4), it is likely that the cerebral PO_2 decreases to an even lower value than the arterial blood during the 20-minute DHCA period. Indeed, Fox et al. showed that decreased but always present cerebral metabolic rate and oxygen requirement by progressive decreases in jugular venous oxygen saturation with decreased flows (to 0.5 L/min/m^2) at 20℃ in humans with CPB (14). Others have confirmed persistent cerebral metabolism during hypothermia (15, 16). Cerebral tissue oxygen tension have been reported by Bloor et al. approached to 0 mmHg after 12 to 15 minutes of circulatory arrest at 20℃ (17).

Cold induced reduction in cerebral metabolic rate is a well known mechanism for protection against anoxic and ischemic insults (18). Indeed, systemic hypothermia decreases the cerebral metabolic rate for oxygen ($CMRO_2$) by reduction of 6%~7% per degree Celcius temperature. Murkin et al. demonstrated a profound reduction in $CMRO_2$ from 1.67 mL/lOOg/min before CPB to 0.42 mL/lOOg/min during hypothermic non-pulsatile CPB at 26℃ (19). Some studies confirming a cerebral Q10 of approximately 2.4 suggest that a drop in cerebral temperature to 20℃ will decrease the metabolic rate and oxygen consumption to 20% of the baseline rate measured at 37℃ (a factor of about 5) (20, 21). Protection exclusively by metabolic rate reduction with this degree of hypothermia gives a fivefold increase in the safe circulatory arrest time at 37℃ (three to four min), which suggest that 15 to 20 minutes of arrest is safe at 20℃. Theoretical calculations based upon adult oxygen reserves and decreases in oxygen consumption with hypothermia suggest safe circulatory arrest times of 6 minutes at 30℃, 18 minutes at 20℃, 30 minutes at 15℃, and 56 minutes at l0℃ (22). Although extensive clinical experiences in many centers have demonstrated that periods of circulatory arrest up to 60 minutes at temperature less than 20℃ are tolerated by the central nervous system (CNS) in infants without demonstrable long-term neurologic dysfunction, results in the adult population are less uniform when DHCA time exceeds 20 minutes (5, 6). Certainly, the lowering of the metabolic rate by deep hypothermia plays a major role in CNS protection. However, hypothermia alone may not be sufficient to explain the prolonged cerebral protection observed clinically. Perhaps, other protective mechanisms are operative. It may be a protective effect by decreasing ATP depletion and lactic acid production (23, 24). But ischemic protection of the CNS during DHCA is poorly understood at this time. However we believe the mechanism of impaired neurologic function is chiefly related to hypoxic injury given the dangerously low PaO_2 documented at the 20-minute mark.

Beginning DHCA with an initially higher PaO_2 may provide additional protective advantages. Likewise limiting DHCA to periods less than 20 minutes combined with short period of low-flow bypass may be beneficial. However these theories have not yet been fully tested in humans.

REFERENCES

1. Kirklin JW, Barratt-Boyes BC. *Cardiac Surgery. Ist ed. New York : Churchill Livingstone, 1993 ; 62-127.*
2. Larson C, Vender J, Seiver A. *Multisite evaluation of continuous intraarterial blood gas monitoring system. Anesthesiology 1994 ; 81 : 543-52.*
3. Winkler MH, Rohrer CH, Ratty SC, Jamieson S, Dembitsky W, Moser K. *Perfusion techniques of profound hypothermia and circulatory arrest for pulmonary thromboendarterectomy. J Extra-Corp Technol 1990 ; 22 : 57-60.*
4. Hickey PR, Anderson NP. *Deep hypothermic circulatory arrest : A review of pathophysiology and clinical experience as a basis for anesthetic management. J Cardiothorac Vasc Anesth 1987 ; 1 : 137-55.*

5. Brunberg JA, Doty DB, Reilly EL. *Choreoathetosis in infants following cardiac surgery with deep hypothermia and circulatory arrest. J Pediatr 1974 ; 84 : 231-5.*
6. Coles JG, Taylor MJ, Pearce JM. *Cerebral monitoring of somatosensory evoked potentials during profoundly hypothermic circulatory arrest. Circulation 1984 ; 70(suppl 1) : 96-102.*
7. Ergin MA, Galla JD, Lansman SL. *Hypothermic circulatory arrest in operations on the thoracic aorta. J Thorac Cardiovasc Surg 1994 ; 107 : 78-99.*
8. Fisk GC, Wright JS, Hicks RG. *The influence of duration of circulatory arrest at 20℃ on cerebral changes. Anaesth lntensive Care 1976 ; 4 : 126-34.*
9. Kirklin JW, Dawson B, Devloo RA, Theye RA. *Open intracardiac operations : Use of circulatory arrest during hypothermia induced by blood cooling. Ann Surg 1961 ; 154 : 769-76.*
10. Messmer Bj, Schallberger U, Gattiker R, Senning A. *Psychomotor and intellectual development after deep hypothermia and circulatory arrest in early infancy. J Thorac Cardiovasc Surg 1976 ; 72 : 495-502.*
11. Shapiro BA. *In vivo monitoring of arterial blood gases and pH. Resp Care 1992 ; 37 : 165-9.*
12. Shapiro BA, Mahute CK, Cane RD, Gilmour IJ. *Clinical performance of a blood gas monitor : A prospective multicenter trial. Crit Care Med 1993 ; 21 : 487-94.*
13. Zimmerman JL, Dellinger RP. *Initial evaluation of a new intraarterial blood gas system in humans. Crit Care Med l993 ; 21 : 495-500.*
14. Fox LS, Blackstone EH, Kirklin JW, Stewart RW, Samuelson PN. *Relationship of whole body oxygen consumption to perfusion flow rate during hypothermic cardiopulmonary bypass. J Thorac Cardiovasc Surg 1982 ; 83 : 239-48.*
15. Fox LS, Blackstone EH, Kirklin JW, Bishop SP, Bradely EL. *Relationship of brain blood flow and oxygen consumption to perfusion flow rate during hypothermic cardiopulmonary bypass. J Thocac Cardiovasc Surg 1984 ; 87 : 658-64.*
16. Govier AV, Reves JG, McKay RD, Karp RB, Zorn GL, Morawetz RB, Smith LR, Adams M, Freeman AM. *Factors and their influence on regional cerebral blood flow during nonpulsatile cardiopulmonary bypass. Ann Thorac Surg 1984 ; 38 : 592-600.*
17. Bloor BM, Hellinger FR, Neville WE. *Oxygen tension of the brain and its modification by hypothermia. Second International Congress of Neurosurgery. Washington DC, 1961.*
18. Steen PA, Newberg L, Middle JH, Michenfelder JD. *Hypothermia and barbiturates : Individual and combined effects on canine cerebral oxygen consumption. Anesthesiology 1983 ; 58 : 527-32.*
19. Murkin JM, Farrar JK, Tweed WA, McKenzie KN, Cuirauden G. *Cerebral autoregulation and flow/metabolism coupling during cardiopulmonary bypass : The influence of $PaCO_2$. Anesth Analg 1987 ; 66 : 825-32.*
20. Astrup J, Sorensen PM, Sorensen HR. *Inhibition of cerebral oxygen and glucose consumption in dog by hypothermia, pentobarbital, and lidocaine. Anesthesiology 1981 ; 55 : 263-8.*
21. Murkin JM, Farrar JK, Tweed WA. *Relationship between cerebral blood flow and O_2 consumption during high-dose narcotic anesthesia for cardiac surgery. Anesthesiology 1985 ; 63 : 44-50.*
22. Vadot L, Estanove S, Gounod R. *Calcul de l'arrest circulatoire admissible en hypothermie. Anesth Analg (Paris) 1963 ; 20 : 61-5.*
23. Carlsson C, Hagerdal M, Siesjo BK. *Protective effect of hypothermia in cerebral oxygen deficiency caused by arterial hypoxia. Anesthesiology 1976 ; 44 : 27-35.*
24. Michenfelder JD, Theye RA. *The effects of anesthesia and hypothermia on canine cerebral ATP and lactate during anoxia produced by decapitation. Anesthesiology 1970 ; 33 : 430.*