Cerebral Oxygenation and Hemodynamics During Induction of Extracorporeal Membrane Oxygenation as Investigated by Near Infrared Spectrophotometry

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ABSTRACT. *Objective.* To investigate cerebral oxygenation and hemodynamics in relation to changes in some relevant physiologic variables during induction of extracorporeal membrane oxygenation (ECMO) in newborn infants.

Methods. Twenty-four newborn infants requiring ECMO were studied from cannulation until 60 minutes after starting ECMO. Concentration changes of oxyhemoglobin (cO_2Hb), deoxyhemoglobin (cHHb), total hemoglobin (ctHb), and (oxidized-reduced) cytochrome aa_3 ($cCyt.aa_3$) in cerebral tissue were measured continuously by near infrared spectrophotometry. Heart rate (HR), transcutaneous partial pressures of oxygen and carbon dioxide ($tcPO_2$ and $tcPCO_2$), arterial O_2 saturation (saO_2), and mean arterial blood pressure (MABP) were measured simultaneously. Intravascular hemoglobin concentration (cHb) was measured before and after starting ECMO. In 18 of the 24 infants, mean blood flow velocity (MBFV) and pulsatility index (PI) in the internal carotid and middle cerebral arteries were also measured before and after starting ECMO using pulsed Doppler ultrasound.

Results. After carotid ligation, cO_2Hb decreased whereas cHHb increased. After jugular ligation, no changes in cerebral oxygenation were found. At 60 minutes after starting ECMO, the values of cO_2Hb, saO_2, $tcPO_2$, and MABP were significantly higher than the precannulation values, whereas the value of cHHb was lower. There were no changes in $cCyt.aa_3$, $tcPCO_2$, and HR, whereas cHb decreased. The MBFV was significantly increased in the major cerebral arteries except the right middle cerebral artery, whereas PI was decreased in all measured arteries. Cerebral blood volume, calculated from changes in ctHb and cHb, was increased in 20 of 24 infants after starting ECMO. Using multivariate regression models, a positive correlation of ΔctHb (representative of changes in cerebral blood volume) with ΔMABP and a negative correlation with $\Delta tcPO_2$ were found.

Conclusions. The alterations in cerebral oxygenation after carotid artery ligation might reflect increased O_2 extraction. Despite increase of the cerebral O_2 supply after starting ECMO, no changes in intracellular O_2 availability were found, probably because of sufficient preservation of intracellular cerebral oxygenation in the pre-ECMO period despite prolonged hypoxemia. The increase in cerebral blood volume and cerebral MBFV may result from the following: (1) reactive hyperperfusion, (2) loss of autoregulation because of prolonged hypoxemia before ECMO and/or decreased arterial pulsatility, or (3) compensation for hemodilution related to the ECMO procedure. *Pediatrics* 1995;95:555–561; *extracorporeal membrane oxygenation, near infrared spectrophotometry, cerebral oxygenation, cerebral hemodynamics, autoregulation.*

ABBREVIATIONS. ECMO, extracorporeal membrane oxygenation; PaO_2, arterial partial pressure of oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide; NIRS, near infrared spectrophotometry; saO_2, arterial oxygen saturation; cO_2Hb, oxyhemoglobin concentration; cHHb, deoxyhemoglobin concentration; ctHb, total hemoglobin concentration; $cCyt.aa_3$, (oxidized – reduced) cytochrome aa_3 concentration; cHb, intravascular hemoglobin concentration; CBV, cerebral blood volume; MBFV, mean blood flow velocity; PI, pulsatility index; HR, heart rate; MABP, mean arterial blood pressure; $tcPO_2$, transcutaneous partial pressure of oxygen; $tcPCO_2$, transcutaneous partial pressure of carbon dioxide; CBF, cerebral blood flow.

Extracorporeal membrane oxygenation (ECMO) is used to treat newborn infants with severe respiratory failure who do not respond adequately to conventional treatment.[1,2] The principle of ECMO is based on prolonged partial cardiopulmonary bypass. The survival rate is over 80%, but cerebrovascular injury is an important complication.[2,3] Generally, the ECMO patient is hypoxemic for hours before ECMO is started. Induction of ECMO may result in significant changes in cerebral circulation caused by ligation of the right common carotid artery and internal jugular vein, decreased arterial pulsatility because of cardiopulmonary bypass, and rapid changes in arterial partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$). However, in humans the effects of these changes on cerebral oxygenation and hemodynamics and their role in the pathophysiology of cerebrovascular injury have not been investigated extensively.

Near infrared spectrophotometry (NIRS) offers the possibility of noninvasive and continuous bedside investigation of cerebral oxygenation in newborn infants.[4,5] We reported preliminary observations of marked changes in cerebral oxygenation and hemodynamics during induction of ECMO.[6,7] In this report, we present further data and describe the relation between changes in cerebral oxygenation and hemodynamics and changes in some physiologic variables during induction of ECMO.

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METHODS

Study Population

After obtaining informed parental consent, we studied 24 ECMO patients (17 male and 7 female, gestational age 35.1 to 40.9 weeks, birth weight 2100 to 4330 g). The study was approved by the University Hospital ethics committee. The indication for ECMO was failure to maintain normoxemia despite adequate conventional treatment using mechanical ventilation, sedation, muscle paralysis, and vasoactive drugs. All infants met the established entry criteria for ECMO[1]; infants with cerebral hemorrhage or cerebral malformation were excluded. The underlying diseases were congenital diaphragmatic hernia (n = 9), meconium aspiration syndrome (n = 6), sepsis (n = 5), and persistent pulmonary hypertension from other causes (n = 4). During cannulation, the infants were anesthetized with fentanyl. Standard venoarterial ECMO was performed.[1] After starting ECMO, flow rate of the bypass was increased gradually during several minutes until reaching a level (ranging from 136 to 205 mL/kg/min) needed to maintain arterial O_2 saturation (saO_2) between 90% and 100% as measured by pulse oximetry. This flow rate is considerably higher than recommended,[1] but proved to be necessary and was not limited by egress of blood from the venous cannula. Subsequently, the ventilator was set at a lower level for pressure, rate, and fraction of inspired O_2 concentration to minimize barotrauma and O_2 toxicity. Systemic heparinization was established. Medication administered before ECMO was continued during the measurement period.

Near Infrared Spectrophotometry

This technique is based on the spectrophotometric measurement of changes in the absorption properties of hemoglobin and cytochrome aa_3 in the near infrared region, depending on their oxygenation state.[8] The NIRS equipment used was developed by the Department of Biomedical Engineering and Medical Physics, University of Keele, and produced by Radiometer (Copenhagen, Denmark).[5] Details of our NIRS measurement have been described elsewhere.[9] Briefly, near infrared light at 3 wavelengths (904, 845, and 775 nm) was transmitted through the skull by fiberoptic bundles. Using the described algorithm, concentration changes of oxyhemoglobin (ΔcO_2Hb), deoxyhemoglobin ($\Delta cHHb$), total hemoglobin ($\Delta ctHb$), and (oxidized – reduced) cytochrome aa_3 ($\Delta cCyt.aa_3$) were calculated from changes in absorption of near infrared light at the 3 wavelengths mentioned. The transmitting and receiving optodes were fixed to the skull at an angle of approximately 90°, one at the anterior fontanelle and the other at the right parietotemporal region. In all infants, the interoptode spacing was greater than 2.5 cm to ensure a constant pathlength multiplying factor,[10] which has been stated to be 4.39 times the interoptode spacing.[11] As the optical pathlength is wavelength dependent, some modification of the algorithm has been made.[12] ΔcO_2Hb and $\Delta cHHb$ reflect changes in cerebral O_2 supply, whereas $\Delta cCyt.aa_3$ reflects changes in cerebral O_2 availability.[13] When the intravascular hemoglobin concentration (cHb) is unchanged, $\Delta ctHb$ reflects changes in cerebral blood volume (CBV). Measurements were started just before the cannulation procedure and continued until 60 minutes after starting ECMO.

Doppler Ultrasound

After having observed a possible increase in CBV after starting ECMO,[6] we decided to add Doppler ultrasound investigation to the study, starting from infant number 7. Therefore, data for Doppler ultrasound investigations are available in only 18 of the 24 infants. Using a 5-MHz pulsed Doppler ultrasound unit (Ultramark 4, Advanced Technology Laboratories, Bothell, WA), the time-averaged mean blood flow velocity (MBFV) in the major cerebral arteries was measured intermittently. The pulsatility index (PI) [(peak systolic blood flow velocity – end-diastolic blood flow velocity)/mean blood flow velocity)] was also calculated. The flow velocities in the supraclinoid internal carotid artery were measured by placing the transducer at the anterior fontanelle. Measurement of the flow velocities in the middle cerebral artery in the Sylvian sulcus was performed by placing the transducer 1 to 2 cm in front of the right ear above the zygomatic process.[14] Using this approach, the insonation angle was assumed to be negligible (less than 10°). Blood flow velocities were calculated using the built-in calipers and calculation program. Measurements were performed just before application of the NIRS optodes at approximately 60 minutes before cannulation, and just after removal of the NIRS optodes at approximately 90 minutes after ECMO was started. The changes in MBFV and PI after induction of ECMO were expressed as percentages of their precannulation levels.

Measurement of Physiologic Variables

Using a neonatal monitor (Sirecust 404N, Siemens, Erlangen, Germany), heart rate (HR) and (umbilical) mean arterial blood pressure (MABP) were recorded continuously. The abdominal transcutaneous partial pressures of oxygen ($tcPO_2$) and carbon dioxide ($tcPCO_2$) (Transend, Sensormedics Corp, Anaheim, CA) and saO_2 at the foot by pulse oximetry (N 200, Nellcor Inc, Hayward, CA) were also measured continuously. Data on $tcPCO_2$ and $tcPO_2$ in three infants and data on saO_2 in one infant were not available because of technical failure. Blood samples for determination of PaO_2, $PaCO_2$, and cHb were drawn from the umbilical artery catheter just before cannulation and at 60 minutes after ECMO was started. Blood gas values and cHb were not corrected during this period.

Data Analysis

From each continuously recorded variable (cO_2Hb, cHHb, $cCyt.aa_3$, saO_2, $tcPO_2$, $tcPCO_2$, MABP, and HR), we obtained data on a 30-second period from six episodes: (A) just before the start of the cannulation procedure, (B) just before carotid ligation, (C) post-carotid ligation just before insertion of the arterial cannula, (D) just before jugular ligation, (E) post-jugular ligation just before insertion of the venous cannula, and (F) at 60 minutes after starting ECMO (see Fig 1). The differences in the mean values over the 30-second period between C and B, between E and D, and between F and A were calculated to determine the effects of carotid ligation, jugular ligation, and ECMO induction, respectively. First, the changes of the variables were analyzed with a multivariate version of the signed-rank test[15] to protect the overall confidence level. Thereafter, statistically significant variables were analyzed further with the signed-rank test. The *P* values presented in the results are those from the (univariate) signed-rank test. The changes in MBFV and PI at 90 minutes and in cHb, pH, PaO_2, and $PaCO_2$ at 60 minutes after starting ECMO, related to their precannulation values, were also calculated. Each difference was statis-

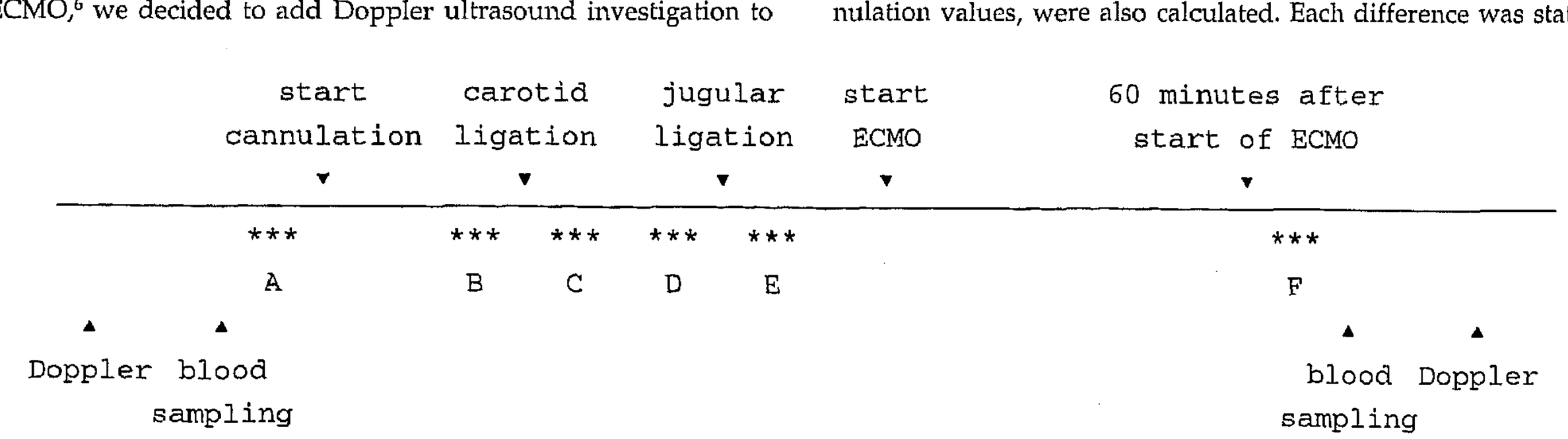

Fig. 1. Schematic representation of data selection from the continuous data registration (see text). ECMO, extracorporeal membrane oxygenation.

tically analyzed by performing the Wilcoxon signed-rank test. For both analyses, the level of significance was .05.

The CBV (expressed in mL/100 g) can be calculated from the following formula:

$$CBV = (4 \cdot ctHb)/(0.69 \cdot cHb),$$

where cHb is expressed in mmol/L and ctHb in μmol/100 g; 0.69 = cerebral-large vessel hematocrit ratio[16] and 4 = correction factor, as ctHb is calculated from changes in light absorption using extinction coefficients based on the tetraheme molecule, whereas cHb determination in blood samples is based on the monoheme molecule.

Because cHb changes after starting ECMO, ΔCBV cannot simply be calculated from ΔctHb. Therefore,

$$CBV + \Delta CBV = 4 \cdot (ctHb + \Delta ctHb)/0.69 \cdot (cHb + \Delta cHb), \text{ and}$$

$$\Delta CBV = (\Delta ctHb - 0.17 \cdot \Delta cHb \cdot CBV)/0.17 \cdot (cHb + \Delta cHb).$$

However, because the initial CBV in the individual infant is unknown, it is impossible to calculate ΔCBV exactly. Wyatt et al[17] found a CBV value of 2.2 ± 0.4 mL/100 g in newborn infants with normal brains. As moderate to severe hypoxemia is the main feature in the pre-ECMO condition, the initial CBV in these infants could be expected to be higher as a result of cerebral vasodilation.[17,18] Assuming that the pre-cannulation CBV in these hypoxemic infants is between 2 and 6 mL/100 g, only the direction of ΔCBV could be estimated:

If ΔcHb is positive: ΔCBV is positive when

$$(\Delta ctHb/0.17 \cdot \Delta cHb) > 6$$

and negative when

$$(\Delta ctHb/0.17 \cdot \Delta cHb) < 2.$$

If ΔcHb is negative: ΔCBV is positive when

$$(\Delta ctHb/0.17 \cdot \Delta cHb) < 2$$

and negative when

$$(\Delta ctHb/0.17 \cdot \Delta cHb) > 6.$$

The distribution of ΔCBV direction among these infants was analyzed by the sign test.

In an attempt to describe the relation between ΔctHb and the changes in selected physiologic variables (ΔcHb, ΔMABP, ΔsaO_2, $\Delta tcPO_2$, ΔPaO_2, $\Delta tcPCO_2$, $\Delta PaCO_2$, and ΔHR) at 60 minutes after starting ECMO, we assessed possible linear regression models with ΔctHb as a dependent variable and the changes in these selected physiologic indices as independent variables. Because not all physiologic variables were recorded in each infant, regression models could be assessed in only 20 or 21 infants. For the three most suitable models, the regression coefficients (β) and the squared multiple correlation coefficients (R^2) are given. Furthermore, to show the relative contribution to the explanation of the variation in ΔctHb, the partial R^2 (taking into account all other variables in the model) is given.

RESULTS

After carotid ligation, significant decreases in cO_2Hb and MABP were found, whereas cHHb increased. The other variables showed no significant changes. Jugular ligation revealed only an increase in MABP (Table 1; Fig. 2).

Immediately after starting ECMO, increases in saO_2, $tcPO_2$, cO_2Hb, and MABP were observed, whereas cHHb decreased. At 60 minutes after starting ECMO, the variables had stabilized in most infants. By then, values of cO_2Hb, saO_2, $tcPO_2$, MABP, and PaO_2 were significantly higher than the precannulation values. The cHb was significantly decreased because of hemodilution by the ECMO priming solution (Table 2; Fig. 2).

After starting ECMO, MBFV increased significantly in the major cerebral arteries except the right middle cerebral artery (Table 3). However, the direction of the blood flow in the right supraclinoid internal carotid artery was reversed in all infants. The PI values decreased significantly after starting ECMO (Table 3).

The CBV increased in 15 of 24 infants after starting ECMO, which was statistically significant ($P < .01$). In the other nine infants, CBV decreased (n = 2) or did not change (n = 7).

After assessing each possible regression model, we found that a model with five independent variables appeared to be most suitable to describe the relation between ΔctHb and the changes in other variables at 60 minutes after starting ECMO. The best model ($R^2 = .67$) had the independent variables ΔcHb, ΔMABP, $\Delta tcPO_2$, $\Delta tcPCO_2$, and ΔPaO_2. The next two best models ($R^2 = .66$) differed from the best model by substituting $\Delta PaCO_2$ for $\Delta tcPCO_2$ and ΔsaO_2 for ΔPaO_2, respectively. As could be expected, there was a strong correlation between ΔctHb and ΔcHb. In these models, after correction for the influence of the remaining independent variables, there was a positive correlation of ΔctHb with ΔMABP and a negative correlation with $\Delta tcPO_2$ ($P < .05$). There was no statistically significant correlation between ΔctHb and ΔsaO_2, ΔHR, ΔPaO_2, or $\Delta PaCO_2$ after this correction.

TABLE 1. Changes in Near Infrared Spectrophotometry and Other Physiologic Variables Related to Carotid and Jugular Ligation (n = 24)*

	Carotid Ligation	Jugular Ligation
ΔcO_2Hb, μmol/100 g	−0.36† (−0.76 to −0.18)	0.02 (−0.18 to 0.17)
ΔcHHb, μmol/100 g	0.21† (0.02 to 0.69)	−0.01 (−0.24 to 0.21)
ΔctHb, μmol/100 g	−0.12 (−0.23 to 0.09)	0.06 (−0.11 to 0.21)
$\Delta cCyt.aa_3$, μmol/100 g	−0.00 (−0.00 to 0.01)	0.00 (−0.00 to 0.01)
ΔsaO_2, %‡	−0.73 (−3.31 to 0.85)	1.01 (−0.21 to 2.30)
$\Delta tcPO_2$, mm Hg§	−0.64 (−2.03 to 0.20)	0.03 (−0.46 to 1.95)
$\Delta tcPCO_2$, mm Hg§	0.22 (−0.38 to 1.03)	0.00 (−0.58 to 1.08)
ΔMABP, mm Hg	−1.90† (−6.41 to 0.32)	1.27† (0.08 to 3.53)
ΔHR, beats/min	−0.16 (−3.56 to 0.85)	−0.55 (−2.15 to 0.82)

* Values are median (interquartile range). Abbreviations: cO_2Hb, oxyhemoglobin concentration; cHHb, deoxyhemoglobin concentration; ctHb, total hemoglobin concentration; $cCyt.aa_3$, (oxidized − reduced) cytochrome aa_3 concentration; saO_2, arterial oxygen saturation; $tcPO_2$, transcutaneous partial pressure of oxygen; $tcPCO_2$, transcutaneous partial pressure of carbon dioxide; MABP, mean arterial blood pressure; HR, heart rate.
† Significant changes ($P \leq .05$).
‡ n = 23.
§ n = 21.

DISCUSSION

Venoarterial ECMO requires ligation of the right common carotid artery. When the collateral circulation through the circle of Willis is completely normal,

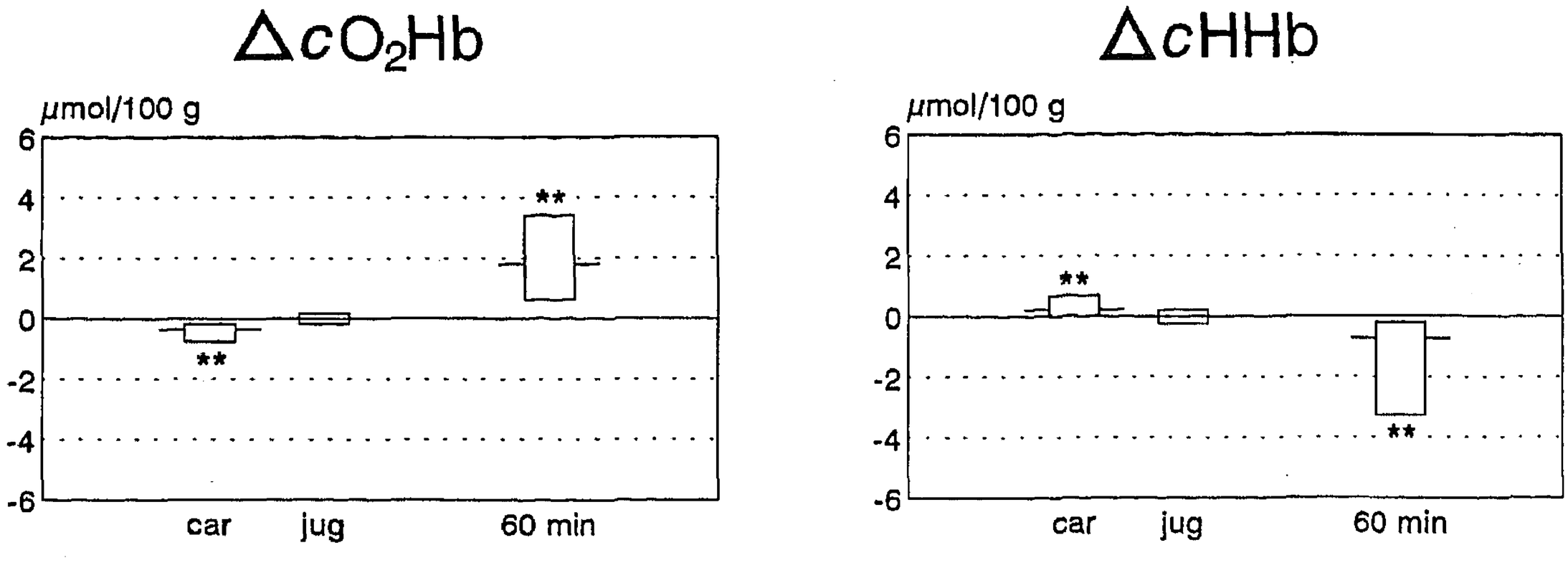

Fig. 2. Changes of NIRS variables during cannulation and after starting ECMO. Car, changes related to carotid ligation; jug, changes related to jugular ligation; 60 min, changes at 60 minutes after starting ECMO as compared with precannulation values. Horizontal line represents the median value; the box covers the interquartile range. cO_2Hb, oxyhemoglobin concentration; cHHb, deoxyhemoglobin concentration; ctHb, total hemoglobin concentration; $cCyt.aa_3$, (oxidized − reduced) cytochrome aa_3 concentration.

perfusion of the right cerebral hemisphere will be sufficiently preserved. However, because incompleteness of the circle of Willis has been described in 0.6% of normal brains,[19] there is a risk of cerebral infarction in the right hemisphere. Conflicting data on lateralization of cerebral lesions in former ECMO patients have been reported.[3,20] In our study, ctHb was unchanged after carotid ligation, reflecting unchanged CBV. Assuming unchanged cerebral venous outflow, cerebral arterial inflow must remain unchanged as well. This is demonstrated by our and other Doppler ultrasound studies showing maintained antegrade blood flow in the right middle cerebral artery.[14,21,22] Reversed blood flow in the right internal carotid artery, as found in our study, is evidence of collateral flow as well. The technique of NIRS may be useful to monitor cerebral hemodynamics during an occlusion test of the right common carotid artery before its definite ligation. When collateral circulation through the circle of Willis reveals inadequacy by showing a fall in CBV, venovenous ECMO should be considered. The advantage of NIRS compared with (color) Doppler ultrasound is the possibility for hands-free continuous monitoring, even during the surgical cannulation procedure.

After carotid ligation, a cO_2Hb reduction with a concomitant cHHb increase was observed. This may reflect increased O_2 extraction in the brain, caused by increased transit time of the blood resulting from diversion of the arterial blood supply to the right hemisphere. This is supported by the observation that, in contrast to the other major cerebral arteries, the right middle cerebral artery did not show a significant increase in MBFV. This compensatory mechanism is probably sufficient, because there is no significant change in $cCyt.aa_3$, reflecting unchanged cerebral O_2 availability. However, there is doubt about the reliability of the cytochrome aa_3 signal, which will be discussed later.

Ligation of the right internal jugular vein might result in cerebral venous congestion[23] and contribute to the occurrence of cerebral vascular lesions during ECMO.[24] However, in our study ctHb and thus CBV did not change after jugular ligation; therefore, it might be concluded that the collateral venous system is sufficient for draining the cerebral venous blood.

The improvement of arterial oxygenation after starting ECMO results in increased cerebral O_2 supply (cO_2Hb). Nevertheless, $cCyt.aa_3$ did not change, reflecting unchanged cerebral O_2 availability, which means sufficient preservation of intracellular oxygenation and energy metabolism in the cerebral tissue in the pre-ECMO period despite prolonged hypoxemia. In newborns, $cCyt.aa_3$ seems to behave more independently from cO_2Hb, as the enzyme remains almost completely oxidized until severe hypoxemia occurs.[13] However, data on $cCyt.aa_3$ should be interpreted with caution because the algorithm

TABLE 2. Changes of the Measured Variables at 60 Minutes After Starting Extracorporeal Membrane Oxygenation (ECMO) as Compared with Precannulation Values (n = 24)*

	Absolute Precannulation Values	Changes 60 min After Starting ECMO
cO_2Hb, µmol/100 g	Not available	1.80† (0.62 to 3.41)
cHHb, µmol/100 g	Not available	−0.72† (−3.27 to −0.20)
ctHb, µmol/100 g	Not available	0.13 (−0.77 to 0.58)
$cCyt.aa_3$, µmol/100 g	Not available	−0.01 (−0.06 to 0.05)
saO_2, %‡	76.35 (66.25 to 88.42)	18.60† (4.57 to 30.37)
$tcPO_2$, mm Hg	27.98 (15.83 to 46.35)	47.63† (18.82 to 64.99)
$tcPCO_2$, mm Hg§	41.02 (33.59 to 64.07)	0.15 (−11.71 to 5.43)
MABP, mm Hg	40.56 (34.80 to 50.95)	11.82† (7.01 to 25.32)
HR, beats/min	159.04 (147.34 to 172.80)	−5.16 (−14.31 to 11.66)
PaO_2, mm Hg	35.25 (24.37 to 49.87)	59.25† (29.75 to 104.25)
$PaCO_2$, mm Hg	38.25 (32.62 to 50.62)	−4.25 (−10.5 to 4.87)
pH	7.34 (7.24 to 7.46)	0.01 (−0.07 – 0.06)
cHb, m Hg	8.75 (7.80 to 9.15)	−1.95† (−2.55 to −0.60)

*Values are median (interquartile range). Abbreviations: PaO_2, arterial partial pressure of oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide; cHb, intravascular hemoglobin concentration; other abbreviations as in Table 1.
† Significant changes ($P \leq .05$).
‡ n = 23.
§ n = 21.

used for calculating $\Delta cCyt.aa_3$ is derived from experiments on rat brains after exchange transfusion with fluorocarbon. Therefore, the data might be affected by noise due to residual hemoglobin after fluorocarbon exchange,[25] as well as from scattering by fluorocarbon, which is different from that of erythrocytes.

After induction of ECMO, we observed an increase in CBV, which may result from increased arterial inflow or decreased venous outflow.[26] Venous outflow decrease is unlikely to occur because during ECMO, venous blood is drained continuously from the right atrium. Increased arterial inflow is more likely the cause of increased CBV, as MBFV in the major cerebral arteries increases significantly, reflecting increased cerebral blood flow (CBF).[27] A high correlation between CBF and CBV changes has been shown in animals.[28] There is no clear-cut explanation for the increases of CBF and CBV after induction of ECMO. Data from the literature are contradictory. Induction of ECMO in normoxemic animals has been shown not to alter CBF[29] or to increase[30] or decrease[31,32] CBF. These conflicting results may be caused by differences in the species used, in the bypass flow rate, and in the duration of ECMO before CBF was measured. However, because many physiologic conditions change during ECMO induction, the cause of hemodynamic changes will be multifactorial.

Some factors could influence cerebral hemodynamics during induction of ECMO. First, changes in arterial blood gas values are probably not responsible for the increases in CBV and CBF found in our study. No changes in arterial PCO_2 and acid-base balance were found. Increased arterial PO_2 would be expected to result in decreases of CBF and CBV. In the selected regression models, the inverse relation between ΔctHb, as a representation of ΔCBV, and $\Delta tcPO_2$ was confirmed. On the other hand, the increases of CBV and MBFV may also be caused by reactive hyperperfusion due to prolonged hypoxemia before ECMO. In hypoxemic newborn piglets, significant cerebral hyperperfusion has been shown after restoration of normoxemia.[33]

Second, the regression models showed a clear relation between ΔMABP and ΔctHb as a representation of ΔCBV. Changes of CBV following changes of MABP are considered to result from disturbed autoregulation,[26] which occurs in distressed newborn infants.[34] However, impairment of cerebral autoregulation occurs in normoxemic newborn lambs undergoing venoarterial ECMO.[35] Disruption of the blood flow-metabolism couple in the brain occurs in pigs undergoing normothermic nonpulsatile cardiopulmonary bypass, indicating "luxury perfusion syndrome," but not in those undergoing pulsatile cardiopulmonary bypass.[36] It seems, therefore, that the ECMO procedure itself is a potential cause of impaired autoregulation. It introduces a reduced arterial pulsatility caused by the use of a roller pump, as reflected by the decreased PI in our patients. This might impair the autoregulatory function, as it has been postulated that the pulse pressure may participate in autoregulation of capillary beds.[36]

Third, significant hemodilution during induction of ECMO will result in a decrease of arterial O_2 content. Therefore, CBF will increase to maintain cerebral O_2 delivery.[18]

It seems that these changes in cerebral hemodynamics after starting ECMO result from both the ECMO procedure itself and the prolonged pre-ECMO hypoxemia. Because fluctuations of cerebral hemodynamics in severely distressed infants might be harmful for the brain, they must be avoided. Further studies are necessary to identify all of the factors responsible for the perturbation of cerebral hemodynamics during ECMO.

In conclusion, NIRS is a valuable tool for studying cerebral oxygenation and hemodynamics during induction of ECMO. We found alterations in cerebral oxygenation reflecting increased O_2 extraction after carotid ligation, but not after subsequent jugular ligation. Despite the increase in the cerebral O_2 supply after starting ECMO, intracellular O_2 availability was unchanged, probably reflecting sufficient preservation of cerebral intracellular oxygenation and energy metabolism in the pre-ECMO period despite prolonged hypoxemia. The observed increases in CBV and cerebral MBFV may result from the following: (1) reactive hyperperfusion, (2) loss of autoregulation

TABLE 3. Changes in Mean Blood Flow Velocity (MBFV) and Pulsatility Index (PI) Values at 90 Minutes After Start of Extracorporeal Membrane Oxygenation (ECMO) (n = 18)*

	MBFV		PI	
	Absolute Precannulation Values, cm/s	Changes 60 min After Starting ECMO, %	Absolute Precannulation Values, cm/s	Changes 60 min After Starting ECMO, %
Internal carotid artery				
Right	21.0 (17.0 to 27.0)	57.47†‡ (34.09 to 103.70)	1.92 (1.25 to 2.56)	−68.37† (−70.53 to −44.33)
Left	20.0 (16.0 to 26.0)	100.61† (52.49 to 166.67)	1.88 (1.28 to 2.44)	−59.60† (−72.60 to −41.18)
Middle cerebral artery				
Right	23.5 (20.0 to 35.0)	18.57 (−14.29 to 44.00)	1.83 (1.50 to 2.65)	−65.92† (−75.12 to −59.24)
Left	23.5 (21.0 to 31.0)	29.26† (5.56 to 42.86)	1.59 (1.13 to 1.87)	−51.46† (−66.06 to −33.63)

* Values are median (interquartile range).
† Significant changes ($P \leq .01$).
‡ Reversed flow.

because of prolonged hypoxemia before ECMO and/or decreased arterial pulsatility, or (3) compensation for hemodilution related to the ECMO procedure.

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NOTICE

Crigler-Najjar Syndrome

A Small Research Conference on this syndrome is to be held in 1996 to discuss new therapies which *might* be available.

I would appreciate hearing from physicians caring for such patients in order to inform them of the meeting and make the proceedings available to them. A newsletter and registry of individuals interested in this topic will be established if there is sufficient interest. **Contact:** Jerold F. Lucey, MD, FAAP, Prof. of Pediatrics, Editor of *Pediatrics,* Medical Center Hospital of Vermont (Fletcher Allen Health Care), Burlington, VT 05401. Telephone: (802) 862-8778.