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Effect of Variation in Arterial Carbon Dioxide Levels on Cerebral-Somatic Oxygenation in Children with Cyanotic Congenital Heart Disease

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Abstract

Background: *Hypocapnia is suggested in decreasing pulmonary vascular resistance in cyanotic congenital heart disease patients undergoing definitive repair. But its effects on cerebral and renal circulation are unclear. Hence the effect of changes in arterial blood carbon dioxide tensions ($PaCo_2$) on cerebral (ScO_2%) and renal (SsO_2%) oxygenation indices using Near Infrared spectroscopy (NIRS) is examined.*

Methods: *We did a prospective observational study in sixty-eight children who underwent elective cardiac surgery for various cyanotic congenital heart diseases. $PaCo_2$, ScO_2% and SsO_2% were obtained before induction of anesthesia, after anesthesia induction at normocapnic or mild hypercapnic ventilation ($EtCo_2$=40 mmHg) and again at hypocapnic ventilation ($EtCo_2$=30 mmHg). Regression analysis was done between $PaCo_2$ and NIRS-C/ScO_2% and $PaCo_2$ and NIRS-R/SsO_2% at both $EtCo_2$ 40 and 30 mmHg. Repeated measure analysis performed to evaluate the significance of change in NIRS-C and NIRS-R from pre-anesthesia induction to when $EtCo_2$ was 40 and then 30 mmHg post anesthesia induction.*

Results: *With decrease in $EtCo_2$, $PaCo_2$ (p=0.0001), NIRS-C (p=0.0001) and NIRS-R (p=0.0001) decreased significantly. At $EtCo_2$ of 40 and 30 mmHg, $PaCo_2$ had significant positive correlation with NIRS-C (R^2=0.77, p=0.0001 and R^2=0.92, p=0.0001 respectively) and had insignificant correlation with NIRS-R (R^2=0.03, p=0.12 and R^2=0.008, p=0.46 respectively). Significant changes in NIRS-C {p=0.0001} and NIRS-R {p=0.0001} occurred from pre-induction to when $EtCo_2$ was 40 and then to 30 mmHg.*

Conclusion: *A decrease in NIRS-C and NIRS-R is probably from decreased cerebral and splanchnic blood flow during hypocapnic ventilation, leading to demand supply mismatch. Hypocapnic ventilation in cyanotic children has potential to cause cerebral hypoxia.*

Abbreviations: CCHD: Cyanotic Congenital Heart Disease; QP: Pulmonary blood flow; Do_2: Oxygen delivery; SpO_2: peripheral pulse oximetry; NIRS: Near Infrared Spectroscopy; NIRS-C/ScO_2%: Regional Cerebral Oxygen saturation; NIRS-R/SsO_2%: Regional Somatic/renal Oxygen saturation; HCT: Hematocrit; ECG: Electrocardiography; CPB: cardiopulmonary bypass; TOF: Tetralogy of fallot; BDG: Bidirectional Glenn Shunt; BT shunt: Blalock Taussig shunt; DORV: Double outlet right ventricle; FiO_2: Inspired oxygen concentration; ABG: Arterial blood gas; PaO_2: Arterial oxygen partial pressure; $PaCo_2$: Arterial carbon dioxide partial pressure; HR: Heart rate; MAP: Mean Arterial Pressure; CVP: Central Venous Pressure

Introduction

The neurodevelopmental disabilities are potentially the most damaging sequelae of children undergoing surgery for cyanotic congenital heart defects (CCHD) [1]. These manifest in the form of seizures in the immediate postoperative period and as developmental delay and impaired cognitive skills in the long-term. Although many factors in the perioperative period can contribute to the cerebral insult [1], scientific literature suggests that these children have decreased cerebral blood flow (CBF) and oxygen delivery preoperatively [2].

In children with CCHD and decreased pulmonary blood flow (Qp), hypocapnic ventilation (arterial carbon dioxide partial pressure ($PaCo_2$) of 25 to 33 millimeter of mercury) to marginally decrease the pulmonary vascular resistance (PVR) is suggested in scientific literature [3] and practiced in some institutions including ours. Evidence suggests that, most often these patients might have a fixed total PVR and so the marginal increase in Qp has negligible impact on increasing the oxygen delivery (DO_2) to systemic end organs [4]. However, if this hypocapnia decreases the cerebral and renal blood flow to a significant extent is unclear. The effect of variations in $PaCo_2$ levels on cerebral vasculature and thereby cerebral blood flow is established [5]. In hypoxemic patients, at a given level of arterial oxygen partial pressure (PaO_2), renal vascular resistance increases by increase in $PaCo_2$ [6]. Acute increments in renal vascular resistance will cause significant decrements in peak systolic velocity of renal blood flow and thereby decline of renal near infrared spectroscopy values [7]. In healthy infants the ratio of oxygen supply to oxygen demand is higher in kidneys in relation to that of brain [8].

Standard monitors like electrocardiography (ECG), pulse oximetry (SpO_2%) and noninvasive blood pressure do not reflect end organ, especially cerebral and renal perfusion or oxygenation. Near Infrared Spectroscopy (NIRS) is a noninvasive continuous method of quantitative measurement of regional cerebral (ScO_2%) and renal (SsO_2%) oxygen saturation. Cerebral (NIRS-C) and Renal NIRS (NIRS-R) values have a good correlation with jugular/central venous and inferior venacaval oxygen saturation in humans [9]. As NIRS provides tissue venous weighted oxyhemoglobin saturation, it is considered a specific indicator of end organ tissue oxygen economy [10]. Some studies have suggested that the high hematocrit (HCT) in children with CCHD precludes use of NIRS [11], albeit the consensus is lacking about the threshold cut off point of HCT.

We aim to examine the effects of normocapnic or mild hypercapnic (end tidal carbon dioxide = 40 millimeter mercury) versus hypocapnic (end tidal carbon dioxide = 30 millimeter of mercury) ventilation on tissue (cerebral and renal) oxygen saturation, using NIRS as a monitoring equipment. We hypothesize that at a given PaO_2, higher carbon dioxide partial pressures will result in significantly higher NIRS-C and NIRS-R values.

Multisite NIRS monitoring provides window on distribution of cardiac output to various tissue and thereby tissue oxygen delivery [10]. This can guide escalation of support at appropriate time.

Material and methods

Study population and study design

This study was approved by the Institute Ethics Committee and a written informed consent was taken from parents of the children.

Ramamoorthy C et al. [12] in their randomized cross over trial studied "the effects of inspired hypoxic and hypercapnic mixtures on cerebral oxygen saturations in single ventricle physiology with increased pulmonary flow". Their Sample size calculation (n=16) was based on a power of 0.8 and α=0.01 to detect a 20% change in ScO_2 (regional cerebral oxygen saturation) from baseline with treatment. In our study, we assumed a similar change in the regional cerebral oxygen saturation with change in ventilation. Hence the required sample size with 90% confidence level and 10% confidence interval would be 66. We recruited 80 children undergoing elective corrective open-heart surgery or palliative cardiac shunt surgery between January 2017 and December 2017.

This was a single center, prospective pretest posttest observational study. Children undergoing emergency surgery, redo surgery, children with active upper and/or lower respiratory tract infection, children in whom cerebral NIRS values were <40% for more than three minutes at any point of time, children with hyperbilirubinemia and children who are diagnosed with any intracranial pathology or neurologic disorder or craniofacial anomaly or cerebralpalsy and mental retardation, were excluded from the study.

Perioperative management

A standard pre-anesthetic checkup was done with routine clinical neurological examination and assessment of room air arterial oxygen saturation. After premedication with promethazine 0.5 milligram per kg weight given orally one hour before surgery, children were taken into operating room. Inside the operating room, ECG, SpO_2, cerebral and renal NIRS moniter and noninvasive blood pressure were applied. After induction of general anesthesia an arterial catheter was inserted in right or left femoral artery. Central venous access was gained by cannulating right internal jugular vein or right or left femoral vein. A transesophageal echocardiography probe of appropriate size was introduced.

Patients underwent mild hypothermic cardiopulmonary bypass (CPB) with or without cold blood cardioplegia to aortic root for intracardiac repair of tetralogy of fallot (TOF), double outlet right ventricle (DORV) and bidirectional Glenn shunt (BDG) respectively. Modified Blalock Taussig (BT) shunt was done without CPB. Rest of the anesthetic management, CPB weaning and postoperative intensive care was as per standard institutional protocols.

NIRS data

Outside the operation theatre, neonatal or pediatric OxyAlert™NIR sensors (COVIDIEN, Mansfield, MA, USA) were placed on child when still he or she was in their mother or father's lap. One was placed on the forehead and the other in the loin at the level of T10-T11 as per the instructions of the manufacturer. Then once child was brought into operation theatre, this was connected to INVOS™ 5100C Cerebral/Somatic Oximeter (COVIDIEN, Mansfield, MA, USA). After obtaining the baseline cerebral and renal NIRS values at room air, general anesthesia was induced and inspired oxygen concentration was maintained at 1.0. After securing the invasive lines and before surgical incision was given, the minute ventilation of the patient was altered to achieve a goal $EtCo_2$ of 40 mmHg. After 5 minutes of pause at this level of $EtCo_2$ an arterial blood gas analysis was done and arterial oxygen saturation (Sao_2%), PaO_2, $PaCo_2$, NIRS-C/ScO_2% and NIRS-R/SsO_2% values were noted. Then minute ventilation was altered to achieve a goal $EtCo_2$ of 30 mmHg and the above parameters were rechecked and noted. Whenever NIRS values were <40% for ≥3 minutes or a fall of >20% from baseline happened hypocapnic ventilation was abandoned and normocapnia was restored. Throughout the procedure heart rate (HR), mean arterial pressure (MAP) and central venous pressure (CVP) were monitored. Surgery commenced once the values at both these time points were noted.

Statistical analysis

Statistical analysis was performed using SPSS software package (SPSS for windows 21.0, SPSS Inc, Chicago, IL, USA) and Stata software package (version 14.0, StataCorp LLC, Lakeway drive, TX, USA) as appropriate. Data are expressed as mean ± standard deviation according to their distribution characteristics. Categorical variables are described using counts and percentages as appropriate. Paired Student's t-test is used to compare pre-test and posttest variables. Using Regression analysis, Pearson correlation coefficient and multiple regression coefficient were obtained to analyze the relation and the quantification of relationship between two quantitative variables. Repeated measure analysis is performed for correlated data. A p value <0.05 is considered as statistically significant.

Results

Of the 80 children with various CCHD enrolled, 7 were excluded from analysis as the NIRS sensors could not detect the saturation either at brain or at kidney site. Two children were excluded because NIRS-C value dropped to 35% and 32% respectively after 3 and 5 minutes of initiation of hypocapnic ventilation. It stayed at the above values for 5 and 8 minutes in those children respectively. Of them, one child was of 18 months age diagnosed with TOF and other was aged 24 months diagnosed with DORV. Three more children were excluded as baseline NIRS-C was <40%. One of them was a 2-month-old diagnosed with TOF with pulmonary atresia for BT shunt. The other 2 children had history of seizures; both were diagnosed with TOF aged 30 and 48 months respectively.

Table 1 shows the diagnostic features and gender distribution of the remaining 68 children. Table 2 shows the demographic data and pre-anesthetic induction parameters considered as baseline. None of these children had any neurological abnormality either by history or physical examination preoperatively. None of them were admitted in ICU preoperatively nor were on any ionotropic/vasopressor support.

42 children were operated for intracardiac repair of TOF, 23 for DORV. In One patient a right sided modified BT shunt was performed as the child was diagnosed with DORV with ventricular septal defect and pulmonic atresia. The other 2 patients were operated to perform a BDG shunt for tricuspid atresia.

	Number of patients
Gender	
Male	37
Female	31
Diagnosis	
TOF	42
DORV VSD PS	23
DORV VSD PA for RMBTS	1
TA for BDG	2

BDG: Bidirectional Glenn, DORV: Double Outlet Right Ventricle, PA: Pulmonary Atresia, PS: Pulmonary Stenosis, RMBTS: Right Sided Modified Blalock: Taussig Shunt, TOF: Tetralogy of Fallot, TA: Tricuspid Atresia, VSD: Ventricular Septal Defect

Table 1: Patient characteristics (n=68).

Baseline tissue oxygenation indices and oxygen saturation

Before induction of anesthesia, the mean NIRS-C was 52.47% (SE=0.34), mean NIRS-R was 62.5% (SE=0.54) and mean Spo_2% was 78.61% (SE=0.74) (Table 2).

Variable	Mean	Standard error (SE)	Median	Range
Age (months)	52.368	3.9	48	44.56-60.16
Weight (kg)	15.24	1.1	12.95	13.04-17043
Height (cm)	102.48	3.41	97	95.67-109.3
Body surface area (m^2)	0.65	0.034	0.57	0.58-0.72
Preoperative Hemoglobin (gm/dl)	17.76	0.203	17.9	17.36-18.17
Preoperative Hematocrit (%)	53.33	0.608	53.7	52.12-54.55
Cerebral NIRS (NIRS-C%/ ScO_2%) before anesthesia induction	52.47	0.34	52	51.77-53.16
Renal NIRS (NIRS-R%/ SsO_2%) before anesthesia induction	62.5	0.54	64	61.41-63.58
Peripheral oxygen saturation (SpO_2%) before anesthesia induction	78.61	0.74	80	77.13-80.1

gm/dl: Gram per Decilitre

Table 2: Demographic characteristics and preanesthetic induction parameters

Arterial carbon dioxide partial pressures

A decrease in $EtCo_2$ from 40 mmHg to 30 mmHg saw a decline in $PaCo_2$ (Table 3). A mean reduction of 9.37 mmHg was statistically significant (p=0.0001).

Variable	At End tidal carbon dioxide = 40mmHg (Mean±SD)	At End tidal carbon dioxide = 30mmHg (Mean±SD)	p value
Arterial carbon dioxide partial pressures ($PaCo_2$ mmHg)	46.69 ± 4.68	37.32 ± 6.16	0.0001
Regional cerebral oxygen saturation (NIRS-C%/ ScO_2%)	59.70 ± 5.16	49.36 ± 6.11	0.0002
Regional renal oxygen saturation (NIRS-R%/ SsO_2%)	74.55 ± 4.29	59.72 ± 3.58	0.0001
Heart rate (per minute)	107.23 ± 13.09	106.32 ± 12.70	0.07
Mean arterial pressure (mmHg)	73.01 ± 6.46	72.5 ± 6.57	0.4
Central venous pressure(mmHg)	10.64 ± 2.24	10.8 ± 2.57	0.28
Hematocrit (%)	55.10 ± 6.47	55.05 ± 6.51	0.77
Arterial oxygen partial pressure (PaO_2 mmHg)	61.10 ± 4.60	60.75 ± 5.07	0.5
Arterial oxygen saturation (SaO_2%)	83.13 ± 4.45	82.77 ± 5.04	0.29

mmHg: Millimeter Mercury, SD: Standard Deviation.

Table 3: Intraoperative variables before initiation of cardiopulmonary bypass

Regional cerebral oxygen saturation

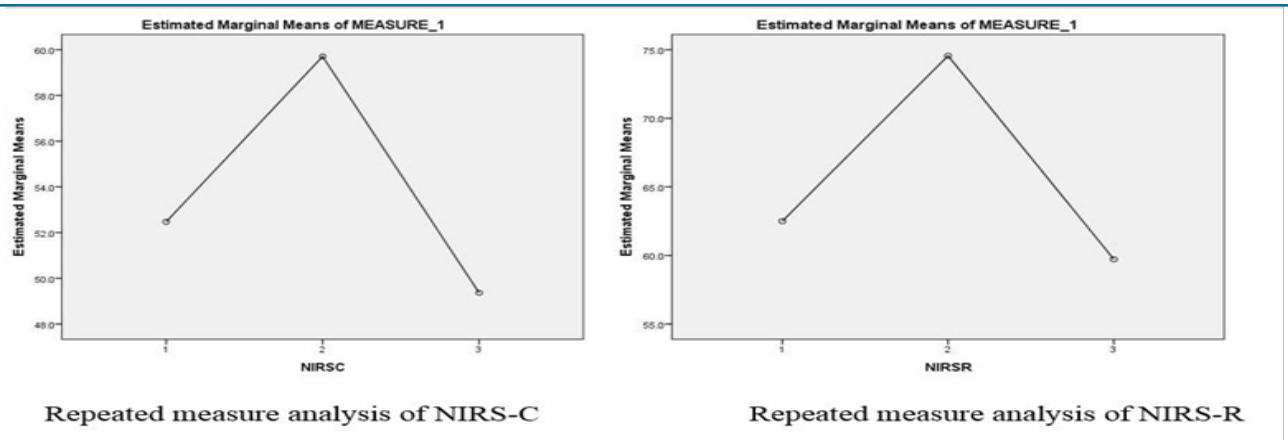
A repeated measure analysis revealed that there was a significant increase in NIRS-C from baseline to when $EtCo_2$ reached 40 mmHg and a significant decrease from there to when $EtCo_2$ became 30 mmHg (Table 4, Figure 1). A regression analysis was done to study the relationship between $PaCo_2$ and NIRS-C at both the levels of $EtCo_2$. This revealed that NIRS-C/ScO_2% had a significant positive correlation with $PaCo_2$ at both the levels of $EtCo_2$ (R^2=0.77, p=0.0001 and R^2=0.92, p=0.0001 respectively) (Table 4, Figure 2).

Regional somatic/renal oxygen saturation

A repeated measure analysis revealed that there was a significant increase in NIRS-R from baseline to when $EtCo_2$ reached 40 mmHg and a significant decrease from there to when $EtCo_2$ became 30 mmHg (Table 4, Figure 2). A regression analysis was done to study the relationship between $PaCo_2$ and NIRS-C at both the levels of $EtCo_2$. This revealed that NIRS-R/SsO_2% had an insignificant correlation with $PaCo_2$ at both the levels of $EtCo_2$ (R^2=0.03, p=0.12, and R^2=0.008, p=0.46 respectively) (Table 4, Figure 3).

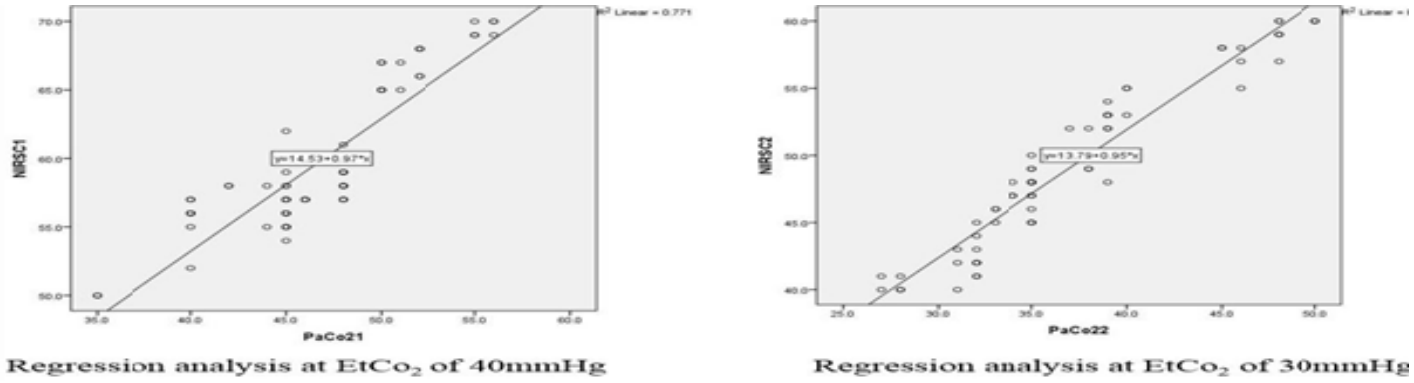
Quantification of factors affecting NIRS-C at 40 and 30 mmHg

Multiple regression analysis revealed that at both 40 and 30 mmHg NIRS-C was significantly affected by PaCo2, SaO2, HR, MAP, CVP and HCT {R^2=0.82 and R^2=0.93 respectively}. Of all these factors $PaCo_2$ was the most significant independent predictor of NIRS-C (β=0.832, p=0.0001 and β=0.962, p=0.0001 respectively) (Table 5).



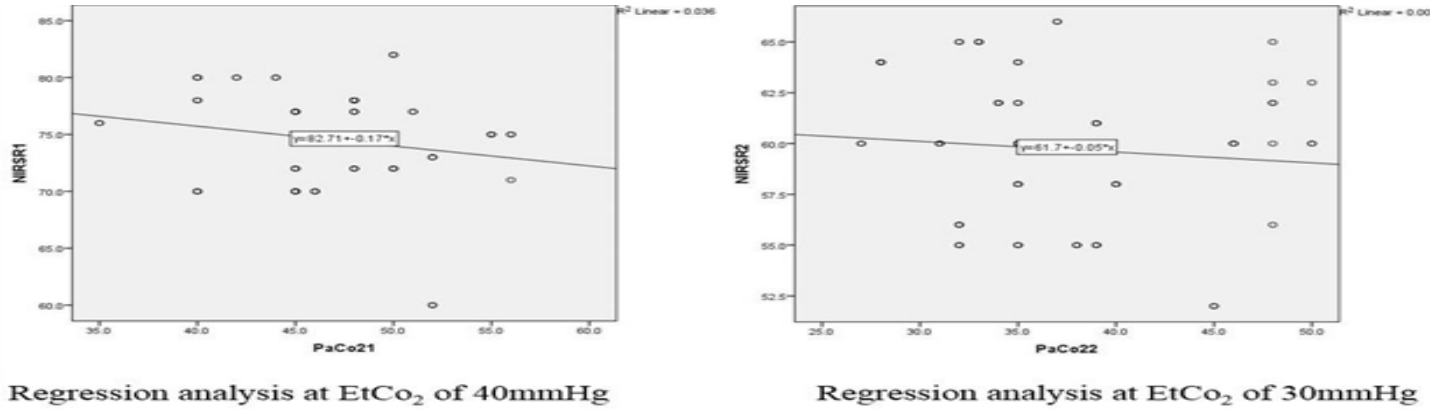
NIRS-C: Near Infrared Spectroscopy-Cerebral, NIRS-R: Near Infrared Spectroscopy-Renal. Timepoint 1: baseline/pre-anesthetic induction, Timepoint 2: at $EtCo_2$ of 40 mmHg, Timepoint 3: at $EtCo_2$ of 30mmHg.

Figure 1: Repeated measures ANOVA of NIRS-C and NIRS-R.



$PaCo_2$-1 and NIRS-C1: $PaCo_2$ and NIRS-C at $EtCo_2$ of 40 mmHg, $PaCo_2$-2 and NIRS-C2: $PaCo_2$ and NIRS-C at $EtCo_2$ of 30 mmHg.

Figure 2: Regression plots between $PaCo_2$ and NIRS-C at $EtCo_2$ of 40 and 30 mmHg.



$PaCo_2$-1 and NIRS-R1: $PaCo_2$ and NIRS-R at $EtCo_2$ of 40 mmHg, $PaCo_2$-2 and NIRS-R^2: $PaCo_2$ and NIRS-R at $EtCo_2$ of 30 mmHg.

Figure 3: Regression plots between $PaCo_2$ and NIRS-R at $EtCo_2$ of 40 and 30 mmHg.

Parameter	F-statistic	Sig	Regression-40				Regression-30			
			R	p	R^2	slope	R	p	R^2	slope
NIRS-C	F(2,134)=91.413	0.0001	0.87	0.0001	0.77	0.97	0.96	0.0001	0.92	0.95
NIRS-R	F(1.59,106.99)=582.337	0.0001	0.19	0.12	0.03	-0.17	0.09	0.46	0.008	-0.05

F-statistic: the result from repeated measures ANOVA test, Sig: p value of F-statistic, Regression-40: regression analysis between the parameter and $PaCo_2$ at $EtCo_2$ of 40 mmHg, Regression-30: regression analysis between the parameter and PaCo2 at $EtCo_2$ of 30mmHg, R: Pearson correlation coefficient, p: p value of β, R^2: coefficient of determination, Slope: slope of regression line.

Table 4: Summary of Regression analysis

Parameter	F-statistic	Sig	Multiple regression-40				F statistic	Sig	Multiple regression-30			
			R	R^2	β	p			R	R^2	β	p
NIRS-C	F(6,67) = 47.239	0.0001	0.907	0.82	0.832	0.0001	F(6,67) = 153.17	0.0001	0.96	0.938	0.962	0.0001
NIRS-R	F(6,67) = 3.352	0.006	0.498	0.248	-0.19	0.15	F(6,67) = 1.839	0.106	0.39	0.153	-0.26	0.07

F-statistic: the result of multiple regression analysis, Sig: p value of F-statistic, Multiple regression-40: multiple regression analysis with $PaCo_2$, SaO_2, HCT, HR, MAP & CVP as independent predictors of NIRS-C/NIRS-R at $EtCo_2$ 40 mmHg, Multiple regression-30: multiple regression analysis with $PaCo_2$, SaO_2, HCT, HR, MAP & CVP as independent predictors of NIRS-C/NIRS-R at $EtCo_2$ 30 mmHg, NIRS-C: near infrared spectroscopy-cerebral, NIRS-R: near infrared spectroscopy-renal, R: Pearson correlation coefficient, R^2: coefficient of determination, β: standardized beta estimate of multiple regression, p: p value of β.

Table 5: Summary of Multiple regression statistic

Quantification of factors affecting NIRS-R at $EtCo_2$ 40 and 30 mmHg

Multiple regression analysis revealed that at 40 mmHg, NIRS-R was significantly affected by PaCo2, SaO2, HR, MAP, CVP and HCT {R2=0.248, p=0.006}. Amongst these factors PaCo2 was insignificant but negative predictor (β= -0.19, p=0.15). However, at 30 mmHg the effect of all the above parameters on NIRS-R became statistically insignificant {R^2=0.15, p=0.10} with $PaCo_2$ still having a negative, albeit statistically insignificant, effect on NIRS-R (β= -0.15, p=0.07) (Table 5).

Hemodynamic and other variables

Heart rate (HR) (p=0.07), Mean arterial pressure (MAP) (p=0.4) and Central venous pressure (CVP) (p=0.28) did not change significantly with reduction in $EtCo_2$ (Table 4). The PaO_2 (p=0.50) and SaO_2 (p=0.29) also did not change significantly, while the Hematocrit (HCT) (p=0.77) remained constant (Table 3).

Comment

The perioperative mortality in cardiac surgery is well under 3% from advancements in surgical techniques, but with about 25% incidence, the postoperative neurological sequelae continue to be high especially in cyanotic neonates and infants [13]. These tend to persist even after 5 to 7 years post-surgery. Cyanotic infants have a lower baseline ScO_2 % as compared to their normal counterparts [14], putting them at substantial risk for neurologic sequelae and perioperative mortality. Among the various intraoperative factors that increase the risk of neurologic injury, hypocapnic ventilation might be an inconspicuous yet significant factor.

NIRS has become a prime monitoring tool in treatment protocols as it helps to detect when oxygen supply versus demand is at risk in this subset of population. It is an optical technique that non-invasively provides tissue venous weighted oxygenation value. The sensor of Somanetics INVOS 5100c monitors a 1 cm3 banana shaped sample tissue volume using near infrared light of 730 and 810 nm wavelengths and the final numerical value displayed is a ratio of oxy-Hb to total Hb [10].

Scientific literature suggests that a 20% fall from baseline or a value below 40% for a minimum of three minutes or a single value of <30% is specific for low cerebral venous oxyhemoglobin saturation [8]. This often has been correlated with increased prevalence of radiographically apparent neurological injury [8]. Cyanotic infants are at higher risk for such injuries as their baseline values are lower to start with [14]. Hypocapnic ventilation to increase the Qp and thereby SaO_2 % is particularly debatable. Based on previous literature, carbon dioxide (Co2) levels in the arterial blood are directly correlated with cerebral blood flow and thereby cerebral DO2 [15]. The significance of this physiological relationship needs to be considered in determining the ventilation strategy, especially in sick cyanotic neonates and infants.

Ramamoorthy et al. have increased Co_2 levels either by adding Co_2 to the inspiratory gas mixture or by normocapnic or hypercapnic ventilation strategies [7]. They concluded that reduction in Co2 is significantly associated with fall in ScO_2 %, putting these infants at higher risk for cerebral injury [7]. In our study, there was a significant decrease in the mean NIRS-C value when the $EtCo_2$ decreased from 40 mmHg to 30 mmHg (p=0.0002) (Table 3). However, at both the levels of $EtCo_2$, children who had relatively higher $PaCo_2$ value for a given level of $EtCo_2$ also had relatively higher NIRS-C value (Figure 2). This probably can be explained as from relatively higher cerebral blood flow because of higher PaCo2, thus higher cerebral DO_2 .

Li and associates observed that with increase in Co_2 levels, Qs increased mainly because of increase in CBF, but not for the splanchnic circulation [15]. Mcquillen et al found that the change in SsO2% is negatively correlated with change in $PaCo_2$ [16]. In our study, NIRS-R values had a weak positive correlation with $PaCo_2$ values at both the levels of $EtCo_2$ (Table 4). However, at both levels of $EtCo_2$ the regression plots showed that the regression line had negative slope, suggesting that at a given $EtCo_2$ children with relatively higher $PaCo_2$ had relatively lower NIRS-R values (Figure 3). Also, multiple regression analysis revealed that $PaCo_2$ was a negative, although statistically insignificant, predictor at both the levels of $EtCo_2$ (p=0.15 and 0.07 respectively) (Table 5). This might be from the increase in renal vascular resistance from increased $PaCo_2$ in that patient. However, the mean NIRS-R values decreased significantly when $EtCo_2$ decreased from 40 mmHg to 30 mmHg (p=0.0001) (Table 3), which might be because of decreased overall systemic blood flow (Qs), including cerebral blood flow, at a lower $PaCo_2$. Yet, the mean or median value of NIRS-R was never below 50% (Table 3), which as demonstrated by Owens et al [17] is the threshold cut off value below which acute postoperative kidney injury would occur. Since both Pearson correlation coefficient and slope of the regression line were not significant, it is difficult to draw

any comprehensive conclusion (Tables 4 and 5).

During this period of decline in $EtCo_2$, other factors determining the Qs, and therefore Cerebral/Renal blood flow, like hemoglobin level, MAP, CVP, HR, SaO_2% ($p>0.05$, for all the factors) (Table 3) and the FiO2 were maintained constant to nullify their effect on cerebral oxygenation. So, the rationale behind this decline in NIRS-C as well as NIRS-R might be from decreased Qs, probably from systemic and cerebral vasoconstriction because of hypocapnia.

Gottlieb et al. stated that NIRS monitoring is not reliable in cyanotic children [11]. Basing on our study results, we opine that NIRS as a monitor need not be universally excluded from usage in cyanotic children. Determining the threshold limit of HCT above which NIRS does not work, is a potential research area.

The limitations of the current study are firstly NIRS can monitor only frontal cerebral cortex oxygenation and does not monitor global cerebral oxygenation. So, the numerical value given by NIRS is non-representative of global cerebral oxygenation. Secondly, to generalize the results of this study, large sample size would be necessary. Thirdly, the findings that both NIRS-C and NIRS-R decline with reduction of $PaCo_2$ and that this happens uniformly across all types cyanotic congenital cardiac lesion categories is yet to be established. Hence, instead of restricting to TOF and DORV predominantly, recruitment of various other complex cyanotic heart disease children should have been done. Finally, no significant clinical neurological outcome was either monitored or described in the postoperative period.

We conclude that hypocapnic ventilation should be cautiously used as it acutely leads to significant untoward effects on cerebral oxygen supply-demand relationship. This in turn might lead to significant long term adverse effects on neurodevelopmental outcome of the child. The acute effects of alterations in arterial carbon dioxide levels on renal vascular bed are obvious, although a comprehensive explanation was elusive to us. Hence the risk-benefit ratio of hypocapnic ventilation needs to be determined by a vigilant clinician on a case to case basis.

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