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Sodium bicarbonate causes dose-dependent increases in cerebral blood flow in infants and children with single ventricle physiology

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Abstract

Background—Sodium bicarbonate ($NaHCO_3$) is a common treatment for metabolic acidemia, however little definitive information exists regarding its treatment efficacy and cerebral hemodynamic effects. This pilot observational study quantifies relative changes in cerebral blood flow (rCBF) and oxy and deoxy-hemoglobin concentrations (ΔHbO_2 and ΔHb) due to bolus administration of $NaHCO_3$ in patients with mild base deficits.

Methods—Infants and children with hypoplastic left heart syndrome (HLHS) were recruited prior to cardiac surgery. $NaHCO_3$ was given as needed for treatment of base deficit. Diffuse optical spectroscopies were employed for 15 minutes post-injection to non-invasively monitor ΔHb, ΔHbO_2 and rCBF relative to baseline prior to $NaHCO_3$ administration.

Results—Twenty-two anesthetized and mechanically ventilated HLHS patients (1 day to 4 years old) received a median (interquartile range) dose of 1.1 (0.8, 1.8) mEq/kg $NaHCO_3$ administered intravenously over 10–20 seconds to treat a base deficit of −4 (−6, −3) mEq/l. $NaHCO_3$ caused significant *dose-dependent* increases in rCBF, however population averaged ΔHb or $\Delta 4HbO_2$ compared to controls were not significant.

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Conclusions—Dose-dependent increases in cerebral blood flow (CBF) caused by bolus $NaHCO_3$ are an important consideration in vulnerable populations wherein risk of rapid CBF fluctuations does not outweigh the benefit of treating a base deficit.

INTRODUCTION

Sodium bicarbonate ($NaHCO_3$) is a commonly used medication to treat metabolic acidemia from a variety of causes. Intravenous $NaHCO_3$ acts by neutralizing excess acid in the blood to yield carbonic acid which then dissociates into carbon dioxide and water, restoring physiologic pH. The efficacy of $NaHCO_3$ treatment for mild to moderate acidemia, however, is widely debated and controversy exists over whether any true benefit results from the therapy (1–4). In fact, some data suggests that $NaHCO_3$ may be harmful in certain populations. In preterm infants, for example, the use of $NaHCO_3$ has been linked to intraventricular hemorrhage, hypernatremia, and death (2, 5, 6). Nevertheless, treatment of metabolic acidemia with $NaHCO_3$ remains a common practice in many pediatric intensive care units and operating rooms.

Further understanding of the cerebral hemodynamic effects of rapid administration of $NaHCO_3$ may illuminate the link between $NaHCO_3$ and brain injury. It is known that administration of $NaHCO_3$ causes an immediate and transient increase in the production of non-metabolic CO_2 (7–10), as well as a slight increase in plasma pH (7, 11), and serum osmolality (12, 13). This increase in serum osmolality leads to a flow of intracellular water into the extracellular space to restore osmotic equilibrium and to an increase in arterial hemoglobin concentration and a decrease in hematocrit (9, 10, 12, 13). However, little definitive and quantitative information exists regarding the effects of $NaHCO_3$ on cerebral hemodynamics.

Several publications studying the effects of $NaHCO_3$ on cerebral blood flow (CBF) report conflicting observations (7, 11, 14–19). Lou *et al* (17) observed substantial *decreases* in CBF measured by the Xenon-133 clearance technique five minutes after $NaHCO_3$ administration in 7 newborn infants with respiratory distress. By contrast, Nakashima *et al* (9) reported significant increases in CBF in 5 healthy adult volunteers following to $NaHCO_3$ administration. Finally, in a study of 6 neonatal dogs, Young *et al* (19) observed no change in CBF (measured with radioactive tracers) 30 minutes after $NaHCO_3$ injection. These conflicting results may reflect the wide variety of experimental subjects studied (both humans and animals), the severity and cause of the acidemia, the dosage and rapidity of injection of $NaHCO_3$, the use of mechanical ventilation, the anesthetic state, the method of CBF measurement, and the time frame for assessing the cerebral hemodynamic effects following drug administration.

The present observational pilot investigation aimed to quantify the immediate cerebral hemodynamic effects of a rapid (10–20 seconds) bolus of $NaHCO_3$. Pilot data was taken 1 to 15 minutes after bolus injection and was obtained from a subset of pre-operative patients with hypoplastic left heart syndrome (HLHS) who were treated for mild acidemia during part of a larger pre-surgical brain imaging study. Noninvasive diffuse optical spectroscopies, namely diffuse optical spectroscopy (DOS) and diffuse correlation spectroscopy (DCS), were employed for 15 minutes post-injection to monitor regional changes in cerebral oxy- and deoxy-hemoglobin concentrations (ΔHbO_2 and ΔHb, respectively), changes in total hemoglobin concentration (ΔTHC), and changes in CBF ($\Delta rCBF$) relative to baseline prior to rapid $NaHCO_3$ administration.

RESULTS

As seen in Table 1,305 patients were approached for this investigation, parental consent was obtained in 133, and 91 were studied with DOS/DCS. Of the 91 HLHS patients monitored with DOS/DCS, 22 received $NaHCO_3$ treatment for a mild or moderate base deficit: N = 8 pre-Norwood, N = 8 pre-Glenn, and N = 6 pre-Fontan. Furthermore, we selected 22 age and gender matched control patients from the remaining 69 patients. These patients received no interventions but were monitored with DOS/DCS as part of the pre-surgical brain magnetic resonance imaging study. Patient characteristics for the treated and control groups are summarized in Table 2. $NaHCO_3$ treated patients were mostly male (64 %) and ranged in age from 1 day to 4 years old.

Arterial blood gas data obtained *prior to* administration of $NaHCO_3$ are summarized in Table 3 for patients in the treated and control groups. Patients received a median (interquartile range) dose of 1.1 (0.9, 1.8) mEq/kg $NaHCO_3$ to treat a median (interquartile range) base deficit of −4 (−6, −3) mEq/l. Of note, the majority of patients were normocapnic but mildly hypoxemic with arterial oxygen tensions of 6.3 (8.0, 6.7) kPa. The below normal partial pressures of oxygen were expected due to the presence of intracardiac shunting, a consequence of single ventricle physiology. Furthermore, arterial blood samples were *not* drawn after $NaHCO_3$ administration, thus changes in the parameters listed in Table 3 due to $NaHCO_3$ are not reported. Baseline heart rate (HR), mean arterial pressure (MAP), and transcutaneous oxygen saturation (SpO_2) are also reported in Table 3 for both treated and control groups. No differences in these baseline parameters between treated and age-matched controls were observed.

Figure 1 provides boxplots of ΔHb, ΔHbO_2, ΔTHC and $\Delta rCBF$ over time for the control and treated group following injection of intravenous $NaHCO_3$. Compared to age matched controls, patients showed significant increases in $\Delta rCBF$ at 1 minute after $NaHCO_3$ injection ($p = 0.0084$). No significant changes in DOS measures of ΔHb, ΔHbO_2, or ΔTHC were observed, nor were any significant differences in these parameters between the treatment group and the control group observed at any time following injection. Additionally, MAP, HR, and SpO2 did not change following $NaHCO_3$ in the treated patients as compared to controls (Figure 2).

In the $NaHCO_3$ treated group, at 1 minute post-injection the increase in $\Delta rCBF$ was highly correlated with $NaHCO_3$ dosage ($R^2 = 0.71$, $p = 2.1e\text{-}6$, slope (95% confidence interval) = 45.7 (32.5, 58.9) %/mEq/kg), see Figure 3. No relationship between change in $\Delta rCBF$ at 1 minute post-injection and baseline pH, pCO2, or pO2 was observed (all $p > 0.1$). The relationship between $\Delta rCBF$ and $NaHCO_3$ dosage weakened slightly by 5 minutes post-injection ($R^2 = 0.51$, $p = 6.0e\text{-}4$), and was no longer highly significant by 10 minutes after $NaHCO_3$ administration (at 10 min $R^2 = 0.12$, $p = 0.085$ and at 15 min, $R^2 = 0.23$, $p = 0.042$). Furthermore, no relationship was observed between cardiac physiology, age, weight, or arterial hemoglobin concentration and the change in ΔHb, ΔHbO_2, ΔTHC or $\Delta rCBF$ at any time point.

DISCUSSION

In this pilot observational study, we quantify the cerebral hemodynamic effects of $NaHCO_3$ administered rapidly to treat metabolic acidemia in paralyzed, mechanically ventilated children with single ventricle physiology. Diffuse correlation spectroscopy demonstrated significant increases in CBF immediately (within 2 minutes) following bolus administration of $NaHCO_3$. These increases in CBF were strongly associated with dosage of the $NaHCO_3$, increasing in a linear fashion. This relationship between CBF and $NaHCO_3$ dose was

observed within all stages of HLHS cardiac physiology studied herein. The present investigation is the first to describe a dose-dependent response of CBF to $NaHCO_3$. Population averaged changes in oxy- or deoxy-hemoglobin concentrations were not significantly different between the control and treated groups. Quantification of the changes in cerebral hemodynamics that occur as a consequence of bolus injection of $NaHCO_3$ may have a significant and beneficial impact on the treatment of metabolic acidemia in patients with congenital heart disease, especially in patients with bidirectional Glenns where pulmonary blood flow is dependent on CBF.

Although this data was obtained on mechanically ventilated patients with single ventricle physiology, these results may be generalized to a larger pediatric population. Understanding the cerebral hemodynamic effects $NaHCO_3$ administration may be especially important in vulnerable populations such as premature infants, patients with impaired autoregulation from hypoxic ischemic injury, or patients with focal or global cerebral edema where the risk of rapid fluctuations in CBF does not outweigh the benefit of treating a metabolic acidemia.

The mechanisms that govern the cerebral hemodynamic responses to a rapid $NaHCO_3$ infusion are complex and not fully understood. Potentially, the observed increase in CBF was caused by an increase in the concentration of CO_2, produced as a byproduct of the reaction of $NaHCO_3$ with acid, leading to an intracellular acidosis (8, 9). Although we did not obtain a post-$NaHCO_3$ administration arterial blood gas, previous work suggests that $NaHCO_3$ causes significant increases in the partial pressure of arterial CO_2 in mechanically ventilated patients (20). CO_2 is a potent vasodilator that induces increases in CBF through local effects on cerebral vasculature. Because our population was paralyzed under general anesthesia, the normal mechanism of responding to elevated arterial CO_2 tension by increasing minute ventilation was eliminated. Therefore, it is possible that a more potent effect from $NaHCO_3$ may have been observed in our population compared to patients who are awake and spontaneously breathing.

Relatedly, the increase in CBF may reflect the increase in plasma osmolality following infusion. Siegel *et al* demonstrated an increase in osmolality as well as a decrease in hematocrit in critically-ill neonates following treatment of metabolic acidemia with $NaHCO_3$ (13). Both increased osmolality and decreased hematocrit have been linked to an increase in CBF via vasodilation and decreased viscosity, respectively (21). Thus, in addition to the vasodilatory effects of CO_2, hyperosmolality and/or a drop in hematocrit could be responsible for our observed increase in CBF.

Interestingly, we did not observe significant population averaged changes in oxy-, deoxy-, or total-hemoglobin concentration. Vasodilation caused by CO_2 and/or hyperosmolality following $NaHCO_3$ might be expected to lead to increases in oxy- and total-hemoglobin concentrations, as well as a slight decrease in deoxyhemoglobin concentration. However, a decrease in hematocrit after $NaHCO_3$ (as shown in (13)) would likely be accompanied by a drop in oxy- and total hemoglobin concentrations, as well as an increase in deoxy-hemoglobin concentration (22). Possibly, these two phenomena (i.e., vasodilation and a concomitatant drop in hematocrit) have opposite effects on tissue hemoglobin concentrations, leading to a population-averaged effect of no net change (i.e. within the error bars of our measured concentration changes).

Little work has been published on the cerebral effects of $NaHCO_3$ to treat metabolic acidemia in human pediatric populations, and to our knowledge, only one publication has investigated the effects in patients with single ventricle physiology (14). On the whole, our results are consistent with several reports of the cerebral hemodynamic effects of $NaHCO_3$ used to correct metabolic acidemia, although we did observe some disparities with other

reports. Van Alfen *et al* (11) employed continuous-wave near-infrared spectroscopy and transcranial Doppler ultrasound to study 15 preterm infants with metabolic acidosis treated with bolus administration of $NaHCO_3$. Their cohort presented with more severe acidemia than our cohort, i.e. a base deficit < −6 mmol/l and pH < 7.3, and their cohort also received half the dose (mEq/kg) of our population. As with our results, Van Alfen *et al* did not observe substantial changes in total hemoglobin concentration at 5 and 15 minutes post-$NaHCO_3$ (they report changes in cerebral blood volume). In contrast to our findings, however, they also did not observe a significant change in CBF as measured by blood flow velocity in the internal carotid artery. This discrepancy may be due to the fact that Doppler ultrasound measures macrovascular changes in arterial flow velocity, while DCS measures microvascular flow directly in cortical tissue, and these two quantities may be disparate. Alternatively, the discrepancy may arise from the differences in age and physiology between the populations, or from the fact that 9 out of 15 patients in their study (11) were spontaneously ventilating, thus permitting the patient to increase their minute ventilation to exhale the extra CO_2 produced by $NaHCO_3$.

Lou *et al* (17) used the ^{133}Xe clearance technique to measure CBF changes five minutes after $NaHCO_3$ injection in seven asphyxiated neonates with respiratory distress and acidosis (base deficit < −8 mEq/l). Interestingly, they found profound *decreases* in global CBF in these infants, contrary to our findings, despite the fact that they administered the same base deficit dependent dose per kilogram of $NaHCO_3$. It is not clear why these results are contradictory; however, a possible explanation could be the difference in patient population. Unlike our otherwise healthy population with palliated congenital heart disease, their cohort was younger, i.e., preterm neonates, and their cohort had suffered asphyxia and potential damage to the blood brain barrier. Thus, bicarbonate ions, which are normally non-permeable ions, may have been able to penetrate from the plasma to the extracellular fluid, leading to cerebrovasoconstriction and hence decreased CBF.

Bradley *et al* (14) monitored fourteen patients following bidirectional superior cavopulmonary connections with transcranial Doppler ultrasound of the middle or anterior cerebral artery. Unlike our study, these patients were not acidemic at baseline, i.e. population averaged baseline pH = 7.39. However, the authors also observed a significant increase in cerebral blood flow velocity for up to 15 minutes after a 4 mEq/kg $NaHCO_3$ bolus, similar to the findings observed in our patients. In addition, they observed an increase in systemic arterial saturations following bicarbonate admministration, contrary to the findings in our bidirectional Glenn population.

In summary, a handful of publications that investigate the cerebral effects of $NaHCO_3$ report findings consistent with the ones presented herein. The discrepancies that do arise may reflect the severity and cause of the acidemia, the dosage and injection rate of $NaHCO_3$, the use of mechanical ventilation, the differences in patient population, the anesthetic state, the method of CBF measurement, and the time frame for assessing the cerebral hemodynamic effects following drug administration.

Study Limitations

The results presented herein have several limitations. First, we did not draw a post-$NaHCO_3$ arterial blood gas, as this was merely an observational pilot study. The current clinical practice at CHOP following $NaHCO_3$ is to not draw another arterial blood sample to confirm increases in pH, CO_2 tension, and bicarbonate ion concentration. Thus, although we suggest that arterial CO_2 levels increased following $NaHCO_3$ due to the abundance of literature suggesting this effect (9, 10, 15, 20) and due to the observed dose-dependent increases in CBF, we cannot definitively confirm that CO_2 increased in our cohort. Furthermore, we did not measure baseline albumin concentration, an important non-

bicarbonate buffer that may also influence CO_2 release following $NaHCO_3$ injection and thus may effect subsequent cerebral hemodynamic changes (20, 23).

Second, we only tracked changes in cerebral and systemic hemodynamics for fifteen minutes following $NaHCO_3$ administration. Despite this limited monitoring time period, by 15 minutes post-injection, CBF was no longer significantly elevated. Thus, we believe a 15 minute window was sufficient to capture the rapid and transient effects of $NaHCO_3$. Additionally, we were limited to studying the effects of rapid infusion of $NaHCO_3$. Future work will investigate variation of the infusion time in order to compare the potential beneficial effects of rapid versus slow infusions.

Third, diffuse optical spectroscopies probe tissues located at shallow depths in the frontal cortex in the region under the optical probe. Although we presume that our frontal cortex measurements are indicative of whole brain response to $NaHCO_3$, absolute quantification of cerebral hemodynamics in other regions of the brain is beyond the scope of this work.

Conclusions

$NaHCO_3$ is a commonly used medication administered for rapid correction of metabolic acidemia in adult, pediatric, and neonatal intensive care units. In pediatric patients with HLHS, we observed substantial increases in CBF following bolus intravenous $NaHCO_3$ administration. These changes in CBF were linearly related to the dose of $NaHCO_3$. On average, cerebral oxy- and deoxy-hemoglobin concentrations did not change with $NaHCO_3$ administration. Future work will benefit from the investigation the effects of infusion rate on the CBF response to $NaHCO_3$.

MATERIALS AND METHODS

Study Protocol

Infants and children with HLHS at various stages of palliation were recruited and and parental consent was obtained for a pre-surgical brain magnetic resonance imaging and hypercapnia study (described in (24, 25)) approved by the Institutional Review Board at The Children's Hospital of Philadelphia. After induction of general anesthesia with paralysis in the operating room, patients were tracheally intubated. The anesthetic consisted of sevoflurane in room air for patients over 3 month of age and fentanyl (5 ug/kg) for neonates. Supplemental oxygen was not utilized. Patients were mechanically ventilated using a tidal volume to achieve an arterial CO_2 of 4.93 – 5.60 kPa. An arterial catheter was placed in the umbical artery in pre-Norwood patients and in an ulnar or radial artery of pre-Glenn and pre-Fontan patients. Patients were then transferred to the magnetic resonance imaging table, and a non-invasive optical probe (see description below) was placed on the forehead for continuous (0.2 Hz) optical monitoring of cerebral hemodynamics. Heart rate (HR) via electrocardiogram and peripheral hemoglobin-oxygen saturation (SpO_2) via pulse-oximetry were monitored and continuously recorded at a rate of 0.5 Hz throughout the duration of the study. Non-invasive (cuff) mean arterial blood pressure (MAP) was measured every 3 minutes.

After the patient was stabilized, an arterial blood gas was drawn. Blood gas analysis was performed using an i-STAT handheld blood analyzer (Abbott Laboratories, Princeton, NJ) to derive blood pH, partial pressure of carbon dioxide and oxygen, base excess or base deficit, bicarbonate ion concentration, hemoglobin concentraction (Hgb), and hematocrit (Hct). As part of routine clinical care during the study, any calculated base deficit less than −2 mEq/l was treated at the attending anesthesiologist's discretion (not protocolized) with bolus intravenous administration of 8.4% $NaHCO_3$ over a 10 to 30 second period. All patients in

this study were hemodynamically stable, including those patients with a base deficit between −2 and −3, where the decision to treat was solely based on practitioner preference. The acuity of patient's illness did not play a role in the decision to treat. The following formula was used to calculate $NaHCO_3$ dosage: Patient weight (kg) × 1/3 (l/kg) × base deficit (mEq/l). If $NaHCO_3$ was given, a second blood gas was *not* obtained following $NaHCO_3$ administration.

Cerebral Monitoring

A hybrid diffuse optical instrument combining diffuse optical spectroscopy (DOS) and diffuse correlation spectroscopy (DCS) was employed to non-invasively monitor cerebral hemodynamics. This instrument has been described previously (24), and the techniques and theoretical analysis have been described at length (26). Briefly, DOS employs 3 near-infrared wavelengths, 688, 787, and 826 nm, and uses a modified Beer-Lambert law (22) to quantify changes in tissue oxy-and deoxy-hemoglobin concentration (ΔHbO_2 and ΔHb, respectively) in the region of brain approximately 1–1.5 cm under the optical probe, i.e. in the cortex surface region. The sum of these changes gives variation of total hemoglobin concentration ($\Delta THC = \Delta Hb + \Delta HbO_2$), a quantity which is generally assumed to be proportional to the change in cerebral blood volume. DCS monitors temporal fluctuations of the reflected light intensity; specifically, the temporal intensity autocorrelation function of detected NIR light is computed using a semi-infinite homogeneous approximation in order to derive a blood flow index (BFI) (26). Previous studies have shown that changes of BFI in various model systems agree with changes in cerebral blood flow relative to baseline ($\Delta rCBF$) measured by other techniques (24–28). The sources and detectors for both DOS and DCS were separated by 2.5 cm and held in place by a black rubber probe.

Data Analysis

To quantify the effects of $NaHCO_3$ on hemodynamics, a 1-minute mean of each of the following parameters was obtained immediately prior to, and at 1, 5, 10, and 15 minutes after injection of $NaHCO_3$: ΔHbO_2, ΔHb, ΔTHC, $\Delta rCBF$, ΔHR, ΔMAP, and $\Delta SpO2$. These time intervals were chosen because the effects of $NaHCO_3$ were expected to be clearly evident due to the rapid onset and transient action of $NaHCO_3$. Changes in each DOS parameter, i.e. Hb, HbO_2, and THC, and vital sign parameter, i.e. HR, MAP, and SpO_2, were quantified as the difference between a 1-minute average taken 1, 5, 10, and 15 minutes after $NaHCO_3$ injection and a 1-minute average immediately prior to injection. Relative changes in DCS-measured CBF were quantified using the following formula:

$$\Delta rCBF = ((\langle BFI \rangle_{Post} / \langle BFI \rangle_{Pre}) - 1) \times 100\%.$$

Here brackets $\langle\ \rangle$ indicate the mean taken over a 1-minute time period, and the subscripts *Pre* and *Post* denote means taken *before* and *after* $NaHCO_3$ injection, respectively. Note, the four *Post* averages were quantified at the time points specified above.

A subset of patients who did not receive sodium bicarbonate treatment were used as controls for the $NaHCO_3$ treated group. These control patients were individually matched with each $NaHCO_3$ treated patient for both age (within 4 months) and cardiac physiology. Vital sign and DOS/DCS monitoring were acquired continuously for these patients although they received no intervention. These control patients were intended to elucidate the normal physiologic variations that occur during the monitoring period. The baseline period for these patients was the first minute of DOS/DCS data acquisition, and changes in DOS, DCS, and vital sign parameters were computed in the same fashion as described above at 1, 5, 10, and 15 minutes after the baseline.

Statistical Analysis

A Wilcoxon signed rank test was carried out to test whether the $NaHCO_3$ treated group showed significantly different changes in vital signs and cerebral hemodynamics compared to age- and physiology-matched controls. Furthermore, to quantify the relationship between the dosage of $NaHCO_3$ and the subsequent change in CBF measured with DCS, we fit a simple linear regression model; using this model we estimated Pearson's correlation coefficient. Pearson's correlation coefficient, R, varies from 0 to 1.0 and measures the extent to which a linear model explains variability in the data. Analyses were performed using R 2.11 statistical software (R Foundation for Statistical Computing, Vienna, Austria). Hypotheses tests and associated p-values (p) were two-sided. A Hochberg correction was used to adjust p-values for multiple comparisons. Statistical significance was declared for p-values < 0.05.

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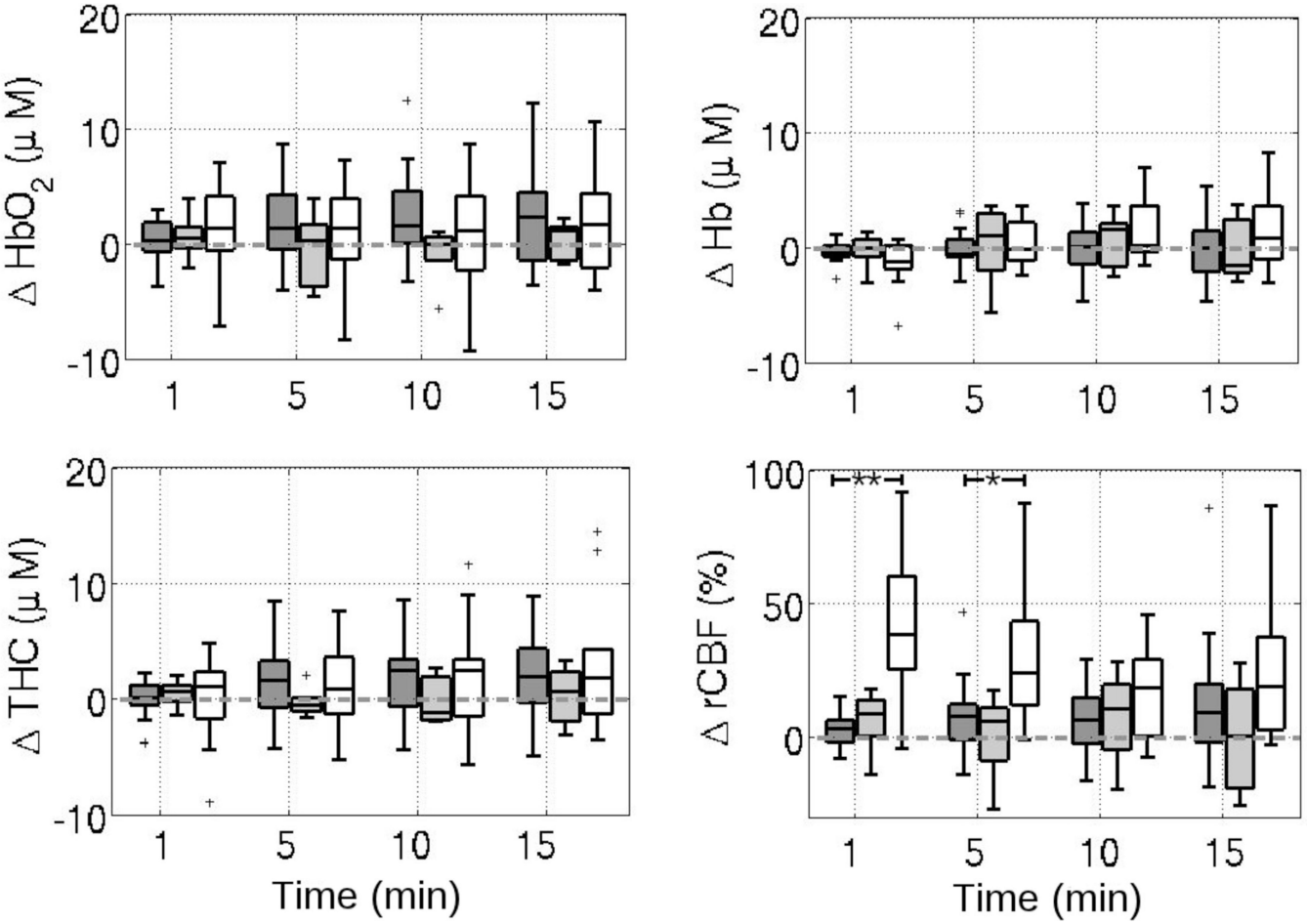

Figure 1.

Boxplots of changes from baseline in (A) deoxy-, (B) oxy-, and (C) total-hemoglobin concentrations (ΔHb, ΔHbO_2, and ΔTHC, respectively) as well as (D) cerebral blood flow (ΔrCBF) at times 1, 5, 10, and 15 minutes following $NaHCO_3$ administration (grey). The control group who received no intervention is shown in white. The dotted grey lines indicate no change from baseline levels. *$p < 0.05$.

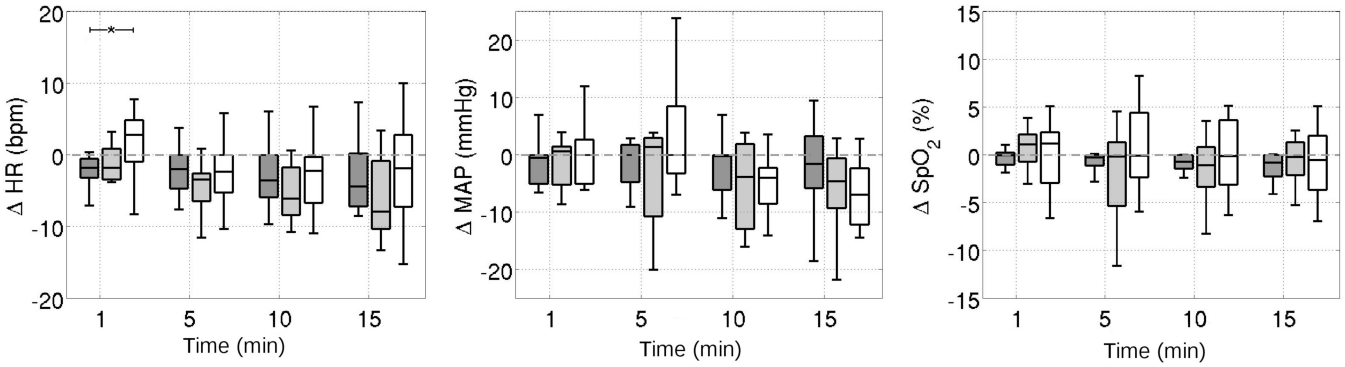

Figure 2.

Boxplots of changes from baseline in (A) heart rate, (B) mean arterial pressure, and (C) transcutaneous oxygen saturation at times 1, 5, 10, and 15 minutes following $NaHCO_3$ administration (grey). The control group who received no intervention is shown in white. The dotted grey lines indicate no change from baseline levels.

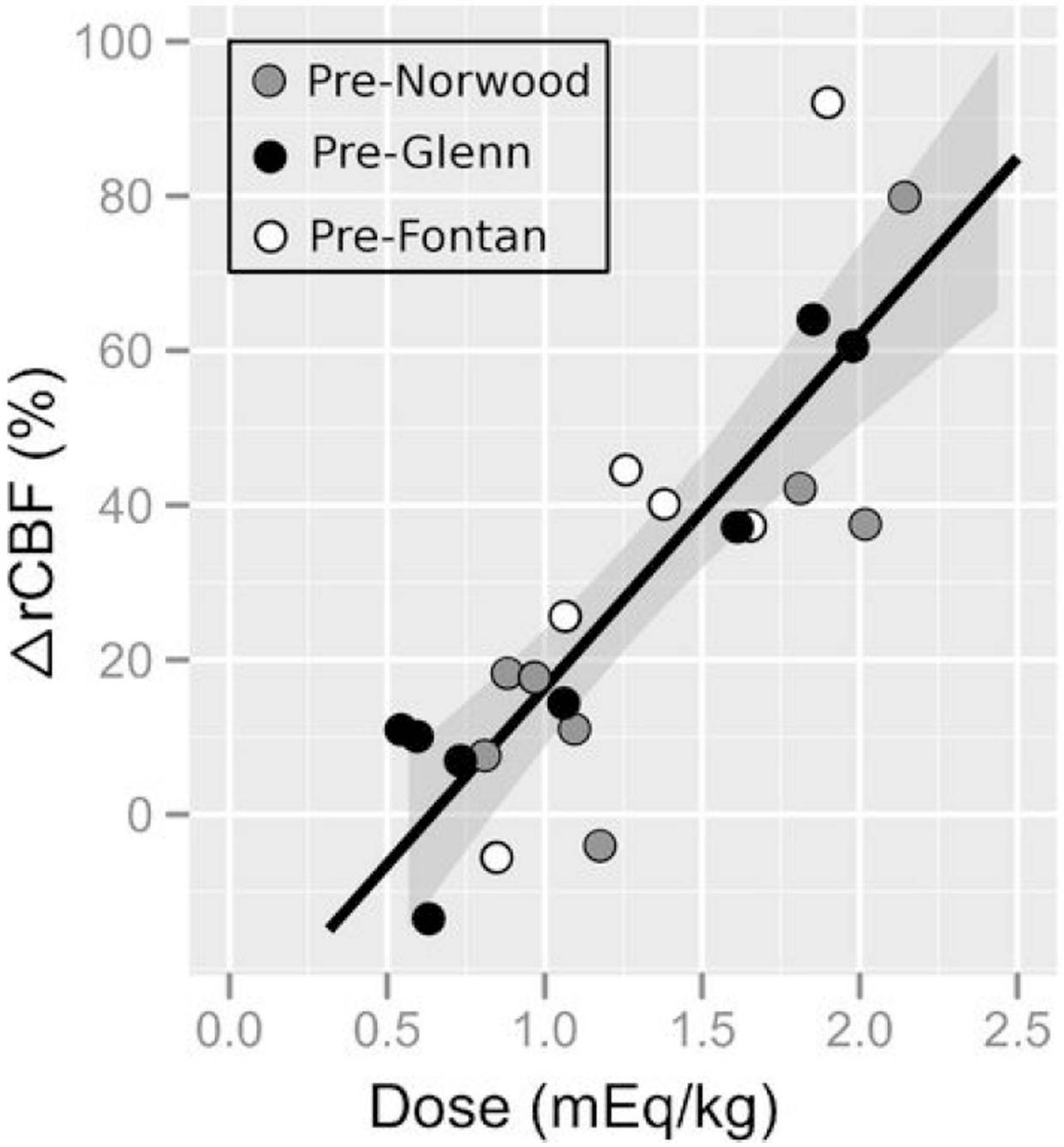

Figure 3.
Relationship between the dose of sodium bicarbonate administered (in mEq/kg) and the associated change in cerebral blood flow (%) 1 minute after injection. The black line indicates the best linear fit to the data, and the 95% confidence interval to the fit is shown in the grey shaded region. Open circles denote pre-Fontan patients, black circles denote pre-Glenn, and grey circles denote pre-Norwood.

Table 1

Summary of patient recruitment.

	Pre-Norwood	Pre-Glenn	Pre-Fontan	Total
Approached	41	264		305
Consented	27	35	71	133
Studied with DOS/DCS	25	24	42	91
Given $NaHCO_3$	8	8	6	22

Of the 91 patients monitored with DOS/DCS, 22 received an intravenous bolus of $NaHCO_3$.

Table 2

Patient Characteristics.

Variable	Level	$NaHCO_3$ Treated	Control
Sex (N (% of total))	Male	14 (64 %)	12 (55 %)
	Female	8 (36 %)	10 (45 %)
Age (years)	--	0.5 (0, 1.8)	0.4 (0, 1.7)
Weight (kg)	--	6.2 (3.4, 11.0)	5.6 (3.3, 8.9)
Cardiac Physiology (N (% of total))	Pre-Stage I	8 (36.4 %)	8 (36.4 %)
	Pre-Stage II	8 (36.4 %)	8 (36.4 %)
	Pre-Stage III	6 (27.3 %)	6 (27.3 %)

Median (interquartile range (IQR)) patient characteristics for both $NaHCO_3$ treated and age matched control patients. Patients were monitored on the day of staged cardiac surgical reconstruction, prior to surgery.

Table 3

Baseline Systemic Hemodynamics.

	Variable	$NaHCO_3$ Treated	Control
Vital Signs	Heart Rate (bpm)	138 (120, 147)	121 (108, 135)
	MAP (mmHg)	64 (61, 68)	63 (56, 71)
	SpO_2 (%)	83 (77, 92)	78 (75, 89)
Arterial Blood Gas	pH	7.35 (7.32, 7.38) *	7.39 (7.37, 7.41)
	Arterial CO_2 tension (kPa)	5.2 (4.7, 5.7)	5.3 (5.1, 5.7)
	Arterial O_2 tension (kPa)	6.7 (6.3, 7.9)	6.5 (5.7, 7.6)
	Bicarbonate (mmol/L)	21 (20, 22) *	24 (22, 26)
	Hemoglobin (g/dL)	14.3 (12.6, 15.6)	14.3 (12.6, 15.3)
	Base Deficit (mEq/L)	−4 (−6, −3) **	−1 (−3, +1)
	Dosage $NaHCO_3$ (mEq/kg)	0.8 (0.6, 0.9)	0

Median (interquartile range) baseline vital signs and measures from arterial blood gas samples taken before administration of sodium bicarbonate in the treated group as well as age matched controls (N = 22). A Wilcoxon signed rank test was carried out to test for differences in each group compared to controls:

* $p < 0.05$,

** $p < 0.001$.