

Sodium bicarbonate use and the risk of hypernatremia in thoracic aortic surgical patients with metabolic acidosis following deep hypothermic circulatory arrest

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ABSTRACT

Objective: Metabolic acidosis after deep hypothermic circulatory arrest (DHCA) for thoracic aortic operations is commonly managed with sodium bicarbonate (NaHCO_3). The purpose of this study was to determine the relationships between total NaHCO_3 dose and the severity of metabolic acidosis, duration of mechanical ventilation, duration of vasoactive infusions, and Intensive Care Unit (ICU) or hospital length of stay (LOS). **Methods:** In a single center, retrospective study, 87 consecutive elective thoracic aortic operations utilizing DHCA, were studied. Linear regression analysis was used to test for the relationships between the total NaHCO_3 dose administered through postoperative day 2, clinical variables, arterial blood gas values, and short-term clinical outcomes. **Results:** Seventy-five patients (86%) received NaHCO_3 . Total NaHCO_3 dose averaged 136 ± 112 mEq (range: 0.0–535 mEq) per patient. Total NaHCO_3 dose correlated with minimum pH ($r = 0.41$, $P < 0.0001$), minimum serum bicarbonate ($r = -0.40$, $P < 0.001$), maximum serum lactate ($r = 0.46$, $P = 0.007$), duration of metabolic acidosis ($r = 0.33$, $P = 0.002$), and maximum serum sodium concentrations ($r = 0.29$, $P = 0.007$). Postoperative hypernatremia was present in 67% of patients and peaked at 12 h following DHCA. Eight percent of patients had a serum sodium ≥ 150 mEq/L. Total NaHCO_3 dose did not correlate with anion gap, serum chloride, not the duration of mechanical ventilator support, vasoactive infusions, ICU or hospital LOS. **Conclusion:** Routine administration of NaHCO_3 was common for the management of metabolic acidosis after DHCA. Total dose of NaHCO_3 was a function of the severity and duration of metabolic acidosis. NaHCO_3 administration contributed to postoperative hypernatremia that was often severe. The total NaHCO_3 dose administered was unrelated to short-term clinical outcomes.

Received: 26-01-16

Accepted: 29-04-16

Access this article online

Website: www.annals.in

DOI:
10.4103/0971-9784.185527

Quick Response Code:



Key words: Deep hypothermic circulatory arrest; Hypernatremia; Metabolic acidosis; Sodium bicarbonate

INTRODUCTION

Metabolic acidosis is common and often severe after deep hypothermic circulatory arrest (DHCA) for elective thoracic aortic operations.^[1] Existing studies suggest that severe metabolic acidosis may cause myocardial depression, hypotension, and

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Cite this article as: Ghadimi K, Gutsche JT, Ramakrishna H, Setegne SL, Jackson KR, Augoustides JG, *et al.* Sodium bicarbonate use and the risk of hypernatremia in thoracic aortic surgical patients with metabolic acidosis following deep hypothermic circulatory arrest. *Ann Card Anaesth* 2016;19:454-62.

decrease the circulatory actions of catecholamines. In addition, respiratory compensation for severe metabolic acidosis may prolong the need for postoperative mechanical ventilator support. Because it is not possible to prevent the obligate lactic acidosis associated with the temporary interruption of systemic perfusion as a consequence of DHCA, alkali therapy is commonly administered to attenuate the decrease in pH after thoracic aortic operations. However, the clinical efficacy of sodium bicarbonate (NaHCO_3) for the treatment of metabolic acidosis among noncardiac surgical patients has remained controversial. Furthermore, the routine postoperative administration of NaHCO_3 may contribute to adverse effects that have not been well characterized. For example, NaHCO_3 may temporarily increase serum pH, but also increase the partial pressure of carbon dioxide in the blood, induce intracellular acidosis, and increase the risk of hyponatremia.^[2]

There is limited evidence to support specific clinical management protocols to guide the use of NaHCO_3 for the treatment of postoperative metabolic acidosis after operations that involve DHCA. For this reason, the management of postoperative metabolic acidosis and the administration of NaHCO_3 to treat postoperative metabolic acidosis vary among individual practices. The objective of this study was to examine the use of NaHCO_3 among patients undergoing elective thoracic aortic operations requiring DHCA in a single, established thoracic aortic surgical practice. The relationship between NaHCO_3 administration with the severity and duration of postoperative metabolic acidosis was studied together with analysis of its impact on postoperative vasopressor requirements, the duration of mechanical ventilatory support, Intensive Care Unit (ICU) length of stay (LOS), and hospital LOS. The incidence and pattern of postoperative hyponatremia, a known complication of NaHCO_3 administration, was also examined.

METHODS

Patient population

Following the Institutional Review Board approval and verification of informed written consent, 100 consecutive adult patients (age ≥ 18 years) undergoing elective thoracic aortic surgery requiring DHCA in combination with retrograde cerebral perfusion (RCP) at the hospital of the University of Pennsylvania from June 2008 to December 2009 were retrospectively studied. Patient information from a prospective database was obtained from the web-based electronic medical record and Sunrise Clinical Manager (Allscripts Healthcare Solutions Inc.,

Chicago, Illinois, USA). Exclusion criteria were patients with dialysis-dependent end-stage renal disease, emergent surgery, evidence of preexisting malperfusion, preoperative hepatic dysfunction, mesenteric ischemia, use of selective antegrade cerebral perfusion, total arch repairs, or hybrid endovascular operations. Thirteen patients met the exclusion criteria and were therefore removed from further analysis. Patient characteristics included age, body mass index (BMI), gender, preoperative laboratory tests, and medical comorbidities [Table 1]. According to the routine clinical protocol, arterial blood gas (ABG) analysis was performed every 30 min (ABL 80 analyzer, Radiometer Inc., Copenhagen, Denmark) in the operating room and approximately every 1–3 h postoperatively while the patient was cared for in a dedicated, Cardiothoracic Surgical ICU (CTICU).

Table 1: Baseline characteristics of the study population

Characteristic	Study population (n=87)
Age (years)	57.0 \pm 15.1 (24-83)
BMI (km^2)	27.8 \pm 4.5 (19.3-41.1)
Weight (kg)	85.5 \pm 16.7 (50.4-130.2)
Male (%)	65 (75)
Female (%)	22 (25)
MDRD eGFR (ml/min^a)	76.4 \pm 20.0 (20.3-144.0)
Preoperative Cr (mg/dL)	1.0 0.3 (0.5-2.6)
Aortic regurgitation (%)	62
Hypertension (%)	55
Bicuspid aortic valve (%)	43
Hyperlipidemia (%)	36
Congestive heart failure (%)	32
Aortic stenosis (%)	26
Atrial fibrillation (%)	24
Coronary artery disease (%)	17
Tobacco use (%)	14
Cardiomyopathy (%)	12
Mitral regurgitation (%)	9
Diabetes mellitus (%)	9
LV dysfunction (%)	6
Stroke (%)	6
Marfan's syndrome (%)	5
COPD (%)	5
Anemia (%)	3
Myocardial infarction (%)	3
Peripheral vascular disease (%)	1
Cerebrovascular disease (%)	1
Tricuspid regurgitation (%)	1

^aMDRD eGFR: Modification of diet in renal disease study Group equation. BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, Cr=Serum creatinine concentration, LV: Left ventricular dysfunction (defined as LVEF<50%), SD: Standard deviation, eGFR: Estimated glomerular filtration rate, LVEF: Left ventricular ejection fraction. Values are listed as the mean \pm SD with the range in parentheses

Blood gas analyzers were inspected and maintained for accuracy according to a schedule recommended by the manufacturer and clinical engineering. All time- and date-stamped ABG samples were analyzed as alpha-stat and included measures of blood concentrations of sodium [Na⁺], chloride [Cl⁻], bicarbonate [HCO₃⁻], glucose, hemoglobin, and hematocrit. The ABG value obtained in the period before cardiopulmonary bypass (CPB) was considered the baseline value for each individual patient. All ABG samples obtained after DHCA until pH normalization (pH ≥7.35) were used in the analysis. Anion gap (AG) was calculated from the ABG sample using $AG = [Na^+] - ([Cl^-] + [HCO_3^-])$. Elevated AG was defined as an AG ≥14 mEq/L. Blood lactate concentrations were measured at the discretion of the caring attending physician and were not routinely measured in every ABG sample, but all lactate samples that were measured in the study population were used in the statistical analysis. The duration of metabolic acidosis was defined as the elapsed time between the end of DHCA to the time of pH normalization.

Anesthesia protocol

All patients underwent general anesthesia with invasive arterial blood pressure monitoring and continuous cardiac output and mixed venous oxygen saturation monitoring (Swan Ganz CCombo Pulmonary Artery Catheter, Edwards Lifesciences, Inc., Irvine, CA, USA). Nasopharyngeal, bladder, venous blood inflow, and arterial blood outflow temperatures were measured continuously. Balanced anesthetic technique was administered using fentanyl, midazolam, isoflurane, and nondepolarizing muscle relaxant.

Transesophageal echocardiography (Philips Healthcare, Bothell, WA, USA) was used to confirm the surgical diagnosis and guide hemodynamic management. Unless contraindicated, epsilon-aminocaproic acid 75 mg/kg intravenous (IV) bolus and 1–2 g/h IV infusion was administered during operation. Heparin anticoagulation for CPB was titrated to maintain the activated clotting time (ACT) at >400 s. About 1500 milliliters of normal saline solution was used to prime the CPB circuit prior to cannulation. Autologous blood priming of the CPB circuit was performed whenever possible in retrograde fashion through the venous cannula just prior to initiation of CPB. The normal saline within the circuit was displaced into a container and utilized on CPB for intravascular volume expansion. This served to minimize crystalloid dilution of hematocrit. Normal saline was used as a carrier fluid for the delivery of vasoactive infusions (25–100 cc/h) and as the primary

crystalloid solution for IV volume expansion. Albumin or plasma protein fraction were not used as volume expanders during our study period.

Cardiopulmonary bypass and deep hypothermic circulatory arrest protocol

RCP was provided via the superior vena cava (SVC) venous cannula. Perfusion management and cannulation for DHCA with RCP was according to a standardized institutional protocol using alpha-stat pH management.^[3] The ascending aorta was cannulated for CPB. Standard retrograde cold blood (4°C) cardioplegia was used for myocardial protection. Mean arterial pressure (MAP) during CPB was maintained in the range of 50–70 mmHg.

During active cooling on CPB (Sarns 8000 Heart-Lung Machine, model 11160 heater/cooler unit, Terumo Cardiovascular Systems, Ann Arbor, MI, USA), the partial pressure of oxygen (PaO₂) was maintained ≥100 mmHg, PaCO₂ between 35 and 45 mmHg, and hematocrit >21%. The rate of cooling on CPB was gradually increased until the onset of ventricular fibrillation or until a CPB venous blood inflow temperature of 27°C was achieved. Cooling was thereafter continued until the target DHCA temperature was achieved or electrocortical silence appeared by electroencephalography. RCP commenced after snaring of the SVC, which consisted of oxygenated blood at 12°C delivered through the SVC cannula at a pressure ≤25 mmHg measured in the SVC. After aortic arch repair was completed, systemic CPB was resumed via cannulation of the aortic graft. Patient rewarming was initiated after a period of at least 5 min of hypothermic reperfusion. During rewarming, ABG was monitored using alpha-stat and the rate of rewarming was controlled to ensure a temperature gradient between the venous inflow and the heat exchanger of no >10°C and a nasopharyngeal temperature <36.5°C.

Separation from CPB was accomplished with external cardiac pacing if necessary, positive pressure mechanical ventilator support, IV phenylephrine to maintain a MAP ≥60 mmHg, and IV epinephrine infusion to maintain a cardiac index ≥2.3 L/min/m². Blood products were transfused to maintain the hematocrit ≥25% and to correct coagulopathy after normalizing the ACT with protamine. Intraoperative administration of NaHCO₃ was at the discretion of the cardiac anesthesiologist, and postoperative NaHCO₃ administration was at the discretion of the CTICU critical care team. The administration of NaHCO₃ was limited to use as

treatment for metabolic acidosis caused by either lactic acidosis, non-AG metabolic acidosis, or a combination of both. There was no established institutional protocol or algorithm to dictate the administration of NaHCO_3 in the CTICU. All patients were managed postoperatively in the CTICU by an intensivist-led critical care team according to a fast-track protocol. Active warming was applied to achieve normothermia (37°C). IV inotropic and vasopressor medications were actively and continuously titrated to achieve a target cardiac index ≥ 2.3 L/min/m² and MAP between 60 and 70 mmHg, then discontinued when no longer necessary. When normothermia was achieved and the FiO_2 on mechanical ventilator support was weaned to 40%, sedatives were discontinued and a spontaneous breathing trial was initiated. Tracheal extubation was performed if circulatory and ABG parameters were satisfactory after 30 min of spontaneous breathing.

Total NaHCO_3 dose in mEq was tabulated from the electronic anesthesia record and postoperative pharmacy medication records through postoperative day 2 for each individual patient. Patients who did not receive NaHCO_3 during the study period were assigned a NaHCO_3 dose of 0 mEq. The duration of mechanical ventilation was tabulated from the end of DHCA to the time of tracheal extubation in the surgical ICU. The duration of inotropic and vasopressor infusion was recorded from the time of initiation of an infusion in the operating room after DHCA to the time of discontinuation of all vasopressor and inotropic infusions in the surgical ICU. Patients who did not receive vasoactive infusions ($n = 9$) during the study period were assigned an infusion duration of 0 h. Elevated AG was defined as an AG >14 mEq/L, hyperchloremia as $[\text{Cl}^-] >110$ mEq/L, hypernatremia as $[\text{Na}^+] >145$ mEq/L, and severe hypernatremia as $[\text{Na}^+] \geq 150$ mEq/L.

Statistical methods

All data were analyzed using STATA 11 (StataCorp LP, College Station, TX, USA). The relationship between total NaHCO_3 dose administered and preoperative patient characteristics, minimum pH, duration of metabolic acidosis, DHCA conditions, clinical parameters, or outcome variables were tested using Pearson product-moment correlation coefficients (r). A relationship was considered significant when the $P < 0.05$. All values were presented as mean \pm standard deviation (range). To establish the relationship between variables, linear regression models were developed first to determine *a priori* univariate predictors and then

parsimonious models were built to determine which univariate predictor(s) contributed significantly in a multivariate model.

RESULTS

A total of 87 patients underwent elective thoracic aortic repair involving the ascending thoracic aorta and aortic arch employing DHCA with RCP. RCP was performed in combination with DHCA in all patients. All patients underwent operations involving the ascending aorta with hemiarch graft. The average DHCA time was 23.7 ± 5.6 min (range: 14.0–46.0 min) with a mean DHCA temperature of $15.3 \pm 2.1^\circ\text{C}$ (range: 10.6–20.7°C). There were no operative deaths and no deaths within 30 days of operation. No patients required re-exploration for operative bleeding in the postoperative period. Three patients in the study population had postoperative delirium based on review of intensivist progress notes, discharge summaries, and consultation notes. Exact criteria for diagnosis of delirium were, however, not defined.

Seventy-six patients (87%) had a minimum pH <7.35 , 55 (63%) had a minimum pH <7.30 , 28 (32%) had a pH <7.25 , and 7 (8%) had pH <7.20 after DHCA. The mean minimum pH was 7.27 ± 0.06 (7.13–7.41) and the mean PaCO_2 at the time of minimum pH was 42.6 ± 6.4 mmHg. The average minimum $[\text{HCO}_3^-]$ was 18.0 ± 2.1 mEq/L (range: 11.0–24.0 mEq/L) [Tables 2 and 3]. The duration of the metabolic acidosis averaged 7.9 ± 5.0 h, but lasted up to 27 h.

Seventy-five patients (86%) received NaHCO_3 for the management of metabolic acidosis after DHCA. The average total dose of NaHCO_3 administered was 136 ± 112 mEq (range: 0–535 mEq). Serum $[\text{Na}^+]$ increased significantly from a mean value before CPB of 136 ± 4 mEq/L (range: 124–144 mEq/L) to a mean maximum postoperative value of 147 ± 3 mEq/L (range: 138–155 mEq/L) ($P < 0.0001$). No patients had preoperative hypernatremia and 58 patients (67%) developed postoperative hypernatremia, defined as a maximum $[\text{Na}^+] >145$ mEq/L. Seven patients (8%) developed severe postoperative hypernatremia, defined as $[\text{Na}^+] \geq 150$ mEq/L. Among the patients with severe hypernatremia, 3 had serum $[\text{Na}^+]$ of 150 mEq/L, 1 had $[\text{Na}^+]$ of 152 mEq/L, 1 had $[\text{Na}^+]$ of 153 mEq/L, and 2 had $[\text{Na}^+]$ of 155 mEq/L. The total dose of NaHCO_3 administered correlated with the maximum postoperative $[\text{Na}^+]$ [Figure 1] ($r = 0.29$, $P = 0.007$), maximum arterial lactate concentration

Table 2: Clinical and laboratory parameters related to sodium bicarbonate administration

Parameter	Sample size	Mean±SD	Range
Minimum pH	87	7.27±0.06	7.13-7.41
Total NaHCO ₃ dose (mEq)	87	135.9±112.2	0.0-535.2
Duration of Metabolic acidosis (h) ^a	87	7.9±5.0	0.0-26.8
Maximum AG (mEq/L) ^b	87	10.4±3.1	2.6-19.8
Maximum serum lactate (mmol/L)	34	7.8±4.1	1.0-16.9
Maximum serum chloride (mEq/L)	87	114.6±3.6	106.0-124.0
Maximum serum sodium (mEq/L)	87	146.6±3.2	138.0-155.0
Maximum serum bicarbonate (mEq/L)	87	27.2±2.4	21.8-33.0
Minimum serum bicarbonate (mEq/L)	87	17.9±2.1	11.0-24.0
Mechanical ventilation (h)	87	38.0±40.6	8.4-202.1
Vasoactive infusion (h)	87	28.1±36.9	0.0-254.7
ICU LOS (days)	87	1.7±1.2	1.0-8.0
Hospital LOS (days)	87	9.6±3.3	6.0-21.0

^aDuration of metabolic acidosis was defined as the elapsed time between the end of deep hypothermic circulatory arrest and first arterial pH ≥ 7.35 . ^bAG: Sodium - (chloride+bicarbonate). ICU: Intensive Care Unit, LOS: Length of stay, NaHCO₃: Sodium bicarbonate, SD: Standard deviation, AG: Anion gap

Table 3: Relationship between sodium bicarbonate dosage and study parameters

Study parameter	Correlation coefficient (r)	P
Minimum pH	-0.41	<0.0001
Minimum serum bicarbonate	-0.40	<0.0001
Time to pH normalization	0.333	<0.001
Maximum serum lactate ^a	0.455	0.004
Maximum serum sodium	0.285	0.004
Hospital LOS	-0.097	0.33
Maximum serum chloride	0.142	0.15
ICU LOS	-0.048	0.62
Maximum serum AG ^b	0.108	0.27
Duration of mechanical ventilation	-0.008	0.94
Duration of vasoactive infusion	0.110	0.26

^aOnly includes patients with recorded lactate values (n=34), ^bAG: Sodium - (chloride+bicarbonate). ICU: Intensive Care Unit, LOS: Length of stay, AG: Anion gap

[Figure 2] ($r = 0.46$, $P = 0.007$), minimum arterial pH ($r = -0.041$, $P < 0.0001$), minimum arterial [HCO₃⁻] ($r = -0.40$, $P < 0.0001$), and the duration of metabolic acidosis ($r = 0.3$, $P = 0.002$) [Table 3]. Postoperative serum [Na⁺] reached its maximum concentration at approximately 10 h after DHCA and gradually returned to normal within 36–48 h after DHCA [Figure 3].

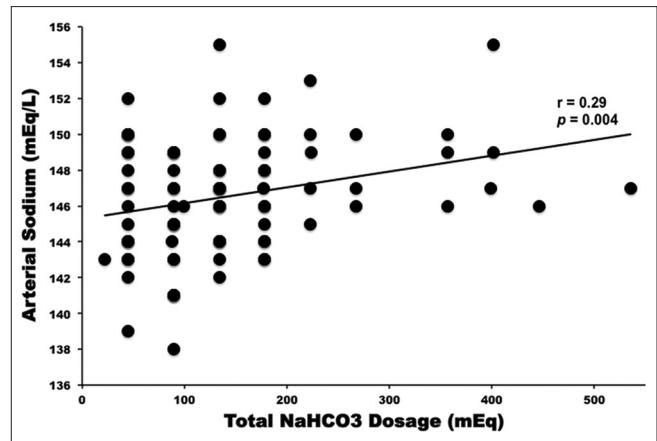


Figure 1: The total dose of NaHCO₃ administered in relation to the maximum postoperative serum sodium concentration among patients undergoing thoracic aortic operations with deep hypothermic circulatory arrest ($n = 87$). The total dose of NaHCO₃ correlated significantly with the maximum postoperative serum sodium concentrations ($r = 0.29$, $P = 0.004$). NaHCO₃: Sodium bicarbonate

One out of the three patients with postoperative delirium had severe hyponatremia (serum Na⁺ ≥ 150 mEq/L) [Table 4 and Figure 4].

Predictors of total NaHCO₃ dosage in the univariate analysis were preoperative estimated glomerular filtration rate ($r = -0.36$, 95% confidence interval [CI]: -0.70 – -0.13 , $P = 0.043$), preoperative creatinine ($r = 56.2$, 95% CI: 10.6 – 101.7 , $P = 0.016$), and BMI ($r = 2.89$, 95% CI: 0.10 – 5.69 , $P = 0.042$). All univariate predictors, however, fell out of regression modeling during multivariate analysis and did not contribute toward prediction. There was no significant correlation detected between the total NaHCO₃ dose administered with the maximum postoperative [Cl⁻], duration of postoperative inotropic and vasopressor infusion, duration of mechanical ventilation, ICU LOS, or hospital LOS. Interestingly, duration of mechanical ventilation was not predicted by dose of NaHCO₃ administration ($P = 0.75$) but rather by patient age ($r = 41.6$, 95% CI: 9.5 – 73.8 , $P = 0.012$) and CPB time ($r = 10.8$, 95% CI: 2.2 – 19.4 , $P = 0.014$).

DISCUSSION

NaHCO₃ was administered frequently with 75 patients (86%) receiving at least 1 dose for the management of metabolic acidosis after DHCA. The average total dose of NaHCO₃ administered was 136 ± 112 mEq, but ranged from 0 mEq to 535 mEq among individual patients. The negative correlation observed between NaHCO₃ and postoperative pH or serum bicarbonate

concentration indicated that NaHCO₃ was more likely to be administered and given in greater doses according to the severity of postoperative metabolic acidosis. The positive correlation between the NaHCO₃ dose and serum lactate concentrations indicated that NaHCO₃ was more likely to be administered among patients who had serum lactate measured and when serum lactate concentrations were abnormally elevated. The positive correlation between NaHCO₃ dose and the time to pH normalization indicated also that the dose of NaHCO₃ administered was greater among patients with prolonged metabolic acidosis. These findings could be interpreted to indicate that NaHCO₃ administration did not decrease the severity nor decrease duration of postoperative metabolic acidosis if it was administered indiscriminately after DHCA. Alternatively, if NaHCO₃ was administered selectively to patients with more severe or prolonged metabolic acidosis, the observed pH values and duration of postoperative acidosis may have been even more extreme in the absence of NaHCO₃ administration. The significance of administering buffered solutions for the management of non-AG

metabolic acidosis (e.g., hyperchloremia) has been discussed in our companion investigation and limiting saline administration may reduce the incidence iatrogenic hyperchloremia.^[1] Future prospective studies may, however, assess the effects of administering buffered solutions on the modulation of hyperchloremic metabolic acidosis after DHCA by evaluating the efficacy of an established algorithm for management of acid-base imbalance and electrolyte disorders.

The absence of an observed relationship between the NaHCO₃ dose administered and the duration of IV inotropic or vasopressor medications suggested that the severity and duration of postoperative metabolic acidosis did not affect the recovery of circulatory

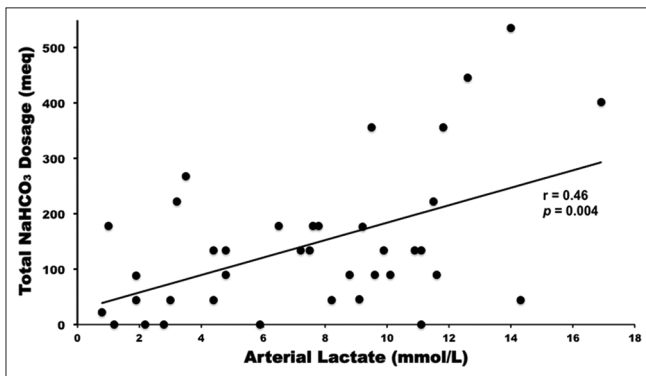


Figure 2: The total dose of NaHCO₃ administered in relation to the maximum postoperative serum lactate concentration among patients undergoing thoracic aortic operations with deep hypothermic circulatory arrest, who had lactate measurements (*n* = 34). Total dose of NaHCO₃ correlated significantly with the maximum postoperative serum lactate concentration (*r* = 0.46, *P* = 0.004). NaHCO₃: Sodium bicarbonate

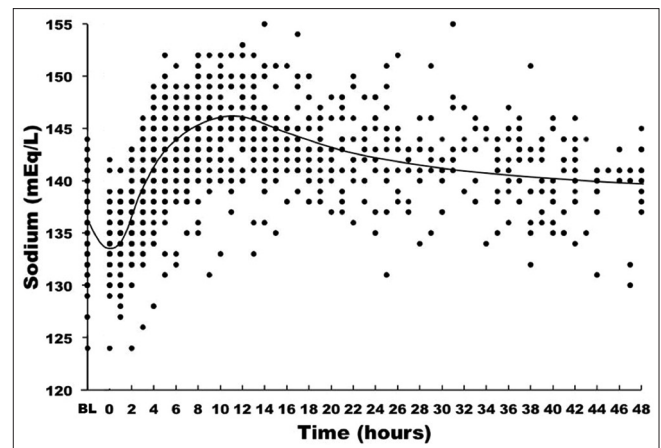


Figure 3: Serum sodium concentrations for patients during the study period. Serum sodium concentration increased significantly after operation among patients (*n* = 87) undergoing thoracic aortic operations with deep hypothermic circulatory arrest to a mean maximum value of 147 ± 3 mEq/L (range: 138–155 mEq/L), *P* < 0.0001. Note that values ranged between 138 and 155 mEq/L and therefore several points overlapped on this graph at similar time points. The maximum postoperative serum sodium concentration correlated with the maximum dose of sodium bicarbonate administered and peaked at approximately 8–12 h after operation. BL values obtained prior to CPB were displayed to the left of time 0 h, on the abscissa. Time 0 h represents the end of deep hypothermic circulatory arrest. BL: Baseline, CPB: Cardiopulmonary bypass

Table 4: Patients with postoperative delirium after deep hypothermic circulatory arrest

Patient	Age	Operation	CPB time (min)	DHCA time (min)	Minimum pH	Preoperative Na ⁺ (mEq/L)	Maximum Na ⁺ Post-DHCA (mEq/L)	Total NaHCO ₃ dose (mEq)
1	72	Composite aortic valve, root, ascending aorta and hemiarch replacement	232	19	7.36	132	144	89.2
2	64	Composite aortic valve, root, ascending aorta and hemiarch replacement	229	27	7.31	135	143	89.2
3	76	Ascending aorta and hemiarch replacement	187	30	7.21	138	150	356.6

CPB: Cardiopulmonary bypass, DHCA: Deep hypothermic circulatory arrest, NaHCO₃: Sodium bicarbonate

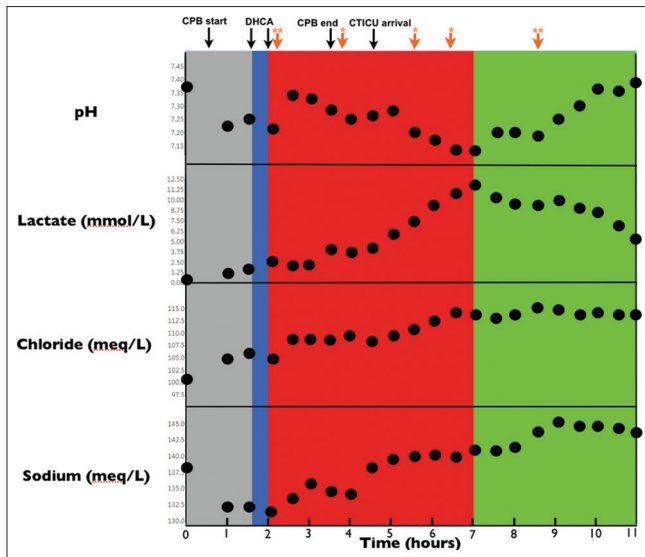


Figure 4: Characteristic postoperative pattern of arterial pH, lactate, chloride, and sodium over time in a representative single patient ($n = 1$) who had undergone deep hypothermic circulatory arrest for ascending aorta and hemiarch graft replacement. The gray zone represents the time prior to the initiation of deep hypothermic circulatory arrest, the blue zone represents the period of deep hypothermic circulatory arrest, the red zone indicates the time period of progressive metabolic acidosis during reperfusion, and the green zone represents the recovery from metabolic acidosis. The black arrows indicate events during the perioperative course. The orange arrows represent times at which sodium bicarbonate was administered (each* = 1 ampule of 44.6 mEq/50 ml). CPB: Cardiopulmonary bypass, CTICU: Cardiothoracic Surgical Intensive Care Unit

function after thoracic aortic operations with DHCA. The absence of a significant relationship between vasopressor requirements and the severity of metabolic acidosis questions the clinical efficacy of NaHCO_3 for the routine treatment of postoperative metabolic acidosis. Alkali for the treatment of lactic acidosis was advocated based on canine studies showing the administration of tris(hydroxymethyl)-aminomethane to increase arterial pH could reverse the effects of acute lactic acidosis, that was shown to depress left ventricular contractility, trigger the release of catecholamines, and decrease the responsiveness of the left ventricle to the actions of catecholamines.^[4] Similar findings in experiments conducted on chick embryos supported also the detrimental effects of acidosis on the circulatory function.^[5] However, the efficacy of NaHCO_3 to treat circulatory consequences of metabolic acidosis has not been reproduced in the clinical setting among ICU patients on vasopressor support.^[2,6] In a prospective case-controlled clinical study, NaHCO_3 administration failed to improve the arterial pressure, pulmonary capillary wedge pressure, and cardiac output among a small sample of noncardiac surgical ICU patients with lactic acidosis.^[2] The findings of this study in thoracic

aortic surgical patients undergoing DHCA tend to support the published clinical experience that NaHCO_3 administration had limited efficacy for augmenting circulatory function in patients with postoperative metabolic acidosis. The alternative interpretation of the findings that routine NaHCO_3 administration attenuated the circulatory consequences of metabolic acidosis to eliminate any relationship between the duration of vasopressor requirements and the severity of postoperative metabolic acidosis was possible, but unlikely.

The absence of a relationship between NaHCO_3 administration and the duration of postoperative mechanical ventilator support also suggested that NaHCO_3 administration had little clinical effect on the recovery of respiratory function after thoracic aortic operations employing DHCA. In clinical studies, although NaHCO_3 administration temporarily increased arterial pH, the improvement in arterial pH was subsequently associated with an increase in arterial PaCO_2 .^[2,6] This may be supported by the slight elevation in mean PaCO_2 recorded at time of minimum pH in our study population. Therefore, the net effect of NaHCO_3 administration on arterial pH and PaCO_2 would not be expected to impact the need for mechanical ventilator support nor the respiratory demands imposed by the presence of metabolic acidosis.

An important finding of this study was the observation that routine NaHCO_3 administration for the treatment of postoperative acidosis was associated with hyponatremia that was often severe and often lasted beyond the duration of metabolic acidosis. The overall incidence of hyponatremia was 67% in our study population. The severity of postoperative hyponatremia correlated with the total dose of NaHCO_3 administered, with 8% of patients developing severe hyponatremia. Acute hyponatremia is an established clinical consequence of hypertonic NaHCO_3 (8.4%, 1 mEq/L or 7.5%, 0.9 mEq/L solutions)^[7] and acquired postoperative hyponatremia has been reported to be associated with increased mortality among CTICU patients.^[8,9] Acute hyponatremia causes intracellular dehydration that predominantly manifests as neurologic symptoms of thirst, irritability, confusion, depressed sensorium, and seizures that have been reported to be present in 36% of patients with serum sodium concentrations above 150 mEq/L.^[10,11] These neurologic signs attributed to hyponatremia are also observed commonly among cardiac surgical patients in the early postoperative

period. Despite the high prevalence of postoperative hyponatremia in the study population, it was not found to be associated with adverse short-term clinical outcomes. Only three patients in the study population were diagnosed with postoperative delirium and 1 of those 3 patients with postoperative delirium had severe hyponatremia [Table 4]. The incidence of delirium may have been underestimated, however, because it was not an outcome assessed in the study protocol. An explanation for the absence of negative outcomes associated with postoperative hyponatremia in the study population may be that NaHCO₃ administration or the underlying condition that led to the development of postoperative hyponatremia was self-limiting.

Limitations

The study achieved the purposes of characterizing the relationships between the total dose of NaHCO₃ administration with the severity of postoperative metabolic acidosis and short-term clinical outcomes in this patient population. However, the retrospective, observational design of the study limited the ability to determine whether the absence of a relationship between NaHCO₃ dose and short-term clinical outcomes was because NaHCO₃ was effective for attenuating the severity and clinical consequences of postoperative acidosis or that clinical outcomes were the same regardless of the dose of NaHCO₃ administered. Furthermore, the study population consisted of elective uncomplicated surgical patients with predictable clinical outcomes. It was possible that clinical findings related to NaHCO₃ use may be different among high-risk patients undergoing operations requiring DHCA. A randomized, clinical trial would be necessary to answer definitively whether NaHCO₃ administration provides clinical benefit for the routine treatment of metabolic acidosis after DHCA. Despite this limitation of the study, the findings provided important insights on the use of NaHCO₃ in postoperative cardiac surgical patients in a typical clinical practice. The findings of the study also support the clinical feasibility and safety of performing a randomized clinical trial to determine the risks and benefits of NaHCO₃ administration to treat postoperative metabolic acidosis. Although the study was not able to establish the clinical efficacy of NaHCO₃, the study findings did reveal that hyponatremia was an important adverse consequence of NaHCO₃ administration. It was possible that the study underestimated the correlation between NaHCO₃ administration and the severity of hyponatremia because only doses of NaHCO₃ that were recorded in the electronic medical records and the ICU pharmacy

records were available for analysis. Despite this limitation, the study did establish that acute, new onset postoperative hyponatremia among patients receiving NaHCO₃ was common, often severe, and related to the total dose of NaHCO₃ administered.

CONCLUSION

The IV administration of NaHCO₃ was common practice in the routine clinical management of metabolic acidosis after DHCA among patients undergoing thoracic aortic operations. The total dose of NaHCO₃ administered was related to the severity and duration of metabolic acidosis. Postoperative serum sodium values should be measured frequently during the administration of NaHCO₃ because it caused dose-dependent, acute postoperative hyponatremia that was often severe. The absence of a significant relationship between NaHCO₃ administration and clinical outcomes suggested that the severity of metabolic acidosis and management with NaHCO₃ did not impact clinical outcomes. Further studies are warranted to establish whether objective evidence exists to support the routine administration of NaHCO₃ for the treatment of the obligate postoperative metabolic acidosis to be expected after cardiac operations that require DHCA.

Acknowledgements

The work for this project was entirely funded by the Department of Anesthesiology and Critical Care at the University of Pennsylvania.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Ghadimi K, Gutsche JT, Setegne SL, Jackson KR, Augoustides JG, Ochroch EA, *et al.* Severity and duration of metabolic acidosis after deep hypothermic circulatory arrest for thoracic aortic surgery. *J Cardiothorac Vasc Anesth* 2015;29:1432-40.
2. Mathieu D, Neviere R, Billard V, Fleyfel M, Wattel F. Effects of bicarbonate therapy on hemodynamics and tissue oxygenation in patients with lactic acidosis: A prospective, controlled clinical study. *Crit Care Med* 1991;19:1352-6.
3. Appoo JJ, Augoustides JG, Pochettino A, Savino JS, McGarvey ML, Cowie DC, *et al.* Perioperative outcome in adults undergoing elective deep hypothermic circulatory arrest with retrograde cerebral perfusion in proximal aortic arch repair: Evaluation of protocol-based care. *J Cardiothorac Vasc Anesth* 2006;20:3-7.

4. Wildenthal K, Mierzwiak DS, Myers RW, Mitchell JH. Effects of acute lactic acidosis on left ventricular performance. *Am J Physiol* 1968;214:1352-9.
5. Marsh JD, Margolis TI, Kim D. Mechanism of diminished contractile response to catecholamines during acidosis. *Am J Physiol* 1988;254(1 Pt 2):H20-7.
6. Cooper DJ, Walley KR, Wiggs BR, Russell JA. Bicarbonate does not improve hemodynamics in critically ill patients who have lactic acidosis. A prospective, controlled clinical study. *Ann Intern Med* 1990;112:492-8.
7. Máttar JA, Weil MH, Shubin H, Stein L. Cardiac arrest in the critically ill. II. Hyperosmolal states following cardiac arrest. *Am J Med* 1974;56:162-8.
8. Lindner G, Funk GC, Lassnigg A, Mouhieddine M, Ahmad SA, Schwarz C, *et al.* Intensive care-acquired hypernatremia after major cardiothoracic surgery is associated with increased mortality. *Intensive Care Med* 2010;36:1718-23.
9. Stelfox HT, Ahmed SB, Zygun D, Khandwala F, Laupland K. Characterization of intensive care unit acquired hyponatremia and hypernatremia following cardiac surgery. *Can J Anaesth* 2010;57:650-8.
10. Arieff AI, Guisado R. Effects on the central nervous system of hypernatremic and hyponatremic states. *Kidney Int* 1976;10:104-16.
11. Ross EJ, Christie SB. Hypernatremia. *Medicine (Baltimore)* 1969;48:441-73.

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