ARTERIAL BLOOD GAS MANAGEMENT DURING CARDIOPULMONARY BYPASS.

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ABSTRACT

This study sought to investigate the effects of α -stat and pH stat regimens on cardiac outcome during moderate hypothermic cardiopulmonary bypass. 100 patients undergoing elective coronary artery bypass grafting (CABG) were randomly assigned with respect to the target value for PaCO_2 during cardiopulmonary bypass (CPB) into 2 groups. In 50 patients the target PaCO_2 was 40 mmHg, measured at a standard electrode temperature of 37 °C while in the other 50 patients the target PaCO_2 was 40 mmHg, corrected to the patients nasopharyngeal temperature (lowest value reached: $32 \pm 0.5^\circ\text{C}$). There were no significant differences between groups with regards to cardiac outcome such as appearance of new 'Q' waves on the electrocardiogram, postoperative creatinine kinase-MB fraction, systemic vascular resistance (SVR), cardiac index (CI), need for inotropic or intra-aortic balloon pump support and the length of postoperative ventilation or intensive care unit stay. These findings support the hypothesis that CO_2 management during CPB at moderate hypothermia has no clinically significant effect on cardiac outcome.

KEY WORDS

Arterial blood gases, cardiopulmonary bypass.

INTRODUCTION

The question of optimal blood gas management during deliberate hypothermia has been the subject of much debate (1-6). Two approaches have been advocated. The first is to adjust the arterial partial pressure of CO_2 to maintain the blood near pH 7.40 at the patient's body temperature. The readings from the blood gas analyzer must then be mathematically corrected because they are conventionally made at an electrode temperature of 37°C. This approach has been known as 'pH stat' management because it seeks to achieve a constant arterial pH as the patient's temperature varies.

The other approach is known as ' α stat' management, which was suggested by Rahn et al (7) as a means to preserve cellular metabolism during varying temperatures by keeping a constant state of electrochemical dissociation of the ionizable amino acids (principally the α -imidazole group of histidine); α -stat management requires that the total CO_2 content of the blood remain constant when cooling (in the absence of metabolic acidosis or alkalosis). Because this mirrors the situation in which a blood sample is

warmed anaerobically for analysis in a blood-gas machine, α -stat can be approximated by adjusting the patient's arterial CO_2 tension to give blood-gas analyzer readings of 40mmHg, without correction, regardless of body temperature. With this approach the increased solubility of CO_2 during hypothermia results in a decrease in PCO_2 producing a respiratory alkalosis when blood-gas values are corrected for temperature.

Studies in dogs have found that alkalosis during hypothermia results in increased cardiac index (8), increased cardiac oxygen utilization and lactate extraction (8, 9) increased myocardial contractility (8), increased subendocardial blood flow (8) and less tendency for ventricular fibrillation (10). However, pH does not influence performance of the isolated rat heart during hypothermia (11).

To determine whether the known physiologic responses to CO_2 management during cardiopulmonary bypass (CPB) with moderate hypothermia affect cardiac outcome in patients this randomized clinical trial was undertaken to compare the α -stat and pH-stat regimens.

MATERIALS AND METHODS

With institutional ethical committee approval and informed patient consent 100 patients undergoing coronary artery bypass grafting (CABG) on cardiopulmonary bypass (CPB) were studied. All patients included in the study had a triple vessel

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coronary artery disease. Exclusion criteria included the following: reoperations, poor left ventricular function (ejection fraction < 30%) and emergency CABG.

Preanesthetic medication consisted of oral diazepam (0.15mg. Kg^{-1}) on the night prior to surgery and intramuscular midazolam (0.1mg.Kg^{-1}) on the morning of surgery. A standardized anesthetic technique was used with oxygen, nitrous oxide and isoflurane. Inj. vecuronium (0.1mg.Kg^{-1}) was used for neuromuscular blockade, Inj. midazolam ($0.1\text{--}0.2\text{mg. Kg}^{-1}$) was used for amnesia and Inj. fentanyl citrate (15mg. Kg^{-1}) was used for analgesia. A triple lumen central line along with a pulmonary artery catheter was inserted through the right internal jugular vein in all the cases.

Prebypass, anticoagulation was achieved by 300 U.Kg^{-1} of heparin, supplemented as needed to maintain an activated clotting time (ACT) of at least 480 seconds during CPB. The bypass circuit was primed with ringers lactate solution and mannitol (1G. Kg^{-1}). Following median sternotomy and heparinization, cardiopulmonary bypass (CPB) was established with a single right atrial cannula and an ascending aortic cannula and a membrane oxygenator. During bypass the haematocrit was maintained between 20 and 25%, pump flow at 2.2 L min^{-1} per square meter body surface area and mean arterial pressures above 50mm Hg. St. Thomas solution was the cardioplegic solution used. Cold blood cardioplegia (10°C) was employed in all the cases. The first dose of cardioplegia was instituted in an antegrade fashion via the aortic root and subsequent doses of cardioplegia were instituted in a retrograde fashion every 20 minutes through the coronary sinus. CPB was conducted under mild hypothermic conditions (32°C). Oxygen inflow to the oxygenator was 6 L. min^{-1} or higher if needed to achieve satisfactory arterial oxygenation. Haemodynamic changes were treated with vasopressors or vasodilators.

A computer generated random number table was used to allocate patients to one of the two groups: 1) Maintenance of PaCO_2 during CPB at 40mmHg at the standard electrode temperature of 37°C (α -stat), or 2) Maintenance at 40mmHg corrected to nasopharyngeal temperature (pH-stat). Blood-gas samples were analyzed every 15 minutes during CPB by a blood-gas analyzer (Nova stat M). The blood-gas instrument performed temperature correction for the pH-stat group automatically. CO_2 inflow into the oxygenator was adjusted according to blood gas results to maintain the desired PaCO_2 .

Cardiac outcome was assessed by conventional clinical methods as follows: Data recorded in the operating room were the number of defibrillations necessary to produce an organized cardiac rhythm

after release of the aortic cross clamp and the need for infusion of inotropic drugs and intra-aortic balloon counter pulsation (IABP). Postoperatively blood samples for creatine kinase (CK) were obtained upon arrival in the intensive care unit (ICU) and again at 12 hours and 24 hours postoperatively. The CK-MB fraction was considered to be elevated if it exceeded 20U. L^{-1} on any sample. 12 lead electrocardiograms (ECG) were obtained upon arrival in the ICU and daily thereafter till the patient remained in the ICU. All postoperative ECG's of patients with elevated CK-MB were reviewed for the presence of new 'Q' waves. The time to extubation, use of inotropic drugs and duration of ICU stay were also recorded.

Comparisons of the two groups were made using the two-sample 't' test. Reported 'p' values have not been adjusted for multiple comparisons. Indices of myocardial injury and performance were compared by the Mann-Whitney test for continuous variables, and the chi-square test (with correction for continuity) or the Fisher's exact test for the binary variables. Statistical comparisons were performed using a SPSS programme. A two-tailed significance level of 0.05 was used throughout.

RESULTS

50 patients were randomized to α -stat management (mean age $\pm$ SD; 59.6 ± 9.1 years) and 50 to pH-stat management (mean age $\pm$ SD; 58.6 ± 9.8 years). There were no differences between groups approaching statistical significance with respect to sex, height, weight, preoperative CK (total and MB fraction) or left ventricular ejection fraction. Intraoperatively, the means of the corrected and uncorrected PCO_2 and pH values over the period of CPB were significantly different between groups, but no significant differences occurred in the other variables related to CPB (table 1).

There were no mortalities in both the groups. No significant differences were found between the CO_2 groups with respect to any of the cardiac measures (tables 2,3). Two variables (CK-MB fraction and defibrillations) were analyzed in both a continuous and dichotomous fashion.

DISCUSSION

The effects of induced hypothermia in cardiac surgical patients are not yet fully understood. Despite numerous studies on the effects of acid base management on organ blood flow, little information is available on the effects of α stat' versus 'pH stat' management on systemic haemodynamics (5, 12).

This study demonstrates that there is no difference in systemic vascular resistance in patients undergoing hypothermic CPB under either α stat' or 'pH stat'

conditions. Changes in systemic haemodynamics during CPB may be related to several factors such as changes in pump flow rate, flow characteristics, hypothermia and viscosity (13, 14). The effects of arterial carbon dioxide tension on systemic haemodynamics and organ blood flow, however, still a matter of discussion (15-17).

Under conditions of spontaneous circulation, Cullen and colleagues have investigated the effects of arterial carbon dioxide tension on systemic haemodynamics (18). They found that an increase in arterial PaCO₂ is associated with a decrease in SVR and a concomitant

increase in cardiac output (CO) (18). Gregory and colleagues and Kazmaier and colleagues have described similar results (19, 20). The effects of arterial carbon dioxide tension have also been investigated in patients undergoing CPB (12, 13, 21, 22). The results of our study are quite comparable with that of Alston and colleagues (13) wherein no significant changes in SVR could be observed when the two groups of patients undergoing either 'α stat' or 'pH stat' management were compared; however, in both groups of patients SVR increased with duration of CPB. The progressive increase in SVR is related to changes in vasomotor tone due to impairment of tissue perfusion

TABLE 1: COMPARISON OF CO₂ GROUPS

	'α stat'	'pH stat'	'p' value
PaCO ₂ (mmHg, Un)	40.2 ± 1.3	46.3 ± 3.4	< 0.001
PaCO ₂ (mmHg, Co)	32.6 ± 1.2	38.1 ± 2.0	< 0.001
pH (Un)	7.37 ± 0.03	7.32 ± 0.05	< 0.001
pH (Co)	7.45 ± 0.02	7.39 ± 0.05	< 0.001
CPB time (min)	90.1 ± 26.2	96.7 ± 32.4	> 0.05
AOT time (min)	48 ± 16	52 ± 18	> 0.05
MNPT (°C)	30.1 ± 1.5	30.1 ± 1.8	> 0.05
MHct (%)	22.8 ± 3.0	23.2 ± 2.0	> 0.05
MAP (mmHg)	71.3 ± 6.0	71.6 ± 7.7	> 0.05
SVR (dynes.sec.cm ⁻⁵)	1502 ± 71	1476 ± 88	> 0.05
CI (min ⁻¹ .m ⁻²)	2.68 ± 0.65	2.72 ± 0.71	> 0.05

Legend : (Values are expressed as means ± standard deviation.)
 CPB: Cardiopulmonary bypass.
 AOT: Aortic cross clamp time.
 MNPT: Minimum nasopharyngeal temperature.
 MHct: Minimum haematocrit.
 MAP: Mean arterial pressure.
 Un: Uncorrected.
 Co: Corrected.
 SVR: Systemic vascular resistance.
 CI: Cardiac index.

TABLE 2: CARDIAC OUTCOMES IN THE STUDY GROUPS

	'α stat'	'pH stat'	'p' value
Defibrillations on CPB	2.1 ± 5.4	1.2 ± 4.2	0.27
Time to extubation (hours)	20.6 ± 11.4	21.0 ± 12.0	0.76
Time in ICU (days)	2.2 ± 1.2	2.2 ± 1.2	0.91
CK, Total (IU)	612.8 ± 476.1	580.1 ± 428.6	0.47
CK-MB fraction (IU)	16.6 ± 11.2	14.8 ± 8.4	0.12

Legend : (Values are expressed as means ± standard deviation).
 CPB: Cardiopulmonary bypass.
 ICU: Intensive care unit.
 IU: International units.

TABLE 3. CARDIAC OUTCOMES BY CO₂ GROUPS, DICHOTOMOUS VARIABLES

	' α stat' n (%)	'pH stat' n (%)	'p' value
Inotropic support in OT	44 (88)	47 (94)	1.1
Balloon pump in OT	3 (6)	2 (4)	0.2
Elevated CK-MB fraction	10 (20)	8 (16)	0.26
New 'Q' waves on ECG*	2 (4)	1 (2)	0.34
Inotropic support in ICU	18 (36)	22 (44)	0.66
<p>Legend : OT: operation theatre. ICU: Intensive care unit. ECG: Electro cardio gram. *Of those patients with elevated CK-MB.</p>			

and active constriction of metaarterioles and pre-capillary sphincters (13). The findings of Alston and colleagues (13) are in accordance with the results of Mundemann and colleagues (21). Paterson (22) in contrast found that hypocapnia during CPB caused an increase in mean arterial pressures. This could be attributed to a non-differing flow rate between groups suggesting an increase in SVR with decreasing PaCO₂.

The findings of our study are quite contrary to that of Buhre and colleagues (23) who concluded that SVR under α stat' acid base management is higher than under 'pH stat' management. The drawback of the study done by Buhre and colleagues (23) was that it was performed in a randomized cross over design and each patient served as his own control. Secondly the target values for α stat' and 'pH stat' management were not reached. Lastly only 20 patients were studied rendering the power of the study to be insignificant to draw any effective conclusions.

The effects of flow rate and flow characteristics on systemic circulation have also been the subject of clinical studies (13, 21, 24). Alston and coworkers (13) studied the effects of flow rates on systemic haemodynamics in 24 patients undergoing CABG. Their findings were that SVR was inversely related to the flow rate because SVR was significantly lower at a pump flow of 1.5 L min⁻¹ m⁻² than at a flow of 2L min⁻¹ m⁻². In our study the additional effect of flow rate on SVR can be excluded because flow rate during CPB was kept constant at 2.2 L min⁻¹ m⁻² and did not differ between the two types of acid base management.

In conclusion, this prospective randomized investigation found no significant difference in cardiac outcome between patients having α stat' versus 'pH stat' management during CPB at moderate hypothermia. However most pediatric and some adult centers employ deeper hypothermia during CPB than we do and our results cannot be extrapolated to those situations. Further research will be necessary to

determine whether CO₂ management effects outcome when lower temperatures are employed.

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