ACUTE HAEMODYNAMIC EFFECT OF SODIUM BICARBONATE IN CANINE RESPIRATORY OR METABOLIC ACIDOSIS

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SUMMARY
This study has examined the acute haemodynamic effects of 7% sodium bicarbonate solution 1 mmol kg\(^{-1}\) (1.2 ml kg\(^{-1}\)) administered into the right atrium over 5 s in 25 anaesthetized dogs allocated randomly to respiratory (arterial pH (\(pH_a\)) 7.18, \(P_{CO_2}\) 10.1 kPa (n = 8)) or metabolic acidosis (\(pH_a\) 7.27, base deficit -9.0 mmol litre\(^{-1}\) (n = 7)) or metabolic neutrality (\(pH_a\) 7.39 (n = 10)). The \(pH_a\) and \(P_{CO_2}\) in the respiratory acidosis group differed from those in the two other groups (P < 0.01). One dog with respiratory acidosis developed progressive circulatory depression and cardiac arrest 6 min after injection of sodium bicarbonate. In the remaining seven dogs with respiratory acidosis, administration of sodium bicarbonate 1 mmol kg\(^{-1}\) produced transient decreases in mean arterial pressure, right ventricular \(dP/dt\), and pulmonary blood flow, with increased right atrial pressure, followed by a gradual return of these variables to the baseline. The magnitude of reduction in pulmonary blood flow after sodium bicarbonate was greater in dogs with respiratory acidosis (P < 0.05) compared with the changes in the two other groups. The haemodynamic depression after bicarbonate was pronounced during respiratory acidosis and this may be attributed to a smaller \(pH_a\) in the respiratory acidosis group, further reduction of intracellular \(pH\), or both. It is suggested that when metabolic acidosis is corrected, bicarbonate should be administered with caution in the presence of respiratory acidosis. (Br. J. Anaesth. 1993; 70: 196–200)

KEY WORDS
Acid-base equilibrium: metabolic acidosis, respiratory acidosis. Complications. hypercapnia. Pharmacology. sodium bicarbonate

Sodium bicarbonate has been used widely for the treatment of metabolic acidosis during cardiopulmonary resuscitation [1–3], although its use during cardiopulmonary resuscitation has recently been questioned [4–8]. Sodium bicarbonate has been reported to cause reductions in arterial pressure and myocardial contractility, and often myocardial ischaemia after the i.v. injection [9–13]. A greater reduction in myocardial contractility has been reported during respiratory acidosis than during metabolic acidosis [14, 15], suggesting that intracellular carbon dioxide tension is more potent as a myocardial depressant than \(pH\) and bicarbonate concentration. Furthermore, several previous reports have indicated significant differences between the partial pressures of carbon dioxide in arterial and venous blood sampled from patients undergoing cardiopulmonary resuscitation or with circulatory failure (reduced and increased partial pressure of carbon dioxide in the arterial and venous blood, respectively) [16–18]. Consequently, it is likely that haemodynamic depression associated with administration of sodium bicarbonate may be exaggerated during respiratory acidosis. However, there has been no reported in \(vivo\) investigation examining the detrimental haemodynamic effects of sodium bicarbonate in acid-base derangements. Therefore, the acute haemodynamic effects of sodium bicarbonate solution have been examined during administration into the right atrium in anaesthetized dogs with respiratory or metabolic acidosis and without acidosis.

MATERIALS AND METHODS
Investigations were carried out in 25 adult mongrel dogs of both sexes, weighing 8–13 kg. The study was approved by the Institutional Animal Care and Use Committee. Animals were anaesthetized with i.v. thiopental 15–20 mg kg\(^{-1}\) and the trachea was intubated. The lungs were ventilated mechanically with room air and supplementary oxygen via a cuffed tracheal tube, using a volume-cycled animal ventilator (model R-60, Aika Co., Ltd, Tokyo). End-expiratory concentration of carbon dioxide was monitored continuously using a carbon dioxide analyser (CO\(_2\) Monitor IH31, NEC San-ei Instruments Co., Ltd, Tokyo). Anaesthesia was maintained with 0.7–1.0 % halothane inspired in oxygen and air. Suxamethonium 20 mg was given i.v. and thereafter 20 mg h\(^{-1}\) was administered i.v. to produce neuromuscular block. During all measurements, pulmonary arterial blood temperature was maintained at 36.5–38.5 °C. Arterial blood was analysed for \(pH_a\), \(P_{CO_2}\), \(P_{O_2}\), and base deficit by Acid–Base Laboratory (model ABL 300, Radiometer, Copenhagen), and for

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blood concentrations of sodium, potassium and ionized calcium (Ca$^{2+}$) by Analyzer (KNAZ Sodium-Potassium Analyzer, Radiometer, Copenhagen).

An i.v. cannula was placed in a forelimb vein for constant administration of lactated Ringer’s solution at a rate of 10 ml kg$^{-1}$ h$^{-1}$. Lead II of an electrocardiogram (model 2236A, NEC San-ei Instruments Co., Ltd, Tokyo) was monitored with subcutaneous electrodes in the legs. Heart rate was measured continuously on a beat-to-beat basis by a cardiotachometer (model 1321, NEC San-ei Instruments Co., Ltd, Tokyo) triggered by lead II of the electrocardiogram. Arterial pressure measurements and samples for blood-gas analysis were obtained from a femoral arterial catheter. A flow-directed, balloon-tipped pulmonary artery catheter (model 93-132-5F, Baxter Edwards Laboratories, Irvine, California) was inserted via the right external jugular vein for continuous monitoring of pulmonary artery pressure. Another catheter was positioned in the right atrium through a femoral vein to permit continuous measurement of right atrial pressure. Another catheter was positioned in the right atrium through a femoral vein to permit continuous measurement of right atrial pressure (RAP). Calibrated Statham P231D transducers (Gould, Cleveland, Ohio) were used for pressure measurements. A 5-French gauge catheter-tipped transducer (model MPC-500, Millar Instruments Inc., Houston, Texas) was inserted through the left jugular vein and positioned in the right ventricle to obtain right ventricular pressure and instantaneous rate of increase in right ventricular pressure (RV dP/dt) using a differential amplifier (model 1323, NEC San-ei Instruments Co., Ltd, Tokyo).

After the pulmonary trunk was dissected free of the surrounding tissues through a left-sided thoracotomy in the fourth interspace, an electromagnetic flow probe of appropriate size (model FR 10–12 mm, Nihon-Kohden Co., Ltd, Tokyo) was placed carefully around the pulmonary trunk for continuous measurement of pulmonary blood flow (PBF). The flow probe was calibrated with 0.9% saline solution in vitro before implantation, and PBF was measured continuously with a square-wave electromagnetic blood flowmeter (model MFV-3200, Nihon-Kohden Co., Ltd, Tokyo). After surgical preparation, all dogs were allowed a stabilization period of at least 60 min. All recordings were made on the eight-channel recorder (model RECTI-HORIZ-8K, NEC San-ei Instruments Co., Ltd, Tokyo) throughout the investigation.

The animals were allocated randomly to three groups: dogs without acidosis (n = 10), with respiratory acidosis (n = 8) and with metabolic acidosis (n = 7). After a period of stabilization in 10 dogs without respiratory (Paco$_2$, 4.5–5.6 kPa) and metabolic acidosis (base deficit > −4 mmol litre$^{-1}$) the haemodynamic effects of 0.9% saline solution 1.2 ml kg$^{-1}$ were observed and recorded continuously for 3 min when administered over 5 s into the right atrium. Subsequently, after another stabilization period of at least 15 min, 7% sodium bicarbonate solution 1 mmol kg$^{-1}$ (1.2 ml kg$^{-1}$) was injected over 5 s into the right atrium, and haemodynamic changes were recorded continuously for 3 min. Ventilator settings were kept constant during these haemodynamic measurements.

Respiratory acidosis of Paco$_2$ 9.1–10.9 kPa was induced by decreasing ventilatory volume in eight dogs, whereas co-existing metabolic acidosis was not corrected. After a period of stabilization, the same haemodynamic measurements were made for 3 min using 0.9% saline solution 1.2 ml kg$^{-1}$ or 7% sodium bicarbonate solution 1 mmol kg$^{-1}$ when these solutions were injected over 5 s into the right atrium. Metabolic acidosis of base deficit less than −6 mmol litre$^{-1}$ was induced in seven dogs by continuous i.v. infusion of hydrochloric acid 0.2 mol litre$^{-1}$ at an approximate rate of 80–120 ml h$^{-1}$, while Paco$_2$ was maintained at 4.5–5.6 kPa. After stabilization for at least 15 min, haemodynamic measurements were made for 3 min when 0.9% saline solution 1.2 ml kg$^{-1}$ or 7% sodium bicarbonate solution 1 mmol kg$^{-1}$ was injected over 5 s into the right atrium.

All values are expressed as mean (SEM). Both mean arterial pressure (MAP) and mean pulmonary artery pressure (MPAP) were calculated as diastolic pressure plus one-third of the pulse pressure. Analysis of changes in haemodynamic variables from baseline (30 s, 1 and 3 min) and comparisons of data among the three groups (baseline values and maximal changes from baseline) were performed using one-way or two-way analysis of variance (ANOVA), respectively, and Student’s t test with Bonferroni correction. Results were considered statistically significant at P < 0.05.

RESULTS

Arterial pH was smallest and Paco$_2$ greatest in the respiratory acidosis group, whereas base deficit was most pronounced in the metabolic acidosis group. Blood sodium concentration was smallest in the metabolic acidosis group, but within the normal range (table 1).
Baseline RAP before administration of 0.9% saline solution was significantly greater in respiratory acidosis compared with the two other groups (P < 0.05) (table II). Administration of 0.9% saline solution 1.2 ml kg⁻¹ into the right atrium over 5 s caused small but significant increases in RAP in all three groups, and significant increases in MPAP and PBF in the metabolic acidosis and non-acidosis groups.

Before administration of sodium bicarbonate, baseline RAP was greater in the respiratory acidosis group compared with the two other groups (P < 0.05) (table III). Both acidosis groups had decreased baseline MAP values; in the metabolic acidosis group, the difference just reached significance compared with the non-acidosis group (P < 0.05).

The most frequently observed haemodynamic changes after administration of sodium bicarbonate included transient decreases in MAP and RV dP/dt, and increased RAP, followed by gradual return to baseline values, or greater. No significant changes in HR were observed in all groups. However, PBF responses to a 5-s administration of sodium bicarbonate were observed in all groups.
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**FIG. 1. Maximal changes (mean, SEM) in mean arterial pressure (MAP) (1), mean pulmonary artery pressure (MPAP) (2) and right atrial pressure (RAP) (3) from baseline values within 1 min after the administration of sodium bicarbonate 1 mmol kg\(^{-1}\) into the right atrium in dogs with no acidosis (NA), respiratory acidosis (RA) and metabolic acidosis (MA). The mean (SEM) times at which maximal changes of MAP, MPAP and RAP occurred after the administration of sodium bicarbonate were: MAP—25 (3) s, 34 (5) s, 24 (4) s; MPAP—20 (1) s, 27 (3) s, 17 (3) s; RAP—24 (3) s, 23 (5) s, 21 (3) s in non-acidosis, respiratory acidosis and metabolic acidosis groups, respectively. There were no significant differences in these haemodynamic variables among the three groups.**

**FIG. 2. Maximal changes (mean, SEM) in right ventricular \(dP/dt\) (RV \(dP/dt\)) (1) and pulmonary blood flow (PBF) (2) from baseline values within 1 min after the administration of sodium bicarbonate 1 mmol kg\(^{-1}\) into the right atrium in dogs with no acidosis (NA), respiratory acidosis (RA) and metabolic acidosis (MA). The mean (SEM) times at which maximal changes of RV \(dP/dt\) and PBF occurred after the administration of sodium bicarbonate were: RV \(dP/dt\)—19 (2) s, 23 (3) s, 21 (1) s; PBF—24 (2) s, 30 (2) s, 24 (2) s in non-acidosis, respiratory acidosis and metabolic acidosis groups, respectively. \(\ast P < 0.05\) compared with non-acidosis and metabolic acidosis groups.

Carbonate were not consistent among the three groups (table I); a profound reduction of PBF occurred immediately after injection of sodium bicarbonate in the respiratory acidosis group.

In one of the eight dogs with respiratory acidosis, progressive circulatory depression and cardiac arrest occurred 6 min after the injection of sodium bicarbonate; the data of this dog were excluded from figures 1 and 2, which show maximal changes in haemodynamic values within 1 min after injection of sodium bicarbonate. Although MAP, MPAP and RAP of the three groups showed comparable alterations from baseline values after administration of sodium bicarbonate (fig. 1), there was a significant reduction in PBF in the respiratory acidosis group compared with those in the two other groups (\(P < 0.05\)) (fig. 2).

**DISCUSSION**

This study has shown that the haemodynamic depression after administration of 7% sodium bicarbonate 1 mmol kg\(^{-1}\) into the right atrium over a period of 5 s was augmented by respiratory acidosis. As the haemodynamic alterations associated with sodium bicarbonate were smaller in dogs without respiratory acidosis, the considerable haemodynamic deterioration after sodium bicarbonate in dogs with respiratory acidosis could be attributed to a decreased pH\(_{a}\) before bicarbonate administration, further reduction of intracellular pH caused by diffusion of carbon dioxide into the myocardial cells or both. The results suggest that, if severe respiratory acidosis exists, sodium bicarbonate should be given cautiously to correct metabolic acidosis.

Although there are conflicting data [12–15, 19, 20] on the major determinants of myocardial performance during acid–base disturbances (intra- or extracellular pH, Pco\(_{2}\) and bicarbonate), Pco\(_{2}\) or intracellular pH appears to be more important. In an animal study [15] of simultaneous changes in intracellular and extracellular pH during acidosis, at the same extracellular pH, it was shown that respiratory acidosis caused greater depression in myocardial contractility and greater intracellular acidosis of the heart than metabolic acidosis. In addition, intracellular acidosis may be aggravated by administration of sodium bicarbonate ("paradoxical" acidosis) [4, 21], because of free diffusion of carbon dioxide, generated by bicarbonate, into the cells. In the present study, extracellular pH in the respiratory acidosis group was 7.18 (table I) and intracellular pH may have decreased to less than 7.00 [21]. This may account for the observation that haemodynamic depression was most marked (table II, fig. 2) and there was a cardiac arrest in the respiratory acidosis group. However, a further study should be undertaken to evaluate the haemodynamic effect of sodium bicarbonate during respiratory and metabolic acidosis at the same arterial pH, as the pH\(_{a}\) was significantly greater in the metabolic acidosis group than in the respiratory acidosis group in the present study, and may have contributed in part to the lesser haemodynamic depression after sodium bicarbonate during metabolic acidosis.

The depressant effect of carbon dioxide on myocardial contractility seems to be evident when the pH\(_{a}\) decreases to less than 7.00 during respiratory acidosis [22–24]. Hypercapnia is accompanied by systemic peripheral vasoconstriction [22]. However, there are also conflicting data showing increased cardiac output associated with systemic vasodilatation during respiratory acidosis [25]. This discrepancy may be attributed to different anaesthetic agents used and the stimulant effect of carbon dioxide on the sympathoadrenal system, which can com-
penis for the direct cardiovascular depressant effect of carbon dioxide. It is likely, therefore, that the significant increase in RAP observed in the respiratory acidosis group (tables II, III) was caused by peripheral vasoconstriction secondary to hypercapnia.

The dose of sodium bicarbonate used in the present study was based on the standards for cardiopulmonary resuscitation [3] and previous reports [7, 9]. The injection rate of sodium bicarbonate is likely to affect the degree of associated haemodynamic alterations to a great extent as the total dose. However, there is no "standard" rate of sodium bicarbonate administration in cardiopulmonary resuscitation [3]. The 5-s period of administration of sodium bicarbonate was chosen according to previous experimental reports in which sodium bicarbonate approximately 1 mmol kg"\(^{-1}\) was given as a bolus injection in or over 5–15 s [1, 2, 7, 9].

In conclusion, this experiment suggests that haemodynamic depression after the i.v. administration of sodium bicarbonate is pronounced during respiratory acidosis. If severe respiratory acidosis exists, bicarbonate should be administered cautiously for the correction of metabolic acidosis.

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REFERENCES