Acid–base changes after cardiorespiratory arrest in the dog

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(Received 5 April 1979; accepted 6 September 1979)

Summary

1. To assess the non-respiratory acid–base disturbance which results from cardiorespiratory arrest experiments were performed on anaesthetized dogs, and circulatory arrest was established either by inducing ventricular fibrillation or by complete occlusion of the great veins.

2. In the first series of experiments (group A) the period of cardiorespiratory arrest was limited to 2-0–3.5 min. It was shown that the non-respiratory component of the ensuing acid–base disturbance as expressed by the non-respiratory pH was small: in nine episodes of circulatory arrest after occlusion of the great veins there was a mean reduction in the non-respiratory pH of 0.04 pH unit (range 0.025–0.055), and in seven episodes of ventricular fibrillation the mean reduction was 0.024 pH unit (range 0–0.055).

3. In the second series of experiments (group B) the period of cardiorespiratory arrest was varied from 3-0 to 11.0 min. It was found that the degree of non-respiratory acidaemia was correlated with the duration of arrest but the magnitude of these changes was not large.

Key words: acid–base balance, cardiac arrest.

Introduction

It is generally accepted that circulatory arrest results in a state of non-respiratory (or metabolic) acidaemia and intravenous administration of alkali has been advocated in resuscitation (Meltzer & Dunning, 1972; American Heart Association Recommendation, 1974; Stephenson, 1974). A chronic inadequacy in the perfusion of tissues results in the accumulation of non-respiratory acids in the blood. However, circulatory arrest of the type which occurs in a coronary or intensive care area of a hospital is an acute phenomenon which has certain unique features: (i) it is of a relatively short duration, (ii) it is invariably accompanied by respiratory arrest which would result in a respiratory acidaemia, and (iii) it is unlikely to occur during an undetected state of acidaemia.

In attempting to assess the degree of non-respiratory acidaemia, which occurs during such a period of circulatory arrest, it is necessary to examine the arterial blood before the arrest and after restoration of the circulation. In addition, the latter measurements should not be interfered with by the administration of alkali. From these standpoints, it is apparent that the data relating to circulatory arrest in man are incomplete (Gilston, 1965; Fillman, Shapiro & Killip, 1970).

Results in animal studies are complicated by the use of 'standard bicarbonate' (Siggaard-Andersen, 1962) to measure the non-respiratory component of acid–base disturbances. This nomogram was derived from data obtained by the titration of blood in vitro with carbon dioxide. It is well known that the carbon dioxide titration curve of blood in vitro differs significantly from that in vivo (Schwartz & Relman, 1963; Linden & Norman, 1966; Pryor-Porter, Kelman & Nunn, 1966), and that these differences lead to an erroneous assessment of non-respiratory disorders of acid–base balance, particularly in the presence of a concurrent respiratory disturbance.
These criticisms led to the description of a scheme for the assessment of acute acid-base disorders based on the titration of blood \textit{in vivo} with carbon dioxide (Kappagoda, Linden & Snow, 1970; Stoker, Kappagoda, Snow & Linden, 1975). The severity of the respiratory acidaemia was assessed in the conventional manner as the change in the arterial Pco\(_2\) from the normal range (4.7–6.0 kPa). The presence of a non-respiratory disturbance was confirmed by plotting the measured values (pH and Pa,co\(_2\)) on a log Pco\(_2\)/pH diagram against a background of carbon dioxide titration \textit{in vivo} curves (Fig. 1). The displacement of the plotted point from the normal line (i.e. the carbon dioxide titration curve passing through pH 7.40 and Pco\(_2\) 5.3 kPa) indicated the presence of a non-respiratory change. The respiratory pH (i.e. the pH which would result if the Pco\(_2\) were altered to 5.3 kPa \textit{in vivo}) was then found by following the titration curve through that point. The difference from pH 7.40 was used as the index of the magnitude of respiratory acid–base change. This scheme was adopted in the present investigation to determine the extent of the non-respiratory acidaemia which occurred during circulatory arrest in dogs.

\textbf{Methods}

\textit{Animals}

Experiments were performed on 14 mongrel dogs weighing 17.2–22 kg (mean 20.2 kg). Anaesthesia was induced by an injection of sodium pentobarbital (Diabutal, Diamond Laboratories Inc., Des Moines, Iowa, U.S.A.; dose 30 mg/kg) given intravenously. Soon after induction of anaesthesia, a tracheostomy was performed and a plastic cannula was inserted into the trachea and tied in place. The dogs were artificially respired through this tube by using a respiratory pump (model 607A, Harvard Instrument Co., Dover, Massachusetts, U.S.A.). In 13 dogs the inspired air was enriched with oxygen to yield an arterial Po\(_2\) in excess of 13.3 kPa (100 mmHg). The remaining dog was ventilated on room air. The anaesthesia was maintained by further injections of pentobarbital at a dose of 3 mg/kg given every hour.

The chest was opened on the right side in the fourth intercostal space. When the chest was opened, an inspiratory resistance was provided by placing the outlet from the pump under 3 cm of water. Loose ligatures were placed around the superior vena cava, inferior vena cava and azygos vein. The pericardium was opened and stimulating electrodes were sutured on to the right ventricle.

The pressure in the descending aorta was recorded from a cannula inserted through the right femoral artery. The respiratory pressure was recorded from a cannula inserted into the trachea. These cannulae were connected to strain-gauge manometers (model P 23BB, Statham Instruments, Hato Rey, Puerto Rico), the output of which, after amplification by carrier and driver amplifiers, was recorded by a pen-recorder (Beckman R. Dynagraph, Beckman Instruments Inc., Schiller Park, Illinois, U.S.A.). The frequency response of the system for recording the femoral blood pressure was tested and found to be flat (+2%) to 30 Hz. The electrocardiogram was recorded with electrodes applied to the right foreleg and the left hind leg. The signals from these electrodes were amplified and recorded. The end tidal Pco\(_2\) was continuously monitored with an infrared analyser (Capnograph, type 146, Godart N.V., Bilthoven, Holland). The output of this analyser was also amplified and recorded. The temperature of the animals was monitored with an oesophageal thermometer (Yellow Springs Instrument Co. Inc., Ohio, U.S.A.).

Samples of arterial blood were withdrawn into heparinized syringes from the descending aorta through a cannula inserted into the femoral artery. The arterial pH, Pco\(_2\) and Po\(_2\) were measured with a conventional blood gas analyser (model IL, Micro 13, Instrumentation Ltd, Lexington, Massachusetts, U.S.A.). The accuracy of the respective measurements as expressed by the 95% tolerance limits were 0.002 pH unit, 0.2 and 0.16 kPa respectively. All the measured values for pH and Pco\(_2\) were corrected for the differences between the temperature of the body and the temperature at which these values were obtained (Bradley, Stupfel & Severinghaus, 1956).

The results of the blood-gas analysis were assessed according to the scheme based on CO\(_2\) titration curves obtained \textit{in vivo} at various levels of non-respiratory acidaemia (Kappagoda et al., 1970; Stoker et al., 1975). The arterial Pco\(_2\) was used as the index of a respiratory acid–base disorder. Non-respiratory acid–base disturbances were assessed on the basis of the non-respiratory pH value, which was defined as a pH of arterial blood when the Pco\(_2\) of the whole animal was corrected to 5.3 kPa (see the Introduction section).

\textit{Experimental protocol}

The experiments were performed in two groups. 

\textit{Group A}. The period of circulatory arrest was
limited to 3 min. Blood samples were collected before and after a period of circulatory arrest according to the schedule shown here.

Sample 1: control sample 5 min before cardiorespiratory arrest.
Sample 2: control sample immediately before cardiorespiratory arrest.
Sample 3: immediately after restoration of cardiac output and ventilation.
Sample 4: 1 min after restoration of cardiac output and ventilation.
Sample 5: 2 min after restoration of cardiac output and ventilation.
Sample 6: 4 min after restoration of cardiac output and ventilation.
Sample 7: 10 min after restoration of cardiac output and ventilation.

Circulatory arrest was achieved either by snaring the veins entering the right atrium or by electrically induced ventricular fibrillation (10 V, 2 ms duration; model SD9B; Grass Medical Instruments, Quincy, Massachusetts, U.S.A.). During the period of circulatory arrest the ventilation was stopped to ensure a simultaneous respiratory arrest. When ventricular fibrillation was instituted, the venous return was occluded immediately before the administration of electrical shocks so as to ensure that the fibrillating heart was not distended. After 3 min of arrest, the circulation was restored either by releasing the snare or by the administration of direct current shocks (275 V, 0·25 s duration; Morris Defibrillator; Corbin Farnsworth Inc., Palo Alto, California, U.S.A.).

No attempt was made to ensure that the non-respiratory pH of arterial blood was within normal limits before each episode of cardiorespiratory arrest. Nevertheless, after completion of the sampling procedures any residual non-respiratory acidaemia was corrected partially by the administration of 10–20 ml of sodium bicarbonate solution (8·4 g/100 ml) intravenously. This procedure ensured a relatively wide range of control non-respiratory pH values.

Group B. In this group (seven dogs) circulation was arrested by snaring the great veins and the period of arrest was varied between 3·0 and 11·0 min. Blood samples were collected according to the schedule shown here.
Sample 1: control sample 5 min before cardiorespiratory arrest.
Sample 2: control sample immediately before arrest.
Sample 3: immediately after restoration of circulation and ventilation.

Sample 4: 5 min after restoration of circulation.
Sample 5: 10 min after restoration of circulation.

The degree of non-respiratory acidaemia caused by the arrest was assessed by comparing the control values (i.e. mean of samples 1 and 2) with those for sample 5.

Results

Control values

The experiments were performed in 14 dogs. At the commencement of the recordings the average arterial pressure and heart rate (+SEM) were 126·9 ± 4·01 mmHg and 151·7 ± 5·08 beats/min respectively. In these dogs the mean arterial Pco₂, Po₂ and pH (+SEM) were 4·59 ± 0·15 kPa, 14·5 ± 0·57 kPa (n = 13) and 7·35 ± 0·01 respectively. In one dog ventilated on room air the arterial Po₂ was 4·3 kPa mmHg.

Group A

A total of 16 episodes of circulatory arrest were studied: nine caused by snaring the superior and inferior venae cavae and seven by ventricular fibrillation. The duration of the circulatory arrest caused by snaring the venae cavae was 3 min (±5 s). In the episodes of circulatory arrest caused by ventricular fibrillation it was often not possible to restart the circulation at a precisely determined time. Of the seven episodes studied, sinus rhythm was restored after 3–3·5 min in five, after 2–2·5 min in two.

The changes in the arterial Pco₂ and pH during an episode of circulatory arrest are analysed in Fig. 1. The results are plotted against a background of the CO₂ titration in vivo curves in Fig. 1(a) (Kappagoda et al., 1970; Stoker et al., 1975). The corresponding non-respiratory pH values for each sample were also obtained and these are shown plotted in Fig. 1(b). It is seen that the circulatory and respiratory arrest was followed by an initial reduction of the pH and a modest elevation of the arterial Pco₂. When the circulation and respiration were restored after 3 min the arterial Pco₂ returned to its control value. The net non-respiratory acidaemia as reflected by the change in the non-respiratory pH was small, as shown in Fig. 1(b).

The overall changes in the non-respiratory pH value of the blood during 17 episodes of circulatory arrest are shown in Fig. 2. The episodes of caval snaring (nine) were considered separately and
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Changes in the pH and $P_{CO_2}$ of arterial blood during one episode of cardiorespiratory arrest (occlusion of venous return). Results are plotted against a background of acute $CO_2$ titration $in vivo$ curves (Kappagoda et al., 1970). The numbers refer to the sampling protocol in group A (see the text). (b) Changes in the non-respiratory pH value of blood corresponding to the data in (a). The bar represents the period of arrest. It is seen that there was a small reduction in the value of the non-respiratory pH. The apparent alkalaemia between samples 3 and 4 was not a constant feature.

In the seven episodes of ventricular fibrillation lasting 2-3.5 min the mean reduction in the non-respiratory pH was 0.024 (range 0.025-0.055). This reduction was also statistically significant ($P < 0.05$). There did not appear to be any significant difference in the magnitude of the reduction in the non-respiratory pH in the two types of circulatory arrest.

**Group B**

In the second part of the study 17 episodes of circulatory arrest varying in duration from 3 to 11 min were studied. It was found that there was a significant relationship between the magnitude of the changes in non-respiratory pH and the duration of circulatory arrest (Fig. 3).

**Discussion**

There has been increasing interest in the various aspects of sudden death after circulatory arrest, with much attention being paid to the procedures of cardiopulmonary resuscitation. One of the aspects of cardiopulmonary resuscitation which has received particular attention is the correction of acid-base disturbances, which are believed to occur during periods of circulatory arrest. It is generally believed that cardiac arrest invariably results in a significant non-respiratory acidemia, which requires correction with alkali. This proposition was based on observations which show that patients successfully resuscitated after an episode of circulatory arrest often exhibited a significant acidemia (Gilston, 1965).

However, the extent and the nature of the acidemia which followed short periods of circulatory arrest in man have not been established with certainty because of the difficulty in per-
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FIG. 3. Changes in the non-respiratory pH of arterial blood during cardiorespiratory arrest in dogs of group B (each symbol represents a different animal). The ordinate shows change in non-respiratory pH (ΔpH/kg body weight) and the abscissa shows duration of cardiorespiratory arrest (min). The curve is defined by the equation: $y = 0.00198 - 0.0003x + 0.00007x^2$ ($r = 0.94; P < 0.05$). The change in non-respiratory pH was expressed as ΔpH/kg body weight because it provided the best fit for the result.

forming a prospective study. However, data are available in man to suggest that an episode of cardiac arrest is usually accompanied by respiratory arrest (Chazan, Stenson & Kurland, 1968). The former would tend to produce a non-respiratory acidaemia and the latter would result in a respiratory acidaemia. The precise contributions of each to the ensuing acid-base disturbance has not been established for two main reasons. First, the analysis is complicated by the administration of sodium bicarbonate or other alkali during cardio-pulmonary resuscitation (Chazan et al., 1968). Secondly, the usual method adopted for analysing these acid-base disturbances (i.e. the Siggaard-Andersen nomogram) tends to overestimate the severity of a non-respiratory disturbance when there is a concurrent severe respiratory acidaemia (Sykes & Vickers, 1970; Stoker, Kappagoda, Grimshaw & Linden, 1972). The magnitude of the error depends on the severity of the respiratory disturbance. For instance, in group A of the present investigation, where the period of arrest was limited to 3 min, the degree of respiratory acidaemia was small. Under these conditions the overestimate in the non-respiratory component of the acid-base disturbance arising from the use of CO₂ titration in vitro curves is minimal. However, where there is an appreciable respiratory disturbance, as in the investigation reported by Ledingham & Norman (1962), the error is significant (Fig. 4; see below).

Owing to difficulties encountered in conducting these studies in man, several investigators have resorted to experiments in animals, particularly dogs. In one of the earliest investigations of this type Ledingham & Norman (1962) subjected anaesthetized dogs to various periods of circulatory arrest by occlusion of the venae cavae. Unfortunately, their data were analysed by use of the Siggaard-Andersen nomogram. On this basis, it was concluded that circulatory arrest for periods of time from 4 to 7 min resulted in a base deficit (i.e. a non-respiratory acidaemia). However, when the data presented in Table 2 of their paper are analysed with carbon dioxide titration in vitro a different interpretation can be made (Fig. 4). In three of the six dogs the episodes of circulatory arrest resulted in minimal changes in the non-respiratory pH. In these three the major contribution to the acidaemia was made by the accumulation of carbon dioxide.

Minuck & Sharma (1977) investigated eight episodes of circulatory arrest in anaesthetized dogs, each of which lasted at least 6 min. In these experiments they observed a mean net change of 0.08 pH unit at a PCO₂ of approximately 4.7 kPa, which is approximately equal to a fall in the non-respiratory pH of 0.07. Since the circulatory arrest was caused by ventricular fibrillation, for 3 min, followed by manual cardiac compression for a further 3
min, it is likely that the circulation was not restored at precisely 6 min in all the experiments.

The present investigation, conducted under more controlled conditions, was undertaken to quantify the non-respiratory acidaemia which followed 3 min of circulatory arrest. This time interval was selected in the first part of the study because of the possibility of irreversible damage to the brain with longer periods of arrest. This study has shown that 3 min of cardiorespiratory arrest did not per se result in a major non-respiratory acidaemia.

The second part of this investigation has shown that there is a significant correlation between the extent of the non-respiratory acidaemia and the duration of cardiorespiratory arrest. It also confirms the proposition that even with relatively long periods of arrest the severity of the acidaemia is not great.

**Possible significance of the results to man**

It is of interest to speculate whether these findings in the dog have any relevance to man. Previous investigations have shown that the carbon dioxide titration curve in vivo in the dog is similar to that in man (Cohen, Brackett & Schwartz, 1964; Brackett, Cohen & Schwartz, 1965; Stoker et al., 1972). Further, short periods of circulatory arrest, such as those examined in the present investigation, do occur in operating theatres, cardiac catheterization laboratories and in intensive and coronary care units. Thus both the method of analysing the acid-base disturbances and the experimental protocol employed form a valid basis for suggesting that the routine administration of sodium bicarbonate in man as a part of the resuscitation procedure after a short period of circulatory arrest could be superfluous.

It is also necessary to examine whether the rapid administration of sodium bicarbonate under these conditions is desirable. For instance, the rapid administration of sodium bicarbonate results in an increase in the arterial Pco₂ (Kappagoda et al., 1970; Berenyi, Work & Killip, 1975). Such an increase is likely to be even greater when the ventilation is inadequate as is the case in the early stages of a resuscitation procedure.

It has been shown in the dog that the rapid injection of sodium bicarbonate solution after a period of ventricular fibrillation (which lasted 4 min) resulted in a marked alkalaemia and a concurrent fall in the pH of the cerebrospinal fluid (Berenyi et al., 1975). The authors attributed the latter to the rapid diffusion of carbon dioxide across the blood–brain barrier and suggested that the reduction in the pH of cerebrospinal fluid could contribute to a depression of cerebral function after successful resuscitation.

An argument which is often presented in favour of the administration of sodium bicarbonate is that the threshold for the ventricular fibrillation is influenced by the degree of acidosis and alkalosis (Gerst, Fleming & Malm, 1966). It was shown that the energy required for defibrillation was related to the degree of non-respiratory acidosis, but it must be emphasized that the change in pH encountered by these authors (see Fig. 3 of Gerst et al., 1966) was far in excess of those observed even after 6 min of circulatory arrest. Thus the relevance of this study to resuscitation in coronary care units and cardiac catheterization laboratories is uncertain. Therefore it is suggested that the recommendation that sodium bicarbonate should be administered routinely in all forms of cardiac arrest merits reappraisal.

**Acknowledgments**

The authors thank Mr Alvin Todd for technical assistance, and the Alberta Heart Foundation for financial support.

**References**


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