pH Changes On the Surface of Brain and In Cisternal Fluid in Dogs in Cardiac Arrest

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SUMMARY: We measured brain surface pH and cisternal cerebrospinal fluid (CSF) acid-base variables in Na-pentobarbital anesthetized dogs during KCl induced cardiac arrest. Electrocardiographically, an agonal rhythm occurred within seconds, presumably resulting in rapid fall in cerebral blood flow. The mean arterial blood pressure fell from 125 ± 22 (mean ± 1 SD) to 35 ± 28 mm Hg at 30 seconds and to 19 ± 3 mm Hg at 60 seconds after KCl injection. The mean brain surface pH (n = 8) dropped abruptly from 7.30 to 6.80 within 3 minutes after induction of cardiac arrest. Changes in cisternal CSF pH, however, occurred slowly with the mean pH falling from 7.33 to 7.27 at 4 minutes and to 6.99 at 10 minutes after induction of cardiac arrest. The fall in cisternal CSF pH was due to a rise in CSF concentration of organic acids as well as a rise in CSF P<sub>CO<sub>2</sub>; the mean cisternal CSF |HCO<sub>3</sub>| fell 3.6 mEq/l while the mean cisternal CSF lactate concentration and the mean CSF P<sub>CO<sub>2</sub></sub> rose, respectively, 2.1 mEq/l and 37.8 mm Hg 10 minutes after induction of cardiac arrest. We conclude that during acute ischemic anoxia pH disequilibria develop between brain extracellular fluid and cisternal CSF; analyses of the latter fluid provide unreliable information about brain metabolic status and its acid-base balance even up to ten minutes after induction of cardiac arrest.

Changes in Ionic Composition: Changes in ionic composition of cerebrospinal fluid (CSF) reflect derangements in brain metabolic function. In man lumbar CSF is most commonly sampled. Wide differences, however, might exist between the composition of lumbar and cisternal CSF during acute events;<sup>1</sup> 2 Kalim and associates<sup>2</sup> have shown that in cardiac arrest the normal compartmental difference between cisternal and lumbar CSF is reversed, with the former being more acidic than the latter. This is due to the closer proximity of the cisternal CSF to the brain which more rapidly reflects the acute acidosis of brain extracellular fluid (ECF) under such circumstances. It might be anticipated, however, that changes in cisternal CSF ionic composition may not immediately reflect ionic changes in brain ECF during acute events, such as cardiac arrest; if true, under such circumstances analyses of cisternal CSF may provide unreliable information about the events occurring within brain ECF.

The purpose of the present study was to quantitate the magnitude of brain ECF acidosis as measured by pH electrodes during cardiac arrest and to see how faithfully cisternal CSF pH changes reflected brain ECF acidity.

Methods

General

Mongrel dogs (n = 16) weighing from 15–20 kg were anesthetized with intravenous injection of sodi-

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mocouple (Model 127, Bailey Instrument, Saddlebrook, New Jersey) with its tip in the fluid adjacent to pH electrodes. Brain surface was heated by a heating lamp when surface temperature fell to 36.5°C.

**Induction of Cardiac Arrest**

After obtaining baseline samples and recording a stable brain surface pH, cardiac arrest was induced by bolus injection of 35–40 ml of saturated KCl. Electrocardiogram was recorded continuously. Brain surface pH was measured in 8 animals; in these cisternal CSF samples were obtained only at 0 time and after 3 minutes of induction of cardiac arrest in order not to disturb the position of the pH electrodes on the brain. In the remaining 8 animals, however, CSF samples were obtained periodically throughout the experiment (see results). In this context, it is emphasized that KCl induced cardiac arrest is an extremely reproducible event.

**Measurements, Analysis and Calculation**

A four-channel recorder (Hewlett Packard, San Diego, California) was used for continuous recording of blood pressure, PE\textsubscript{CO\textsubscript{2}} and brain surface pH. Gases of known concentration were used to calibrate the infrared CO\textsubscript{2} analyzer (LB—2 Bechman, Medical Gas Analyzer). Arterial blood P\textsubscript{O\textsubscript{2}}, P\textsubscript{CO\textsubscript{2}} and pH and cisternal CSF P\textsubscript{CO\textsubscript{2}} and pH were measured immediately in cisternal CSF and pH were measured in 8 animals; in these cisternal CSF samples were obtained only at 0 time and after 3 minutes of induction of cardiac arrest in order not to disturb the position of the pH electrodes on the brain. In the remaining 8 animals, however, CSF samples were obtained periodically throughout the experiment (see results). In this context, it is emphasized that KCl induced cardiac arrest is an extremely reproducible event.

| Table 1 | Changes in the Mean Arterial Blood Pressure (MABP), Brain Surface [H\textsuperscript{+}] and Cisternal Cerebrospinal Fluid (CSF) P\textsubscript{O\textsubscript{2}}, P\textsubscript{CO\textsubscript{2}}, and H\textsuperscript{+}, HCO\textsubscript{3}-, Lactate and K\textsuperscript{+} Concentrations During Cardiac Arrest (Mean ± so) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Time (min)      | 0.0             | 0.5             | 1.0             | 2.0             | 4.0             | 10.0            |
| MABP (mm Hg)    | 125             | 35*             | 19*             | 8*              | 8*              | 8*              |
| ±22             | ±28             | ±6             | ±2              | ±2              | ±2              |
| Surface [H\textsuperscript{+}] (nmol/l) | 50.3            | 55.2*           | 69.6*           | 129.8*          | —               | —               |
| ±3.0            | ±6.0            | ±6.3           | ±17.4           | —               | —               |
| Surface pH      | 7.30            | 7.26            | 7.16            | 6.89            | —               | —               |
| CSF [H\textsuperscript{+}] (nmol/l) | 46.3            | 47.5            | 48.5            | 49.5            | 54.1*           | 101.7*          |
| ±4.5            | ±6.2            | ±6.5           | ±5.9            | ±6.7            | ±20.3           |
| CSF pH          | 7.33            | 7.32            | 7.31            | 7.31            | 7.27            | 6.99            |
| CSF P\textsubscript{CO\textsubscript{2}} (mm Hg) | 45.7            | 46.6            | 46.5            | 46.6            | 49.8*           | 83.5*           |
| ±3.7            | ±2.0            | ±2.3           | ±5.8            | ±3.0            | ±14.0           |
| CSF [HCO\textsubscript{3}-] (mEq/l) | 22.9            | 22.2            | 22.4            | 21.3            | 21.1            | 19.3*           |
| ±2.8            | ±2.9            | ±2.6           | ±1.8            | ±2.6            | ±1.6            |
| CSF P\textsubscript{O\textsubscript{2}} (mm Hg) | 124.0           | 111.0           | 100.0           | 96.0*           | 63.0*           | 34.0*           |
| ±22.0           | ±14.0           | ±28.0          | ±15.0           | ±12.0           | ±7.0            |
| CSF [K\textsuperscript{+}] (mEq/l) | 3.1             | —               | —               | —               | 3.5             | 5.5*            |
| ±0.2            | ±0.7            | ±1.8           | ±0.2            | ±0.5            |
| CSF lactate (mEq/l) | 1.8             | —               | —               | —               | 2.1             | 3.9*            |

*Indicates statistical significance with p < 0.05 compared to values at time 0.0 (KCl injection). The brain surface pH had fallen to 6.80, three minutes after KCl injection in all animals studied (n = 8). For CSF values there are at least 5 measurements at each time. For comparison of surface and CSF [H\textsuperscript{+}] see page 8.
brain surface pH and end-tidal PE\textsubscript{CO\textsubscript{2}} (PE\textsubscript{CO\textsubscript{2}}) vs time during cardiac arrest. The events suggested that the blood-brain barrier had remained intact. Changes in the brain surface pH and cisternal CSF pH during cardiac arrest. Most important, however, such pH changes are reflected very slowly in cisternal CSF. The latter grossly underestimated the severity of the metabolic events which occurred within the brain during acute anoxic ischemia.

The continuous recording of brain surface pH coupled with periodic measurements of cisternal CSF pH in this study, clearly demonstrated the time dependent pH disequilibria which might exist between brain and cisternal CSF during acute events. This observation makes measurement of the changes in the latter fluid a poor candidate for assessment of brain tissue acid-base balance under such circumstances.

Four minutes after induction of the cardiac arrest, the mean CSF PE\textsubscript{CO\textsubscript{2}} and HCO\textsubscript{3}\textsuperscript{-} decreased, K\textsuperscript{+} and lactate concentrations had changed very little (table 1); the mean brain surface and CSF pH had fallen, respectively by about 0.5 and 0.2 pH units 3 minutes after cardiac arrest (fig. 2). We are not aware of any other studies in the literature to compare our data with, but the notable difference in pH changes between the two fluids should reflect the time-dependent diffusion processes occurring between CSF and ECF during cerebral ischemia; specifically this represents the delayed permeation of CO\textsubscript{2} and organic acids into CSF from ECF as they diffuse into the latter compartment from within the brain cells. The rise in CSF PE\textsubscript{CO\textsubscript{2}} as measured in the cerebral spinal fluid (CSF) pH during KCl induced cardiac arrest. pH values were obtained from the respective mean (H\textsuperscript{+}) shown in table 1.
present study and tissue $P_{CO_2}$ as measured by Severinghaus and Feustel was mainly due to nonmetabolic CO$_2$ generation via titration of HCO$_3^-$ with organic acids produced in excess during cerebral ischemia; in this context it is noted that in cisternal CSF the fall in the mean $|HCO_3^-|$ was 3.6 and the rise in lactate concentration was 2.1 mEq/l, 10 minutes after induction of cardiac arrest.

The development of rapid and profound brain surface acidosis measured by surface pH electrodes in the present study is similar to the previously reported pH changes during acute cerebral ischemia as measured by pH electrodes (see later) or biochemically. We have observed similar brain surface pH changes during Na-pentobarbital induced cardiac arrest in dogs. Such profound pH changes are due to excessive production of organic acids (or their equivalents; see reference 18) as a result of anaerobic consumption of glucose during cerebral ischemia. Assuming that similar brain pH changes may occur in man, it is noteworthy that brain function can return to normal after 3 to 4 minutes of cardiac arrest.

It may be argued as to how accurately the changes in brain surface pH as measured in the present study as well as several other studies represent actual changes which occur within the brain tissue, particularly in view of the acute nature of the study and the potential influence of a slow or an asymmetric DC potential shift developing during cerebral ischemia and affecting the surface pH values. The latter argument i.e. the influence of asymmetric potential changes on pH is also applicable to pH measurements by microelectrodes when the reference barrel is not side by side to the actual pH barrel.

To this end, in one animal we simultaneously measured both brain surface fluid pH, by placing our surface electrode on one cerebral hemisphere, and brain ECF pH by inserting a double-barrelled microelectrode 5 mm below the cortex into the other hemisphere. Although the steady state pH values were different, the slopes of changes were remarkably similar during induction of cardiac arrest (fig. 3).

The double-barrelled microelectrodes had a tip-diameter of 30 µM with the tip of the reference barrel (10 µM) next to the tip of the pH barrel (20 µM). The resemblance of the two pH tracings, therefore, suggests that the pH changes recorded by the surface electrodes were not affected by either artifactual cortical $P_{CO_2}$ changes or asymmetric or slow DC potentials developing during cardiac arrest. Further studies using intracerebral pH microelectrodes have shown similar pH changes during cardiac arrest (unpublished observations).

In conclusion, profound changes occurred in brain ECF pH during cardiac arrest and analyses of cisternal CSF provided unreliable information about the magnitude of the severity of brain metabolic derangements under such circumstances. We have also shown that time dependent pH disequilibria exist between cisternal CSF and brain surface fluid during respiratory arrest as well as during transients of acute metabolic acid base perturbations. In this context, other investigators have shown that during ischemia or hypoxia rapid and pronounced changes occur in cerebral ECF electrolyte composition specifically ECF $K^+$ and lactate concentrations have been shown to rise relatively abruptly while respective changes in CSF as shown in the present study (table 1) as well as by others occur relatively slowly. Therefore, taken together, all these studies suggest that caution should be taken in relying on changes in cisternal CSF for an assessment of brain metabolic status during acute events.

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