Influence of Alterations in Arterial Blood pH and Carbon Dioxide Tension on Plasma Potassium Levels in Humans Anesthetized With Nitrous Oxide, Thiopental and Succinyldicholine

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ABSTRACT


It was the purpose of this study to determine, under carefully controlled conditions in human subjects, whether similar alterations in plasma potassium occur as a result of alterations in arterial pH and carbon dioxide tension.

METHODS AND PROCEDURES

The investigation was made on 30 normal healthy adults. The majority of the subjects were studied immediately before any surgery was performed. However, observations were made on several patients after relatively minor surgical procedures had been completed. In these few, surgical hemorrhage was judged to be minimal, and blood was not administered before or during the experiments.

All patients were given pentobarbital, 100 mg orally, 1-2 hours before surgery, and atropine sulfate, 0.6 mg intravenously, 10 minutes prior to induction of anesthesia. Each patient was in the supine position. General anesthesia was produced and maintained with thiopental, succinyldicholine and nitrous oxide-oxygen (administered at equal flow rates). After intubation, controlled mechanical ventilation was continued throughout the experiment with an intermittent positive pressure, nonrebreathing, precision volume respirator (10). Total respiratory paralysis was maintained continuously throughout the experiment by the slow intravenous administration of a 0.3% solution of succinyldicholine. Electrocardiographic recordings were

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made intermittently during this study with a Cambridge Simpli-Scribe direct-writing electrocardiograph.

The end-expiratory carbon dioxide tension was monitored continuously by a portable gas mass spectrometer (11). Arterial blood samples were drawn anaerobically from the brachial artery into heparinized, oiled syringes. These samples were iced immediately and were analyzed for pH and total plasma carbon dioxide content within 1 hour. The total plasma carbon dioxide content was determined by the manometric method of Van Slyke and Neill (12), with re-extraction for nitrous oxide content (13). The pH of arterial blood was measured with a constant temperature Beckman glass electrode pH meter (Model G) at 37°C. The tension of arterial carbon dioxide was calculated from the total plasma carbon dioxide and the pH using the Henderson-Hasselbalch equation. Blood samples for potassium were centrifuged immediately and the plasma was quick-frozen for subsequent analysis by flame photometry.

Following induction and intubation, ventilation of each patient was adjusted until the alveolar carbon dioxide tension was normal. When no alterations in ventilation were required over a 20-minute interval, the patient was considered to have reached a steady state. Arterial blood was then drawn for carbon dioxide, pH and potassium control determinations.

Three experimental groups, each containing 10 patients, were managed as follows: Group I was maintained in a state of normal acid-base balance for a period of at least 60 minutes. During this time the alveolar carbon dioxide tension was maintained continuously at 39 mm Hg. Group II was subjected to a 60-minute period of acute respiratory acidosis. The acidosis was produced by the addition of sufficient carbon dioxide to the inspired gas mixture to maintain the alveolar carbon dioxide tension at approximately 75 mm Hg. Group III was subjected to a 60-minute period of acute respiratory alkalosis, produced by mechanical hyperventilation sufficient to maintain the alveolar carbon dioxide tension at approximately 19 mm Hg.

At the conclusion of the 60-minute experimental period, arterial blood samples were drawn from each group for determination of pH, total plasma carbon dioxide content and plasma potassium.

Two additional experiments were conducted upon certain of the subjects. Following the 60-minute period of carbon dioxide breathing, nine of the acidic (group II) patients were hyperventilated vigorously with inspiratory gas mixtures containing no carbon dioxide to reduce the arterial carbon dioxide tension. Multiple arterial blood samples were drawn at intervals during this period of carbon dioxide ‘washout’ for determinations of the same variables.

Random patients from groups II and III (5 subjects from each group) were subjected to multiple sampling of arterial blood at 2-minute intervals for 10-15 minutes following the onset of acidosis and alkalosis, respectively, in an attempt to identify any early variation in plasma potassium which might be missed by the 60-minute analysis.

RESULTS

Steady State. At the end of the 20-minute steady state period, all patients exhibited normal acid-base and potassium values. Plasma potassium levels ranged from 3.88 to 4.17 mEq/l. and were statistically homogeneous by analysis of variance at the 20% level.\(^3\)

Normocapnea. There was no significant change in plasma potassium among the group I patients maintained in a state of normal pH and carbon dioxide tension during the hour of study. Since the values after 1 hour of normocapnea were comparable to those of the steady state, one may assume that neither the method of experimental management nor the anesthetic agents or technique influenced the plasma potassium concentrations.

Hypercapnea. In group II, in which the alveolar carbon dioxide was raised to approximately 75 mm Hg and kept at that level for 1 hour, the mean pH fell to 7.19 and the mean arterial blood carbon dioxide tension rose to 73.20 mm Hg, and the mean total carbon dioxide content became 29.34 mm/l. The mean plasma potassium value was 4.142 mEq/l. This represents an insignificant change in potassium (0.034 mEq/l.) from the control value.

Hypocapnea. The third (alkalotic) group of

\(^3\) Five tables giving additional numerical data of the results obtained have been deposited as document number 5177 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. Copies may be secured by citing the document number and by remitting with the order $1.25 for photoprints, or $1.25 for 35 mm microfilm. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.
patients, after 1 hour of hyperventilation, had a mean pH of 7.63. The mean arterial carbon dioxide tension fell to 19.24 mm Hg and the total carbon dioxide content was 10.90 mM/l. The mean potassium value fell from the control level of 3.88 to 3.53 mEq/l, the average fall being 0.35 mEq/l. This was of statistical significance as shown by the P value of 0.004.

In groups II and III no detectable transient alteration in plasma potassium levels was demonstrated by the multiple arterial blood analysis during the first 15 minutes of acidosis or alkalosis.

In an attempt to identify posthypercapnic potassium changes (6, 7), nine patients were subjected to a washout of carbon dioxide over a mean period of 16 minutes. It is impossible to analyze the washout period statistically because of variables in time and in rate of elimination of carbon dioxide. Nevertheless, it is interesting to note that, of the nine cases studied, seven showed an increase and two a decrease in the plasma potassium. The mean average increase was 0.298 mEq/l. The tendency toward a rise in potassium seems to be present, but it is not possible at this time to quantitate accurately the degree of change.

The blood pressure never was noted to drop below the preinduction level with this washout technique.

No significant electrocardiographic alterations were noted.

DISCUSSION

From these data it may be assumed that the anesthesia technique had no influence on the plasma potassium level, since no significant difference existed between the steady state and the 1-hour normocapnic values. Furthermore, plasma potassium did not change during acute respiratory acidosis of 1 hour duration with alveolar carbon dioxide levels between 70 and 75 mm Hg tension (approximately 10%). This finding is in striking contrast to the changes observed by others in laboratory animals. When dogs were caused to inspire 10% carbon dioxide for 1 hour, there occurred a small but definite increase in plasma potassium in four of six animals (personal communication from Dr. E. B. Brown, Jr.). There was a marked rise in potassium when similar animals were subjected to higher (20–40%) carbon dioxide levels.

Failure to demonstrate any hyperkalemia in these patients might be attributable to a variable species response to hypercapnea. Such a disparity of response among cats and dogs has been elicited by several workers (1, 3, 6, 7).

A more attractive hypothesis, however, is found in the application of recent animal data of Fenn (3) who suggests a dual potassium response to carbon dioxide inhalation. This author describes a purely physicochemical effect of pH upon the plasma-tissue equilibrium of potassium. This action produces a shift in potassium from the plasma into the tissues, since the tissues tend to become more acidotic than the highly buffered blood. Thus, a hypokalemia results when the purely physicochemical effect of acidosis is manifest. In addition, Fenn identifies a hepatic reaction to severe hypercapnea (20–40% CO₂) which results in hyperkalemia due to progressive liberation of potassium from the liver. The hepatic effect then tends to counterbalance and, in many instances, may even exceed the physicochemical effect. Thus, the plasma level of potassium reflects the algebraic sum of these two effects. Fenn further showed that a threshold of CO₂ inhalation existed, below which the hepatic response did not occur. The critical level was placed somewhere between 10% and 20% carbon dioxide.

It is possible that, in the clinical experiments described herein, a similar dual response was elicited, the physicochemical tendency to depression of the plasma potassium being exactly offset by a mild hepatic response in the hyperkalemic direction. Further indication that this mechanism may be in play is found when the washout experiments are considered. Under this circumstance, the tendency for the potassium to rise is compatible with the sudden withdrawal of the physicochemical effect of acidosis, with a resultant shift of the cation from the tissue into the plasma.

It is more difficult to explain the mechanism of the production of the hypokalemia observed in the alkalotic (group III) patients. Here, applying the dual response theory, one would expect the plasma level of potassium to be elevated. However, the renal response to
alkalosis is one of hydrogen ion retention and increased potassium excretion (14). In the face of the sharply elevated pH (average 7.63), it is conceivable that augmented renal output of potassium was sufficient to lower the plasma level 0.35 mEq/l. Although this decrease is significant statistically it is questionable whether this slight change is of any real clinical importance.

The above factors may be implicated in the failure to demonstrate the posthypercapnic hypotensive response previously observed in anesthetized humans (15), although variables of duration of hypercapnea and speed of washout doubtless are important in this comparison.

The findings in this investigation do not necessarily indicate that plasma potassium concentrations remain unaltered in human patients subjected to acidosis. The patients studied in these experiments were all healthy individuals and were carefully controlled throughout the study. Although prudence dictated limitation of the severity of the acidosis during this experimental period, it should be recognized that certain patients undergoing clinical anesthesia and surgery may develop carbon dioxide tensions of much greater magnitude. Also, longer duration of hypercapnea, intercurrent disease conditions and stresses associated with surgical intervention may exaggerate the potassium responses. Under these conditions, it is quite possible that acidosis may be sufficient to cause profound changes in electrolyte balance and cardiovascular homeostasis. By the same token, alka-

REFERENCES