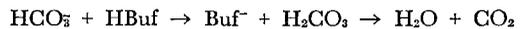


Acid-base effects of hypertonic sodium bicarbonate solutions: A commentary

THE OCCURRENCE of respiratory acidosis in infants with respiratory distress syndrome accompanied by some degree of metabolic acidosis is well documented. This has led to the widespread acceptance of alkali therapy for such infants in the belief that correction of the low blood pH is generally beneficial and superficially may be accompanied by a decrease in pulmonary arterial vasoconstriction with subsequent decrease in the degree of right-to-left shunting of blood. At first glance such treatment is deceptively simple; one need only provide an amount of sodium bicarbonate necessary to increase plasma bicarbonate concentration which, even in the face of an elevated plasma P_{CO_2} , will cause a rise in blood pH. The specific amount of bicarbonate required for any given patient cannot be precisely determined from any of the several widely used "recipes"; rather the approach should be a strictly empirical one in which the bicarbonate dosage is determined on the basis of serial blood acid-base studies. Because relatively large amounts of base are required, hypertonic rather than isotonic solutions of bicarbonate are usually employed in order not to exceed water requirements of the infant.

Finberg¹ has already pointed out the potentially dangerous consequences of this practice with respect to the effects of hypertonicity of the body fluids upon the central nervous system. Another possible danger in this practice is suggested by the study of Ostrea and Odell² published elsewhere in this issue of the JOURNAL. These authors studied the acid-base properties of blood in vitro and

demonstrated clearly that the bicarbonate buffer system is far from ideal when studied in a closed system—i.e., a system where CO_2 cannot escape. CO_2 is produced by the non-bicarbonate buffers of blood (HBuf, principally hemoglobin) via the following reactions:



The CO_2 generated by these reactions cannot escape and the P_{CO_2} as well as the bicarbonate concentration rise. The resulting rise in pH is smaller than if the CO_2 were eliminated by the lungs as it is under normal in vivo conditions. Therefore, a given amount of bicarbonate will produce a larger rise in blood pH in vivo than in a closed system.

If bicarbonate is added to a closed system as a hypertonic solution in amounts which produce an increase in osmolality, a second factor becomes operative. With the addition of a nonpermeable solute (sodium) to this system, water shifts from the erythrocytes into the plasma, and hemoglobin as well as intracellular potassium become more concentrated. Hemoglobin behaves as an acid (HBuf in the above equation), and like many other proteins, the strength of this acidic property of hemoglobin is influenced by the density of electrical charges contributed by other electrolytes (i.e., the ionic strength). With increasing ionic strength, hemoglobin becomes a stronger acid and converts more of the added bicarbonate to CO_2 . The reaction shown above is pushed from left to right to a greater extent than is the case with addition of isotonic bicarbonate. This factor, well documented in the study of

Ostrea and Odell, accounts for the seemingly paradoxical result that addition of hypertonic bicarbonate may actually produce a fall in blood pH rather than the expected rise. The results observed with hypertonic mannitol—a neutral, nonpermeable solute—provide strong support for this interpretation. Addition of hypertonic mannitol, as in the case with hypertonic bicarbonate, causes a shift of water from the erythrocytes to the plasma leading to an increase in intraerythrocyte ionic strength thereby making hemoglobin a stronger acid. This “new” source of hydrogen ions in effect pushes the reaction shown above to the right consuming bicarbonate already present with a corresponding rise in P_{CO_2} and an accompanying fall in pH.

At first glance, the experiments of Ostrea and Odell may appear to be far removed from clinical practice. But this may not be the case when one considers that there are a variety of clinical circumstances in which a severe limitation of CO_2 excretion may exist—e.g., apnea from any cause including birth asphyxia, cardiac arrest, severe respiratory distress, etc. Physiologically all of these clinical circumstances, at least transiently, approximate the conditions of a closed system. Therefore, hypertonic bicarbonate administration in such instances could be accompanied by the type of adverse changes in blood acid-base status observed by Ostrea and Odell in their experiments.

Even if the system were “partially open,” transient or prolonged rises in P_{CO_2} during or after completion of the bicarbonate infusion may occur; a number of such instances are documented and reviewed by Ostrea and Odell. Such elevations could be quite harmful. For example there is abundant evidence³ available from study of cerebrospinal fluid acid-base composition to show that CO_2 rapidly passes the blood-brain barrier, while bicarbonate does not. The same is likely to be true of neurons although this issue, for technical reasons, is much more difficult to study. An abrupt increase in P_{CO_2} in the nervous system and/or in the cerebrospinal fluid incident to a bicarbonate infusion in an

infant who cannot excrete the added load of CO_2 may actually produce a general depression in the function of the central nervous system including the central respiratory drive. All of these considerations should give pause to those who would infuse bicarbonate into patients with apnea or inadequate ventilation. Certainly abundant clinical evidence in the resuscitation of the newborn infant or of the patient with cardiac arrest demonstrates that the essential first steps are to establish adequate artificial ventilation and adequate circulation before bicarbonate is administered. Similar considerations apply to the treatment of the infant with respiratory distress. Admittedly this is a more difficult feat to accomplish, but hopefully continuing research will lead to technical advances in the ventilatory therapy of such patients.

The key to treatment of respiratory acidosis of any cause must be a primary attack upon ventilatory insufficiency. Bicarbonate therapy at best only ameliorates the resulting acid-base disturbance but does not definitively correct it. Ostrea and Odell's studies now cause us to re-examine this use of bicarbonate particularly in the case of the inadequately ventilated infant in respiratory failure.

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