Sodium Bicarbonate Controversy in Lactic Acidosis

To the Editor:

We read with interest the review article by Drs. Forsythe and Schmidt (January 2000). The use of sodium bicarbonate in the treatment of lactic acidosis has been very controversial and will probably remain so for a long time.

The argument that giving IV sodium bicarbonate causes paradoxical intracellular acidosis is overly simplistic and is not convincingly shown (despite several studies that the authors also point out). As in medicine in general, this is a multifactorial process. As outlined in the more recent literature, whether paradoxical intracellular acidosis really develops or not depends on several factors: the presence of nonbicarbonate buffering systems acting as proton donors to react with HCO₃⁻ to form more CO₂; the ability to ventilate and eliminate CO₂ in proportion to its formation, and therefore the dose and rate of bicarbonate administration; and some other factors that are not yet well understood.

The fact that the administration of IV sodium bicarbonate has not been beneficial in lactic acidosis is difficult to interpret for several reasons. First, lactic acidosis that is severe enough to warrant this therapy is associated with very high mortality to begin with. As long as the underlying etiology is not corrected, survival is unlikely. Therefore a significant benefit, especially in terms of survival, should not be expected from any tempozizing measure short of reversing tissue hypoxia, improving lactate metabolism or uptake. Second, under these circumstances, any benefit to hemodynamic parameters is also difficult to interpret because there are so many confounding variables. It is very hard to control for these factors, despite the use of various scoring systems or sophisticated statistical analysis. It is also possible that the observation period may not be long enough to note any benefit. Third, to prove a possible marginal benefit (as common sense would dictate), by keeping the pH close to the physiologic range where all the cells function, may require the study of large numbers of subjects in a disease state that has very high mortality.

We respect the opinion of the authors, of not using bicarbonate administration routinely in lactic acidosis; however, we think we should be cautious in discarding treatment options that are not harmful if appropriately used, especially if there are no alternatives and if their use is based on a logical explanation. Even though we believe in the current concept of evidence-based medicine, history has shown that it may take time to provide the evidence. Along with others, we do not think we should discard its use, unless further data show that bicarbonate is actually harmful despite appropriate and controlled use (careful rate and dosing, avoiding hypernatremia, hyperosmolality), and/or until there are other, easily available alternatives for clinical use. There is a physiologic range for everything in nature, and there must be a reason for this. Why should we not attempt to maintain the physiologic range where the cells normally function? How many humans have the authors seen who could survive with a pH < 7.0?

What is wrong with trying to maintain a living milieu reasonably close to the physiologic one and with supporting the human body while the disease process takes its course? After all, isn’t this what we do in medicine? (Some examples, although somewhat exaggerated, might include the use of ventilation for patients while their pneumonia is resolving; provision of hemodynamic support, etc.)

To the Editor:

Thank you for reporting your experience with chronic IV epoprostenol in patients with pulmonary hypertension associated with systemic sclerosis. I apologize if my editorial was misinterpreted to imply that chronic IV epoprostenol therapy should not be considered as a therapeutic option for patients with pulmonary hypertension associated with various connective tissue disorders. My comments were only meant to alert physicians to our not currently having the same experience with these patients as we have with patients who have primary pulmonary hypertension. We obviously are cautiously optimistic and hopeful that chronic IV epoprostenol in patients with pulmonary hypertension associated with systemic sclerosis is efficacious for various patients with pulmonary hypertension associated with other disorders, including collagen vascular diseases, particularly in light of many of these patients not being candidates for transplantation due to their associated collagen vascular diseases. Your experience appears similar to previously published experiences with these patients, eg, chronic IV epoprostenol does appear to be efficacious, although whether or not its efficacy is as good as we and others have seen with primary pulmonary hypertension remains to be determined. In the meantime, consideration of looking at these patients in a registry may allow us to evaluate the relative efficacy of epoprostenol and rank the efficacy of chronic IV epoprostenol for various groups of patients with pulmonary vascular disease, including primary pulmonary hypertension, pulmonary hypertension associated with the various collagen vascular disorders (subdivided into the specific collagen vascular disorders, since their responses may be different), as well as pulmonary hypertension associated with portal hypertension, HIV, and appetite suppressant-induced primary pulmonary hypertension.

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REFERENCES
1 Barst RJ. Experience and reason [editorial]. Chest 2000; 117:2–5
support for patients with septic, cardiogenic, or anaphylactic shock; treatment with dialysis for patients with acute renal failure while the tubules or glomeruli regenerate; or administration of analgesics and anti-inflammatory agents during traumatic edema/inflammation.

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To the Editor:

We agree that the use of sodium bicarbonate in lactic acidosis is controversial and probably will remain so. Regarding the impact on intracellular pH, Dr. Cuhaci and colleagues hold out hope that “several factors” such as buffering systems, dose or rate of bicarbonate, compensation by increasing ventilation, or other speculative mechanisms might allow bicarbonate to reveal its salutary effects. We would counter that nearly all in vivo studies to date have failed to show any rise in intracellular pH (as our table shows1), despite many different methodologies.

In our view, the fact that the administration of bicarbonate has not been shown beneficial is not “difficult to interpret.” The purpose of cross-over studies, such as those cited in our review, is to minimize the impact of “confounding variables.” We would never go so far as to say that the studies published to date are definitive, however. An area in which current data are seriously lacking is the longer-term effect of bicarbonate. We can imagine that some method of bicarbonate administration would have a hemodynamic effect distinguishable from saline, but until such a method is published, interpretation is simple: the studies are negative.

We vigorously challenge the statement that keeping the pH close to the physiologic range is “common sense.” Examples abound in medicine for which keeping some parameter close to the physiologic range is dangerous or even negligent. Where would modern medicine be without cold cardioplegia, hypotensive surgery, or therapeutic anticoagulation? Recent studies have even called into question some age-old practices such as blood transfusion in the critically ill and fluid resuscitation of victims of penetrating trauma. In this regard, permissive hypercapnia is one of the most dramatic recent innovations to challenge common sense. It is now widely accepted that using a ventilator to keep the PCO2 close to the physiologic range in patients with status asthmaticus or ARDS worsens the outcome (eg, barotrauma, auto-positive end-expiratory pressure, ventilator-induced lung injury, and hemodynamic depression).

We are asked not to discard a treatment that has not been shown harmful, especially if there are no alternatives. This is emotionally seductive, but unpersuasive. First, it is not true that bicarbonate has never been shown to have detrimental effects, as we discussed in our review.1,2 Further, in data published after our review was completed, Laffey and colleagues3 showed in an animal model that both respiratory and metabolic acidosis defended the lung against ischemia-reperfusion injury, a form of ARDS. Particularly interesting was their demonstration that the correction of hypercapnic acidosis compounded lung injury. Second, and most importantly, ineffective treatments should not be defended, even if some view them as logical. If not for the long history of bicarbonate use, who would actually propound its use today? Imagine trying to convince a knowledgeable patient, one’s colleagues, or the US Food and Drug Administration that you want to infuse into a critically ill patient a substance that has never been proven to be beneficial in any animal or human trial.

We have the means for testing such unproven therapies: controlled clinical trials approved by an institutional review board, which we believe is the only setting in which patients with lactic acidosis should be treated with bicarbonate.

The use of sodium bicarbonate is surrounded by many strong convictions, on both sides of the aisle. We hope that our article generates discussion, causes critical evaluation of the data, and provokes clinicians to rethink the use of bicarbonate for patients with lactic acidosis.

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