Is Bicarbonate Therapy Useful?

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KEYWORDS

• Metabolic acidosis • Lactic acidosis • Diabetic ketoacidosis • Kidney disease
• Ionized calcium • Potassium

KEY POINTS

- Sodium bicarbonate therapy is likely to increase extracelluar pH but will be associated with paradoxic intracellular acidosis.
- Despite concerns that acidosis can have negative effects on cardiovascular performance, bicarbonate therapy has not been shown to improve cardiovascular function in the face of metabolic acidosis.
- Sodium bicarbonate therapy is associated with adverse effects, including hypernatremia, hyperosmolality, hypokalemia, and decreased serum ionized calcium concentration.
- Sodium bicarbonate treatment can enhance ketogenesis in patients with diabetic ketoacidosis and may delay resolution of the disease.
- Sodium bicarbonate is thought to play an important role in bicarbonate-losing diseases such as renal tubular acidosis or diarrhea.

INTRODUCTION

Sodium bicarbonate is a buffer or alkalinizing agent used commonly for the treatment of metabolic acidosis, despite a growing body of literature questioning its benefit. This controversy is based on concerns about both questionable benefits and potential adverse effects. Given the lack of high-quality evidence supporting the use of sodium bicarbonate, there remains debate surrounding its use in specific clinical scenarios, and it is largely left to clinical judgment.[1] In order to make an informed clinical decision, a full understanding of the potential benefits and potential adverse effects of bicarbonate administration is needed.

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POTENTIAL BENEFITS OF BICARBONATE THERAPY

The primary premise for the benefit of bicarbonate therapy is that acidemia is harmful and resolution of acidemia will remove these harmful effects. Changes in pH will alter protein structure and function. Commonly cited adverse effects of acidemia include decreased myocardial contractility, arterial vasodilatation, decreased vascular responsiveness to vasopressors, shifts in the oxyhemoglobin dissociation curve, impairment of coagulation, and cellular dysfunction.[2–4] Although these effects have been identified in various experimental settings, the effects of acidemia in clinical patients are not consistent.[5–7] Human patients with permissive hypercapnia and severe diabetic ketoacidosis (DKA) have been found to tolerate acidemia with minimal cardiovascular or other adverse effects.[8–10]

POTENTIAL DETRIMENTAL EFFECTS OF BICARBONATE THERAPY

Acid-Base Changes

It has been assumed that administration of sodium bicarbonate will increase pH, removing the potential adverse effects of acidemia. The acid-base effects of bicarbonate administration are complicated by the production of carbon dioxide (CO_2) following the buffering of hydrogen ions, according to the equation:

$$HCO_3^- + H^+ \Leftrightarrow H_2CO_3 \Leftrightarrow H_2O + CO_2$$

For every 1 mol of hydrogen ions neutralized by bicarbonate, an equimolar amount of CO_2 is produced. Carbon dioxide generation after bicarbonate therapy has been well documented in clinical and experimental studies to date.[11] In order for bicarbonate to have an alkalinizing effect, it is necessary for CO_2 to be removed through effective alveolar minute ventilation. As the Henderson-Hasselbalch equation describes, pH is dependent on the ratio of bicarbonate to P_{CO_2}, (pH α $[HCO_3^-]/P_{CO_2}$). If both bicarbonate concentration and P_{CO_2} increase with the administration of bicarbonate, there may be persistence, or even worsening of the acidemia. As a result, bicarbonate administration should be limited to patients with adequate minute ventilation.

Paradoxic Intracellular Acidosis

The production of CO_2 following bicarbonate administration can also lead to paradoxic intracellular acidosis. After bicarbonate is administered, there is an increase in CO_2 production, and this CO_2 will diffuse into cells leading to intracellular hypercapnic acidosis. Intracellular pH has been shown to decrease consistently in experimental and clinical studies of bicarbonate therapy in humans.[11] Even in patients with adequate alveolar minute ventilation, there is a period of time when blood P_{CO_2} is increased following bolus infusion of bicarbonate.[7] Studies that have reported negative outcomes in association with bicarbonate administration have suggested that these outcomes may be attributable to the intracellular pH changes.

Increased Intravascular Volume and Hypernatremia

Sodium bicarbonate administration can cause hypervolemia, hyperosmolality, and hypernatremia. Acquired hypernatremia in hospitalized patients may have a negative impact on outcome, suggesting that therapies that induce hypernatremia should be avoided.[12,13] A common formulation of sodium bicarbonate is an 8.4% solution, which represents 1 mmol/mL of sodium bicarbonate, has a sodium concentration of 1000 mmol/L, and has an osmolality of 2000 mOsm/L. Rapid infusion of undiluted sodium bicarbonate can cause hypotension as a result of its hypertonic nature and the