



## Sodium Bicarbonate for Metabolic Acidosis?

### Key Article

- Jaber S, Paugam C, Futier E, et al. Sodium bicarbonate therapy for patients with severe metabolic acidemia in the intensive care unit (BICAR-ICU): a multicenter, open-label, randomized controlled, phase 3 trial. *Lancet*. 2018; 392:31-40.

### Background

- Acute acidemia frequently observed in critically ill patients; an acidotic environment can cause cellular dysfunction
- Incidence ranges from 14% to 42%
- Mortality is greater than 50% when the pH stays  $< 7.20$
- Recent surveys demonstrate that the majority of clinicians use sodium bicarbonate for the treatment of acidemia with hyperlactemia.
- The effect of bicarbonate for the treatment of metabolic acidemia remains controversial
- The 2016 SSC Update suggests that the effect of bicarbonate on hemodynamics and vasopressor requirements at lower pH remains unknown

### Objective

- Evaluate whether sodium bicarbonate infusion would improve clinical outcome in critically ill patients with severe metabolic acidemia
- (Investigators hypothesized that bicarbonate infusion would result in fewer deaths from any cause at 28-days and lower incidence of at least 1 organ failure at 7 days)

### Study

- Multicenter, open-label, randomized, controlled phase 3 trial
- 26 ICUs in France
- Inclusion Criteria
  - Adults patients  $\geq 18$  years of age
  - Admitted within 48 hours to the ICU
  - Severe acidemia: pH  $< 7.2$ , PaCO<sub>2</sub>  $\leq 45$  mm Hg, bicarb  $\leq 20$  mmol/L
  - Total SOFA of 4 or more
  - Arterial lactate concentration of 2 mmol/L or more
- Excluded
  - Respiratory acidosis
  - Digestive or urinary disorder with loss of bicarbonate
  - Stage IV kidney disease
  - Ketoacidosis
  - Bicarb infusion within 24 hours before screening
- Randomization
  - Randomly assigned patients in 1:1 ratio
    - Bicarb infusion

- 4.2% sodium bicarbonate
    - Aim to achieve pH of 7.20 or more during the 28-day ICU admission or ICU discharge
    - 125 to 250 mL in 30 min with a maximum of 1L in 24 hours after inclusion
    - Measurement of ABG should be 1-4 hours after the end of each infusion
      - No bicarb infusion
  - A-priori stratified by site and 3 factors
    - Age (65 years)
    - Presence or absence of sepsis
    - Presence or absence of AKIN score of 2 or 3
- Outcome
  - Primary: composite of death from any cause at 28 days after randomization AND presence of at least 1 organ failure at 7 days after randomization
  - Secondary
    - Use, duration, and number of days alive free of life support interventions
    - SOFA score at enrollment and at days 1, 2, and 7 days after enrollment
    - Total fluid intake
    - Adverse events
    - ICU-acquired infections
    - ICU LOS
- Analyses: all done on data from intention-to-treat population

## Results

- 400 patients randomly assigned to the study groups (201 to control group; 199 to bicarb group)
- Total of 389 included in ITT analysis; 341 of 389 patients adhered to the planned treatment in their randomization group
- Characteristics well balanced
- Proportion of patients whom targeted pH of 7.30 was reached and maintained for 36 hours from enrollment to day 2 was 26% in control group and 60% in bicarb group
- **Primary outcome**
  - **71% in the control group**
  - **66% in the bicarb group**
  - **p=0.24**
  - **No significant effect of the treatment group**
- After multivariate analysis, bicarb was associated with fewer deaths than control group at day 28
- In a-priori defined stratum of patients enrolled with AKI with AKIN scores of 2 or 3, primary outcome occurred in 82% of control group and 70% of bicarb group
  - Univariate and multivariate analysis demonstrated that bicarb was significantly associated with better outcome than no bicarb at day 28
- Renal Replacement Therapy During the ICU Stay
  - 52% in the control group
  - 35% in the bicarb group
- No difference in days free of mechanical ventilation
- No difference in ICU LOS
- More patients in bicarb group free from vasopressors

- Metabolic alkalosis, hypernatremia, and hypocalcemia observed more frequently in bicarb group but no life-threatening complications observed

#### Limitations

- No specific control group fluid solution was recommended
- Physicians caring for the patient was not masked
- Bicarb infusion titrated to maintain pH target of 7.3
- Protocol suggested a range volume of 4.2% bicarb – did not use a formula to calculate the base deficit and provide a tailored bicarb infusion
- Did not stratify patients based on mechanism of acidemia – causes were heterogeneous.

#### Take Home Point from Authors

- Sodium bicarbonate infusion had no effect on 28-day mortality or the presence of at least 1 organ failure at day 7 for this patient population.
- It did decrease the mortality in the a-prior defined stratum of patients with AKI.