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Early sodium bicarbonate therapy for critically ill patients with septic shock and acute moderate metabolic acidosis

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To the editor:

In recent decades, septic shock has continued to be a life-threatening health problem around the world.[1] Meanwhile, metabolic acidosis (MA) is also well known in critically ill patients, and even moderate metabolic acidosis (MMA) is associated with higher mortality than sepsis.[2] Although the administration of sodium bicarbonate (SB) is widely used in sepsis shock with MA in the intensive care unit (ICU), its clinical efficacy is not well established. In the 2021 update of the Surviving Sepsis Campaign guidelines, Evans et al. recommend the administration of SB in adults with septic shock, severe metabolic acidemia (pH ≤7.2), and acute kidney injury (AKI, AKIN score 2 or 3).[3,4] However, clinical evidence for the efficacy of the administration of SB in critically ill patients with septic shock and acute MMA is still limited.

We retrospectively investigated a large ICU database (MIMIC-IV, https://www.physionet.org/) from 2008 to 2019 in 6 ICUs at a single-center hospital (Beth Israel Deaconess Medical Centre; Boston, MA). All adults with septic shock and acute MMA (7.2 < pH < 7.3, bicarbonate concentration <20 mmol/L, and $PaCO_2$ <50 mmHg) within the first 48 hours after ICU admission were included in this study. Propensity score analysis[5] (PSA) was performed to account for differences in the probability of receiving or not receiving SB. For the PSA, we matched patients 1 to 1. The marginal structural Cox model[5] (MSCM) was developed to adjust for both baseline and time-varying confounding variables. The primary outcome was ICU and in-hospital mortality.

Variables, including sex, age, body mass index, comorbidities on ICU admission, mechanical ventilation, vasopressors, and renal replacement therapy, were extracted from the MIMIC-IV database for the first 24 hours of ICU admission. Serum creatinine within the first 48 hours of an ICU stay was used to identify AKI stages. Administration of lactate solution for the first 24 hours was also included in the study. To account for the possible influence of clinical practice in previous years, the year of admission was used as a random factor in a mixed-effects model. Laboratory variables (PaO_2, $PaCO_2$, pH, and bicarbonate concentration) were recorded throughout the ICU period. For patients who underwent multiple tests, the highest values of lactate and $PaCO_2$ and the lowest values of PaO_2, bicarbonate concentration, and pH on each day were used for analysis. The above variables included in the PSA and MSCM are listed in Supplemental Table 1 (http://links.lww.com/ECCM/A58).

A total of 577 patients with septic shock and MMA were identified, of whom 194 were included in the SB and 383 in the non-SB groups (Supplemental Table 2, http://links.lww.com/ECCM/A58). In the PSA group, early SB infusion was associated with both lower ICU mortality (hazards ratio [HR]: 0.61; 95% confidence interval [CI]: 0.40–0.93; $P < 0.05$) and lower in-hospital mortality (HR: 0.69; 95% CI: 0.50–0.97; $P < 0.05$; Fig. 1). In MSCM, our study also found a statistically significant positive effect of early SB infusion on ICU mortality (HR: 0.31; 95% CI: 0.13–0.72; $P < 0.01$) and hospital mortality (HR: 0.55; 95% CI: 0.31–0.97; $P < 0.05$) in patients with septic shock and MMA (Supplemental Figure 1, http://links.lww.com/ECCM/A59).

Our observational study suggests that early infusion of SB in critically ill adult patients with septic shock and MMA within the first 48 hours after ICU admission has a significant beneficial effect on both ICU and hospital mortality. Further large, randomized, controlled clinical trials are needed to provide high-quality evidence to improve the Surviving Sepsis Campaign guidelines.

Conflict of interest statement

The authors declare no conflict of interest.

Author contributions

The study was designed by Feng C, who was responsible for data collection, analysis, and interpretation and for writing the manuscript. Huang S and Peng Y contributed to data analysis and interpretation and wrote the manuscript. Zhang X conducted the data interpretation. Yao Y performed the data interpretation and reviewed the manuscript.

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Ethical approval of studies and informed consent

Data collection was passive and had no impact on patient safety. The data set was deidentified in compliance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.

The data sets generated during and/or analyzed during the current study are available in the https://physionet.org/.

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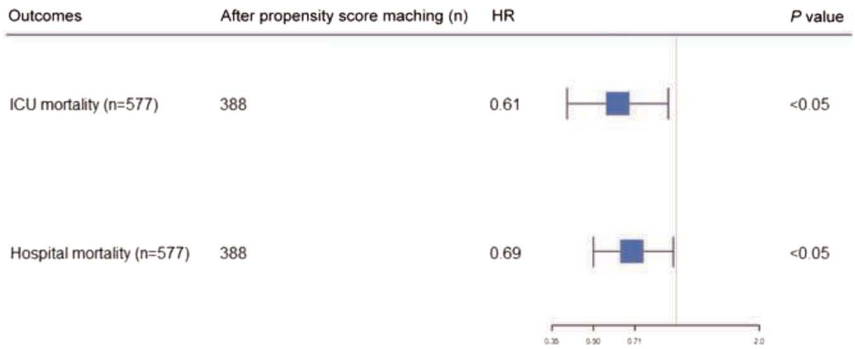

Figure 1. Forest plot showing the effect of early sodium bicarbonate infusion on ICU and hospital mortality in the PSA for critically ill patients with septic shock and acute moderate metabolic acidosis. The hazard ratios were estimated using the PSA. After propensity score matching, 194 patients from the non-SB group were matched to SB group (n = 194) to balance the baseline differences in the probability to receive SB or not. The x-axis tick marks follow a logarithmic scale. ICU, intensive care unit; PSA, propensity score analysis; SB, sodium bicarbonate.

Data extraction from the database was certified by the team at the Laboratory for Computational Physiology at the Massachusetts Institute of Technology (MIT-LCP), which provides and maintains MIMIC-IV. Since the study was an analysis of an anonymized, publicly available third-party database that had already been approved by the Institutional Review Board (IRB), our institution's IRB approval was exempt.

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