Weekly Pharmacy Pearl #31 – Sodium Bicarbonate: The Whole Truth

Hard Data/Evidence

- Both retrospective and prospective studies have consistently documented that sodium bicarbonate therapy **does not** improve metabolic responses, biochemical parameters, acid-base balance normalization, or clinical outcomes among patients with DKA
- **No benefit** from sodium bicarbonate therapy has been found in the management of lactic acidosis regarding clinical outcomes or mortality
- Accordingly, the 2016 update of the Surviving Sepsis Campaign guidelines **recommends against the use of sodium bicarbonate** therapy to improve hemodynamics or to reduce vasopressor requirements in patients with hypoperfusion-induced lactic acidemia **with pH ≥ 7.15** (weak recommendation, moderate quality of evidence)

Theoretical Advantages

- Improved myocardial contractility
- Elevated ventricular fibrillation threshold
- Improved catecholamine tissue response
- Decreased work of breathing

Known Disadvantages

- Worsening hypokalemia
- Paradoxical CNS acidosis
- Worsening intracellular acidosis
- Impaired (shift to left) oxyhemoglobin dissociation
- Hypertonicity and sodium overload
- Delayed recovery from ketosis
- Elevation in lactate levels
- Possible precipitation of cerebral edema
- Tissue necrosis if extravasated from an IV push

Acceptable Times to Use Bicarb

Lactic Acidosis

- **Severe acidemia pH < 7**
- May paradoxically depress cardiac performance and exacerbate acidosis by enhancing lactate production
    - Bicarb stimulates phosphofructokinase
- May cause fluid overload and HTN from the massive amount required when lactic acid accumulation is relentless
- Goal should be arterial pH ~ 7.2 and bicarb to no more than 12 mEq/L over 30 – 40 mins
- When the underlying cause of lactic acidosis can be remedied, blood lactate will be converted to bicarb and may result in an overshoot alkalosis if excessive amounts of bicarb have been administered

DKA

- **Initial pH < 6.9**
- Acidotic patients routinely recover from DKA without alkali therapy
- Slowing the ketoacid production from infused insulin allows the generation of bicarbonate ion as ketoacids are oxidized

References or Fun Readings

- Ghauri SK, Javaeed A, Mustafa KJ, et al. Bicarbonate therapy for critically ill patients with metabolic acidosis: a systematic review. Cureus. 2019 Mar;11(3).
- Adeva-Andany MM, Fernández-Fernández C, Mouriño-Bayolo D, et al. Sodium bicarbonate therapy in patients with metabolic acidosis. The Scientific World Journal. 2014 Oct;2014.
- Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock: 2016. Intensive care medicine. 2017 Mar;43(3):304-77.
- Waskowski J, Hess B, Cioccari L, et al. Effects of sodium bicarbonate infusion on mortality in medical–surgical ICU patients with metabolic acidosis—A single-center propensity score matched analysis. Medicina Intensiva. 2021 Jun 11.
- Fujii T, Udy AA, Nichol A, et al. Incidence and management of metabolic acidosis with sodium bicarbonate in the ICU: An international observational study. Critical Care. 2021 Dec;25(1):1-0.
- Nyce A, Byrne R, Lubkin CL, Chansky ME. Diabetic Ketoacidosis. Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 9e. McGraw-Hill; Accessed June 16, 2021.

Commentary on Fujii T, Udy AA, Nichol A, et al. **Incidence and management of metabolic acidosis with sodium bicarbonate in the ICU: An international observational study**. *Crit Care*. 2021;25(1):45.

*This study has several limitations and did NOT show meaningful clinical outcomes in the overall population

Table 4 Association between administration of sodium bicarbonate and clinical outcomes

	Overall population ($N=360$)			Vasopressor dependent at the diagnosis of metabolic acidosis ($N=187$)			Severe metabolic acidosis at the time of diagnosis ($N=46$)		
	aOR, β	95% CI	*p* Value	aOR, β	95% CI	*p* Value	aOR, β	95% CI	*p* Value
ICU mortality	0.85	0.44 to 1.62	0.63	0.52	0.22 to 1.19	0.13	0.86	0.08 to 9.03	0.90
Hospital mortality	0.96	0.51 to 1.76	0.89	0.84	0.38 to 1.85	0.68	1.07	0.09 to 12.3	0.96
Vasopressor dose at 6 h	−0.02	−0.08 to 0.03	0.36	0.01	−0.07 to 0.09	0.81	−0.23	−0.50 to 0.03	0.11
Vasopressor dose at 24 h	0.04	−0.01 to 0.08	0.10	0.04	−0.03 to 0.11	0.24	−0.004	−0.16 to 0.16	0.97
Mean arterial pressure at 6 h	2.85	−0.50 to 6.15	0.09	5.99	1.84 to 10.2	0.01	6.60	−3.65 to 17.2	0.23
Mean arterial pressure at 24 h	−1.07	−4.28 to 2.13	0.52	−1.03	−5.21 to 3.15	0.63	8.90	−1.44 to 19.2	0.13
Delta mean arterial pressure per vasopressor dose at 6 h	3.66	−0.78 to 8.09	0.11	8.87	3.34 to 14.48	0.002	8.53	−8.60 to 25.4	0.35
Delta mean arterial pressure per vasopressor dose at 24 h	1.26	−3.68 to 6.22	0.28	3.65	−2.56 to 9.88	0.26	13.7	0.79 to 26.6	0.06

Delta mean arterial pressure per vasopressor dose = mean arterial pressure at 24 h/(vasopressor dose at 24 h + 1) − mean arterial pressure at 6 h/(vasopressor dose at 6 h + 1)

- No findings were statistically significant except for 'delta MAP per vasopressor dose at 6 h' and 'vasopressor dose at 6 h' in the 'vasopressor dependent at the diagnosis of metabolic acidosis' subgroup.
- There was a small sample size of 187 in this subgroup.
- ICU mortality and hospital mortality did not have any statistically significant findings.
- The study conclusion stated that the lack of a significant signal of harm supports that sodium bicarb in early metabolic acidosis is safe.
- The study results should be interpreted with caution due to several limitations including being an observational study and having a small sample size.
- Further randomized controlled studies are warranted to truly distinguish its significance.