TREATMENT OF SEVERE ACIDEMIA

What’s so bad about severe acidemia?  pH > 7.2 important to maintain optimal cellular function AND cardiovascular function.

- Optimal intracellular pH >7.2 needed for optimal function of many metabolic intermediates (need to be in ionized state so as not to escape cell), enzymes (such as phosphofructokinase important in the rate limiting step in glycolysis), and in the synthesis of DNA, RNA and proteins.
- **Direct myocardial depression:** directly correlates with myocardial depression, at pH <7.2
  - In vitro heart studies, observed with a decrease of pH from 7.4 to 7.2 to be associated with a decrease in LV function, of 5-10 % with metabolic acidosis and 25 % with respiratory acidosis.
  - Animal studies observed only detectable myocardial depression with pH <7.2; and actually an increased contractility for pH >7.2. This was worsened with administration of beta blockers and with lactic acidosis.
- **Generation of cardiac arrhythmias** by reducing the ventricular fibrillation threshold and impairing myocardial repolarization.
- **Direct arterial vasodilation,** causing a decrease in SVR. However, a huge catecholamine response then leads to vasoconstriction, so the net effect on SVR depends on their interplay. In the midst of this, the vasculature is less responsive to both alpha and beta stimulation. Note acidemia is associated with venoconstriction, displacing blood into central circulation and elevating right side filling pressures.
- **Impaired oxygen delivery:** initially, a decrease in pH reduces the affinity of HgB for oxygen immediately, thus enhancing the oxygen delivery to tissues (Bohr effect). By 12-36 hours, a decrease in RBC glycolysis depletes 2,3-DPG, thus HgB gets an increased affinity for oxygen, thus impairing oxygen tissue delivery.
- **Electrolyte abnormalities:** increased serum potassium levels due to cellular shift out of cells (beware that in some metabolic acidosis there is net k depletion due to enhanced potassium urinary excretion); ionized calcium levels are initially elevated (good for myocardial contractility) but then vary depending on renal function.

SHOULD WE TREAT WITH BICARBONATE THERAPY?  NOT BENEFICIAL IN DKA, NO EFFECT ON CARDIAC DYSFUNCTION, MORTALITY OR ACIDEMIA IN TYPE A LACTATE ACIDOSIS EXCEPT IN VERY LARGE QUANTITIES IN SETTING OF ULTRAFILTRATION AND MAY WORSEN MYOCARDIAL ACIDEMIA POST CARDIAC ARREST

- Normal compensatory mechanisms in place to deal with acidemia include:
  - Anion gap acidosis: within minutes to hours, the direct metabolism of the organic anions replete HCO3 stores; after about 8 hours, renal HCO3 synthesis picks up the slack.
  - Normal anion gap acidosis: no organic anion and chloride is not converted to HCO3, so depends on renal HCO3 synthesis, which takes hours to days.
- There is great debate about exogenous bicarbonate therapy in the treatment of severe acidemia due to Type A lactate acidosis, diabetic ketoacidosis and metabolic and respiratory acidosis s/p cardiac arrest (these three clinical scenarios are responsible for > 90 % cases of severe acidemia, thus the bulk of research concentrated on them). **The main opponent view is that it can lead to deterioration in hemodynamics, volume overload, hyperosmolality, CSF acidosis and increased organic acid production.**
  - DKA: theory that severe acidemia increases insulin resistance. Animal studies confirmed increased insulin resistance, but also observed increased hepatic ketogenesis and lactate production. In humans, many small case series revealed NO change in the rate of decrease in glucose or resolution of ketoacidosis. One study actually extended the period of ketoacidosis and hospitalization. May actually exacerbate CSF acidosis.
due to suppressed ventilation with HCO3 treatment, but this was also seen in recovering DKA treated without HCO3 therapy.

- **Lactic acidosis**: Type A due to severe hypoxemia or impaired tissue perfusion.
  - Animal studies observed a decrease in cardiac output due to a decrease in arterial and intracellular pH due to increased CO2 generation and rapid entry into cells, especially myocardial, liver, skeletal muscle, RBC’s and brain. Other observations include: increased venous PCO2, decrease in HCO3 concentration, increased lactate production, decrease in ionized calcium (increase arterial pH increases binding to albumin), increase of myocardial intracellular calcium (due to enhanced function of NA-H pump exchanger resulting in increased intracellular Na which decreases efflux of calcium through NA-Ca exchanger), and a decreased ratio of ATP and phosphocreatintine ratio to inorganic phosphate (interference with energy production). However, another study administered large quantities of HCO3 (20 mEQ/liter) and noted a profound decrease in cardiac output for just thirty minutes, then returned to baseline; and survival was prolonged but only for an additional hour, then mortality rates the same.
  - In humans, very few studies (total 500 patients over the past 50 years) to base practice on. In summary, studies have revealed NO effect on cardiac output, NO change in morbidity or mortality, and equivocal impact on pH and HCO3. In subset of patients with Class III and IV CHF, there was a decrease in cardiac output reported. A review of 177 patients treated with large quantities of HCO3 and ultrafiltration did show some improvement in acidemia, hemodynamics and mortality.

- **Cardiac arrest**: potentially detrimental because net pathology is a severe decrease in myocardial pH (more so than arterial pH) and increase in venous PCO2; which would be exacerbated by HCO3 administration. Minimal human studies. Lots of animal studies, best outcome when co-administer pressors and hyperventilated. 

**IS THER ANYTHING ELSE WE CAN DO?**

- **THAM** (a biologically inert amino alcohol) : very effective buffer (pK 7.8 at T 37), penetrates quickly into cells. Animal studies have observed an increase in both arterial and intracellular pH while a reduction in PCO2, improved myocardial contractility and survival post arrest and with sepsis. Recent study here at SFGH, used THAM in patients with ARDS being treated with permissive hypercapnea and reported less depression of myocardial contractility.

**BOTTOM LINE**

- Stop the production organic acid first and foremost!!!
- Hyperventilate as much as you can!
- Bicarbonate has many potential detrimental effects (increasing venous and intracellular CO2 and pH) and not consistently shown to improve hemodynamics, mortality or even pH levels unless administered in large quantities that will get you into trouble with osmolality and volume.
- THAM better buffer, does not increase CO2 and improves cardiac dysfunction.

**References:**