Acid-Base Conference

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PGY4
Case Presentation

HPI: 65yo M with PMH significant for CKD stage III (Cr: 1.6), OSA (noncompliant w/CPAP), CHF (EF of 45%) and morbid obesity admitted to MICU 6/15 with shortness of breath. Found to be in CHF exacerbation and started on aggressive diuresis

- Course complicated by GI Bleed and MSSA bacteremia during which time he required frequent PRBC transfusions and diuresis was held for hypotension

- Renal Consult requested 7/8 for AKI on CKD and for assistance with diuresis
PMH: IDDM, HTN, AFib not on AC 2/2, small bowel arteriovenous malformations

PSx: CABG 1997 and Nephrectomy due to trauma in 1968

SH: ~50 pack year hx, denied EtOH/illicit drug use

FH: no FH of renal disease

ROS: +orthopnea, DOE, LE edema
  • No nausea, vomiting, fever/chills, abdominal pain, chest pain or changes in mental status
Physical Exam

- **VS:** T: 98  BP: 103/54  P: 64  R: 24  O2: 92%
  - BIPAP: 12/7  FiO2: 30%
- **Gen:** NAD, morbidly obese M
- **CVS:** +s1s2, irregularly irregular, +JVD
- **RESP:** decreased BS at bases, crackles up to mid-lung fields
- **ABD:** soft, obese, +BS, NT/ND
- **EXT:** +3 pitting edema up to thighs, +sacral edema
- **NEURO:** AOx3, non-focal
Diagnostic Studies

- CBC:  H/H: 7.4/27.4
- ABG: ph: 7.39  pCO2: 43.5 pO2: 220 HCO3: 25.7 (FiO2: 40%)
- Urine microscopy: 1+ protein, few granular casts, no RBCs or WBCs
- UNa: 12  UCreat: 222  FeUrea: 14%  UCl: not sent
- Renal US: Non-visualization of the right kidney. No evidence of left hydronephrosis
- CXR: moderate vascular congestion
Hospital Course

- Transferred to CCU and started on an aggressive diuresis regimen with lasix gtt and diuril
- Net negative 2-3L daily over the next 7 days with a significant improvement in volume status by clinical exam and decrease in weight by 24kg
- Intermittent agitation and non-compliance with BIPAP
Repeat labs

- ABG: pH: 7.39 pCO2: 75.4 pO2: 85.9 HCO3: 44.8
- BMP: NA: 144 K: 3.7 Cl: 89  CO2: 45 BUN: 96 Creat: 1.6

DX: Non-Respiratory Alkalosis / Compensated Mixed Respiratory Acidosis and Metabolic Alkalosis)

- primary respiratory acidosis; expected HCO3 of 36
- primary metabolic alkalosis; expected pCO2 of 54
- Worsening respiratory acidosis secondary to non-compliance with NIPPV and as compensatory mechanism for metabolic alkalosis due to diuresis

- Diuretics were held and he was placed on continuous BIPAP

- Started on acetazolamide 500mg daily and KCL supplementation

Blood Gas [HCO3]
Serum CO2
Acetazolamide in the Treatment of Metabolic Alkalosis
Metabolic Alkalosis

- severe alkalosis itself is associated with increased mortality
- increased incidence in patients with severe sepsis and trauma
  - due to factors that are directly consequent upon vigorous correction of shock, hypotension and acidosis where large quantities of citrated blood, LR, and alkali itself are administered
- in a study of 1415 critically ill patients, 177 developed severe alkalosis (pH >7.55) and found that mortality rose with pH
  - 41% in 61 patients with pH of 7.55 to 7.56
  - 47% in 61 patients with pH of 7.57 to 7.59
  - 65% in 40 patients with pH of 7.56 to 7.64
  - 80% in 15 patients with pH of 7.65 to 7.70

Critical Reviews in Clinical Laboratory Sciences, 1999
Alkalosis Secondary to Diuretic Use

- Diuretics diminish reabsorption of NaCl by the loop of Henle and the distal tubule with associated loss of Cl- → resulting in inappropriate H+ secretion due to Cl- depletion in CT

- ECF contraction with activation of the renin-angiotensin system → increased Na delivery to the distal tubule and hypoK → leading to new HCO3 formation

- Increased secretion of H+ ion both generates and maintains a mild metabolic alkalosis

- Alkalosis compounded by hypokalemia resulting from diuretic therapy
  - Stimulation of the H+/K+ ATPase pump resulting in increased H+ secretion

Treatment of Severe Metabolic Alkalosis in patient with CHF; Am J Kidney Disease 2013
Chronic Hypercapnia

- Respiratory acidosis compensated by accelerated renal bicarbonate resorption and increased urinary Cl-excretion

- In chronic respiratory acidosis, Cl- depleted state maintained until hypercapnia is corrected

- When the acidosis is corrected, accelerated HCO3-reabsorption, which is no longer appropriate, persists if sufficient Cl- is not available and “post-hypercapneic” metabolic alkalosis remains.
Carbonic Anhydrase

A - Intercalated cells

B - Intercalated cells
Carbonic Anhydrase Inhibitor

- Inhibits Na and HCO3- reabsorption in the proximal tubule through the inhibition of CA-2 and CA-4
- Impairs collecting duct H+ secretion mediated via H+ ATPase in A-intercalated cells through inhibition of CA-2
- Optimizes CO2 release by inhibiting CA isoenzymes in red cells and muscle tissue and improves delivery of CO2 to alveoli for gas exchange
Acetazolamide-mediated decrease in strong ion difference accounts for the correction of metabolic alkalosis in critically ill patients

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This is an open access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
• Studied the mechanism of action of acetazolamide in critically ill patients with metabolic alkalosis using the Stewart approach

• Serum Ion difference was calculated using the equation SID = [Na] + [K+] + [Ca+] + [Mg+2] – [Cl-] – [lactate]

• By inhibiting carbonic anhydrase in the proximal tubules, acetazolamide causes excretion of strong cations (Na+ and K+) along with HCO3 and retention of Cl- → decreasing the SID

• The decrease in SID, due to the rise in Cl- then corrects the alkalosis by causing dissociation of water and formation of H+ ions

• After normalization of pH at 24hrs, duration of the pharmacologic effect of 500mg of acetazolamide exceeds its serum half-life (6-8hrs) due to altered urinary Na+ and Cl- excretion
Efficacy of acetazolamide treatment of patients with hypercapnia and superimposed metabolic alkalosis

• Prospective study with 45 patients who had chronic respiratory acidosis and metabolic alkalosis

• 500 or 750mg acetazolamide were administered daily for 48hr

• After treatment, a clinical improvement was observed in patients by a decrease in PaCO2, pH and HCO3 and an increase in PaO2 (p<.001).

• Hypochloremia (82.2%) and Hypokalemia (33.3) were the most common electrolyte abnormalities before therapy and improved after treatment

*Acetazolamide is an efficient alternative for treatment of patients with respiratory acidosis and metabolic alkalosis – particularly when discontinuation of diuretics and/or volume replacement have failed

Rev Clin Esp 1997
Acetazolamide improves oxygenation in patients with respiratory failure and metabolic alkalosis

- evaluated the effectiveness of short-term treatment with acetazolamide for combined respiratory failure and metabolic alkalosis
- randomized, placebo-controlled and double blind group trial
- acetazolamide 250mg TID PO x5 days administered to patients with respiratory failure because of pulmonary disease (PaO2<60 and/or PaCO2>52) who had concurrent metabolic alkalosis (base excess >8mmol/L)
- During the 5 day treatment, PaO2 increased on average by 6mmHg in the placebo group and 10.5 in the acetazolamide group. PaCO2 decreased in both groups but the different was not statistically significant.
- Acetazolamide is a useful adjuvant treatment in patients with respiratory failure combined with metabolic alkalosis or where non-invasive ventilation is insufficient or infeasible.
Acetazolamide in the treatment of metabolic alkalosis in critically ill patients

- after correcting for fluid and electrolyte abnormalities, examined the effect of acetazolamide 500mg IV on acid-base status of 30 ventilated patients

- in all patients, there was a fall of total serum HCO3; mean reduction at 24hrs was 6.4mmol/L with a normalization of the base excess and pH

- onset of action was rapid, within 2 hours, and the maximal effect occurred at a mean of 15.5 hours

- the effect of acetazolamide was still apparent at 48 hrs

(Heart Lung 1991 September)