

**Guidelines
For the Management of
Metabolic Alkalosis**

By

**Dr. Sinan Butrus
F.I.C.M.S**

2009 AD

2709 K

Clinical Standards & Guidelines

**Kurdistan Board
For Medical Specialties**

Bordê Kurdistan Bo Psporayati Pzîstî

Setting Clinical and Professional Excellence

Metabolic alkalosis is a primary increase in serum bicarbonate (HCO_3^-) concentration as a result of loss of H^+ from the body or a gain in HCO_3^- manifests as alkalemia ($\text{pH} > 7.40$); usually compensated by alveolar hypoventilation with a rise in arterial carbon dioxide tension (PaCO_2) to decrease change in pH.

Elevated HCO_3^- can also represent a compensatory response to primary respiratory acidosis, however; a bicarbonate concentration > 35 mEq/L is almost always caused by primary metabolic alkalosis.

Normally, arterial PaCO_2 increases by 0.5-0.7 mm Hg for every 1 mEq/L increase in plasma bicarbonate concentration. If the change in PaCO_2 is not within this range, this results to a mixed acid-base disturbance. For example, if the increase in PaCO_2 is more than 0.7 times the increase in bicarbonate, then metabolic alkalosis coexists with primary respiratory acidosis. Likewise, if the increase in PaCO_2 is less than the expected change, then a primary respiratory alkalosis is also present

Presentation:

The patient may experience weakness, myalgia, polyuria, hypoventilation and cardiac arrhythmias.

Signs of hypocalcemia (tetany, Chvostek sign, Trousseau sign, seizures & mental changes)

Physical examination should include an evaluation for hypertension and for volume status (orthostatic changes in blood pressure and heart rate, mucous membranes, presence or absence of edema, skin turgor, weight change, urine output).

Work up:

- Measure serum electrolytes, HCO_3^- and arterial blood gases as the only definitive way to diagnose metabolic alkalosis is with a simultaneous blood gases analysis that shows elevation of both pH and PaCO_2 and increased calculated bicarbonate.

Serum bicarbonate concentration can be calculated from a blood gas sample:

$$\text{HCO}_3^- = 24 \times \text{PaCO}_2 \div [\text{H}^+]$$

The H^+ can be estimated by subtracting the last 2 digits (hundredths value) of the pH value from 80 when the pH is 7.0 – 7.55, e.g. if the pH is 7.25 then the H^+ concentration will be 80-25

- Measure serum anion gap to differentiate between primary metabolic alkalosis and metabolic compensation for respiratory acidosis. $\text{AG} = (\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-)$.

The anion gap is frequently elevated to a modest degree in metabolic alkalosis because of the increase in the negative charge of albumin and the enhanced production of lactate.

- If the etiology of metabolic alkalosis is not clear from the clinical history and physical examination, including drug use and the presence of hypertension, then a urine chloride ion concentration can be obtained to differentiate between

Chloride-responsive metabolic alkalosis (low urine chloride ion concentration < 20 mEq/L)

Chloride-resistant metabolic alkalosis (high urine chloride ion concentration > 20 mEq/L)

- Measuring the plasma renin activity and aldosterone level to find the etiology of metabolic alkalosis, especially in patients with hypertension, hypokalemic (renal potassium wasting) without diuretic use as low renin activity and high plasma aldosterone levels are found in primary hyperaldosteronism, including glucocorticoid-remediable hyperaldosteronism.

Management

depends primarily on the underlying etiology and on the patient's volume status.

In the case of vomiting, administer antiemetic, if possible.

If continuous gastric suction is necessary, gastric acid secretion can be reduced with H₂-blockers or more efficiently with proton-pump inhibitors.

In patient on thiazide or loop diuretics, the dose can be reduced or the drug can be stopped if appropriate. Alternatively, potassium-sparing diuretics or acetazolamide can be added.

Chloride-responsive alkalosis

- Volume depletion: treat the alkalosis with an intravenous infusion of isotonic sodium chloride solution and as this type of alkalosis is usually associated with hypokalemia, use potassium chloride to correct the hypokalemia.

- Edematous states (e.g., congestive heart failure CHF), use potassium chloride instead of sodium chloride to correct the alkalosis and avoid volume overload.

If diuresis is needed, a carbonic anhydrase inhibitor (acetazolamide) or a potassium-sparing diuretic (spironolactone, amiloride, triamterene) can be used to correct the alkalosis.

Chloride-resistant metabolic alkalosis

Management is based on the specific cause. Aldosterone antagonist (spironolactone, amiloride, triamterene) is helpful in hyperaldosteronism.

Intravenous HCl is indicated (0.1N HCL at a rate < 2 mEq/Kg/hr or < 125 mEq/hr)

- Severe metabolic alkalosis (pH >7.55).

- Unable to administer sodium or potassium chloride because of volume overload or advanced renal failure.

- Rapid correction of severe metabolic alkalosis is warranted (cardiac arrhythmias, hepatic encephalopathy, and digoxin cardiotoxicity).

Hemodialysis & peritoneal dialysis

The main indication of dialysis in metabolic alkalosis is in patients with advanced renal failure, who usually have volume overload and are resistant to acetazolamide.

Dialysis can be used to correct metabolic alkalosis with certain modifications of the dialysate.

In hemodialysis; use a low-bicarbonate dialysate (bicarbonate can be as low as 18 mmol/L).

Otherwise, use acetate-free biofiltration (buffer-free dialysate) in which bicarbonate is not present in the dialysate but is infused separately as needed, may be used.

In peritoneal dialysis; use isotonic sodium chloride solution as the dialysate.

Take home message:

- The most common causes are volume depletion (particularly when involving loss of gastric acid and Cl from recurrent vomiting or nasogastric suction) and diuretic use.
- Metabolic alkalosis involving loss or excess secretion of Cl is termed Cl-responsive managed by treating the cause and give patients with Cl-responsive metabolic alkalosis 0.9% saline IV.
- Cl-resistant metabolic alkalosis is due to increased aldosterone effect so management involves the correction of hyperaldosteronism.

Further reading

Two factors are needed to establish metabolic alkalosis *generation & maintenance*

Generation of metabolic alkalosis through one of the following mechanisms:

- Loss of hydrogen ions either through the GI tract (vomiting or nasogastric NG suction) or through renal tract when the distal delivery of sodium increases in the presence of excess aldosterone.
- Shift of hydrogen ions into the intracellular space mainly develops with hypokalemia
- Alkali administration in amounts that exceed the capacity of the kidneys to excrete as observed in renal failure or in volume depletion.
- Contraction alkalosis: contraction of extracellular fluid volume caused by diuretic therapy or chloride diarrhea.

Maintenance of metabolic alkalosis through one of the following mechanisms:

- Decreased perfusion to the kidneys caused by either volume depletion or a reduction in effective circulating blood volume (eg, edematous states such as heart failure or cirrhosis) which stimulates the renin-angiotensin-aldosterone system leading to increased renal sodium ion reabsorption and enhanced hydrogen ion secretion. Aldosterone may also independently increase the activity of the apical proton pump in the collecting duct. Whenever a hydrogen ion is secreted into the tubular lumen, a bicarbonate ion is gained into the systemic circulation.
- Chloride depletion may occur through the GI tract by loss of gastric secretions or through the kidneys with loop diuretics or thiazides. Chloride depletion, even without volume depletion, enhances bicarbonate reabsorption
- Many of the causes of metabolic alkalosis are also associated with hypokalemia. In turn, hypokalemia maintains metabolic alkalosis by 5 different mechanisms.
 1. Hypokalemia results in the shift of hydrogen ions intracellularly. The resulting intracellular acidosis enhances bicarbonate reabsorption in the collecting duct.
 2. Hypokalemia stimulates the apical H^+/K^+ ATPase in the collecting duct leading to appropriate potassium ion reabsorption but a corresponding hydrogen ion secretion with net gain of bicarbonate, maintaining systemic alkalosis.
 3. Hypokalemia stimulates renal ammonia genesis, reabsorption and secretion which generate bicarbonate that is returned to the systemic circulation.
 4. Hypokalemia leads to impaired chloride ion reabsorption in the distal nephron with enhancement of hydrogen ion secretion.
 5. Hypokalemia reduces the glomerular filtration rate (GFR) which decreases the filtered load of bicarbonate. In the presence of volume depletion, this impairs renal excretion of the excess bicarbonate.

Causes of metabolic alkalosis

Chloride-responsive alkalosis (urine chloride < 20 mEq/L):

- Loss of gastric secretions - Vomiting, NG suction
- Loss of colonic secretions - Congenital chloridorrhea, villous adenoma
- Thiazides and loop diuretics (after discontinuation)
- Posthypercapnia
- Cystic fibrosis

Chloride-resistant alkalosis (urine chloride >20 mEq/L) with hypertension:

- Primary hyperaldosteronism - Adrenal adenoma, bilateral adrenal hyperplasia, adrenal carcinoma, glucocorticoid-remediable hyperaldosteronism
- 11 β -HSD2 - Genetic, licorice, chewing tobacco, carbenoxolone
- CAH - 11-Hydroxylase or 17-hydroxylase deficiency
- Current use of diuretics in hypertension
- Cushing syndrome
- Exogenous mineralocorticoids or glucocorticoids
- Liddle syndrome
- Renovascular hypertension

Chloride-resistant alkalosis (urine chloride >20 mEq/L) without hypertension:

- Bartter syndrome
- Gitelman syndrome
- Severe potassium depletion
- Current use of thiazides and loop diuretics
- Hypomagnesemia

Other causes:

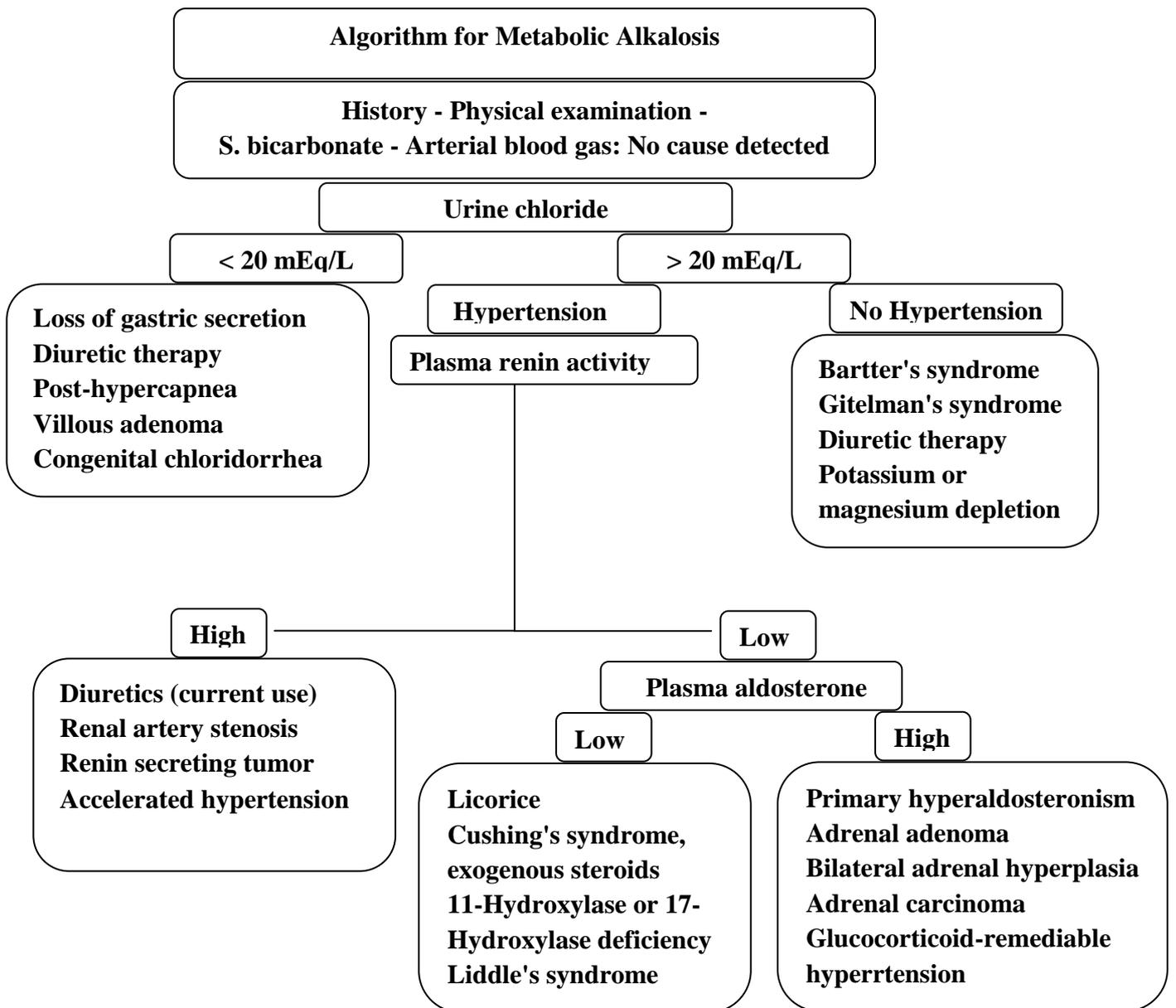
- Exogenous alkali administration - Sodium bicarbonate therapy in the presence of renal failure, metabolism of lactic acid or ketoacids
- Milk-alkali syndrome
- Hypercalcemia
- Intravenous penicillin
- Re-feeding alkalosis
- Massive blood transfusion

Low plasma renin activity and aldosterone levels are found in:

- Cushing syndrome
- Exogenous steroid use
- Congenital adrenal hyperplasia (CAH)
- Liddle syndrome

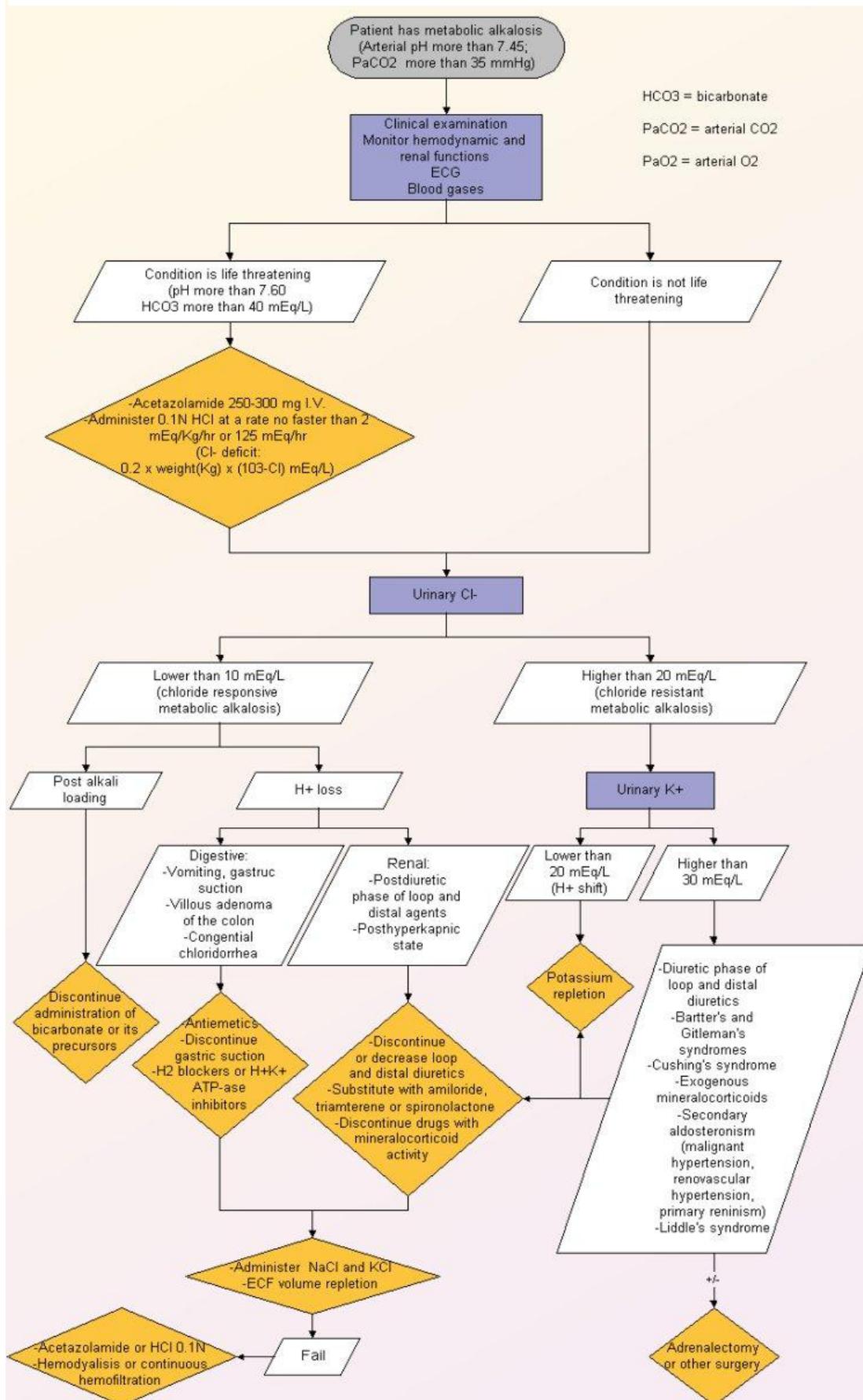
High plasma renin activity and aldosterone levels are found in:

- Renal artery stenosis
- Diuretic use
- Renin-secreting tumors
- Bartter syndrome
- Gitelman syndrome



<http://img.medscape.com/pi/emed/ckb/gps1/large/1339ALKALG.PD>

Management of Metabolic Alkalosis



References:

1. Christie P Thoma Metabolic Alkalosis Treatment & Management. Dec 26, 2014
<http://emedicine.medscape.com/article/243160-treatment>
2. James L. Lewis. Metabolic Alkalosis. February 2013
www.merckmanuals.com/professional/endocrine-and-metabolic-disorders/acid-base-regulation-and-disorders/metabolic-alkalosis#
3. Metabolic Alkalosis. University of Connecticut.2006
http://fitsweb.uhc.edu/student/selectives/TimurGraham/Metabolic_Alkalosis_diagnosis_and_treatment.html
4. N Shah, C Shaw, LG Forni. Metabolic alkalosis in the Intensive Care Unit.
neth j crit care. volume 12 No 3. June 2008
http://njcc.nl/sites/default/files/pdf/NJCC_03%20Forni.pdf
5. Arterial blood gas analysis workshop. 2012
<http://www.resus.org.uk/pages/alsabgGd.pdf>
6. www.med-online.ro/eng/clinical/eng_005/eng_005_e.php
7. Hypokalaemic Alkalosis. 29/8/2014
<http://www.patient.co.uk/pdf/1847.pdf>.