In the name of god

Metabolic Alkalosis
management

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Metabolic Alkalosis

Metabolic alkalosis is the result of an increase in plasma HCO 3 due to either

gain of HCO 3

or

extracellular volume contraction

Phases of Metabolic Alkalosis

Initiation and maintenance are the two phases of metabolic alkalosis.

The alkalosis can persist after the initiating process has resolved only if there are additional factors maintaining it.

Initiation

- Renal or extra renal losses of H+ (vomiting, nasogastric suction, use of diuretics)

- Gain of HCO 3 (NaHCO 3 administration, citrate in transfused blood)

Maintenance

- **Chloride depletion**:

✓ Decrease the activity of the Na+-K+â€“2Cl-(secondary hyperaldosteronism)
✓ involve Cl-/HCO-3 exchange across the luminal membrane
✓ The luminal H+-ATPase pump in the intercalated cells in the collecting tubules

- **Potassium depletion**: Bicarbonate reabsorption in both the proximal and distal tubules is increased in the presence of potassium depletion.

- **Volume contraction** augments fluid reabsorption in the proximal tubule increasing bicarbonate reabsorption and maintains alkalosis.

- **Reduced glomerular filtration rate** (GFR) due to volume contraction limits the filtration of HCO 3 .

A. *Chloride responsive*: *loss of acid* (spot urine chloride <20 mmol/l)

Extra renal losses:

- Gastric losses – vomiting, nasogastric drain, pyloric stenosis
- Diarrhea – villous adenoma, congenital chloride diarrhea
- Post-hypercapnia
- Cystic fibrosis (chloride loss in sweat)
- Dietary chloride depletion

Renal losses: diuretic use (remote)

B. *Chloride resistant*: *gain of base* (spot urine chloride >20 mmol/l)

Normotensive: Bartter syndrome, Gitelman's syndrome, diuretics (recent)

Hypertensive

- Mineralocorticoid excess: associated with hypokalemia, hypertension
- Primary aldosteronism: adenoma, hyperplasia
- Apparent mineralocorticoid excess: 11β and 17α hydroxylase deficiency
- Glucocorticoid remediable hypertension, Liddle's syndrome, drugs: licorice, carbenoxolone
- Secondary hyperaldosteronism: reninoma, renovascular hypertension, malignant hypertension

Others: laxative abuse, milk alkali syndrome, bicarbonate use

- Hypercalcemia, hypokalemia
- Hypoalbuminemia
- Blood transfusion (citrate)

Mild metabolic alkalosis (HCO_3 <36 mEq/l): asymptomatic
Moderate metabolic alkalosis (HCO_3 36–42 mEq/l): paresthesias, weakness, orthostatic hypotension, fatigue, muscle cramps, lethargy, hyporeflexia, muscular irritability
Severe metabolic alkalosis: (HCO_3 >45–50 mEq/l): arrhythmias, tetany, seizures, delirium, stupor
Complications: hypoventilation, hypoxemia, difficulty in weaning from ventilator, increased digoxin toxicity, worsening of hepatic encephalopathy
Features of hypokalemia: muscle weakness, paralytic ileus, arrhythmias
Features of decrease in ionized calcium: neuromuscular irritability, tetany

TREATMENT

Metabolic alkalosis can be corrected most easily be the urinary excretion of the excess HCO-3.

This does not occur spontaneously because, in the patient with relatively normal renal function, volume, Cl-, and/or K+ depletion leads to enhanced net HCO-3 reabsorption.

Therefore, the **aim of therapy** is to repair these deficits, which will have two beneficial effects:

volume, Cl-, and K+

also Treatment should also be directed at the **underlying disease** and at diminishing further H+ loss.

In patients with continued vomiting or nasogastric suction, for example, the administration of an H2-blocker or proton pump inhibitor can markedly reduce the rate of gastric H+ secretion

Management

Chloride-Responsive Metabolic Alkalosis

• Correct the hydration status with **normal saline infusion** @ 10 ml/kg over 10–30 min. May repeat the bolus, if indicated. **Do not use Ringer's lactate**.

• Associated **hypokalemia** should be **corrected**.

• **For GI losses**: decrease frequency of nasogastric drainage, use antiemetics and drugs that inhibit gastric acid secretion.

• **In diuretic-induced metabolic alkalosis**: stop or decrease the dose of diuretics, use of K + -sparing diuretics and KCl supplementation.

This regimen can lower the plasma HCO-3 concentration in three ways:

By reversal of the contraction component.

By **removing the stimulus to renal Na+ retention**, thereby permitting NaHCO3 excretion in the urine.

By increasing **distal Cl- delivery**, which will promote HCO-3 secretion in the cortical collecting tubule.

The therapeutic effectiveness of this regimen can be followed at the bedside by **measuring the urine pH**.

The **urine pH** is often below 5.5 prior to therapy as a result of enhanced H+ secretion.

However, when volume and Cl- replacement are sufficient to allow the excess HCO-3 to be excreted, the **urine pH will exceed 7.0 and occasionally 8.0**.

The urine Cl- concentration will remain below 25 meq/L until the Cl- is corrected.

The efficacy of fluid repletion is dependent upon the administration of **Na+** **with the only reabsorbable anion, Cl-.**

As this Na+ enters the glomerular filtrate, it is reabsorbed with Cl-, resulting in volume expansion. The outcome is different if Na+ is given with an impermeant anion, such as SO2-4.

As with Na+, the administration of **K+** with any anion other than Cl- results in an increase in H+ secretion, preventing correction of the alkalosis.

This is important clinically, since many of the commercial K+ supplements contain HCO-3, acetate, or citrate. Only KCl will be effective.

Chloride-Resistant Metabolic Alkalosis

- **Treat the underlying cause**

The administration of saline is occasionally ineffective in correcting the alkalosis.

in those disorders in which K+ depletion, not hypovolemia

Adrenal adenoma – surgical removal

Primary hyperaldosteronism – NaCl restriction, KCl supplementation, **spironolactone**

Glucocorticoid remediable aldosteronism – low-dose **dexamethasone**

Apparent mineralocorticoid excess – K+ supplements, **K+ -sparing diuretics**

Bartter syndrome – K+ supplementation, **K+ -sparing diuretic**, indomethacin

Gitelman's syndrome – K+ supplementation, **K+ -sparing diuretics**, magnesium replacement

Liddle's syndrome – salt restriction, K+ supplementation, K+ -sparing diuretics (**triamterene, amiloride**)

Edematous states

Patients with **heart failure, cirrhosis, or the nephrotic syndrome** often develop metabolic alkalosis following diuretic therapy.

Both a **reduction in the effective circulating volume**, leading to **Na+-avidity**, and renal insufficiency can contribute to the inability to excrete the excess HCO-3 in these disorders.

However, the **administration of saline is not indicated**, since it will increase the degree of **edema**, perhaps precipitating **pulmonary edema** in the presence of heart failure.

Corrective therapy consists of:

withholding diuretics if possible
acetazolamide
HCl
dialysis

Acetazolamide (250 to 375 mg, once or twice a day, given orally or intravenously) is a carbonic anhydrase inhibitor that increases the renal excretion of $NaHCO_3$

This serves the dual purpose of **treating both the edema and the alkalosis**.

As with the use of saline in saline-responsive states, the efficacy of acetazolamide can be assessed by monitoring the urine pH, which should exceed 7.0 if HCO_3^- excretion is substantially enhanced. K^+ balance must be carefully followed, since acetazolamide increases urinary K^+ excretion

Mineralocorticoid excess

States of primary mineralocorticoid excess are characterized by mild volume expansion and a rate of urinary Na+ excretion that is equal to intake (due to aldosterone escape;).

The alkalosis in this setting is **resistant to saline**, since neither renal Na+ avidity nor Cl- depletion is the limiting factor in HCO-3 excretion.

In contrast, it is the combination of hypokalemia and hypersecretion of aldosterone that is responsible for perpetuation of the alkalosis.

Correction of the hypokalemia tends to lower the plasma HCO-3 concentration in two ways:

by allowing increased HCO-3 excretion

by causing H+ ions to move out of the cells into the extracellular fluid

Successful treatment requires the restoration of normal mineralocorticoid activity

This can be achieved by :

surgical removal of an adrenal adenoma

by the use of a K+-sparing diuretic

such as amiloride or the aldosterone antagonist spironolactone

Severe hypokalemia

Patients with metabolic alkalosis and hypovolemia may be resistant to saline therapy in the presence of severe K+ depletion.

In this setting, the plasma K+ concentration generally is less than 2.0 meq/L, and the urine Cl- concentration exceeds 15 meq/L despite the presence of volume depletion.

These effects of severe hypokalemia are readily reversible. The replacement of **only one-half** of the K+ deficit will normalize Cl- reabsorption and restore saline responsiveness, as the administration of saline will now correct the alkalosis.

Hypokalemia is a potent stimulus to H+ secretion and HCO-3 reabsorption

1)The concurrent intracellular acidosis, induced by transcellular K+/H+ exchange, will tend to increase H+ secretion.

2)There is a second proton pump in the distal nephron, a H+-K+â€“ATPase that actively reabsorbs K+ as well as secreting H+. Active K+ reabsorption by this pump appears to be appropriately stimulated by hypokalemia, an effect that could also enhance H+ secretion.

3)Severe hypokalemia may cause, by an **unknown mechanism**, a reduction in chloride reabsorption in the distal nephron. As a result, Na+ reabsorption at this site is associated with a greater luminal electronegativity and therefore a greater tendency for H+ secretion.

Diminished Cl- reabsorption could also impair corrective HCO-3 secretion in the cortical collecting tubule, a process that appears to be mediated by Cl-/HCO-3 exchange.

If Cl- reabsorption is impaired and the availability of K+ for exchange with Na+ is limited, then Na+ reabsorption must be accompanied by increased H+ secretion and HCO-3 reabsorption, thereby preventing a HCO-3 diuresis

Treatment of Refractory Metabolic Alkalosis

• A cetazolamide orally @ 5 mg/kg OD or up to 8–30 mg/kg/day in 2–3 divided doses or intravenously @ 8–30 mg/kg/day in 2–3 divided doses; monitor serum K + .

• **Life-threatening metabolic alkalosis** (HCO 3 >50 mmol/l) with problems in mechanical ventilation warrants the following options:

– **Renal replacement therapy** (hemodialysis or peritoneal dialysis) dialysate fluid may be modified with reduced/absent base. Continuous form of renal replacement therapy (e.g., CVVH) may be preferred.

– **Direct titration with HCl infusion**.

The goal of HCl therapy is to decrease HCO 3 by:

50 % aiming at reducing the pH <7.55 and HCO 3 <40 mEq/l

Intravenous 0.1 M HCl (100 mEq H + per liter) via central vein is infused or added to dextrose/amino acids/electrotype solution.

Pediatric dose not firmly established. Rate of infusion should not exceed >0.2 mEq/kg/h.

Limitations: volume of fluid required, hemolysis, venous thrombosis.
For example, 30-kg child, HCO 3 = 50, pH = 7.60

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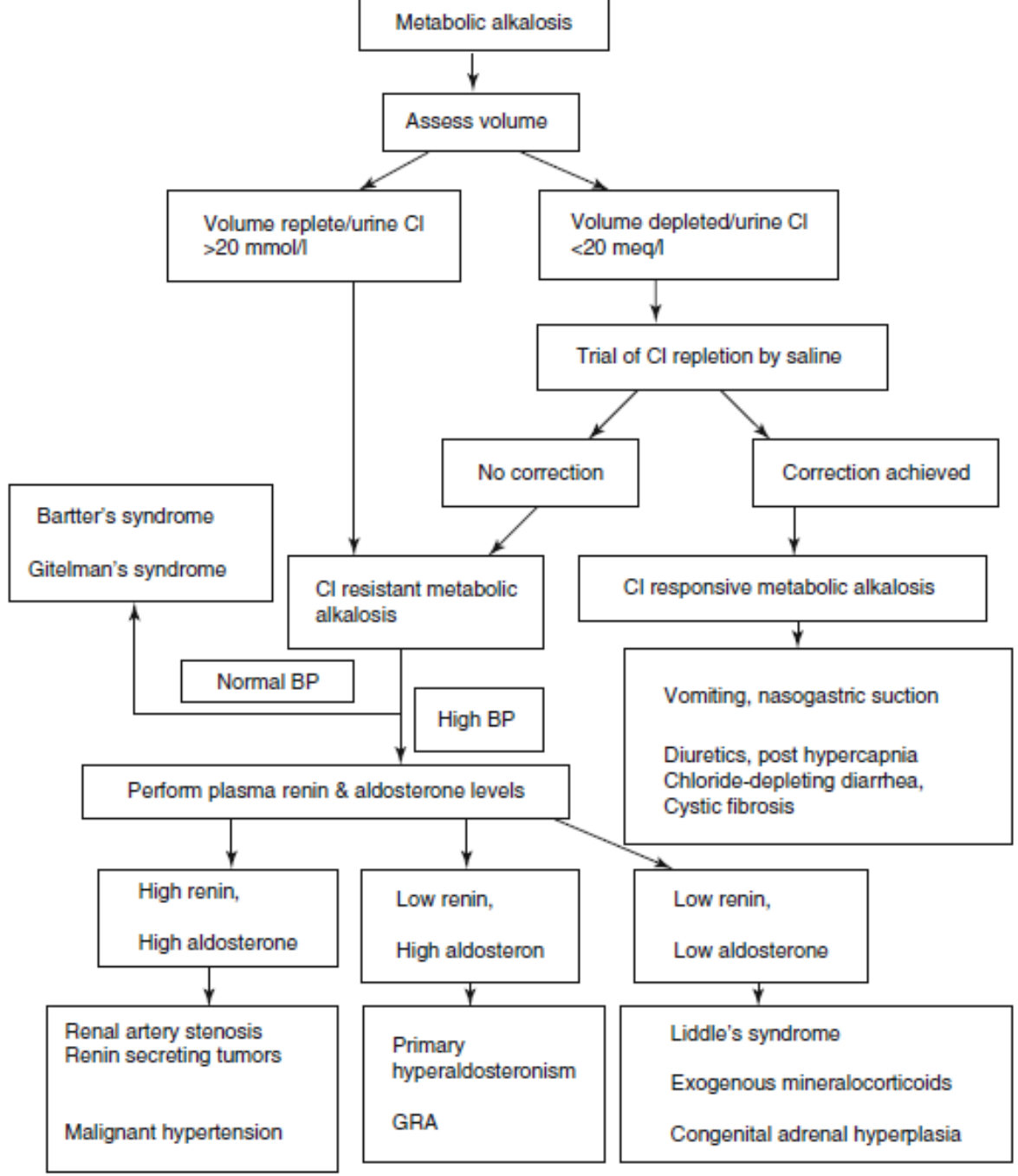
$$\begin{aligned}\text{HCl required} &= 0.5 \times \text{body weight} \times (\text{observed} - \text{desired bicarbonate}) \\ &= 0.5 \times 30 \times (50 - 40) \\ &= 150 \text{ mEq} \ @ \ 10 \text{ mEq/h} \ (0.1 \text{ M HCl} \ @ 100 \text{ ml/h})\end{aligned}$$


Metabolic alkalosis
Assess volume
Volume replete/urine Cl >20 mmol/l
Volume depleted/urine Cl <20 meq/l
Trial of Cl repletion by saline
No correction
Correction achieved
Bartter's syndrome
Gitelman's syndrome
Cl resistant metabolic alkalosis
Cl responsive metabolic alkalosis
Normal BP
High BP
Vomiting, nasogastric suction
Diuretics, post hypercapnia
Chloride-depleting diarrhea,
Cystic fibrosis
Perform plasma renin & aldosterone levels
High renin,
High aldosterone
Low renin,
High aldosteron
Low renin,
Low aldosterone
Renal artery stenosis
Renin secreting tumors
Malignant hypertension
Primary hyperaldosteronism
GRA
Liddle's syndrome
Exogenous mineralocorticoids
Congenital adrenal hyperplasia

THANK YOU