Pathophysiology, Evaluation, and Management of Metabolic Alkalosis

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Abstract

Metabolic alkalosis is an increase in blood pH to >7.45 due to a primary increase in serum bicarbonate (HCO3⁻). Metabolic alkalosis results from alkali accumulation or acid loss, and it is associated with a secondary increase in carbon dioxide arterial pressure (PaCO2). Metabolic alkalosis is a common acid-base disorder, especially in critically ill patients. The pathogenesis of chronic metabolic alkalosis includes two derangements, generation of metabolic alkalosis via gain of alkali or loss of acid and maintenance of metabolic alkalosis by increased tubular HCO⁻³ reabsorption (failure of the kidneys to excrete excess alkali). Metabolic alkalosis is the most common acid-base disorder in hospitalized patients, particularly in the surgical critical care unit. Mortality increases as pH increases.

Introduction And Background

The focus of this review article is the pathophysiology of metabolic alkalosis, as well as its causes, diagnosis, and management. The PubMed database was searched for relevant basic science and clinical articles in addition to the leading journals in nephrology, endocrinology, critical care, and internal medicine. The articles reviewed included clinical trials, comprehensive reviews, and case studies deemed of clinical significance. Chapters from the major textbooks were reviewed as well.

Intracellular pH is 7.0-7.30 while normal arterial blood pH is 7.35-7.45 [1-2]. Arterial blood pH is kept in a narrow range due to renal and respiratory regulations and multiple intracellular and extracellular buffers. Arterial blood gases (ABGs) are required to ascertain the diagnosis of acid-base disorders. For example, high serum HCO³⁻ can result from metabolic alkalosis or metabolic compensation for respiratory acidosis. A high blood pH >7.45, i.e., low arterial blood hydrogen (H+) defines alkalemia, if serum HCO³⁻ is high, the alkalemia is due to metabolic alkalosis, while if carbon dioxide arterial pressure (PaCO₂) is low, the alkalemia is due to respiratory alkalosis. In metabolic alkalosis, arterial HCO³⁻ is >28 mmol/l and venous total CO₂ is >50 mmol/l [3]. A gain of alkali or loss of acid leads to metabolic alkalosis. If serum HCO³⁻ is high and PaCO₂ is low, the alkalemia is due to a mixed acid-base disorder, namely, metabolic alkalosis and respiratory alkalosis [4]. A simple acid-base disorder is due to a change in either PaCO₂ or serum HCO³⁻ with appropriate metabolic or respiratory compensation, respectively. A mixed acid-base disorder is the presence of two or three acid-base disorders simultaneously [5]. Metabolic alkalosis is usually accompanied by hypokalemia and hypochloremia. This reduction in chloride (Cl⁻) is not accompanied by hyponatremia [6]. Serum anion gap (AG) is usually slightly elevated in metabolic alkalosis due to an increase in the net negative charges of plasma proteins [7]. To summarize, in simple acid-base disorders, serum HCO³⁻ and PaCO₂ move in the same direction (both are up in metabolic alkalosis and respiratory acidosis and both are down in metabolic acidosis and respiratory alkalosis). In mixed acid-base disorder, serum HCO³⁻ and PaCO₂ move in the opposite direction.

The next step after diagnosing metabolic alkalosis is the determination of respiratory compensation. For every 1 mmol/l rise in HCO³⁻ above 24 mmol/l, there is a 0.6 mmHg rise in PaCO₂ as per the following equation:

\[ \text{PaCO}_2 \text{(mmHg)} = 40 + 0.6 \times (\text{HCO}_3^- - 24 \text{mmol/l}) \]

For example, if HCO³⁻ is 40 mmol/l, the rise in HCO³⁻ is 40-24 = 16 mmol/l, the rise in PaCO₂ is 0.6 x 16 = 9.6 mmHg, and the expected PaCO₂ is 40 + 9.6 or approximately 50 mmHg. A quick way to determine...
P$_{2}$CO$_2$ is by adding 15 to HCO$_3^−$ [8]. Metabolic alkalosis is accompanied by alveolar hypoventilation, which takes minutes to hours to occur [9]. Respiratory compensation usually does not result in complete pH normalization [9]. In metabolic alkalosis, P$_{2}$CO$_2$ is rarely over 55 mmHg. A pH that is close to the normal range may indicate a mixed acid–base disorder, namely, metabolic alkalosis and respiratory acidosis [10]. An example of such disorder is a patient with chronic respiratory acidosis due to chronic obstructive pulmonary disease (COPD) who develops a concomitant metabolic alkalosis due to diuresis. It is helpful to remind the reader of the concept of base excess, which is routinely reported on ABGs. An ABG sample under standard (normal) conditions has a pH of 7.40, P$_{2}$CO$_2$ of 40 mmHg, a temperature of 37°C, and a base excess of 0 mmol/l. Base excess is defined as the amount of strong acid in mmol/l that needs to be added to one liter of fully oxygenated blood in vitro to return an ABG sample to the above-defined standard conditions [11]. Base excess is negative in metabolic acidosis and positive in metabolic alkalosis. The normal range of base excess is -2 to +2 mmol/l. For example, an ABG sample in a patient with severe metabolic alkalosis showed pH 7.55, P$_{2}$CO$_2$ 49 mmHg, HCO$_3^−$ 38 mmol/l, and a base excess of 14 mmol/l.

**Review**

**Incidence**

Metabolic alkalosis was the most common acid–base disorder in patients in the intensive care unit (ICU) in a large Norwegian study [12]. The study analyzed 138,523 ABGs. On admission to ICU, acidosis (metabolic and respiratory) is more common. HCO$_3^−$ increases over time. Alkalosis was defined as base excess > 0 on ABGs and was found in 118,014 samples (85%). A stricter definition of alkalosis as base excess > 2 mmol/l would have led to a lower reported incidence. Alkalosis was found as a simple or mixed acid–base disorder, including post-hypercapnic alkalosis in patients with COPD on mechanical ventilation. A prospective study by Okusawa et al. enrolled 293 general surgical patients [13]. Six ABGs were taken from each patient starting on postoperative day 0 and ending on postoperative day 7. The vast majority of patients (87.5%) had a normal acid–base balance preoperatively. Postoperatively, 50.5% of patients developed metabolic alkalosis. Other acid–base abnormalities were uncommon. Metabolic alkalosis persisted in 31 patients and carried a high mortality rate of 32%. The administration of fresh frozen plasma (FFP) was a major cause of metabolic alkalosis postoperatively. Hodgkin et al. analyzed 13,430 ABGs obtained from hospitalized patients [14]. Metabolic alkalosis was by far the most common acid–base disorder (51%), followed by respiratory alkalosis (29%), then respiratory acidosis (27%), and, finally, metabolic acidosis (12%). The reported incidence adds to more than 100% due to the presence of mixed acid–base disorders in some patients. For example, metabolic alkalosis was simple in 70% of cases and mixed with respiratory or metabolic acidosis in the remaining 30%. An earlier study by Wilson et al. in 1415 critically ill surgical patients showed that 177 (12%) developed severe metabolic alkalosis defined as arterial pH >7.54 [15]. More severe metabolic alkalosis was associated with higher mortality. Mortality was 41% in patients with pH 7.55-7.56, 47% in patients with pH 7.57-7.59, 65% in patients with pH 7.60-7.64, and 80% in patients with pH 7.65-7.70. A prospective study by Anderson et al. in a group of 409 medical and surgical patients showed that mortality was 48.5% in patients with pH >7.60 [16].

**Pathophysiology of metabolic alkalosis**

The kidneys play a major role in acid-base regulation. The three components of renal net acid excretion are ammonium (NH4+), titratable acid, and urinary HCO$_3^−$ (U$_{HCO3^−}$) [1-2]. All of the HCO$_3^−$ filtered through the glomeruli is reabsorbed under normal physiological conditions [17]. The kidneys generate new HCO$_3^−$ to replace the HCO$_3^−$ used to buffer acid in the body. About 80% of filtered HCO$_3^−$ is absorbed by the proximal tubule (PT) while the thick ascending limb (TAL) of the loop of Henle reabsorbs 15%. The cortical collecting duct (CCD) and the inner medullary collecting duct (IMCD) reabsorb the remaining 5% [1]. The two cell types of the CCD are the intercalated cells, which regulate acid–base balance, and the principal cells, which, under the effect of aldosterone, secrete potassium (K$^+$), and reabsorb sodium (Na$^+$). There are two subtypes of intercalated cells (they are the functional mirror images of each other), alpha-intercalated cells, which secrete H$^+$, and beta-intercalated cells, which secrete HCO$_3^−$ in exchange for Cl$^−$ and, therefore, play a role in the correction of metabolic alkalosis. The medullary collecting duct does not contain beta-intercalated cells [1-2]. In the alpha-intercalated cells, the generated HCO$_3^−$ exits the cell via a basolateral Cl$^−$-HCO$_3^−$ exchanger. The beta-intercalated cells generate HCO$_3^−$, which exits the cell and enters the tubular lumen via an apical Cl$^−$-HCO$_3^−$ exchanger (SLC26A4 protein [pendrin]) [18-19] (Figure 1). HCO$_3^−$ secretion in the collecting duct (CD) requires luminal Cl$^−$ and is inhibited by Cl$^−$ depletion. As we shall see, Cl$^−$ depletion is critical in the generation of metabolic alkalosis [5]. Cl$^−$ depletion increases distal Na$^+$ delivery and reabsorption, which stimulates K$^+$ and H$^+$ secretion. This explains the importance of isotonic saline solutions in the correction of metabolic alkalosis. The density of beta-intercalated cells and pendrin are both reduced in the case of hypokalemia [20]. Therefore, hypokalemia limits HCO$_3^−$ excretion, which explains the importance of the correction of hypokalemia in the management of metabolic alkalosis.
FIGURE 1: Pendrin is an apical chloride-bicarbonate exchanger in beta-intercalated cells

ATP: adenosine triphosphate

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Two steps are required for metabolic alkalosis to persist. The first step is the generation of metabolic alkalosis and the second step is the maintenance of metabolic alkalosis [21]. In other words, when faced with metabolic alkalosis, one has to answer two questions. First, what is the source of the excess $\text{HCO}_3^-$ and second, why is the excess $\text{HCO}_3^-$ not excreted by the kidneys?

**Generation of Metabolic Alkalosis**

The generation of metabolic alkalosis is due to excess $\text{HCO}_3^-$ accumulation originating from endogenous or exogenous sources (Table 1).

| Infusion or ingestion of $\text{HCO}_3^-$ (e.g. NaHCO$_3$) or $\text{HCO}_3^-$ precursors (citrate, lactate, or acetate) |
| Hydrochloric acid (HCl) loss as in vomiting, Cl$^-$-rich diarrhea, or nasogastric (NG) suction |
| Hypokalemia leads to extracellular K$^+$ shift balanced by concomitant intracellular H$^+$ shift |
| Excess $\text{HCO}_3^-$ generation by the distal tubule (due to increased H$^+$ excretion) due to increased distal delivery and subsequent absorption of Na$^+$ as in primary hyperaldosteronism, use of thiazide or loop diuretics, Gitelman and Bartter syndromes, and infusion of Na penicillin (penicillin is a poorly absorbed anion) |

**TABLE 1: Exogenous and endogenous mechanisms resulting in the generation of metabolic alkalosis**

An example of exogenous ingestible Na$^+$ and K$^+$ alkali salts include baking soda (60 mmol/teaspoon), NaHCO$_3$ tablets (7.8 mmol/650 mg tablet), KHCO$_3$ tablets, K citrate tablets, Polycitra-K® and Cytra-2®. Na citrate is added as an anticoagulant to whole blood or fresh frozen plasma (FFP) and can be an important source of alkali in patients needing massive amounts of blood products as in those treated with large dose plasma exchange [9]. HCO$_3^-$ is generated upon complete oxidation of citrate, acetate, and lactate, all of which are organic anions. Loss of HCl due to vomiting or NG suctioning results in HCO$_3^-$ generation [8]. It is
useful to recall that loss of acid (H\(^+\)) is equivalent to the gain of alkali (HCO\(_3^-\)) and vice versa. Infusion of large amounts of Na penicillin or other Na\(^+\) salts of nonreabsorbable anions, such as sulfate or phosphate, will generate HCO\(_3^-\) if Na\(^+\) reabsorption via the distal tubule is enhanced by volume depletion or mineralocorticoids (aldosterone) \([9,22]\). Na\(^+\) is reabsorbed while HCO\(_3^-\) is generated and H\(^+\) is excreted as titratable acid or NH\(_4^+\).

**Maintenance of Metabolic Alkalosis**

Under normal circumstances, the kidneys excrete excess HCO\(_3^-\) and restore the acid-base balance. Normal kidneys have an enormous ability to excrete large amounts of HCO\(_3^-\) when ingested chronically \([23]\). Some advocate the use of NaHCO\(_3\) to improve athletic performance. When NaHCO\(_3\) was given progressively and chronically in amounts up to 400 mg/kg, it was well-tolerated \([23-24]\). The failure of the kidneys to excrete excess HCO\(_3^-\) is due to the presence of a mechanism that leads to the maintenance of metabolic alkalosis (Table 2).

| Decreased HCO\(_3^-\) filtration due to a decline in glomerular filtration rate (GFR) |
| Increased HCO\(_3^-\) reabsorption in the proximal tubule due to volume (and Cl\(^-\)) depletion |
| Increased H\(^+\) secretion and NH\(_4^+\) excretion due to hypokalemia or increased aldosterone |

**TABLE 2: Mechanisms of maintenance of metabolic alkalosis**

Some clinical events activate more than one mechanism for the maintenance of metabolic alkalosis. For example, volume (and Cl\(^-\)) depletion decreases HCO\(_3^-\) filtration due to a decrease in GFR, increases proximal tubular reabsorption of HCO\(_3^-\), and enhances H\(^+\) secretion and NH\(_4^+\) excretion due to increased aldosterone and subsequent hypokalemia \([8]\).

**Etiology of Metabolic Alkalosis**

Metabolic alkalosis is divided into two major categories base on extracellular fluid (ECF) volume status, metabolic alkalosis with ECF volume contraction, and metabolic alkalosis with ECF volume expansion \([8-9]\). Urine chloride (UCl\(^-\)) is helpful in differentiating the two categories. UCl\(^-\) is <20 mmol/l in ECF volume contraction and UCl\(^-\) >20 mmol/l in ECF volume expansion (Table 3). Contraction alkalosis occurs whenever there is ECF volume depletion (contraction) associated with a fixed amount of HCO\(_3^-\).

<table>
<thead>
<tr>
<th>ECF volume contraction</th>
<th>ECF volume expansion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting, nasogastric (NG) suction</td>
<td>Primary aldosteronism</td>
</tr>
<tr>
<td>Congenital chloridorrhea (Cl(^-)-rich)</td>
<td>Renal artery stenosis</td>
</tr>
<tr>
<td>Villous adenoma</td>
<td>Renin-secreting tumors</td>
</tr>
<tr>
<td>High volume ileostomy output</td>
<td>Glucocorticoid remediable aldosteronism</td>
</tr>
<tr>
<td>Post-hypercapnic state</td>
<td>Cushing's syndrome or disease</td>
</tr>
<tr>
<td>Thiazide or loop diuretics (U(_{\text{U}}) is variable)</td>
<td>Exogenous mineralocorticoids</td>
</tr>
<tr>
<td>Cystic fibrosis associated with severe perspiration</td>
<td>Congenital adrenal hyperplasia due to 11-beta or 17-alpha hydroxylase deficiency</td>
</tr>
<tr>
<td>Bartter syndrome</td>
<td>Licorice (reduced activity of 11-beta hydroxysteroid dehydrogenase)</td>
</tr>
<tr>
<td>Gitelman syndrome</td>
<td>Liddle syndrome</td>
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**TABLE 3: Causes of metabolic alkalosis**
Other important causes of metabolic alkalosis in which volume status is variable include, hypokalemia, hypomagnesemia, milk-alkali (calcium-alkali) syndrome (where many patients have reduced GFR limiting HCO₃⁻ excretion), alkali load especially with reduced GFR, nonreabsorbable anions, such as penicillin and carbenicillin, and refeeding post fasting or starvation [25].

Typical causes of metabolic alkalosis associated with ECF volume contraction are vomiting and NG suction. The gastric H⁺-K⁺ ATPase secretes HCl into the stomach lumen. When HCl reaches the small bowel, it is neutralized by an equal amount of HCO₃⁻ secreted into the lumen of the small bowel. The removal of gastric HCl due to vomiting or nasogastric (NG) suction results in metabolic alkalosis because HCO₃⁻ is added to the ECF (rather than secreted into the small bowel lumen). HCO₃⁻ is subsequently excreted by the kidneys as NaHCO₃, resulting in volume depletion [9]. Metabolic alkalosis is maintained in this case due to volume depletion, secondary aldosteronism, loss of K⁺ (due to secondary aldosteronism and increased distal delivery of NaHCO₃). Moreover, hypokalemia shifts K⁺ extracellularly and subsequently H⁺ (a positive cation) intracellularly [26]. Intracellular acidosis stimulates further HCO₃⁻ generation. UCl⁻, in this case, is <20 mmol/l, while UNa⁺ can be elevated due to the excretion of Na⁺ with HCO₃⁻ by the kidneys. Diarrhea usually results in non-anion gap metabolic acidosis. Villous adenoma results in metabolic alkalosis due to loss of K⁺ in stool and volume depletion. Likewise, congenital chloride diarrhea also results in metabolic alkalosis. The latter is a rare autosomal recessive disorder due to mutation in the gene SLC26A3 resulting in loss of function of the ileal HCO₃⁻-Cl⁻ exchanger and subsequent HCO₃⁻ retention [27]. Thiazide and loop diuretics can result in metabolic alkalosis with ECF volume contraction and hypokalemia due to enhanced distal delivery of water and Na⁺ and secondary hyperaldosteronism [28]. UCl⁺ is variable, it is elevated (>20 mmol/l) when diuretics are working and low (<20 mmol/l) when their effect wears off. Bartter syndrome is due to a loss of function mutation in the TAL resulting in effects similar to the use of a loop diuretic.

Gitelman syndrome is due to loss of function mutation of the Na⁺-Cl⁻ cotransporter in the distal collecting duct (DCT) mimicking the effects of a thiazide diuretic [29]. Liddle syndrome is a rare genetic cause of severe hypertension due to gain of function mutation of the epithelial sodium channel (ENaC) resulting in hypokalemia and hyporeninemic hypoaldosteronism [8]. UCl⁺ is elevated (>20 mmol/l) in Bartter and Gitelman syndromes. In patients with acute respiratory acidosis, HCO₃⁻ goes up by 1 mmol/l for each 10 mmHg increase in P₅CO₂, while in chronic respiratory acidosis, HCO₃⁻ goes up by 4 mmol/l for each 10 mmHg increase in P₅CO₂. For example, a patient with chronic respiratory acidosis and a P₅CO₂ of 70 mmHg, is expected to have serum HCO₃⁻ of 36 mmol/l (24 +[4×3]) due to metabolic compensation. In the post-hypercapnic state, the respiratory acidosis has improved (as in COPD patients who are placed on mechanical ventilation) but the elevation of HCO₃⁻ persists, resulting in metabolic alkalosis [30]. Excessive perspiration can cause metabolic alkalosis in patients with cystic fibrosis (CF) [31]. Unexplained metabolic alkalosis with volume depletion and hyponatremia should raise the possibility of cystic fibrosis; this presentation is more common during a heatwave. Aminoglycosides activate the calcium-sensing receptor (CaSR), resulting in inhibition of the Na⁺-K⁺-2Cl⁻ transporter in the TAL with subsequent increase in urinary Na⁺, K⁺, Ca²⁺, and Mg²⁺ [32-33]. The intact PTH level is low despite hypokalemia due to the activation of CaSR. A typical cause of metabolic alkalosis associated with ECF volume expansion is primary aldosteronism commonly caused by unilateral aldosterone-secreting adenoma or adrenal hyperplasia. Adrenal carcinoma is rare. Primary aldosteronism manifestations are hypertension, hypokalemia, metabolic alkalosis, and ECF volume expansion [9]. Distal Na⁺ reabsorption is enhanced by aldosterone, resulting in ECF volume expansion. This, in turn, increases K⁺ excretion resulting in hypokalemia. HCO₃⁻ generation and retention are increased with hypokalemia as explained above [26]. Metabolic alkalosis is maintained due to autonomous aldosterone secretion. UCl⁻ in this case is >20 mmol/l due to ECF volume expansion [29].

Diagnosis of Metabolic Alkalosis

Metabolic alkalosis is an elevation in blood pH to >7.45. ABGs are required to ascertain the diagnosis of acid-base disorders because high serum HCO₃⁻ can result from metabolic alkalosis or metabolic compensation for respiratory acidosis. History can identify potential causes of metabolic alkalosis such as vomiting, diuretic use, licorice intake, cystic fibrosis, exogenous sources of HCO₃⁻, or primary aldosteronism. Physical examination helps in evaluating ECF volume status. Most clinicians make the diagnosis of metabolic alkalosis in appropriate clinical settings (such as vomiting, NG suction, primary aldosteronism) based on history, physical exam, and basic chemistry profile without doing ABGs. A basic chemistry profile is needed for the diagnosis of metabolic alkalosis. Measurement of other electrolytes (other than serum HCO₃⁻), including Na⁺, K⁺, Cl⁻, and Mg²⁺, is critical. Urea and creatinine help in evaluating renal function. Urine electrolytes are obtained. UCl⁻ is elevated (>20 mmol/l) in case of ECF volume expansion and low (<20 mmol/l) in case of ECF volume contraction. Obtaining UCl⁻ concentration from a random urine sample is adequate and 24-hour urine collection is usually not necessary. Patients suspected of having primary aldosteronism require further testing [34]. Surreptitious diuretic use is an important cause of metabolic...
Bartter syndrome is treated with K⁺ should be identified. Patients should be instructed to avoid licorice or licorice-containing tobacco products. or H₂ blockers may be helpful in patients with ongoing gastric fluid losses symptomatically and the cause of vomiting should be investigated. The use of proton pump inhibitors (PPIs) The etiology of metabolic alkalosis should be addressed. Patients with vomiting should be treated hyperkalemia due to the extracellular shift of K⁺ should be replaced as well. The underlying etiology, such as adrenal adenoma, should be the main focus of treatment. Patients with bilateral adrenal hyperplasia are treated with aldosterone blockers such as spironolactone or eplerenone. A low Na⁺ diet is helpful in patients with hyperaldosteronism because it reduces distal Na⁺ delivery. Peritoneal dialysis or hemodialysis (with a low HCO₃⁻ in the dialysate 30-32 mmol/l) are helpful in correcting metabolic alkalosis in patients with advanced chronic kidney disease (CKD) or who are already on dialysis. Continuous renal replacement therapy (CRRT) is particularly helpful in the management of severe metabolic alkalosis due to the ability to modify electrolytes in replacement solutions and dialysate.[3]. Prolonged exposure to inappropriately high dialysate HCO₃⁻ is associated with increased mortality due to post-dialysis metabolic alkalosis.[41]. Currently, HCO₃⁻ in the dialysate is kept around 35 mmol/l. Infusion of dilute HCl (0.1 normal HCl, 0.1N HCl = 100 mmol/l H⁺) or ammonium chloride (NH₄Cl) is rarely done.[42]. HCl should be placed in a glass container and infused through a central venous catheter; it can cause severe hemolysis and venous thrombosis and should be discontinued once pH is around 7.50. IV tubing has to be changed every 12 hours. NH₄Cl is metabolized into urea and HCl and is associated with central nervous system toxicity and gastrointestinal adverse reactions. NH₄Cl can be also given orally. Arginine–HCl is no longer used because it may cause life-threatening hyperkalemia due to the extracellular shift of K⁺.

The etiology of metabolic alkalosis should be addressed. Patients with vomiting should be treated symptomatically and the cause of vomiting should be investigated. The use of proton pump inhibitors (PPIs) or H₂ blockers may be helpful in patients with ongoing gastric fluid losses.[43]. Exogenous sources of alkali should be identified. Patients should be instructed to avoid licorice or licorice-containing tobacco products. Bartter syndrome is treated with K⁺ depletion, K⁺-sparing diuretics, such as spironolactone and amiloride, and nonsteroidal anti-inflammatory drugs (NSAIDs) due to their prostaglandin blocking effect.[29]. Gitelman
syndrome is treated in a similar manner in addition to Mg²⁺ repletion. Blanchard et al. evaluated treatment with indomethacin, eplerenone, or amiloride in 30 patients with Gitelman syndrome [44]. Indomethacin was the most efficacious with a 0.38 mmol/l increase in plasma K⁺, followed by amiloride (0.19 mmol/l increase), and then eplerenone (0.15 mmol/l). Forty percent of patients receiving indomethacin discontinued treatment due to gastrointestinal adverse reactions.

Conclusions
Metabolic alkalosis is the most common acid-base disorder in hospitalized patients, and it is associated with increased mortality. It is generated by a gain of alkali or loss of acid and is maintained by the failure of the kidneys to excrete excess alkali. Metabolic alkalosis is either associated with volume depletion or volume expansion. Volume depletion metabolic alkalosis is Cl⁻-sensitive and is treated with isotonic saline solutions and K⁺ replacement while volume expansion metabolic alkalosis is Cl⁻-insensitive and is treated with K⁺ repletion and by addressing the underlying cause. Recently, the molecular mechanisms of several genetic disorders associated with metabolic alkalosis have been elucidated such as the Bartter, Gitelman, Liddle, and Pendred syndromes.

Additional Information
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