Evaluation and Treatment of Alkalosis in Children

Matjaž Kopač¹

¹ Division of Pediatrics, Department of Nephrology, University Medical Centre Ljubljana, Ljubljana, Slovenia

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Address for correspondence Matjaž Kopač, MD, DSc, Division of Pediatrics, Department of Nephrology, University Medical Centre Ljubljana, Bohoričeva 20, 1000 Ljubljana, Slovenia (e-mail: matjaz.kopac@siol.net).

Abstract

Alkalosis is a disorder of acid–base balance defined by elevated pH of the arterial blood. Metabolic alkalosis is characterized by primary elevation of the serum bicarbonate. Due to several mechanisms, it is often associated with hypochloremia and hypokalemia and can only persist in the presence of factors causing and maintaining alkalosis. Respiratory alkalosis is a consequence of dysfunction of respiratory system's control center. There are no pathognomonic symptoms. History is important in the evaluation of alkalosis and usually reveals the cause. It is important to evaluate volemia during physical examination. Treatment must be causal and prognosis depends on a cause.

Keywords

- alkalosis
- children
- chloride

Introduction

Alkalosis is a disorder of acid–base balance defined by elevated pH of the arterial blood. According to the origin, it can be metabolic or respiratory. Metabolic alkalosis is characterized by primary elevation of the serum bicarbonate that can result from several mechanisms. It is the most common form of acid–base balance disorders. This was confirmed in a study on 3,300 patients where gas analysis of the arterial blood was done in 13,000 samples.¹ Respiratory alkalosis is a consequence of dysfunction of respiratory system's control center.² The pH of the arterial blood is elevated in metabolic alkalosis and lowered or normal in respiratory acidosis although there is increased concentration of bicarbonate and hypercapnia (elevation of partial pressure of carbon dioxide–pCO₂) in both disorders.¹

The relationship between the pCO₂, the bicarbonate concentration, and the hydrogen ion concentration can be presented by rearranged Henderson–Hasselbach equation:

$$[H^+] = 24 \times pCO_2 / (HCO_3^-)$$

An increase in the bicarbonate concentration or a decrease in the pCO₂ decreases the hydrogen ion concentration and the pH increases. On the other hand, a decrease in the bicarbonate concentration or an increase in the pCO₂ increases the hydrogen ion concentration and the pH decreases.³

Regarding terminology, acidemia is a pH below normal (< 7.35), and alkalemia is a pH above normal (> 7.45). An acidosis is a pathologic process that causes an increase in the

hydrogen ion concentration and an alkalosis is a pathologic process that causes a decrease in the hydrogen ion concentration. Therefore, acidemia and alkalemia indicate the pH abnormality while acidosis and alkalosis indicate the pathologic process that is taking place.³

Regulation of hydrogen ion balance is basically similar to the regulation of other ions in the body. There must be a balance between the intake or production of hydrogen ions and their net removal from the body to achieve homeostasis. The kidneys play a key role in regulating hydrogen ion removal but much more is needed to achieve precise control of extracellular fluid hydrogen ion concentration. There are also several other acid–base buffering systems involved, such as the blood, cells, and lungs that are crucial for maintaining normal hydrogen ion concentrations in both the extracellular and the intracellular fluid.⁴

To determine the primary acid–base disorder, we must examine the pCO₂ and the bicarbonate concentration. In general, there is pCO₂ below 35 mm Hg in respiratory alkalosis, serum bicarbonate concentration above 26 mm Hg in metabolic alkalosis, pCO₂ above 45 mm Hg in respiratory acidosis, and serum bicarbonate concentration below 22 mm Hg in metabolic acidosis.⁵ However, acid–base disorders are not accompanied by appropriate compensatory responses in some instances. When this occurs, the abnormality is referred to as a mixed acid–base disorder. This means that there are two or more underlying causes for the acid–base disturbance.⁴

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Physiological Aspects

Increased concentration of bicarbonate in metabolic alkalosis elevates serum pH which triggers alveolar hypoventilation, leading to hypercapnia. The $p\text{CO}_2$ in metabolic alkalosis rarely exceeds value 7.3 kPa (55 mm Hg) because there is no full response with hypoventilation due to hypoxia. Respiratory compensation of metabolic alkalosis is impaired in some diseases, such as obstructive airway diseases, severe liver diseases, cardiac failure, and others. Metabolic alkalosis is often associated with hypochloremia and hypokalemia.¹ Addition of chloride (Cl^-) is therefore often important part of alkalosis treatment. Base excess is at least 2 mmol/L.⁶ Carbon dioxide (CO_2) production is fairly constant in the body. During hypoventilation the amount of CO_2 excreted exceeds the amount formed in the metabolic processes. The potassium (K^+) loss is also important for generation and maintenance of alkalosis because it enhances excretion of hydrogen ions and bicarbonate reabsorption. This is important clinically in mineralocorticoid excess.⁷

Increased concentration of bicarbonate is a consequence of gastrointestinal hydrogen loss, excessive renal hydrogen loss, administration and retention of bicarbonate ions, volume contraction, or intracellular shift of hydrogen ions. Normally, gastric hydrogen ion secretion does not lead to metabolic alkalosis, since the hydrogen ions are not lost from the body but instead are neutralized by bicarbonate secreted by the pancreas, liver, and intestines in response to the acid that enters the small bowel. The hydrogen and bicarbonate ions combine within the intestinal lumen to form carbonic acid and water, and the secreted chloride, sodium, and potassium ions are reabsorbed into the systemic circulation. When vomiting or nasogastric tube suction removes hydrogen chloride from the body and prevents it from reaching the duodenum, the bicarbonate that is added to the extracellular fluid is not neutralized by the subsequent secretion of bicarbonate into the more distal gastrointestinal lumen.⁸

Hyperventilation reduces $p\text{CO}_2$ in blood and consequently amount of carbonic acid in respiratory alkalosis. Non-bicarbonate buffer system releases hydrogen ions that bind to serum bicarbonate. This reduces its amount which corrects or attenuates incipient alkalosis. The bicarbonate concentration decreases in this way while concentrations of other buffer systems increase. Therefore, there is no base excess.² Respiration is regulated through central chemoreceptors in the respiratory center which respond to changes in $p\text{CO}_2$ and blood pH, and through peripheral chemoreceptors in the walls of great blood vessels which respond primarily to hypoxia. Respiratory alkalosis is a common disorder in complex patients. Respiratory center can be stimulated by some toxins (e.g., released in gram negative sepsis), hyponatremia, ammonia (in liver dysfunction), the pons tumors and by signals from the cortical centers (in psychogenic hyperventilation). Respiratory alkalosis can also be a consequence of some lung diseases (such as pneumonia, lung embolia, lung edema) where pathological process (inflammation, edema) activates juxtacapillary receptors or receptors in the airway epithelia, which stimulate respiratory center.⁷

Pathogenesis

Metabolic alkalosis can only persist in the presence of factors causing alkalosis (there is a source of base) and factors maintaining alkalosis, when there is impaired ability to excrete excess bicarbonate in the urine due to different causes, such as: hypovolemia, reduced effective arterial blood volume, chloride depletion, hypokalemia, reduced glomerular filtration rate, hyperaldosteronism, or combinations of these factors. Normally, bicarbonate is excreted through the kidneys regardless of the cause.^{1,8}

Factors Causing Alkalosis

Loss of Acid from the Extracellular Fluid

Gastrointestinal causes: The most common cause of hydrogen loss is the loss of gastric secretions due to vomiting or nasogastric suction. Other causes are diarrhea in patients with rare disorders that block intestinal chloride absorption (such as congenital chloridorrhea) and villous adenomas. There is a good response to infusion of normal saline (containing chloride), therefore it is named saline-responsive or chloride-depletion.¹ Gastric secretions can be significantly enhanced with appropriate stimuli (even 20 times or more). One mEq of bicarbonate is formed per 1 mEq of hydrogen ion. In vomiting the equilibrium is disturbed because hydrogen is removed and bicarbonate remains. In this way metabolic alkalosis is generated that can be accentuated by hypovolemia and hypokalemia.⁷

Renal causes: It is the most common cause of metabolic alkalosis due to acid loss from the extracellular fluid. It is most commonly due to diuretic therapy, either with loop or thiazide diuretics. These drugs stimulate acid excretion via increased distal sodium delivery and tubular flow which then causes secondary hyperaldosteronism.¹ Additionally, diuretics increase secretion of some electrolytes (Na^+ , K^+ , Cl^-) more compared with bicarbonate.⁷ Other renal causes of metabolic alkalosis are Bartter syndrome, hypoparathyroidism, posthypercapnic metabolic alkalosis, and hypersecretion of mineralocorticoids. In the latter group, we should mention primary hyperaldosteronism, such as Liddle syndrome, or the combination of secondary mineralocorticoid secretion with a diuretic whose site of action is proximal to the site of hydrogen ion secretion.^{1,8}

Intracellular shift of hydrogen: Hydrogen ions move from the extracellular fluid into the cells in hypokalemia (exchange of K^+ with hydrogen ions) which is not a common cause of metabolic alkalosis.¹ This happens mostly when serum concentration of K^+ is less than 2 mmol/L with a consequent efflux of K^+ from the cells due to concentration gradient and influx of hydrogen ions into the cells to maintain electroneutrality. This results in extracellular alkalosis and paradoxical intracellular acidosis.⁷

Cystic fibrosis: There can be metabolic alkalosis with hypokalemia due to excess of chloride loss in the sweat. This leads to enhanced Na^+ reabsorption in the distal tubules of the kidney, in exchange for K^+ and hydrogen ions.⁹

Increased Bicarbonate Concentration in the Extracellular Fluid

Metabolism from bicarbonate precursors: Citrate, acetate, and lactate are bicarbonate precursors that can be converted to bicarbonate. This can happen during massive transfusions because blood and blood products are anticoagulated with citrate salts.¹ Infusion of large amounts of fresh frozen plasma (e.g., during plasmapheresis) and the use of citrate as an anticoagulant during hemodialysis or continuous renal replacement therapy can also generate alkalosis. In these situations, the alkali load is not readily excreted because of reduced effective arterial blood volume or renal impairment.⁸

Alkali administration: Alkali administration, orally or parenterally, is another important cause of increased bicarbonate concentration in the extracellular fluid. It can be found in cases of total parenteral nutrition, during resuscitation and in milk-alkali syndrome. In the latter, there is a combination of chronic kidney disease, hypercalcemia, nephrocalcinosis, metabolic alkalosis, and continued ingestion of milk or dairy products and Ca^{2+} -containing antacids.¹ However, the short-term administration of even large amounts of sodium bicarbonate to normal individuals usually results in very rapid renal excretion of the entire alkali load with minimal increase in the bicarbonate concentration. Metabolic alkalosis may develop, especially when renal function is poor, as a consequence of ingestion of cocaine that is often produced in illicit laboratories using a strong base, such as household drain cleaner.⁸

Drugs: Some patients take large amounts of antacids in treatment of gastritis or ulcer disease. When using some aluminum-containing antacids there is no significant base absorption. However, hydroxide in Mg-hydroxide containing antacid binds with hydrogen ion and neutralizes it while Mg^{2+} binds to bicarbonate, phosphate, and fat. As a result of this, part of bicarbonate remains unbound and is reabsorbed.⁷ During parenteral high-dose penicillin salts administration, the penicillin part does not absorb and consequently, Na^+ reabsorbs in exchange for K^+ and hydrogen ion which leads to hypokalemia and metabolic alkalosis. In salicylate intoxication, respiratory alkalosis develops at the beginning due to direct stimulation of the respiratory center but later metabolic acidosis ensues.⁷

Factors Maintaining Alkalosis

Factors maintaining alkalosis are a consequence of inability to excrete the excess bicarbonate in the urine due to intravascular volume contraction, reduced effective arterial blood volume (e.g., due to heart failure), chloride depletion, hypokalemia, renal impairment, excess mineralocorticoid activity, parathyroid hormone deficiency, or combinations of these factors.^{1,8}

Clinical Features

Clinical features of metabolic alkalosis result from pathological influences of alkalemia on various organ systems with a consequent dysfunction. Alveolar hypoventilation is most prominent manifestation of alkalosis which is a physiological response of organism to this disorder.¹ Clinical manifestations

directly related to the metabolic alkalosis are uncommon. Patients with metabolic alkalosis may be asymptomatic or may complain of symptoms that are primarily related to the alkalemia, to the underlying etiology of the metabolic alkalosis, or to accompanying electrolyte abnormalities.¹⁰

Metabolic Disturbances

Metabolic alkalosis is often associated with hypokalemia which is due to K^+ loss in the context of a disease that also leads to metabolic alkalosis or due to K^+ shift in the cells. It is also accompanied by reduced concentration of ionized Ca^{2+} (and normal concentration of the entire Ca^{2+}) due to increased protein binding and increased production of citrate and lactate. In addition, alkalosis increases anion gap (up to 12 mmol/L) and stimulates glycolysis and thus lactate production. Reduced volume of extracellular fluid leads to increased plasma protein concentration with their increased negative charge.¹ Patients may consequently present with lassitude, easy fatigability, muscle cramps, and postural dizziness. Hypokalemia may produce muscle weakness, cardiac arrhythmias, and if persistent, polyuria and polydipsia due to impaired urinary concentrating ability, and/or direct stimulation of thirst.¹⁰

Disturbances of Cardiovascular System

Supraventricular and ventricular arrhythmias may often appear that may not respond to treatment in cases of prolonged alkalosis. There is often hypokalemia (due to cellular shift), hypotension (due to alkalosis mediated vasodilatation), and hypovolemia with decreased minute volume of the heart.^{1,7}

Disturbances of Nervous and Muscular System

There is increased release of acetylcholine in the peripheral nerves and reduced concentration of ionized Ca^{2+} . This results in increased neuromuscular excitability that presents clinically with muscle cramps, muscle weakness, tetany, paresthesias around mouth or in the extremities, and carpopedal spasms with a positive Chvostek and Trousseau sign. Laryngeal spasms are rare.^{1,7}

Central Nervous System Disturbances

Alkalosis, especially when pH of arterial blood exceeds 7.55, causes nausea, disorientation, and later stupor. This may be associated with simultaneous reduced brain blood perfusion and oxygenation.^{1,7}

Diagnostic Evaluation

History is important first step in the evaluation of alkalosis, especially information about vomiting, diarrhea, or drug intake (prescribed or self-intake). History usually yields the necessary information to identify the cause. During physical examination, it is important to assess volume with evaluation of skin turgor, pulse, presence of edema, orthostatic signs, and blood pressure. In addition to gas analysis, we should check blood concentrations of electrolytes (especially K^+) and urine concentration of Cl^- .¹

Metabolic Alkalosis with Hypovolemia

Causes can be renal or extrarenal. Alkalosis is maintained due to hypovolemia and hypokalemia with a consequent increased reabsorption of bicarbonate in the proximal kidney tubules and due to reduced glomerular filtration rate that decreases bicarbonate excretion. There is Cl^- depletion with urine concentration of Cl^- less than 15 mmol/L. This is hypovolemia with a good response to infusion of normal saline, named saline-responsive or chloride-responsive alkalosis. After restoration of plasma volume with saline infusions bicarbonate excretion increases.¹ In addition to bicarbonate, Cl^- is the only anion in a body that is present in a large amount. This is important to achieve enough renal bicarbonate excretion with simultaneous Na^+ reabsorption in the proximal kidney tubules and parts of loop of Henle. In some patients, urine concentration of Cl^- may be high in hypovolemia due to impaired mechanisms of Cl^- reabsorption in the kidney tubules and therefore, it does not reflect the true situation and is not diagnostic in these cases.⁷

Renal Causes

Diuretics: Thiazide and loop diuretics are a common cause of metabolic alkalosis with hypovolemia as they cause secondary hypokalemia, hypovolemia, and hyperaldosteronism. Alkalosis is present in 3 to 50% of patients treated with diuretics. Thiazide diuretics increase serum bicarbonate concentration for 2 to 7 mmol/L and loop diuretics for up to 15 to 20 mmol/L. There is increased concentration of Na^+ and Cl^- in the urine despite hypovolemia in these patients. After treatment cessation, the urine concentration of Cl^- is less than 15 mmol/L.¹

Bartter syndrome: This is a rare syndrome characterized by metabolic alkalosis, hypokalemia, hypochloremia, hyperuricemia, increased concentration of renin and aldosterone and sometimes hypomagnesemia. Blood pressure is normal. There is increased synthesis of prostaglandins and increased urine concentration of Cl^- . Histologically, there is juxtaglomerular apparatus hypertrophy. Disease presents in children and young adults with polyuria, paresthesias, and muscle weakness with cramps.¹ Etiologically, Bartter syndrome is a consequence of mutation of at least five genes, coding for several protein transporters in the ascending part of Henle's loop:

- Bumetanide-sensitive Na-K-2Cl cotransporter (type 1, gene *SLC12A1* on chromosome locus 15q15–21): impaired reabsorption of Na^+ in the thick ascending part of Henle's loop.
- Inwardly rectifying renal potassium channel (Renal Outer Medullary potassium (K) [ROMK], type 2, gene *KCNJ1* on chromosome locus 11q24–25): impaired transfer of K^+ molecules in the tubular lumen with a consequent too low K^+ concentration in the tubular lumen for normal function of Na-K-2Cl cotransporter.
- Renal chloride channel (type 3, gene *CLCKNB* on chromosome locus 1p36): responsible for voltage dependent Cl^- transport across basolateral membrane back to the circulation with a concomitant defect of NaCl reabsorption at the luminal membrane.
- Barttin (type 4, gene *BSND* on chromosome locus 1p31): the barttin subunit is also expressed in inner ear and these

patients can have Bartter's syndrome associated with sensorineural deafness (very rarely).^{9,11}

- Calcium sensing receptor (type 5, due to gain-of-function mutation of *CASR* gene): thick ascending loop of Henle's is affected tubular region. Disease onset is variable. Other features are hypocalcemia, low parathyroid hormone levels, hypercalciuria, and elevated urine prostaglandins (PGE2); it is an uncommon cause of Bartter's syndrome.¹²

Mutations in the first two of the above-mentioned genes were proven in patients with Bartter syndrome with associated hypercalciuria and nephrocalcinosis–neonatal Bartter syndrome or Bartter syndrome type 1 and 2. These children are born after pregnancies complicated with polyhydramnios and premature delivery. Mutations in the gene for renal chloride channel were discovered in patients without nephrocalcinosis–classic or Bartter syndrome type 3. In these patients there is no hypercalciuria but there can be severe dehydration.¹¹ There is impaired urinary concentrating ability with a consequent water loss through kidneys in all children with Bartter syndrome. For this reason, they are prone to develop hypernatremic dehydration. Clinical features in these patients can vary from prenatal presentation with polyhydramnios, premature delivery, severe and life-threatening dehydration with hypotension (due to salt loss in the first year of life), and failure to thrive (especially neonatal Bartter syndrome) to gradual progression to chronic kidney disease. On the other hand, they can be asymptomatic and identified incidentally in adulthood.⁹ The evaluation of these patients should include gas analysis of the blood (revealing metabolic alkalosis) and blood analysis of electrolytes: K^+ , Cl^- (both decreased), Mg^{2+} (normal or decreased), Na^+ (variable), Ca^{2+} (usually normal), urea, creatinine, and albumin (to assess renal function and hydration). It should also include analysis of electrolytes in urine: Na^+ , K^+ , Cl^- , Mg^{2+} (elevated fractional excretion–FE), Ca^{2+} (variable), and creatinine (to calculate FE). Ultrasound of the abdomen and genetic analysis should also be done. All types of Bartter's syndrome are inherited in an autosomal recessive way, with exception of type 5, which is inherited in an autosomal dominant way.^{9,12}

Gitelman syndrome: It is a rare syndrome characterized by metabolic alkalosis, hypokalemia, hypomagnesemia (due to increased excretion of Mg^{2+} in the urine), hypocalciuria, and decreased urine concentration of Cl^- .¹ It results from mutation of the gene *TSC*, coding for thiazide-sensitive NaCl cotransporter, located in the distal convoluted kidney tubule. This results in reduced delivery of NaCl to the distal convoluted tubule with NaCl loss in urine, hypovolemia, enhanced renin-angiotensin-aldosterone system, hypokalemia, and metabolic alkalosis. Patients can suffer from tetany, seizures but can also be asymptomatic.¹¹ Others can suffer from hypotension, dizziness, joint pains, muscle weakness, cramps or nocturnal enuresis. A prolonged QT-interval on ECG (electrocardiogram) occurs in 10% of patients. Inheritance is autosomal recessive.⁹

Extrarenal Causes

Upper gastrointestinal loss: The most common cause of metabolic alkalosis with hypovolemia is vomiting or nasogastric suction with subsequent fluid, electrolytes, and hydrogen loss from the extracellular fluid. Hypovolemia causes hyperaldosteronism that enhances K^+ loss in urine with subsequent hypokalemia and hypochloremia.¹

Other extrarenal causes: Other forms of metabolic alkalosis associated with hypovolemia and chloride depletion are laxative abuse, cystic fibrosis with excessive sweating (loss of a large volume of chloride-rich sweat), congenital chloride diarrhea, and alkalosis in infants given a chloride-deficient synthetic formula.¹⁰

Metabolic Alkalosis with Hypervolemia

The kidneys cause and maintain metabolic alkalosis with elevated urine concentration of Cl^- above 20 mmol/L in this disorder that is not responsive to infusion of a normal saline. It is therefore called saline-resistant or chloride-resistant alkalosis. This disorder can be divided according to the presence or absence of hypertension.¹

Hypervolemia and Hypertension with Mineralocorticoid Excess

Mineralocorticoid excess causes reabsorption of salt and hypervolemia, hypokalemia, and increased excretion of K^+ and Cl^- in the urine. Mineralocorticoid excess with elevated plasma concentration of renin can be found in renovascular hypertension (e.g., renal artery stenosis) and in malignant hypertension with associated hypokalemic alkalosis in 10 to 20%. Mineralocorticoid excess with reduced plasma concentration of renin can be found in primary hyperaldosteronism where metabolic alkalosis is accompanied by hypokalemia, hypernatremia, and arterial hypertension.¹ Aldosterone directly enhances hydrogen excretion through the kidneys that causes additional production of bicarbonate or bicarbonate reabsorption that would have been otherwise filtered and excreted. As a consequence, there is increased bicarbonate concentration, hypokalemia, and hypochloremia.⁷ Mineralocorticoid excess (without elevated aldosterone) with hypervolemia and hypertension (together with metabolic alkalosis and hypokalemia) can be found in Cushing syndrome, either intrinsic or iatrogenic.¹

There are some monogenic forms of hypertension associated with hypervolemia and alkalosis. One of them is Liddle syndrome, the autosomal dominant disorder, secondary to an activating mutation of the sodium channel in the distal nephron. Since it is continuously open in Liddle syndrome, these children have hyperaldosteronism with hypertension, hypokalemia, metabolic alkalosis, and low serum levels of aldosterone.³ In glucocorticoid-remediable aldosteronism (also called glucocorticoid-suppressible hyperaldosteronism or familial hyperaldosteronism type I), an autosomal dominant disorder, there is excess production of aldosterone because of the presence of an aldosterone synthase gene that is regulated by adrenocorticotrophic hormone (ACTH). This disorder can be treated with glucocorticoids which inhibit ACTH production by the pituitary, leading to a decrease of aldosterone production.³ In congenital adrenal hyperplasia

due to 17 α -hydroxylase deficiency, there is often hypertension, hypokalemia, and metabolic alkalosis as well. This disorder responds to glucocorticoids because the concurrent excess production of mineralocorticoid 11-deoxycorticosterone is under the control of ACTH. In 11 β -hydroxysteroid dehydrogenase deficiency, also called apparent mineralocorticoid excess, cortisol is not converted in the kidney to cortisone. The latter does not bind to the mineralocorticoid receptor. Cortisol can therefore bind to the mineralocorticoid receptor in the kidney and act as a mineralocorticoid. Patients with this deficiency, despite low levels of aldosterone, have hypertension, hypokalemia, and metabolic alkalosis.³

Hypervolemia without Hypertension and without Elevated Plasma Concentration of Renin and Mineralocorticoids

Hypervolemia without hypertension and without elevated plasma concentration of renin and mineralocorticoids can be associated with metabolic alkalosis due to increased alkali administration, transfusion of large amount of blood, or blood products or with milk-alkali syndrome.¹

► **Fig. 1** schematically shows the diagnostic process using some clinical and laboratory data in the evaluation of children with alkalosis.¹

Treatment and Prognosis

Treatment of metabolic alkalosis must be causal. When there is reduced amount of extracellular volume in a patient, this must be corrected with infusion of a normal saline. Metabolic alkalosis with hypovolemia and urine concentration of Cl^- less than 15 mmol/L has, in general, a good response to infusion of a normal saline (saline-responsive alkalosis). On the other hand, metabolic alkalosis with hypervolemia and elevated urine concentration of Cl^- above 20 mmol/L is not responsive to it (saline-resistant alkalosis).¹

Hypokalemia must be corrected with the administration of potassium chloride, either orally or parenterally. Sometimes (very rarely) we can use acetazolamide which increases urinary bicarbonate and also K^+ excretion. We must be careful with fluid replacement in patients with kidney or heart failure as this can worsen an underlying disease.¹ Rarely, patients with very severe alkalosis, with blood pH value above 7.6, can be treated with intravenous infusion of hydrochloric acid (HCl) that must be given in a central vein, to reduce pH value below 7.5. An HCl precursor, such as ammonium chloride or arginine chloride, can be used but only when liver function is normal. Dialysis is available for anuric patients, using dialysis solution with reduced bicarbonate concentration.¹ Fluid and electrolytes replacement (normal saline) is mandatory in Bartter syndrome. Indomethacin (or other inhibitor of prostaglandin synthesis) can be used to reduce renal losses but not in the neonatal period because of the risk for necrotizing enterocolitis. Treatment with spironolactone is an option in some cases but can cause severe hypotension.⁹ Supplementation of electrolytes (K^+ , Cl^- , Mg^{2+}) is necessary in Gitelman syndrome to maintain electrolyte and acid-base balance and to prevent neurological symptoms. Treatment is lifelong. Patients are encouraged to maintain a high-salt diet.

Fig. 1 Schematic diagram of evaluation of alkalosis.¹ BP, blood pressure; decr., decreased; ECF, extracellular fluid; incr., increased; malig., malignant; Sy, syndrome.

Spironolactone and amiloride can be used to correct severe hypokalemia but may lead to severe hypotension.⁹

Prognosis of metabolic alkalosis depends on a cause and on factors maintaining it. Treatment of an underlying disease which has led to alkalosis, generally corrects it. Sometimes it takes longer to reveal a cause that cannot be removed in some cases (e.g., genetic disease, such as Bartter syndrome). In these cases, treatment is lifelong and consists of correcting alkalosis and associated electrolyte abnormalities with supplementation of electrolytes. Nevertheless, progression to chronic kidney disease can occur over time. The prognosis is generally excellent in Gitelman syndrome with preserved renal function.⁹

Conflict of Interest

None declared.

References

- 1 Hojs R. Metabolic alkalosis (Presnovna alkaloza). In: Kandus A Buturović Ponikvar J Bren AF, eds. Evaluation of Electrolyte, Water and Acid-Base Balance Disturbances (Obravnava Motenj Elektrolitskega, Vodnega in Acidobaznega Ravnotežja). Ljubljana: University Medical Centre Ljubljana; 2002:74–78
- 2 Drinovec I. Respiratory acidosis and respiratory alkalosis (Respiracijska acidoza in respiracijska alkaloza). In: Kandus A Buturović Ponikvar J Bren AF, eds. Evaluation of Electrolyte, Water and Acid-Base Balance Disturbances (Obravnava Motenj Elektrolitskega, Vodnega in Acidobaznega Ravnotežja). Ljubljana: University Medical Centre Ljubljana; 2002:79–87
- 3 Greenbaum LA. Acid-base balance. In: Kliegman RM Stanton BF St Geme JW III Schor NF Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Elsevier; 2016:369–383
- 4 Hall J Guyton A. Regulation of acid-base balance. In: Guyton AC Hall JE, eds. Textbook of Medical Physiology. 11th ed. Philadelphia, PA: Elsevier/Saunders; 2005:383–401
- 5 Hines EQ. Fluids and electrolytes. In: Tschudy MM Arcara KM, eds. The Harriet Lane Handbook, 19th ed. Philadelphia, PA: Elsevier Mosby; 2012:271–292
- 6 Appendix A: acid-base balance. In: Samuels M Wieteska S, eds. Advanced Pediatric Life Support. 5th ed. Blackwell Publishing Ltd.; 2012:271–278
- 7 Varl J. Alkalosis (Alkaloza). In: Keber D Fras Z, eds. Recognizing of Internal Diseases. Diagnostic Algorithms (Razpoznavanje Notranjih Bolezni. Diagnostični Algoritmi). 1st ed. Ljubljana, Republic of Slovenia: Medicinski razgledi. Littera picta; 1994:4–12–4–16
- 8 Emmett M Szerlip H. Causes of metabolic alkalosis. 2017. Available at: <https://www.uptodate.com/contents/causes-of-metabolic-alkalosis#> Accessed June 29, 2017
- 9 Rees L Brogan PA Bockenhauer D Webb NJA, eds. Paediatric Nephrology. 2nd ed. Oxford, United Kingdom: Oxford University Press; 2012
- 10 Emmett M Szerlip H. Clinical manifestation and evaluation of metabolic alkalosis. 2017. Available at: <https://www.uptodate.com/contents/clinical-manifestations-and-evaluation-of-metabolic-alkalosis>. Accessed June 29, 2017
- 11 Bettinelli A Tsygin A. Bartter and Gitelman syndromes. In: Cochat P, ed. ESPN Handbook. Lyon, France: European Society for Pediatric Nephrology; 2002:229–232
- 12 Sreedharan R Avner ED. Bartter and Gitelman syndromes and other inherited tubular transport abnormalities. In: Kliegman RM Stanton BF St Geme III JW, Schor NF Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Elsevier; 2016:2533–2534