

Contraction Alkalosis: A Case-Based Review

Ashaq Hussain Parrey, MD, FACP,¹ Hilal Bhat, MD,², Murtaza Noor MD, and Mohd. Ismail MD¹

Abstract. Metabolic alkalosis is defined as an increase in blood pH to more than 7.45 and serum bicarbonate greater than 26 mmol/L. Metabolic alkalosis is the most common acid-base disturbance in hospitalized patients. It usually occurs due to an underlying predisposing condition, which includes reduced effective arterial blood volume, chloride depletion, hypokalaemia, hypoalbuminemia, hyperaldosteronism, or combinations of these factors. Severe metabolic alkalosis can have deleterious consequences and contribute to organ dysfunction, manifesting generally as agitation, disorientation, seizures, and coma. Increased morbidity and mortality are observed with severe alkaline blood pH, especially when it is associated with other life-threatening conditions like sepsis, acute coronary events, and stroke. Here, we report two cases: a 68-year-old man and a 19-year-old female, both presenting with severe metabolic alkalosis. The 68-year-old man, with underlying comorbid conditions, died, while the young woman survived, highlighting the importance of underlying comorbid conditions in elderly patients, which can determine mortality in such cases.

Keywords. Contraction alkalosis, Sepsis, Nephrotic syndrome, Diuretics

Introduction

Metabolic alkalosis is a common entity, comprising nearly 50% of all acid-base disorders in hospitalized patients [1]. Mortality as high as 80% has been reported with a blood pH above 7.65 [2]. Despite such deleterious effects, metabolic alkalosis is often overlooked in hospitalized patients. The most common cause of metabolic alkalosis is the loss of bicarbonate-rich secretions, as seen in diarrhoea, laxative overuse, diuretic misuse, and hypokalaemia. For management purposes, it is classified based on the response to chloride-containing fluids as chloride-responsive and chloride-resistant metabolic alkalosis [2,3].

Usually, symptoms are non-specific and can range from apathy, disorientation, irritability, seizures, and coma. Other findings may be related to the concomitant presence of hypokalaemia (e.g., weakness, myalgias, and polyuria) or resultant hypocalcaemia. Some patients can develop life-threatening hypercarbia due to inhibition of the respiratory centre [4], along with other deleterious effects causing organ dysfunction [1]. Metabolic alkalosis further worsens the prognosis when it occurs in association with conditions like sepsis [5], intracranial haemorrhage (ICH) [6], or liver failure (both acute and chronic) [7].

We report two cases to highlight the course of these patients during their hospital stays.

Case One

A 68-year-old man, a chronic smoker with a history of cannabis use, presented with underlying uncontrolled hypertension on erratic treatment, sub-nephrotic proteinuria, and oedema managed with torsemide 20 mg as prescribed by a nephrologist. He also had chronic idiopathic constipation managed with lactulose. The patient had stopped smoking cannabis one week prior on the advice of his treating physician and presented with a six-day history of anorexia, anxiety, chills, breathlessness on exertion, fatigue, insomnia, restlessness, agitation, and altered mental status.

On examination, the patient was found to have altered sensorium with a GCS of 9/15, irritability, fever, tachycardia with a pulse rate of 120 beats/min, blood pressure of 90/60 mmHg, oxygen saturation of 82% on room air, and a respiratory rate of 26/min. Chest auscultation revealed bilateral diffuse wheezing. Jugular venous pressure was normal, and there was no peripheral oedema, but skin turgor was markedly reduced.

Serial blood gas (Table 1) revealed severe metabolic alkalosis (pH = 7.72) with very high serum bicarbonate (59.5 mmol/L) and PCO₂ of 72 mmHg (uncompensated metabolic alkalosis). The PCO₂ of the patient was lower than the expected PCO₂ for compensation (95–99 mmHg) as calculated by Winter's formula for acid-base disorders. Additionally, severe hypokalaemia (K⁺ 1.4 mmol/L) and low ionized calcium (0.65 mmol/L) were noted, urea 70mg/dl creatinine 1.35mg/dl, however during hospital stay the renal functions deteriorated and

¹Section of Internal Medicine, Government Medical College Srinagar, India
Corresponding author: Ashaq Hussain Parrey, MD, FACP
Email: chogalpora@gmail.com

12 hours before death creatinine was 6.3mg/dl and urea was 243mg/dl.

Chest X-ray revealed bilateral overinflation of the lung fields, and ECG showed prominent U waves in anterior precordial leads. The patient was intubated due to low GCS and hypercarbia.

Laboratory Results:

- Urine Chloride: 10 mEq/L
- Blood Culture (Day 1): Sterile after 24 and 48 hours of incubation

- Urine Culture (Day 1): Sterile after 24 hours of incubation
- Tracheal Aspirate Culture (Day 4): Acinetobacter species sensitive to tigecycline and meropenem.

Despite being on culture-appropriate antibiotics, the patient's condition deteriorated over the next three days. Tracheal aspirate cultures on Day 4 of mechanical ventilation grew Acinetobacter species, and chest X-ray showed right lower zone consolidation. The patient developed septic shock and died on Day 6 of hospitalization.

Table 1. Serial ABGs of case one

Time	pH	PCO2	HCO3-	PO2	Lac	Ca ²⁺	Cl-	Na+	K+
0 hour	7.72	72	59.5	52	3.5	0.65	80	141	1.4
1hour	7.51	72	57.5	283	0.9	0.65	-	145	1.5
2 hours	7.48	76	56.6	204	1.0	0.75	-	146	1.9
6 hours	7.40	83	51.4	65	1.3	1.00	-	150	2.2
12hours	7.55	61	53.4	241	1.2	0.92	-	156	2.6
24 hours	7.57	40	36.6	129	1.1	0.87	-	154	2.9
36 hours	7.53	33	27.6	99	1.3	0.79	-	146	2.4
3 days	7.22	52	21.3	90	1.6	0.79	-	145	4.6
4 days	7.12	58	18.9	88	1.7	0.61	-	144	4.5

Case Two

A 19-year-old female, recently diagnosed with nephrotic syndrome five days ago based on the presence of anasarca, ascites, and pleural effusion, with a 24-hour urinary protein of 5 g/day, was prescribed high doses of oral loop diuretics (torsemide 80 mg and metolazone 5 mg) and high-dose steroids (prednisolone 1 mg/kg body weight). She was simultaneously scheduled for a renal biopsy by a nephrologist.

She presented to the emergency department with generalized weakness, myalgias, and lower limb paraesthesia's. She also reported a history of anorexia and a few episodes of vomiting.

On examination, she was conscious, with a pulse of 88 bpm and a blood pressure of 100/70 mmHg. Her respiratory rate was 16 per minute, and oxygen saturation was 98% on room air. Her systemic examination was unremarkable except for lower limb weakness with sluggish deep tendon reflexes.

Her complete blood count (CBC) and chest X-ray were unremarkable. Liver function tests revealed low albumin

levels (1.9 g/dL), and the 24-hour urinary protein was 5.7 g/day. An arterial blood gas analysis showed severe metabolic alkalosis (pH 7.74) with hypokalaemia and hyponatremia, which was confirmed twice (Table 2). The CBC was normal, and kidney function tests revealed a urea level of 74 mg/dL and a serum creatinine level of 1.3 mg/dL. Her random blood sugar was normal, but ionized calcium was low.

A diagnosis of drug-induced metabolic alkalosis with severe hypokalaemia was made, and she was managed conservatively with IV saline and IV potassium replacement. Loop diuretics were stopped. Close monitoring of vitals, electrolytes, and pH was conducted.

Over the course of three days, the patient responded to treatment, and her pH improved significantly. Serum potassium and sodium levels also normalized. Clinically, her weakness improved, and deep tendon reflexes returned.

She was later subjected to a renal biopsy for definitive diagnosis, which revealed membranous glomerulopathy.

Table 2. Serial electrolytes and PH of case two during hospital stay.

Na	K	PH	HCO ₃	PCO ₂
122	1.4	7.74	60.4	47
123	1.3	7.70	>60	-
127	1.3	7.62	43	42
127	2.5	7.59	42	-
131	2.6	7.57	38	-
129	2.2	7.51	33.5	42
127	4.4	7.39	21.8	36
131	3.3	7.34	21.6	40
130	3.4	7.38	17.2	29

Discussion

Case one's initial symptoms can be attributed to acute cannabis and tobacco withdrawal. The severe metabolic alkalosis and hypokalaemia (which exacerbated the metabolic alkalosis) can be explained by a combination of underlying laxative overuse and diuretic use weeks before hospitalisation. The hypokalaemia caused muscle weakness, and the metabolic alkalosis led to respiratory depression, resulting in severe hypercapnia. Thus, the combined effects of alkalosis and hypercapnia contributed to the coma.

Post-intubation, the patient was managed with an infusion of normal saline and intravenous (IV) potassium chloride replacement, leading to a gradual correction of the deficits. Close monitoring of serial arterial blood gases (ABGs) revealed a gradual resolution of the metabolic alkalosis (indicating chloride-responsive alkalosis). The respiratory failure and hypercapnia were managed by placing the patient on mechanical ventilation.

Metabolic alkalosis accounts for about half of all acid-base disorders in hospitalised patients [8]. This is unsurprising, as many hospitalised patients experience vomiting, receive chloruretic drugs, or undergo nasogastric suction [9]. An inverse correlation has been reported between alkalosis and mortality [10]. Recent studies demonstrated that mortality rates are higher in medical patients compared to surgical patients when the pH exceeds 7.48. The mortality rate is 45% in patients with an arterial blood pH of 7.55 and 80% when the pH exceeds 7.65 [1].

Metabolic alkalosis results from the loss of acidic secretions or a gain of bicarbonate in the body. Once established, it tends to sustain itself by promoting increased bicarbonate absorption and decreased bicarbonate secretion in the distal tubules. Chloride depletion plays a major role in the development of metabolic alkalosis by increasing bicarbonate reabsorption (by enhancing the entry of H⁺ and Cl⁻ into the lumen, facilitating bicarbonate generation and reabsorption) [10] and by inhibiting bicarbonate secretion (through suppression of the Cl⁻/bicarbonate anion exchanger protein called pendrin) [11]. Hypokalaemia also promotes alkalosis through similar mechanisms. Both the cases had low ionised calcium

which could be explained as alkalosis causes increased avidity of calcium with albumin and decreases ionised calcium.

Thus, volume loss from nasogastric suction, vomiting, or diarrhoea, and diuretic use leads to alkalosis due to chloride depletion. Hyperaldosteronism causes metabolic alkalosis by directly stimulating the H⁺ ATPase on the luminal side of distal tubular cells, promoting acid secretion [12].

Clinical manifestations of metabolic alkalosis include signs of hypocalcaemia, cardiac arrhythmias, neuromuscular irritability, lethargy, and seizures. Other effects include altered consciousness, reduced oxygen release to tissues from haemoglobin, increased ammonia generation by the kidney, and, in some cases, depression of respiratory drive, leading to hypoventilation and a rise in arterial PCO₂ [13-16].

Metabolic alkalosis is reasonably classified into two types based on the patient's response to chloride. Chloride-responsive metabolic alkalosis, with a urinary chloride <15 mEq/L, is caused by chloride depletion and includes vomiting, nasogastric suction, chloruretic diuretic use, volume depletion, and laxative abuse. This type improves promptly with the infusion of isotonic saline. In contrast, chloride-resistant cases, characterized by a urinary chloride >25 mEq/L, include mineralocorticoid excess, severe hypokalaemia, and liquorice ingestion. These patients are typically volume-expanded and do not respond to isotonic saline [17].

The management of metabolic alkalosis aims to correct the underlying pathophysiology, which, in most cases, involves chloride and potassium depletion [18]. An infusion of normal saline corrects alkalosis caused by chloride and volume depletion. The volume to be infused depends on the chloride deficit. However, in oedematous states (usually accompanied by hypokalaemia that perpetuates metabolic alkalosis), administration of potassium chloride helps correct the alkalosis.

Saline-resistant metabolic alkalosis (e.g., primary hypoaldosteronism) is treated with IV potassium administration, as most cases involve hypokalaemia. Resistant cases with concomitant hypomagnesaemia [19] require prompt magnesium correction. Acetazolamide

[20] inhibits bicarbonate reabsorption in renal tubules, thereby increasing bicarbonate excretion, and is used after potassium replacement.

Rare cases of metabolic alkalosis unresponsive to potassium replacement and acetazolamide are treated with IV hydrochloric acid infusion as per the H⁺ deficit [21].

It is evident that metabolic alkalosis is a significant acid-base disturbance that must be recognised early, as untreated cases can lead to deleterious consequences. Alkalosis shifts the cytoplasmic redox balance, favouring lactate production [22], and promotes tissue hypoxia by shifting the oxygen dissociation curve to the left [23]. Furthermore, metabolic alkalosis increases overall mortality, especially among medical patients with a pH >7.48. Its presence also worsens the prognosis of other life-threatening conditions like sepsis, liver failure, and intracranial bleeding [24].

Case two had an uneventful course during her hospital stay. Prompt intervention, including stopping diuretics to prevent further intravascular volume contraction and appropriate use of volume and potassium replacement, along with monitoring, helped stabilise this patient.

Conclusion

The effect of diuretics in patients with hypoalbuminemia secondary to protein loss due to renal disease is a common cause of contraction alkalosis encountered in day-to-day practice. This condition can result in significant morbidity and mortality, as evidenced by the two cases described. Both patients had protein-losing renal disease. However, comorbid conditions play a major role in determining the mortality in such patients.

Conflict of Interest

The authors declare no conflict of interest.

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