Severe metabolic alkalosis in pregnancy

Charlotte Frise¹, Muna Noori² and Catherine Williamson³

Abstract

Metabolic alkalosis is uncommon in pregnancy and is most often the result of severe vomiting. If this is present at the time of delivery, transient metabolic derangement in the fetus can occur, potentially requiring additional organ support. A 22-year-old woman is described, who presented at 37 weeks gestation with a severe metabolic alkalosis, vomiting and acute renal and hepatic impairment. The investigations, management options and maternal and fetal outcome are described.

Keywords

high-risk pregnancy, metabolism, gastroenterology, maternal–fetal medicine

Introduction

A pure metabolic alkalosis is uncommon (2.2% of all alkalotic patients¹) and only four cases have been described in pregnancy.^{2–5} Most cases can be explained by gastrointestinal or renal chloride loss but it is important to understand the differential diagnosis so that rarer causes are not missed. We report a patient who presented at term with severe vomiting and a profound metabolic alkalosis. The aetiology, investigation and management strategy are described.

Case

A 22-year-old presented 37 weeks into her second pregnancy with pruritus, right upper quadrant pain and vomiting. She had been vomiting intermittently throughout pregnancy and was admitted at 32 weeks gestation for rehydration. The vomiting had worsened prior to the current admission and she had been unable to tolerate oral fluids. She felt weak, was experiencing leg cramps and had lost 12 kg in weight during pregnancy. Blood pressure was normal throughout.

Her previous pregnancy ended in a stillbirth secondary to placental insufficiency at 29 weeks gestation and had not been complicated by vomiting. Medical history included depression, schizophrenia and alcohol misuse prior to pregnancy. She reported intermittent cocaine and cannabis use during pregnancy but not prior to this presentation. She had no history of diuretic abuse. Her mood remained stable on depot zuclopenthixol. She had no significant family history. She smoked 5–10 cigarettes a day, was unemployed and lived alone.

On examination she appeared dehydrated. Examination was normal except for oxygen saturations of 92% on room air, with a respiratory rate of 12 breaths per minute. Blood pressure was 122/76 mmHg and her pulse rate was 100 beats per minute. On abdominal palpation there was mild right upper quadrant discomfort, the uterus was soft and the symphysis-fundal height was within normal limits. Urinalysis revealed 3+ protein and 3+ ketones.

Arterial blood gas analysis showed a profound hypochloraemic metabolic alkalosis with partial respiratory compensation and hypokalaemia (Table 1).

Blood results revealed acute renal and hepatic dysfunction (creatinine 195 µmol/L, bilirubin 37 µmol/L, alanine transaminase 417 IU/L, aspartate transaminase 319 IU/L) and markedly raised uric acid (1.01 mmol/L), all of which had been normal when measured earlier in pregnancy. Full blood count was normal apart from leukocytosis (total white cell count $16.3 \times 10^9/L$). The protein:creatinine ratio was mildly elevated at 60 mg/mmol. Urine chloride concentration was less than 20 mmol/L. Random serum bile acid concentration a week prior to admission was mildly elevated (29 µmol/L).

Four litres of intravenous normal saline with a total of 100 mmol potassium chloride was administered in the first 24 hours of her admission, with normalization of her serum potassium and a gradual resolution of the alkalosis. Spontaneous labour ensued and a male infant weighing 2.8 kg was delivered vaginally in good condition, with umbilical cord arterial and venous pH of 7.37 and 7.43 respectively.

The vomiting ceased immediately after delivery with rapid clinical and biochemical recovery. The placenta was macroscopically normal and histological analysis was not performed. Ultrasound of the abdomen was unremarkable. The patient declined further investigation and was discharged.

Discussion

Vomiting is common in pregnancy but significant vomiting with a marked alkalosis is very uncommon and only three cases have been described previously.^{2–4} One further case of metabolic alkalosis was associated with pica and oral bicarbonate ingestion.⁵ Consideration of the cause of vomiting was also required, and the worsening of her symptoms, in combination with right upper quadrant pain, leucocytosis, deranged renal and liver function, prompted the clinical team to consider a diagnosis of acute fatty liver of pregnancy.⁶ However, this would not explain the protracted vomiting or the associated weight loss, which may have reflected inadequately treated hyperemesis gravidarum.

Aetiology

Metabolic alkalosis results from increased bicarbonate concentration from renal or gastrointestinal hydrogen ion loss, or from an increased intake of bicarbonate ions for example with administration of bicarbonate containing compounds. The kidney can rapidly compensate for an increased bicarbonate load and so for a metabolic alkalosis to be

¹John Radcliffe Hospital, Oxford University Hospitals NHS Trust

²Queen Charlotte's and Chelsea Hospital, Imperial College Healthcare NHS Trust

³Queen Charlotte's and Chelsea Hospital, Imperial College London, London, UK

Corresponding author:

Catherine Williamson, Maternal and Fetal Disease Group, Institute of Reproductive and Developmental Biology, Imperial College London, Du Cane Road, London W12 0NN, UK.

Email: catherine.williamson@imperial.ac.uk

Table 1. Arterial blood gas on admission.

Parameter	Value	Normal range
pH	7.62	7.35–7.45
PaCO ₂	5.3	4.7–6.0 kPa
PaO ₂	10.8	11–13 kPa
Base excess	18	–2 to +2 mmol/L
HCO ₃	38.8	22–26 mmol/L
Cl	79	95–105 mmol/L
K	2.6	3.5–5.5 mmol/L
Anion gap	12.8	12–16 mmol/L

maintained there is likely to be impairment of this compensatory mechanism, resulting in inappropriately high bicarbonate re-absorption. This can result from hypovolaemia which stimulates renal sodium re-absorption. To maintain electrochemical neutrality, either chloride or bicarbonate ions also have to be re-absorbed. Therefore in a state of chloride deficiency, bicarbonate re-absorption occurs. Sodium can also be re-absorbed in exchange for hydrogen and potassium ions, and hence hypovolaemia can cause a hypokalaemic metabolic alkalosis. Hypokalaemia alone can also lead to the maintenance of a metabolic alkalosis, because hydrogen ions are excreted by the kidney in exchange for potassium ions. Mineralocorticoid excess has similar consequences as aldosterone leads to re-absorption of sodium via the epithelial sodium channel in the collecting duct and hydrogen and potassium ions are then secreted into the lumen. However, pregnant women are relatively protected against the biochemical consequences of primary hyperaldosteronism due to their high levels of progesterone that have an antagonistic effect on aldosterone.

Bartter and Gitelman syndromes are autosomal recessive conditions which cause hypokalaemia, metabolic alkalosis, hyperaldosteronism and in some patients, hypomagnesaemia, as a result of impaired sodium chloride re-absorption in the kidney in the loop of Henle and distal tubule, respectively. Bartter syndrome tends to present in childhood, whereas Gitelman syndrome may present later, including during pregnancy.⁷ If a patient has these features, in the absence of another cause such as vomiting, the diagnosis can be supported by measuring the urinary calcium (this is normal or high in Bartter syndrome and below normal in Gitelman syndrome).

Diuretic abuse can also cause hypokalaemia and metabolic alkalosis, and is important to exclude in patients who present with these clinical features.

Consequences of alkalosis

Severe alkalosis is associated with significant morbidity and mortality, particularly in critically ill patients.¹ An increase in pH results in a shift of the oxygen dissociation curve to the left, which represents increased oxygen affinity to haemoglobin and therefore reduced oxygen delivery to the tissues, which is exacerbated by the hypoxia that may result from compensatory physiological respiratory depression. Arrhythmias, confusion and impaired myocardial contractility can result from reduced oxygen delivery. Cerebral blood flow may be impaired but can be partially balanced by increased partial pressure of the carbon dioxide that is present.

Effects of pregnancy on acid–base balance

Pregnancy is a state of physiological respiratory alkalosis, which can reduce the buffering capacity if acidosis develops. There are insufficient cases described to ascertain whether pregnancy has any effect on the development of a metabolic alkalosis.

Table 2. Causes of metabolic alkalosis.

Exogenous administration	
Alkali administration (e.g. milk alkali syndrome)	
Intravenous penicillin	
Current use of diuretics	
Low urinary chloride (<20 mEq/L)	
Loss of gastric secretions, e.g. vomiting, villous adenoma	
Congenital chloridorrhea	
Following an episode of hypercapnoea	
Previous diuretic treatment	
Increased urinary chloride without hypertension	
Hypokalaemia	
Hypomagnesaemia	
Bartter's syndrome	
Gitelman's syndrome	
Increased urinary chloride with hypertension	
Cushing syndrome (or exogenous steroid use)	
Congenital adrenal hyperplasia	Low-plasma renin activity
11 β hydroxysteroid dehydrogenase deficiency	Low-aldosterone level
Liquorice consumption	
Congenital adrenal hyperplasia	
Liddle's syndrome	
Renal artery stenosis	High plasma renin activity
Diuretic use	High aldosterone level
Renin-secreting tumours	
Primary hyperaldosteronism (adrenal adenoma, bilateral adrenal hyperplasia or rarely adrenal carcinoma)	Low plasma renin activity High aldosterone level

Effects of alkalosis on pregnancy

The three previous published cases were all identified because of neonatal illness, including a neonate with hypoventilation and episodic cyanosis and a significant alkalosis at birth, associated with maternal hypochloraemic alkalosis (pH 7.63, PaCO₂ 7.0 kPa, HCO₃[–] 34.6 mmol/L, base excess 10.5 mmol/L, Cl[–] 84 mmol/L, K⁺ 1.5 mmol/L), thought to have resulted from an eating disorder.² The second describes a neonate with respiratory distress, possible sepsis and significant alkalosis immediately following birth. The mother had a hypochloraemic alkalosis (pH 7.57, PaCO₂ 7.0 kPa, HCO₃[–] 48 mmol/L, Cl[–] 78 mmol/L, K⁺ 1.7 mmol/L), thought to be the result of reduced oral intake and vomiting as an attempt to conceal her pregnancy.⁴ The third case describes an infant born by caesarean section at 36 weeks gestation, to a mother with severe vomiting from 24 weeks and significant metabolic alkalosis (pH 7.59, base excess 11 mmol/L). The neonate was irritable with hypertonia.³

Investigation

A history of severe vomiting, previous gastrointestinal procedures, or other features such as hypertension, all help narrow the differential diagnosis. Examination is important because the volume status of the patient also helps identify the cause of the metabolic derangement and can guide treatment.

Urinary chloride concentration is a useful diagnostic tool as a low result reflects appropriate chloride handling in the kidney in response to low plasma chloride. Appropriate reduction in renal chloride excretion is seen in volume deplete states and makes other causes such as mineralocorticoid excess less likely.

A raised urinary chloride is not specific for one diagnosis, but an elevation is seen in disorders that are not related to volume depletion, such as mineralocorticoid excess. Measurement of plasma renin activity and aldosterone concentration therefore aid the diagnosis and alongside the presence or absence of hypertension, may distinguish between the less common causes (Table 2).

Management

The intervention required depends on the patient's clinical condition and the potential cause of the alkalosis.

Metabolic alkalosis associated with hypochloraemia and hypovolaemia requires the administration of sodium chloride containing fluid. Histamine receptor antagonists or proton pump inhibitors reduce the volume and acidity of secretions in patients with large volume gastric fluid loss and therefore may aid resolution of the metabolic abnormalities.⁸

In extreme cases haemodialysis has been used, initially with an acid dialysate,⁹ but more recently case reports have described successful resolution with normal bicarbonate dialysate.¹⁰

Acetazolamide can also be used to correct serum pH in alkalotic patients. In one study, a single dose was administered to 15 consecutive patients on an intensive care unit, which caused an increased ratio for renal excretion of sodium to chloride, resulting in an increase in serum chloride and a resolution of the alkalosis.¹¹

Conclusions

In the absence of an obvious cause of alkalosis in this patient, the absence of a history of diuretic abuse and the prompt resolution following rehydration and delivery supports the hypothesis that protracted vomiting caused her metabolic derangement, with dehydration and malnutrition contributing to renal and hepatic dysfunction. There are no reports of medication such as zuclopenthixol creating a similar picture, and the prompt resolution following delivery without alteration of the dose or regimen of this medication would suggest that this was not relevant to the current presentation. Elevated serum bile acid concentration in combination with pruritus and deranged liver function tests support a diagnosis of intrahepatic cholestasis of pregnancy (ICP), however profound vomiting is not a feature of ICP and therefore ICP is unlikely to be the cause of the alkalosis in this case.

This case emphasizes the importance of pharmacological intervention for vomiting in pregnancy, to prevent the severe morbidity and mortality that can be seen in hyperemesis gravidarum, which results in approximately one maternal death each year.¹²

Acknowledgements

None.

Declaration of conflicting interests

None declared.

Funding

None.

Ethical approval

The authors obtained written patient consent to publish this case report.

Guarantor

CW.

Contributorship

MN and CJF wrote the case summary and discussion respectively. CJF, MN and CW reviewed the draft and approved the final version of the manuscript.

References

1. Anderson LE and Henrich WL. Alkalemia-associated morbidity and mortality in medical and surgical patients. *South Med J* 1987; 80: 729–733.
2. Schimert P, Bernet-Buettiker V, Rutishauser C, Schams M and Frey B. Transplacental metabolic alkalosis. *J Paediatr Child Health* 2007; 43: 851–853.
3. Martí Fernández J, Salcedo Abizanda S and Peguero Monforte G. Transplacental hypochloremia. *An Pediatr* 1988; 29: 261–262.
4. Benaron DA, Yorgin PD, Lapuk S, Gibson R and Dennery PA. Alkalemia in a newborn infant. *J Pediatr* 1992; 120: 489–494.
5. Grotegut CA, Dandolu V, Katari S, Whiteman VE, Geifman-Holtzman O and Teitelman M. Baking soda pica: a case of hypokalemic metabolic alkalosis and rhabdomyolysis in pregnancy. *Obstet Gynecol* 2006; 107: 484–486.
6. Ch'ng CL, Morgan M, Hainsworth I and Kingham JGC. Prospective study of liver dysfunction in pregnancy in Southwest Wales. *Gut* 2002; 51: 876–880.
7. de Bustros A, Aleppo G and Zikos D. Hypokalemia in pregnancy: clue to Gitelman syndrome. *Endocrinologist* 2001; 11: 447–450.
8. Hixson R and Christmas D. Use of omeprazole in life-threatening metabolic alkalosis. *Intensive Care Med* 1999; 25: 1201.
9. Ponce P, Santana A and Vinhas J. Treatment of severe metabolic alkalosis by 'acid dialysis'. *Crit Care Med* 1991; 19: 583–585.
10. Hsu S-C, Wang M-C, Hsin-Liang L, Tsai M-C and Huang J-J. Extreme metabolic alkalosis treated with normal bicarbonate hemodialysis. *Am J Kidney Dis* 2001; 37: 1–4.
11. Moviat M, Pickkers P, van der Voort PHJ and van der Hoeven JG. Acetazolamide-mediated decrease in strong ion difference accounts for the correction of metabolic alkalosis in critically ill patients. *Crit Care* 2006; 10: R14.
12. Cantwell R, Clutton-Brock T, Cooper G, et al. Saving mothers' lives. Reviewing maternal deaths to make motherhood safer: 2006–2008. The eighth report on confidential enquiries into maternal deaths in the United Kingdom. *BJOG* 2011; 118(Suppl. 1): 1–203.