Case report

AN ATYPICAL CASE OF SEVERE METABOLIC ALKALOSIS BY INJECTION ACYCLOVIR

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Abstract

Metabolic alkalosis is a rare condition in ICU settings mostly found due to vomiting, use of diuretics, hypochloremia or hypokalemia. Conditions like Cushing's syndrome and Hyperaldosteronism may also aid in development of metabolic alkalosis. The management of the causative factor along with the supportive care is usually sufficient to treat such a condition. We report a case of metabolic alkalosis, which couldn't be attributed to any pathology but could be finaly managed by stopping the drug of choice; Injection Acyclovir.

Keywords: Acyclovir, Metabolic alkalosis

Introduction

Metabolic alkalosis is characterized by hyperbicarbonatemia (>27 mmol/L) and alkalemia with pH (> 7.45)[1]. It may be due to metabolic origin by loss of acid, by gain of excess HCO_3^- or in post-hypercapnic state[2]. Injection Acyclovir is widely available as the drug of choice for Herpes virus infections. Acyclovir administration may lead to local adverse reactions of inflammation, nausea or vomiting.[3] Here; we report a case of severe metabolic alkalosis as one of the complications of Injection Acyclovir, a first of its kind in the treatment of Herpetic infections.

Case report

A sixty six year old lady was received in the intensive care unit with fever and status epilepticus. Seizure was controlled by Midazolam intravenous infusion which was continued for 48h. The patient was not suffering from any other co-morbid disease or under any medication. The only significant clinical finding was bilateral constricted pupil, not reacting to light. MRI of brain revealed features of encephalitis involving midbrain, basal ganglia and bilateral temporal lobes. The management involved mechanical ventilation, antibiotics and Injection Acyclovir with other supportive care. Continuous day to day monitoring of the patient was done.

For the first 3 days the patient's vitals were stable. On day 4, patient started developing metabolic alkalosis (pH: 7.48; HCO_3^- : 33mMol/L; PCO_2:48 mmHg).The patient continued in the comatose state though she didn't develop any dyselectrolytemia or any

other organ dysfunction. After scrutinizing the drugs, intravenous Acyclovir was stopped on day 10. Though the clinical condition remained status quo, the patient showed improvement in the blood gas parameters within 48h-72h of intervention and alkalosis was settled in the next 3-4 days **(Table 1)**

Discussion

Metabolic alkalosis contributes to half of all the acid-base disorders[4]. The mortality associated with severe metabolic alkalosis is substantial; a mortality rate of 45% in patients with an arterial blood pH of 7.55 and 80% when the pH greater than 7.65 has been reported[5].

Metabolic alkalosis is characterized by hyperbicarbonatemia and alkalemia[2]. It occurs when a primary pathophysiologic process leads to the net accumulation of base within or the net loss of acid from the extracellular fluid[6] **(Table 2)**.

Though hypochloremia and hypokalemia remains the major cause, bicarbonate or base loading may rarely be the sole cause of significant metabolic alkalosis[2]. Such states may occur during and immediately after an oral or intravenous infusion of $NaHCO_3$ or base equivalent, *e.g.*, citrate in transfused blood or fresh frozen plasma. But such alkalosis is only transient as kidney is very efficient to excrete the extra bicarbonate[7]. In our case, we presume the alkalosis was due to infusion of highly alkaline Acyclovir preparation **(Fig 1).** Acyclovir is marketed in lyophilized powder form, prepared by adding normal saline to make a solution of 25mg/ml. This patient received around 500mg Acyclovir thrice daily which may attribute to be the causative agent for developing metabolic alkalosis.

Fig.1: pH of Acyclovir preparation checked by litmus paper.

Administration of Injection Acyclovir is usually well tolerated, although it is associated with side effects like lethargy, tremor and nephropathy in cases of dehydration[3]. Metabolic alkalosis is not a documented side effect though in our patient it appears to be the causative factor as both the generation and resolution of alkalosis was related to the starting and stopping of the drug.

Table1. Various monitoring parameters of the patient from day 4 to day 16 of admission

	Day 4	**Day 5**	**Day 6**	**Day 7**	**Day 8**	**Day 9**	**Day 10**	**Day 11**	**Day 12**	**Day 13**	**Day 14**	**Day 15**	**Day 16**
pH	7.48	7.43	7.46	7.47	7.47	7.45	7.41	7.48	7.5	7.49	7.42	7.44	7.42
PCO2	48	45	55	52	52	55	52	40	40	35	45	40	35
CO_3^-	33	30	40	38.9	40	39	33	35	35	27	29	27	25
PO_2	90	97	108	95	89	184	102	130	130	100	171	134	112
Na^+	131	129	134	140	132	128	132	129	135	131	128	139	141
K^+	3.0	3.3	3.3	2.9	3.4	3.4	3.2	3.2	3.3	3.1	3.3	2.9	3.0
Cl^-	101	108	94	106	100	108	102	114	99	104	107	110	109
Urine output (L)	2.25	2.1	2.27	2.5	2.75	2.65	2.4	2.15	2.85	2.1	1.9	2.3	2.35

Table2. Causes of metabolic alkalosis

S. no.	**Cause**	**Example**
1.	Loss of acid from extracellular space	
	A. Loss of gastric fluid	Vomiting
	B. Acid loss in urine	Primary aldosteronism Diuretic use
	C. Acid shifts into cells	Hypokalemia
	D. Loss of acid in stool	Congenital chloride loosing diarrhoea
2.	Excessive HCO_3^- load	
	A. Absolute	
	1. Oral or parenteral HCO_3^-	Milk alkali syndrome
	2. Metabolic conversion of the salts of organic acids to HCO_3^-	Lactate, acetate, or citrate administration
	B. Relative	$NaHCO_3$ dialysis
3.	Post hypercapnic states	Correction(e.g. by mechanical ventilator support) of chronic hypercapnia

The mechanism of metabolic alkalosis varies as per the causative factor[2] e.g. hypokalemia decreases GFR and increases proximal tubular reabsorption of HCO_3^-; hypochloremia increases proton secretion in medullary collecting duct; renal hypoperfusion causes increased fractional HCO_3^- reabsorption[1]. This patient never showed hypokalemia or hypochloremia; also adequate urine output excludes the possibility of renal hypoperfusion in our patient. Hormonal disturbances like hypercortisolism[8] and hyperaldosteronism[1] can cause metabolic alkalosis by increasing Na- dependant proton secretion in cortical collecting duct and Na- independent proton secretion in both cortical and medullary collecting duct. Serum Cortisol (12.50mcg/dl) and serum Aldosterone (10.40 ng/dl) level were within normal limits in our patient, and thus excludes this possibility of hormonal disturbances. **(Table 1)**

Clinically, metabolic alkalosis manifests as apathy, confusion, cardiac arrhythmias, and neuromuscular irritability[2,9] .The increase in arterial blood pH predictably depresses ventilation resulting in increased PaCO2 and buffering of alkalemia. The PaCO2 increases about 0.5 to 0.7 mmHg for every 1.0 mM increase in plasma HCO3 concentration [10]. Although a PaCO2 greater than 55 mmHg is uncommon, compensatory increase upto 60 mmHg have been documented in severe metabolic alkalosis[2]. In this case, patient being comatose, the assessment of mental condition was difficult. Only hypoventilation was evident by significant hypercarbia.

Certain laboratory parameters like serum albumin, urinary chloride and urinary pH are also important in the diagnosis of metabolic alkalosis. Hypoalbuminemia, due to loss of negative charge and urinary chloride <10meq/L, confirms alkalosis. Urine pH >6.2 is evident in cases of alkalosis developed after correction of ketoacidosis or lactic acidosis. Our patient had serum albumin 3.2-3.8g/dL and urinary pH 5.0 and urinary chloride >140meq/L, thus excluding the possibility of such causative factors.

Treatment of metabolic alkalosis is cause dependant. Nonetiologic treatments include expansion of intravascular volume, administration of potassium causes increase in serum chloride and decrease in serum HCO_3^-. Administration of Acetazolamide, infusion of Ammonium chloride, Arginine hydrochloride, 0.1N Hydrochloric acid has also been found to be effective. In this patient, stoppage of intravenous Acyclovir was sufficient to correct metabolic alkalosis.

Conclusion

Parenteral administration of Acyclovir can cause metabolic alkalosis and administration of such highly alkaline drugs should be monitored closely to avoid clinical deterioration of critically ill patients.

References

1. Donald S, Prough, J. Sean Funston, Christer H. Svensen, Scott W. Wolf. Fluids, electrolytes and Acid-Base Physiology. In: Barash, editor. Clinical Anaesthesia 6th Ed. Philadelphia: Lippincott Williams & Wilkins;2009. p. 290-325.

2. John H Galla. Metabolic alkalosis. J Am Soc Nephrol. 2000; 11: 369–75.

3. Lindesey R. Baden, Raphael Dolin. Antiviral chemotherapy, Excluding Antiretroviral Drugs. In: Longo, editor. Harrison's principles of internal medicine, 15th Ed. United States of America: Mc-Graw Hill Companies; 2001. p. 1092-1100.

4. Hodgkin JE, Soeprono FF, Chan DM. Incidence of metabolic alkalemia in hospitalized patients. Crit Care Med. 1980; 8: 725–32.

5. Anderson LE, Henrich WL. Alkalemia-associated morbidity and mortality in medical and surgical patients. South Med J. 1987; 80: 729–33.

6. Tannen RL. Effect of potassium on renal acidification and acidbase homeostasis. Semin Nephrol. 1987;7: 263–73.

7. Singer RB, Clark JK, Barker ES, Crosley AP Jr, Elkington JR. The acute effects in man of rapid intravenous infusion of hypertonic sodium bicarbonate solution. Medicine. 1955; 34: 51–95.

8. Miguel Angel Martínez-Valles, Asael Palafox-Cazarez, Jose Antonio Paredes-Avina. Severe hypokalemia, metabolic alkalosis and hypertension in a 54 year old male with ectopic ACTH syndrome: a case report. Cases Journal. 2009; 2:6174.

9. Adrogue HJ, Madias NE. Management of life-threatening acidbase disorders. N Engl J Med. 1998;338: 107–11.

10. Javaheri S, Kazemi H. Metabolic alkalosis and hypoventilation in humans. Am Rev Respir Dis. 1987;136: 1101–1016.

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