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Metabolic Alkalosis Induced by Plasmapheresis in a Patient with Systemic Lupus Erythematosus

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We report a patient with systemic lupus erythematosus (SLE), who had developed metabolic alkalosis during plasmapheresis. The metabolic alkalosis could be promptly corrected by reducing the amount of citrate load. The development of metabolic alkalosis can be explained by the citrate load during plasmapheresis. Careful monitoring of acid base status is mandatory in patients with limited renal function and the reduction of citrate load may be advisable in plasmapheresis.

Key Words: *Metabolic alkalosis, Systemic lupus erythematosus Plasmapheresis*

INTRODUCTION

Metabolic alkalosis due to administration of parenteral alkali, especially in the setting of renal failure, has previously been reported. The administration of plasma protein fractions that are very rich in sodium acetate (Rahilly et al., 1979), regional citrate hemodialysis of patients with bleeding tendency (Kelleher et al., 1987) and administration of large amounts of fresh frozen plasma and acid-citrate-dextrose solution during plsmapheresis (Pearl et al., 1985) could induce metabolic alkalosis.

We have recently observed a patient with SLE in whom metabolic alkalosis developed, when she was treated with plasmapheresis. The development of metabolic alkalosis during plasmapheresis can be explained by the large amount of sodium citrate load during the procedure. The metabolic alkalosis was prevented by appropriate modifications in the plasmapheresis protocol.

CASE REPORT

A 15-year-old girl was admitted because of fever, dyspnea, anuria, generalized edema and seizure. The patient had been healthy until one month earlier, when she first noted facial rash, weakness and generalized edema. Two days before admission, she experienced anuria and seizure. She had no specific past or family history.

Vital signs were pulse rate; 108/min, respiration rate; 24/min, blood pressure; 180/100 mmHg and body temperature; 38.1°C. On physical examination, she was alert but febrile and puffy. There was an erythematous rash on both cheeks. The head and neck were normal, the conjunctivae were slightly anemic, the sclerae were anicteric. The lung sounds were coarse with rale on both lung fields and the heart sound was rapid but regular without murmur. The abdomen was soft without distention and hepatosplenomegaly. Moderate pitting edma was observed. Neurologic examination was negative.

The urinalysis revealed proteinuria (+++), 1 to 3 WBC and many RBC per high power field without any sorts of casts. The hematocrit was 26% and the hemoglobin 8.7 g/dl. The WBC was 8,800/μl, with 87% of neutrophils and 12% of lymphocytes. The platelet count was 40,000/μl, the corrected reticulocyte count was 0.9%. RBC indices were 92 fl of MCV, 30.7 pg of MCH and 34.5% of MCHC. Peripheral blood smear showed evidence of microangiopathic hemolytic anemia; 5 to 7 schistocytes per oil immersion field. Fasting blood sugar was 110 mg/dl, creatinine 7.6 mg/dl, total protein 5.3 g/dl and albumin 2.4 g/dl. Sodium was 141 mEq/L, potassium 4.8 mEq/l, calcium 8.6 mg/dl,

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phosphate 7.4 mg/dl and chloride 101 mEq/L. Total bilirubin was 0.3 mg/dl. Serum aspartate aminotransferase was 14 unit, serum alanine aminotransferase 5 unit, LDH 1187 unit and CPK 173 IU/L. PT and aPTT were 78% and 28.2 sec (control 27.0 sec). Fibrinogen was 420 mg/dl and fibrin degradation product was negative (below 8 μg/dl). On the arterial blood gas analysis, pH was 7.381, Pco_2 27.5 mmHg, Po_2 84.7 mmHg, Hco_3 16.5 mmol/L and O_2 saturation was 96.5%. The complement C_3 was 24.1 mg/dl, the C_4 below 10.5 mg/dl. LE cell was positive and FANA was positive (1:160, homogeneous type). Anti-ds DNA Ab was 100 IU/ml and anti-platelet Ab was positive. VDRL and RA factor were negative and ESR was 32 mm/hr.

The chest x-ray showed an enlarged heart and diffuse reticulonodular pattern in both lung fields and increased linearity of the peripheral lung field. On the 1st hospital day, the patient was transfused platelet concentrates and was treated with hemodialysis. On the 2nd day, she received pulse therapy of intravenous methylprednisolone and was followed by oral prednisolone administration.

On the 5th hospital day, corrected reticulocyte count and LDH were elevated to 4.6% and 1973 unit respectively. Thrombocytopenia was advanced to 30,000/ml and MAHA was persistent. So, we performed plasmapheresis on alternate days under the clinical impression of SLE. The plasma exchanges were performed with a Haemonetics model V50; approximately 2000ml of patient's plasma was removed and 1000 ml of fresh frozen plasma which is contained about 7.5 g of sodium citrate, 80 ml of cryoprecipitate, 500ml of acid-citrate-dextrose (ACD) solution as anticoagulant which contained 11 g of sodium citrate and 500 ml of 4 percent albumin solution was administered as replacement solution at each session. Hemodialysis was performed for four hours on alternate days using a standard bath with a bicarbonate concentration of 30 mEq/L.

After the 2nd trial of plasmapheresis, an arterial blood gas measurement demonstrated severe metabolic alkalosis; pH was 7.52, Pco_2 55.4 mmHg, Po_2 59.4 mmHg, and Hco_3 43.6 mmol/L. The patient didn't have any other causes for metabolic alkalosis such as alkali therapy, nasogastric suction, vomiting, or hypokalemia.

On the 15th hospital day, plasmapheresis procedure was altered by reducing the volume of ACD solution to 200 ml. The volume ratio of blood vs anticoagulant was changed from 8:1 to 16:1 while the ACD solution was reduced from 500 m to 200 ml. Subsequent to this modification in procedure, the metabolic alkalosis was promptly resolved; pH was 7.40, Pco_2 34.2 mmHg, Po_2 62.7 mmHg, and Hco_3 23.9 mmol/L (Fig. 1).

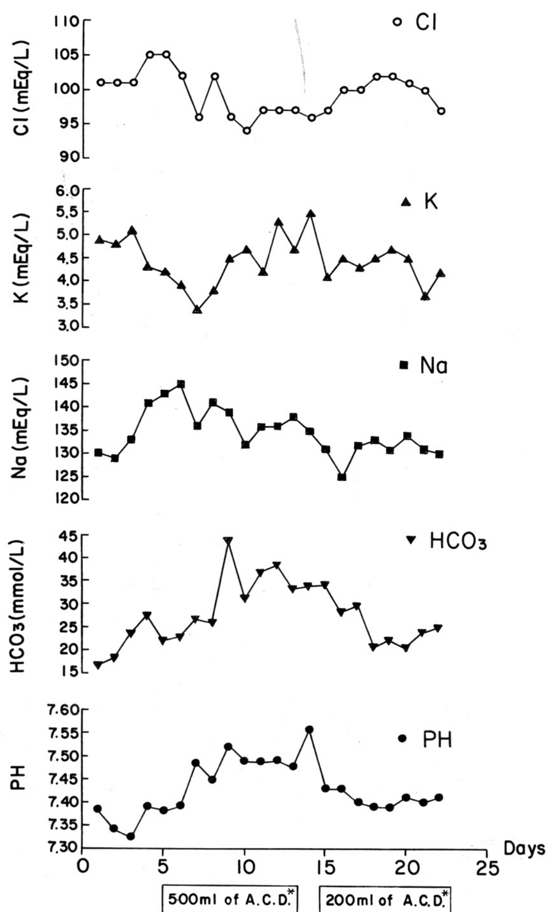


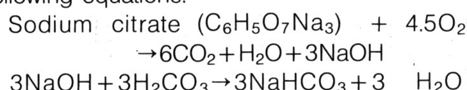
Fig. 1. Serum electrolytes and arterial acid-base status before and after reducing amount of citrate load.
* A.C.D.: acid-citrate-dextrose

DISCUSSION

The impairment in acid excretion that accompanies decreases in renal function makes patients with renal insufficiency prone to the development of a metabolic acidosis (Relman, 1968). If all renal function were lost approximately 80 mmol of H^+ per day (1 mmol/Kg body weight) could not be excreted.

However, metabolic alkalosis due to vomiting in patients with uremia has been reported in 1991 (Quintanilla et al., 1991). We observed metabolic alkalosis develop in a patient with SLE during plasmapheresis. Since this patient had no evidence of acid losses

(e.g., vomiting) or alkali ingestion by mouth, some other exogenous source of alkali must have been responsible for the acid base disturbance (Seldin et al., 1972). One possible causative or at least potentiating factor of metabolic alkalosis could be the sodium citrate load during the plasmapheresis. Most plasmapheresis protocols use fresh frozen plasma as the replacement solution for the removed plasma. The administered fresh frozen plasma is prepared from citrated blood. The sodium citrate both in the anticoagulant solution and fresh frozen plasma can proceed down normal metabolic pathways to form sodium bicarbonate on a milliequivalent for milliequivalent basis as shown in the following equations:



$$\text{Sodium citrate } (C_6H_5O_7Na_3) + 4.5O_2 \rightarrow 6CO_2 + H_2O + 3NaOH$$

$$3NaOH + 3H_2CO_3 \rightarrow 3NaHCO_3 + 3H_2O$$

The administration of citrate solutions has been recognized as a cause of metabolic alkalosis following massive transfusion (Litwin et al., 1959). There has been the report that metabolic alkalosis developed in patients with limited renal function and at increased risk for bleeding due to regional citrate hemodialysis (Kelleher et al., 1987). Also, the development of metabolic alkalosis during plasmapheresis can be prevented by replacing removed plasma with 3 percent albumin solution and cryoprecipitate rather than with fresh frozen plasma (Pearl et al., 1985). On the other hand, Pinnick et al. reported no acid-base disorders and no other side effects during citrate dialysis in patients at high risk for bleeding (Pinnick et al., 1983). The development of metabolic alkalosis in patients with limited renal function may be caused by decreased capacity of renal bicarbonate excretion. In our patient, ACD solution and fresh frozen plasma were administered simultaneously as a anticoagulant or replacement fluid during plasmapheresis. The ACD solution used for this patient contained approximately 130 mEq of sodium citrate. The fresh frozen plasma was prepared from blood containing approximately 90 mEq of sodium citrate. The maximal amount of bicarbonate that could be potentially produced from the sodium citrate contained in the replacement solution therefore exceeded 200 mEg on alternate days in this patient. The actual amount of sodium citrate could be significantly low due to removal of sodium citrate in the discarded plasma, distribution of sodium citrate to red blood cells during preparation of fresh frozen plasma and removal of sodium citrate by dialysis (Pearl et al., 1985). Since our patient was essentially anuric and unable to excrete excess bicarbonate, she was therefore particularly prone to the development of severe metabolic alkalosis as a result of the citrate load. By reducing the amount of ACD, we were able to prevent the potential bicarbonate production by up to 70 mEq at each plasmapheresis session. This modification in the plasmapheresis procedure resulted in rapid correction of the metabolic alkalosis.

We recommend careful acid-base monitoring of all patients undergoing repeated plasmapheresis procedures, especially when the renal function is compromised. If metabolic alkalosis developed during plasmapheresis, modifications of the procedure to alkali load should be considered.

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