

Fatal Fluctuation of Serum Potassium Level during Barbiturate Coma Therapy

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Severe hypokalemia and rebound hyperkalemia is rare side effect of barbiturate. The authors report an experience of life-threatening fluctuation of serum potassium level from barbiturate coma therapy (BCT) in severe brain injury patient. A 54-year-old man falling from a golf-cart suffered multiple hemorrhagic contusion and traumatic subarachnoid hemorrhage. He was treated with barbiturate coma therapy conservatively for 20 hours. One hour after cessation of barbiturate infusion, cardiac arrest happened. Meanwhile serum potassium level was 1.5 mmol/L. 24 hours after discontinuation of barbiturate, another asystole occurred, and the serum potassium level was 8.5 mmol/L. This rare side effect of barbiturate is mediated by transcellular shift of potassium. Clinicians should monitor closely the electrolyte balance during barbiturate infusion, and possibility of rebound hyperkalemia after the cessation must be borne in mind. (J Kor Neurotraumatol Soc 2009;5:99-102)

KEY WORDS: Hypokalemia · Hyperkalemia · Barbiturate · Head trauma.

Introduction

Coma therapy using barbiturate has been widely used for control of increased intracranial pressure caused by brain swelling from diverse neurosurgical crises.¹¹⁾ However, using high-dose barbiturate for a prolonged period sometimes leads to considerable well-known side effects which include arterial hypotension, immunosuppression, hepatic dysfunction, renal dysfunction, pneumonia and decrease in cortical activity.^{1,11)} Extreme changes in serum potassium occurring in a severe brain injury patient during high-dose barbiturate coma therapy (BCT) are so rare that only a few reports have been published.^{1,6,8,11,12)} We present an experience of life-threatening fluctuations of serum potassium during the coma therapy with thiopental sodium and discuss the proper management of such condition.

Case Report

A 54-year-old man was transferred to emergency unit due

to altered mentality after the fall from a golf-cart. His initial Glasgow Coma Scale (GCS) was E3M4V1 and pupillary response was intact. Initial brain computed tomography (CT) at arrival revealed multiple hemorrhagic contusions in bilateral frontal bases and anterior temporal areas. Traumatic subarachnoid hemorrhage was diffuse, and small amount of falcian and tentorial subdural hemorrhage together with linear skull fracture in the left frontal bone continuing to sagittal suture existed. However, there was no lateralizing lesion causing profound mass effect, we decided to manage the patient conservatively with high-dose BCT along with intracranial pressure (ICP) monitoring. His all blood samples including serum potassium level (3.3 mmol/L) were in their normal or near-normal range.

He was admitted to intensive care unit and BCT was started 5 hours from the accident. BCT was applied because mannitolization alone was not considered sufficient to control his ICP. As his body weight was 66 kg, loading dose of infused thiopental sodium was 350 mg (5 mg/kg) for the first 10 minutes, followed by continuous infusion at a rate of 350 mg/h (5 mg/kg/h) during the first 24 hours. Because sufficient sedative effect could not be shown at the standard dose, we increased the infusion rate up to 450 mg/h. During the higher-dose coma therapy, the ICP as well as proper cerebral perfusion pressure could be maintained in normal range. Careful mechanical ventilation had been performed for prevention of hypercapnea and for lowering

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Potassium Level during Barbiturate Therapy

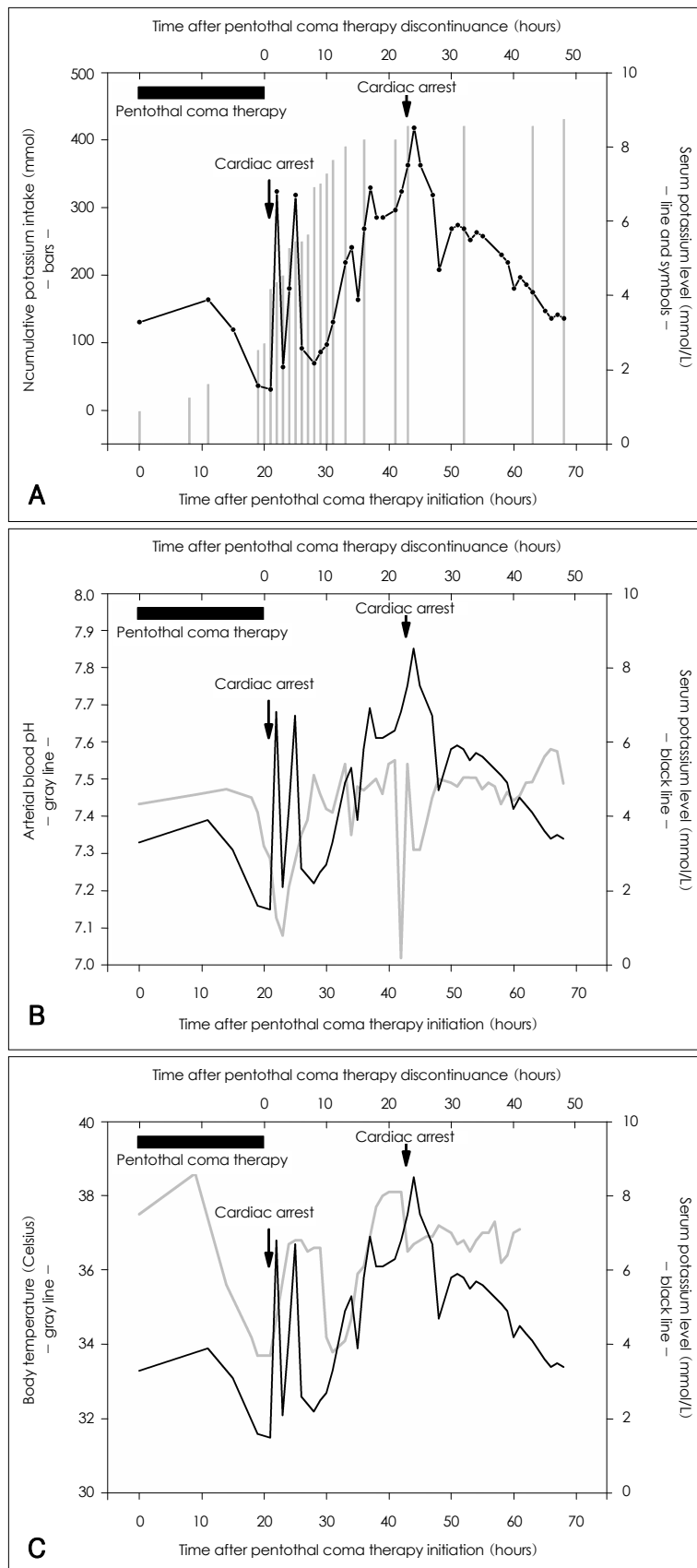


FIGURE 1. Time course changes in serum potassium level with cumulative potassium intake (A), arterial blood pH (B), and body temperature (C).

body temperature. Sixteen hours from the initiation of the therapy, significant hypotension occurred. For the purpose of maintaining blood pressure and cerebral perfusion pressure, continuous infusion of dopamine (5–15 mcg/kg/min) was started. During the following 3 hours, depression of ST element on the electrocardiography occurred prior to ventricular tachycardia. At that time serum potassium level was 1.6 mmol/L. Therefore, the patient was managed with cardioversion and with potassium replacement. As soon as the cardiac rhythm converted to normal, subsequent bradycardia and hypotension followed. We discontinued BCT 20 hours after its initiation and added inotropics such as dobutamine and norepinephrine to maintain the blood pressure. The results of echocardiography and cardiac enzyme tests showed no evidence of underlying cardiac disease. One hour after cessation of thiopental sodium infusion, ventricular tachycardia recurred and cardiac arrest followed. At that time, serum potassium level was 1.5 mmol/L. Cardiac resuscitation with potassium replacement enabled him to recover normal cardiac sinus rhythm. During 16 hours after discontinuation of thiopental sodium infusion, extreme range of fluctuations in serum potassium level needed frequent injection of potassium or calcium gluconate. Intermittent potassium dose was 20 mEq/hr, but it was temporarily increased to 80 mEq/hr whenever cardiac arrest occurred. Subsequently, gradual increase of serum potassium reached its peak level of 8.5 mmol/L at 24 hours by virtue of discontinuation of thiopental sodium infusion. At the end of that phase, another event of asystole occurred, but it was reversible after cardiac resuscitation. Hyperkalemia was treated with calcium gluconate injection and kalliminate enema. The serum potassium level became normalized in 24 hours and it could be maintained afterwards without further management. Serum potassium level, cumulative potassium intake, and arterial blood pH, body temperature measured during the clinical course are illustrated in Figure 1. Fortunately, during this life-threatening event, ICP was maintained in tolerable range and the patient has fully recovered without any permanent neurological deficit except transient personality change.

Discussion

Although the phenomenon of hypokalemia resulted from barbiturate injection had been known previously, significant hypokalemia induced by continuous barbiturate infusion was first reported by Schälén et al.¹¹⁾ in 1992. Since then, information from sporadically reported cases of severe potassium imbalance associated with BCT failed to suggest any risk factors.^{1,6,8,12)} However, most of reported cases in-

cluding ours shared common clinical features. Typically severe hypokalemia occurred within 48 hours after initiation of BCT, and fatal rebound hyperkalemia followed shortly after cessation of the barbiturate infusion.^{1,6,8,12)} The amount of barbiturate infused varies and therefore it seems to have no relations to the development of such event.^{1,6,8,12)}

Theoretically, several mechanisms can be proposed to the serum potassium imbalance in neurointensive care setting. Barbiturate can induce reversible intracellular shift of potassium by inhibiting neuronal voltage-dependant potassium currents or by decreasing lactate and pyruvate production through the inhibition of phosphofructokinase.^{2,5,7)} This can increase intracellular pH that may produce intracellular potassium shift.^{2,5,7)} Factors other than barbiturate that can affect serum potassium level include catecholamine, body temperature, acid-base balance, and usage of diuretics.⁸⁾ Endogenous catecholamine release secondary to intracranial hypertension can induce hypokalemia through β_2 -stimulation of the sodium-potassium pumps.^{1,10)} It is known that severe brain injury may induce an adrenergic stress response by two-to tenfold increase in plasma catecholamine levels.³⁾ Hypothermia is also related with hypokalemia, hypophosphatemia and hypomagnesaemia.⁹⁾ During therapeutic cooling, excessive urinary loss of potassium can be combined with hypothemic diuresis.⁹⁾

Because, in our case, the severity of brain injury was not so severe to induce endogenous catecholamine release by brainstem compression, the occurrence of rebound hyperkalemia was not correlated with recovery of brain injury. Hypothermia might have contributed to the hypokalemia, however, the recovery of body temperature has no exact relation to the rebound hyperkalemia. Other contributors such as mannitol and dopamine might have influenced the electrolyte imbalance, especially for the hypokalemia.^{4,10)} However, they are discontinued after the first attack of cardiac arrest and it is hard to say that they are responsible for successive fluctuations of potassium level. Therefore, considering the time sequences of fluctuations of serum potassium level in relation to barbiturate infusion and cessation, barbiturate is the principal cause of those events. Reciprocal changes of levels between serum potassium level and arterial blood pH seen our case can be a good evidence of intracellular shift of potassium by barbiturate effect (Figure 1).

Although such a severe hypokalemia and rebound hyperkalemia event is rare side effect of barbiturate, it is important to monitor potassium level closely during BCT as it can result in serious consequences. Once severe hypokalemia occurs, barbiturate infusion should be discontinued and potassium should be replaced slowly under intensive

monitoring of serum potassium level and electrocardiogram. Clinicians should also prepare for possible rebound hyperkalemia. Slow tapering of barbiturate after the hypokalemia might be helpful in reversing the intracellular shift of potassium for we could minimize the amount of potassium replacement and prevent rebound hyperkalemia.

Conclusion

BCT can develop fatal fluctuation of serum potassium level due to transcellular shift of potassium. Clinicians should monitor the electrolyte balance intensively during barbiturate infusion, and bear in mind potential risk of rebound hyperkalemia after the cessation of barbiturate infusion.

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