

# Hypokalemia after cessation of the therapeutic barbiturate coma- an unusual complication

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## Abstract

Barbiturate coma is one of the treatment modalities used to prevent secondary brain damage in refractory malignant intracranial tension both in traumatic and non-traumatic brain injuries. Complications such as hypotension, myocardial suppression, hepatorenal dysfunction and delayed return of consciousness have been reported following barbiturate coma therapy. In addition, potassium changes have also been reported, in particular hypokalemia during barbiturate coma therapy and a rebound hyperkalemia *after* cessation of therapy. We however report an unusual complication of refractory hypokalemia occurring after stopping barbiturate therapy. A 24-year-old patient was treated with a thiopentone infusion for management of increased intracranial pressure after severe head

injury. The patient developed persistent hypokalemia (1.6 mmol) 8 hours after withdrawing thiopentone infusion. Severe disturbance of plasma potassium balance is a rare but life-threatening complication of therapeutic barbiturate coma. We recommend that clinicians be aware of the potential occurrence of severe hypokalemia, which is rare but fatal, not only during barbiturate coma therapy but also following cessation of thiopentone infusion. We recommend close monitoring of serum potassium *during* as well as *after* discontinuing barbiturate coma therapy in order to prevent fatal complications secondary to potassium abnormalities. Further studies are needed to elucidate the precise mechanism of this clinical event.

## Introduction

Barbiturate coma is one of the treatment modalities used to prevent secondary brain damage in refractory malignant intracranial tension both in traumatic and non-traumatic brain injuries. Complications such as hypotension, myocardial suppression, hepatorenal dysfunction have been reported following barbiturate coma therapy. (1) In

addition, potassium changes have also been reported, in particular hypokalemia during barbiturate coma therapy and a rebound hyperkalemia after cessation of therapy. We however report an unusual complication of refractory hypokalemia occurring *after* stopping barbiturate therapy.

## Case description

A 24-year-old man was admitted to the neurosurgical intensive care unit following traumatic head injury. His initial GCS (Glasgow coma scale) score was 7. He was intubated for airway protection. His injuries included a traumatic extradural, subdural, subarachnoid and intracerebral hemorrhage (without midline shift) and a left tibial fracture (**Figure 1**). Intracranial pressure (ICP) monitoring was instituted and his initial ICP reading was very high (>60 mmHg).

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Measures for the prevention of secondary brain damage were instituted. This included sedation with propofol, ventilation to normocapnea, maintenance of normoglycemia, normothermia, and inotropic support (noradrenaline up to 0.1 µg/kg/min for this patient) to achieve a cerebral perfusion pressure of more than 70 mmHg. Following these measures, a repeat CT brain was done. This however showed gross midline shift. An emergency craniectomy was subsequently performed for evacuation of the intracerebral hematoma (**Figure 2**). The extradural and subdural hematomas were small and did not require any evacuation. Mannitol was also administered at regular intervals to control the ICP. Despite these measures, his ICP continued to remain elevated (>40 mmHg). Barbiturate coma therapy was therefore started due to the refractory malignant intracranial tension. The patient received a bolus dose of 250 mg of thiopentone followed by an infusion of 250 mg/hr for 20 hours in order to achieve burst suppression and to maintain the ICP <20 mmHg. The thiopentone infusion was stopped once the ICP fell to less than 20 mmHg.

Eight hours after stopping thiopentone infusion, the patient developed severe hypokalemia. The lowest measured potassium level following cessation of barbiturate therapy was 1.6 mmol/L. During this period, the patient developed a transient supraventricular tachycardia and ventricular ectopics which reverted spontaneously to sinus rhythm. Aggressive potassium replacement was commenced and only stopped when measured serum potassium levels reached 5.5 mmol/L. This subsequently normalized over 12 hours without further supplementation. Other causes which could contribute to the hypokalemia were also excluded. The patient was on minimal inotropic support, no excessive urine output was noted and his blood sugar was controlled without any insulin. His plasma biochemistry was normal and pH was within normal range. Urinary electrolytes and adrenocortical function however were not measured.

## Discussion

Barbiturate coma is one of the treatment modalities used to prevent secondary brain damage in refractory malignant intracranial tension both in traumatic and non-traumatic brain injuries. Complications such as hypotension, myocardial

suppression, hepatorenal dysfunction, immunosuppression and delayed return of consciousness have been reported following barbiturate coma therapy. However, one of the less well-recognized complications is that of severe potassium disturbance. Thiopentone has been associated with potassium imbalance for many years without any clinical significance. This effect went largely unrecognized until Schälén and his colleagues published a case series describing metabolic and electrolyte imbalances (especially refractory hypokalemia) associated with morbidity and mortality in their patients who received barbiturate coma for malignant intracranial tension. They reported a high incidence of hypokalemia (<3.5 mmol) in 38 patients (82%) who were treated with thiopentone, without any rebound hyperkalemia. (1)

Sequential occurrences of hypokalemia and rebound hyperkalemia have been reported by few authors *during* barbiturate coma therapy in the intensive care. Cairns et al reported one death in three patients who developed hypokalemia during thiopentone infusion. (2) Few of the later reports subsequently describe life-threatening arrhythmias after stopping the infusion of thiopentone. (3-5) We observe however that in our patient, the phenomena of persistent hypokalemia did not develop during barbiturate therapy but only eight hours *after* stopping therapy, with the effect lasting for 12 hours, requiring aggressive potassium replacement. We were not able to find any other similar report of this observed phenomenon in the literature.

Hypokalemia in severe head injury can be attributed to several causes. These include catecholamines, mannitol, insulin, excessive diuresis, preexisting hypokalemia, and hypothermia. These interventions and drugs are usually part of the armamentarium of neuroprotection. The potassium disturbance observed during thiopental infusion has distinct pattern with hypokalemia usually within the first 48 h, followed by the rapid development of hyperkalemia upon withdrawal or cessation of the infusion. Various theories have been proposed to explain this characteristic biphasic pattern of potassium disturbances. (5) Carlsson and his colleagues after studying the effects of thiopentone on the cerebral cortex of the rats have proposed the following possible mechanisms that can account for the observed potassium disturbances. The first mechanism can be due to thiopentone causing an inhibition of phosphofructokinase

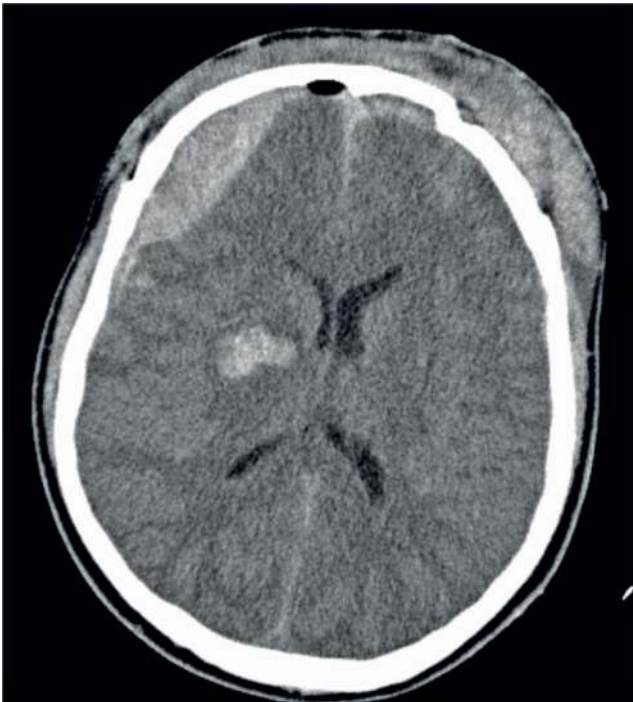
which in turn causes a decrease in intracellular lactate and pyruvate production. These results in increased intracellular pH and potassium concentration. (6)

The second possible mechanism is due to the reversible inhibition of neuronal potassium currents which is a concentration-dependent effect. This leads to a decrease in extracellular potassium. However Friedrich and his colleagues have described that this effect is less likely, as voltage-dependent potassium channels that are opened during repolarization will be inactive during barbiturate coma. A similar effect has been observed with other sedatives such as benzodiazepines without any incidence of potassium disturbances. (7) The incidence of potassium disturbance is an area for further study, as the biochemical disturbance occurs earlier than what we would expect from conventional understanding of thiopentone's pharmacology.

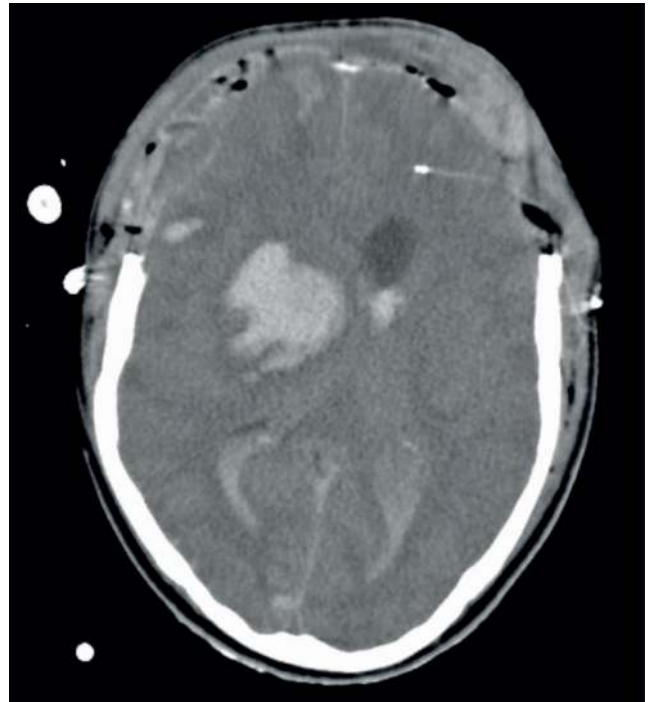
## Conclusion

In conclusion, there are many possible reasons for potassium disturbance in severely head-injured patients. The hypokalemia is usually mild and easily correctible. However, this may not be the case in patients who are on barbiturate coma. From previous case reports, the hypokalemia which commonly occurs during therapy and possibly after therapy (as seen with our patient), followed by a rebound hyperkalemia after cessation of therapy can lead to life-threatening arrhythmias. We therefore recommend that clinicians must be aware of these phenomena and monitor serum potassium closely *during* as well as *after* discontinuing barbiturate coma therapy in order to prevent fatal complications secondary to potassium abnormalities. Further studies are needed to elucidate the precise mechanism of this clinical event.

**Figure 1.** CT brain on admission to intensive care unit



**Figure 2.** CT brain - post craniectomy



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