Case Report

Life-Threatening Dyskalaemia after Barbiturate Coma Therapy: The Strategy of Management

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Abstract

Barbiturate coma therapy (BCT) is a treatment option that is used for refractory intracranial hypertension after all other options have been exhausted. Although BCT is a brain protection treatment, it also has several side effects such as hypotension, hepatic dysfunction, renal dysfunction, respiratory complications and electrolyte imbalances. One less concerning but potentially life-threatening complication of BCT is dyskalaemia. This complication could present as severe refractory hypokalaemia during the therapy with subsequent rebound hyperkalaemia after cessation of the therapy. Judicious potassium replacement during severe refractory hypokalaemia and gradual cessation of the therapy to prevent rebound hyperkalaemia are recommended strategies to deal with this complication, based on previous case series and reports. In this case report, we show that these strategies were applicable in improving severe hypokalaemia and preventing sudden, life-threatening rebound hyperkalaemia. However, even with use of these strategies, BCT patients could still present with mild, asymptomatic hyperkalaemia.

Keywords: *barbiturate coma, intracranial hypertension, hypokalemia, hyperkalemia, thiopentone*

Introduction

Barbiturate coma therapy (BCT) is the second-tier option for the treatment of refractory intracranial hypertension and can be started either before or after an emergency decompressive craniectomy, depending on the severity of the primary insult and its subsequent effects on intracranial pressure (ICP) (1). In our case, we started BCT because of persistently high ICP after an emergency decompressive craniectomy and hypertonic saline (HTS) therapy.

Despite its therapeutic effects, BCT can also lead to several complications. In one study of traumatic brain injury (TBI) patients on BCT, 87% had hepatic dysfunction, 82% had hypokalaemia, 76% had respiratory complications, 58% had arterial hypotension, 55% had infections and 47% had renal dysfunction (2). Even though the occurrence of hypokalaemia in TBI patients on BCT had been previously reported as being up to 82%, the fatal effects of the severe refractory hypokalaemia and rebound hyperkalaemia that can occur after the cessation of BCT have only recently been discovered.

The aim of this case report is to highlight the success of dyskalaemia management following BCT based on two recommended strategies: judicious potassium replacement during the severe hypokalaemic phase and a gradual cessation of the therapy to prevent life-threatening rebound hyperkalaemia.

Case Report

A 53-year-old gentleman with a known case of hypertension presented with severe TBI, a left haemothorax and a left clavicular fracture following a road traffic accident. A computed tomogram (CT) scan of the brain showed a mild acute right hemispheric subdural haemorrhage with brain contusions and a midline shift (Figure 1). He was intubated because of his Glasgow coma scale (GCS) score of 8/15 and subsequently underwent an emergency decompressive craniectomy with clots evacuation as well as external ventricular drainage insertion.

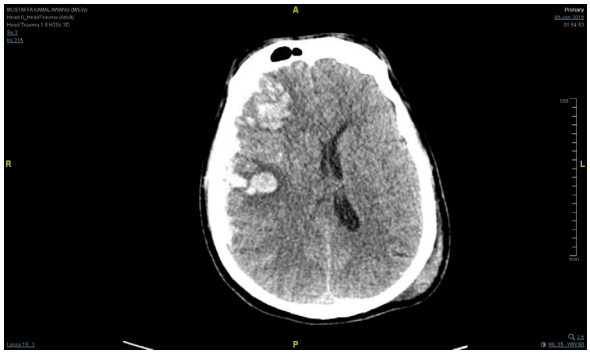

Figure 1. CT Scan of the brain on admission

Cerebral protection strategies to prevent secondary brain damage were implemented immediately after the operation, in the neurosurgical intensive care unit (Neuro ICU). These strategies included normocapnic ventilation, maintenance of normoglycaemia, therapeutic induction of normothermia, an infusion of noradrenaline and an infusion of sedation using propofol and fentanyl to achieve the targeted cerebral perfusion pressure (CPP) of more than 60 mmHg. Nevertheless, his ICP was persistently very high—up to 40 mmHg–55 mmHg—and did not respond to the treatments, including the HTS 7.4% infusion at a rate of 30 ml/hour.

Therefore, BCT using sodium thiopentone (STP) was initiated ten hours after the surgery, while the patient was still on HTS 7.4% infusion. An intravenous (IV) bolus of 350 mg STP was slowly given over 10 minutes and was followed by a maintenance dose between 3 mg/kg/hour–5.5 mg/kg/hour in titration, aiming to achieve bispectral index ≤20, ICP ≤20 mmHg and burst suppression on the electroencephalogram monitor. Serum electrolytes were closely monitored every six hours for hypernatremia and hypokalaemia. HTS 7.4% was stopped after 29 hours of surgery due to hypernatremia up to 160 mmol/L. The serum potassium level prior to BCT was 4.3 mmol/L.

Hypokalaemia was first detected 18 hours after BCT with serum potassium level of 3.2 mmol/L. At the 36th hour of infusion, the lowest potassium level recorded was 1.6 mmol/L with the electrocardiograph (ECG) showing inverted T waves on leads V2–V6 and flattened T waves on leads 1, aVL and V1. Potassium replacement with IV potassium chloride was started during the event. We planned an aggressive intermittent bolus and ongoing slow maintenance replacement for the patient with the aim of achieving the minimum potassium level of 3.0 mmol/L. In total, 248.6 mmol of potassium chloride was given during the acute hypokalaemic phase.

The other factors that also potentially contributed to hypokalaemia in this patient were compensatory metabolic alkalosis on arterial blood gases (ABG) and the noradrenaline infusion, which was titrated at the lower dosage between 0.13 mg/min–0.67 mg/min in order to maintain mean arterial pressure (MAP) and CPP. However, the acid-base imbalance was subsequently improved and the noradrenaline infusion was also subsequently stopped after MAP was maintained within normal value. HTS could also contribute to hypokalaemia, but it was stopped earlier because of hypernatremia. There were no other potential factors that might lead to hypokalaemia in this patient, such as diarrhoea; hypothermia; hypomagnesaemia; renal failure; a high volume of nasogastric aspiration; underlying endocrinal pathologies such as Conn's syndrome or Cushing's syndrome; or drug-induced hypokalaemia such as diuretic, insulin, carbenicillin, gentamicin, corticosteroids or amphoteracin B.

On the third day of the barbiturate coma, the patient's potassium level was gradually improving with a level between 3.0 mmol/L–4.0 mmol/L, despite the fact that no further correction was given. The ECG also indicated a return to sinus rhythm. The potassium level continued to increase up to 4.3 mmol/L, despite the continued infusion of STP at 5.5 mg/kg/hour. On the fifth day of BCT, a repeat CT scan of the brain showed a right middle cerebral artery (MCA) territory infarct with uncal herniation. The basal cistern was effaced, but there was no worsening of the right-sided contusion. During that time, the ICP was still on the high side, between 35–50 mmHg. The patient's pupils were not reactive and were unequal on both sides.

On the same day, after the subsequent ICP showed a trend of reduction to between 18 mmHg–30 mmHg, the neurosurgical team decided to terminate the BCT. In view of our concern of potential rebound hyperkalaemia following the sudden cessation of barbiturate coma, we planned to taper off the STP infusion gradually. It was initially halved to 2.6 mg/kg/hour and slowly reduced by 0.3 mg/kg/hour every 2 hours. The infusion was totally withheld after 21 hours of the gradual tapering process. During this period, two peaks of hyperkalaemia were seen. There were no observed ECG changes of tall T waves. The highest potassium level was 5.6 mmol/L, which responded to the cocktail lytic regime treatment comprised of 2 mmol of IV calcium gluconate, 10 units of IV actrapid and 50 ml of IV dextrose 50%. The potassium level normalised after the treatment. During this period, the ABG showed mild compensated metabolic acidosis. The sequence of potassium level changes throughout BCT is shown in Figure 2. Subsequent blood gases and electrolytes were normal throughout the patient's stay in the Neuro ICU. His condition was gradually improved, and the best GCS was 7 with tracheostomy in situ (E4 V [tracheostomy] M3). He was successfully discharged from the Neuro ICU to the normal ward after three weeks of Neuro ICU stay.

Discussion

BCT is an effective treatment method for severe intracranial hypertension patients. A review of 10 years' experience of BCT in severe brain injury patients showed that a group treated with BCT had better good outcome rates (Glasgow outcome scale = 4 and 5) at three months after insult and better one-year survival rates than a group without BCT (3). The mortality among patients on BCT was previously reported at 47.4% and was mainly caused by an untreatable increase in ICP. In only 2.6% of patients, the mortality may have been influenced by fatal outcomes of BCT complications (2). Among the barbiturates that could be used for BCT, sodium thiopentone and pentobarbital are the two most common types that have been widely used.

Dyskalaemia is less concerning than other BCT complications, even though Schalen et al. documented that 82% of TBI patients treated with BCT using thiopentone developed hypokalaemia. However, severe hypokalaemia (serum potassium < 2.0 mmol/L) occurred in only 25.8% of patients. The fluctuation of potassium during titration and during an interruption dose of thiopentone infusion has also been observed in this study, but the study did not emphasise on any serious problems (2). In another recent retrospective study, Ng et al. reported that 89.4% of patients on thiopentone BCT for refractory intracranial hypertension developed hypokalaemia after induction of the therapy and severe hypokalaemia was reported in only 23.4% of patients. In this study, 34% of patients developed hyperkalaemia during the weaning of BCT (4).

The onset of hypokalaemia after the initiation of BCT and the subsequent onset of hyperkalaemia after the cessation of BCT was varied. Based on a recent retrospective review on 47 patients who received BCT, the median onset time of severe hypokalaemia was 11 (6–23) hours after induction of BCT and the median time to lowest serum potassium levels was 25 (15–41) hours. The median onset time of hyperkalaemia was 31 (25–44) hours after cessation with the peak potassium levels occurring at a median time of 31 (28–56) hours. This review recorded that the mean serum potassium before cessation was 3.1 ± 0.9 mmol/L and the mean peak serum potassium was 6.2 ± 0.8 mmol/L after cessation. This was the only review that applied slow weaning of the infusion over 12–24 hours (4). In other reports that applied an abrupt cessation of BCT, the fastest onset of hyperkalaemia documented was 2 hours after cessation, and the serum potassium level increased very fast—from 4.7 mmol/L–8.9 mmol/L within only four hours (5). In our case, the onset of hypokalaemia was initially recorded after 18 hours of BCT, and within 21 hours of weaning the infusion, only two peaks of mild hyperkalaemia were recorded. There was no other episode of hyperkalaemia after full cessation of the therapy.

The issue of dyskalaemia following BCT has become a serious concern after a few case reports described fatal complications of either severe resistant hypokalaemia following induction of BCT or rebound hyperkalaemia after cessation. Cairns et al. reported three cases of dyskalaemia following thiopentone BCT. This report highlighted that severe hypokalaemia resistant to potassium therapy may be seen during thiopentone BCT and that life-threatening rebound hyperkalaemia may occur following the cessation of the infusion. The report also highlighted that abrupt cessation of the thiopentone infusion might be the cause of rebound hyperkalaemia and suggested to

tolerate asymptomatic hypokalaemia to prevent this complication (6). Neil et al. also reported the same issue and suggested a less aggressive treatment of hypokalaemia that occurs during thiopental infusion, with a tapering dose used on cessation to limit the rebound phenomenon. There were some other variants of dyskalaemia that have been reported like persistent refractory hypokalaemia, even a few hours after withdrawing thiopentone infusion (7), and refractory hyperkalaemia following the reintroduction of the pentobarbital infusion while it was still in rebound hyperkalaemia following cessation of the initial infusion (8).

Most of the case reports practiced aggressive potassium replacement, and only one report by Ng et al. mentioned the practice of gradual cessation of BCT over 12–24 hours. They recommended being cautious when correcting the hypokalaemia, because the risk of hyperkalaemia following cessation was significantly associated with the total dose of replacement potassium. Their mean potassium replacement of patients who developed hyperkalaemia was significantly higher than those who did not (230 ± 135 mmol versus 66 ± 70 mmol). This report suggested that a lower potassium replacement target threshold of 3.0 mmol/l might be appropriate in the absence of cardiac arrhythmias. Controlled weaning of BCT, instead of abrupt termination, was recommended, and frequent serum potassium monitoring up to 72 hours following cessation is warranted (4). In other reports that applied abrupt cessation and subsequently patient developed life-threatening hyperkalaemia, the management required a combination of medical treatment and renal dialysis (5).

In our case, we have been aware of the potential of dyskalaemia from the beginning and have been planning to use those management strategies. We managed to correct the hypokalaemia from 1.6 mmol/L, the lowest value, up to 3 mmol/L–4 mmol/L before cessation, with a total replacement of 248.6 mmol of potassium chloride. Our gradual weaning started with a reduction of the infusion dosage to half (5.5 mg/kg/hour–2.6 mg/kg/hour), before further reductions by 0.3 mg/kg/hour every two hours for total duration of 21 hours. During the period of gradual weaning, there were still two peaks of hyperkalaemia recorded, with the highest peak being 5.6 mmol/L, but the hyperkalaemia responded to our medical therapy. There was no other documented hyperkalaemia after complete cessation of the therapy. The sequence of serum potassium level changes is shown in Figure 2.

There are several mechanisms that may explain the occurrence of dyskalaemia as a result of thiopentone infusion. Thiopentone inhibits voltage-dependant potassium currents, which causes intracellular sequestration of potassium (9). It also inhibits phosphofructokinase, causing a reduction of intracellular pyruvate and lactate production, increasing intracellular pH and then resulting in a shift of potassium towards intracellular compartment (10). The subsequent

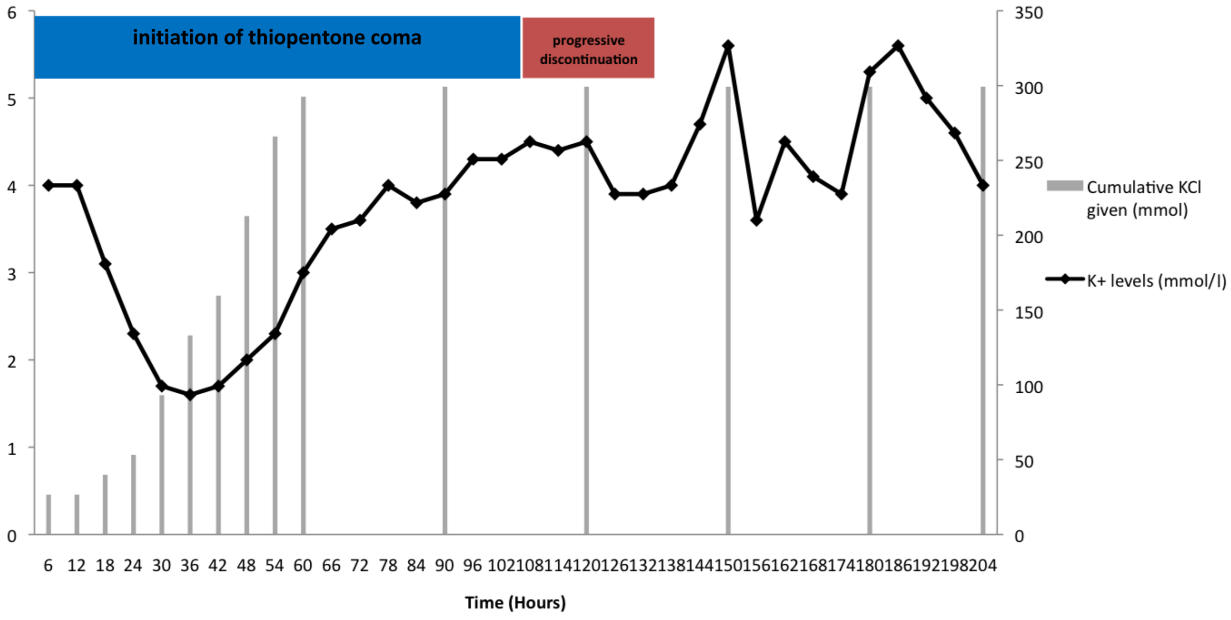

Figure 2. Time course of changes in serum potassium level with cumulative potassium replacement.

hyperkalaemia event following the cessation of BCT may be due to the reduction of barbiturate-induced Na^+-K^+-ATPase activity, resulting in extracellular potassium redistribution (5).

In comparison to previous reports, we have already anticipated the potential of dyskalaemia complications following BCT and prospectively planned ahead the strategies to treat it. We proved that judicious potassium replacement for severe hypokalaemia with a total of about 250 mmol of potassium chloride could improve the potassium level between 3 mmol/L–4 mmol/L, and gradual cessation lasting up to 21 hours could prevent life-threatening rebound hyperkalaemia. Nevertheless, mild hyperkalaemia was still present during the weaning process. This was most likely because our total dose of potassium replacement was still slightly high. If we based our treatment strategy on previous reports that mentioned a mean potassium replacement of 66 ± 70 mmol in a group without hyperkalaemia complications following BCT, we should try to limit the replacement of potassium to probably less than 100 mmol and prolong the gradual weaning of the therapy in the future.

Conclusion

Dyskalaemia complications during BCT can be fatal to patients. Our case report shows that judicious potassium replacement and gradual cessation of the therapy are key strategies for the prevention of life-threatening dyskalaemia. However, dyskalaemia could still present with mild and asymptomatic hyperkalaemia.

Authors' Contributions

Conception and design: YBT, WMNWH
Analysis and interpretation of the data: YBT, WMNWH
Drafting of the article: YBT, WMNWH
Critical revision of the article for important intellectual content: YBT, WMNWH, TYC, ARIG
Final approval of the article: YBT, WMNWH, TYC, ARIG
Provision of study materials or patients: YBT, WMNWH, TYC, ARIG
Administrative, technical, or logistic support: WMNWH
Collection and assembly of data: YBT

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References

1. Latorre JGS, Greer DM. Management of acute intracranial hypertension. A review. *The Neurologist*. 2009;**15**:193–207. 1. https://doi.org/10.1097/NRL.0b013e31819f956a

2. Schalen W, Messeter K, Nordstrom CH. Complications and side effects during thiopentone therapy in patients with severe head injuries. *Acta Anaesthesiol Scand*. 1992;**36**:369–377. https://doi.org/10.1111/j.1399-6576.1992.tb03483.x

3. Kim YI, Park SW, Nam TK, Park YS, Min BK, Hwang SN. The effect of barbiturate coma therapy for the patients with severe intracranial hypertension: a 10-year experience. *J Korean Neurosurg Soc*. 2008;**44**:141–145. https://doi.org/10.3340/jkns.2008.44.3.141

4. Ng SY, Chin KJ, Kwek TK. Dyskalaemia associated with thiopentone barbiturate coma for refractory intracranial hypertension: a case series. *Intensive Care Med*. 2011;**37**:1285–1289. https://doi.org/10.1007/s00134-011-2240-2

5. Jung JY, Lee C, Ro H, Kim HS, Joo KW, Kim Y, et al. Sequential occurrence of life-threatening hypokalemia and rebound hyperkalemia associated with barbiturate coma therapy. *Clin Nephrol*. 2009;**71**:333–337. https://doi.org/10.5414/CNP71333

6. Cairns CJ, Thomas B, Fletcher S, Parr MJ, Finfer SR. Life-threatening hyperkalaemia following therapeutic barbiturate coma. *Intensive Care Med*. 2002;**28**:1357–1360. https://doi.org/10.1007/s00134-002-1399-y

7. Hassan WMNW, Najid NM, Muslim HS, Ghani ARI. Refractory hypokalemia during barbiturate coma therapy used for treating refractory intracranial hypertension in traumatic brain injury. *Asian J of Neurosurgery*. 2015;**10**:149–151. https://doi.org/10.4103/1793-5482.151528

8. Greenwood BC, Adams CD, Khalpey ZI, Hou PC. Barbiturate coma: rebound and refractory hyperkalemia. *Case Reports in Clinical Medicine*. 2014;**3**:304–308. https://doi.org/10.4236/crcm.2014.35067

9. Friedrich P, Urban B. Interaction of intravenous anaesthetics with human neuronal potassium currents in relation to clinical concentration. *Anesthesiology*. 1999;**91**:1853–1860. https://doi.org/10.1097/00000542-199912000-00040

10. Carlsson C, Harp JR, Siesjo BK. Metabolic changes in the cerebral cortex of the rat induced by intravenous pentothalsodium. *Acta Anesthesiol Scand*. 1975;**57**:1–17. https://doi.org/10.1111/j.1399-6576.1975.tb05407.x