

Successful treatment of Propofol induced refractory status epilepticus with calcium gluconate

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Abstract

Propofol-induced seizure-like phenomena (SLP) is well described following anesthesia or sedation with this drug. The episode is usually benign and responds well to standard anti-convulsant therapy. The occurrence of status epilepticus refractory to conventional treatment and successful treatment with intravenous Calcium has been rarely reported. We describe a patient who developed status epilepticus refractory to standard treatment during recovery from Propofol anesthesia and successfully treated with intravenous calcium. The report highlights a potentially harmful complication of the Propofol and suggests that intra-venous calcium may be effective as an anticonvulsant treatment for Propofol-induced status epilepticus.

Key words: Propofol, seizure, calcium, status epilepticus

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Introduction

Seizure like phenomena is a known complication of Propofol following sedation or anesthesia [1,2] Propofol induced status epilepticus is rare complication and could be detrimental. Conventional treatment to abort drug induced status epilepticus could be ineffective. We present a 40 day old infant who received Propofol anesthesia for her-nia repair and during recovery period developed seizure like phenomena which progressed to status epilepticus refractory to standard treatment. Empirical intravenous calcium bolus given resulted in successful seizure cessation. This report stresses on the importance of rare and rather serious complication associated with Propofol anesthesia and suggests that calcium may be an effective intravenous treatment strategy.

Case Report

A 40 day old male infant presented to our institution for urgent repair of right inguinal hernia under general anesthesia. Preoperative evaluation revealed a completely healthy infant who was born via NSVD at term gestation, birth weight 3.37 Kg, with uneventful natal and postnatal period and no history of neurological disease, or a seizure disorder. Preoperative investigations showed normal values of CBC, serum electrolytes, ECG and chest X-ray. Anesthesia was induced with Propofol intravenously (IV) and maintained with a continuous Propofol infusion and low dose isoflurane. Several minutes after arrival in the Recovery care unit the patient began to have symmetrical tonic-clonic seizure refractory to all standard intravenous medications which included in sequence: Diazepam, Midazolam, and Propofol. Patient's condition deteriorated further and he was intubated to maintain airway. Calcium gluconate (10%) was given in a dose of 1.5 ml/Kg empirically in assumption of hypocalcaemia. Status has resulted in successful cessation. Interestingly metabolic and electrolyte screen including total serum calcium at the time of the seizures showed no evidence of a metabolic cause, and his blood pressure was normal for age.

Patient was transferred to the pediatric intensive care unit (PICU), and extubated shortly thereafter and remained hemodynamically stable without evidence of seizure like episodes throughout PICU course. CT brain study was unremarkable.

Patient was then transferred to the pediatric ward for further 36 hours observation, He made an uneventful recovery from his surgical procedure. Neurological assessment at hospital discharge revealed complete recovery.

Discussion

Propofol has many favorable pharmacological characteristics, including lack of accumulation and the relatively short recovery time, which make it one of the most popular sedative and anesthetic agent used for minor and emergency surgery [3,4] Propofol is also considered as a promising agent in treating status epilepticus owing to its modulating property on γ -aminobutyric acid receptors [5-7]. In contrast, this agent has also been associated with a variety of neuroexcitatory events including: opisthotonos, muscle rigidity, myoclonus, and seizures [8] collectively termed as seizure-like phenomenon (SLP) [9]. The Committee on the Safety of Medicines in the United Kingdom has estimated the incidence of seizures associated with Propofol to be 1 in 47 000 patients [10]. This adverse neurologic events occur during induction, anesthesia termination, or delayed up to 5 days after the surgical procedure [8,9] usually characterized by self limited grand-mal type seizures occurring unexpectedly in patients with no previous history of epilepsy. All of the patients recovered without sequelae [9].

Despite several case reports and systematic review, there is no clear consensus regarding risk factors, prevention and management of such adverse events, furthermore it is not known whether this "seizure activity" is primarily, secondarily, or not at all a cerebral cortical event [11-13].

Calcium is a very important ion for the normal functioning of nervous system. Any condition such as acute illness, surgical procedure or drugs ingestion could decrease the availability of calcium in the extracellular fluid which could result in increase the excitability of the nerve cells.

Propofol is one of the drug that might have negative relationship with Ca^{++} , by modifying the sarcoplasmic permeability to Ca^{++} , thus reducing its availability at the cellular level. Propofol may cause a decrease in inflow and a release of Ca^{++} at the sarcolemma level, a reduction of Ca^{++} availability for contraction, and a lower sensibility of myofibrillae to Ca^{++} ions. [14,15]. In one study by Tritapep et al demonstrated that simultaneous administration of calcium chloride has counteracted the undesirable hemodynamic effect of Propofol in Patients undergoing Coronary artery bypass grafting [16].

We hypothesized that Propofol proconvulsant mechanism could result from its effect on the availability of extracellular Ca^{++} level which would explain the resistance nature of the seizure and immediate response to calcium therapy.

Being a case report the possibility of the observer and selection bias is quite possible for example the combinations of other anesthetic drug like isoflurane in our case could have resulted in clinically evident seizures,[17] making the sole role of Propofol impossible. However the frequent reported association between seizure and Propofol plus the normal electrolytes including serum calcium level and negative neurologic assessment in our case, probably made the Propofol the most likely cause.

The seizure attack associated with our patient's presentation as side effect of Propofol are similarly described in previous reports. However the severity and refractory nature of the seizure and the unexpected response to calcium bolus therapy is indeed rarely reported. Since usage of Propofol for emergency surgery is quite common and in the future probably will be even more common, we provide another evidence that Propofol is not totally safe and might be associated with serious neuroexcitatory sequelae which could be disturbing, frightening to the child's parents and all health care providers. Furthermore this undesirable effect of Propofol could result in increase in the cost of treatment for two reasons. These patients have to be admitted to the intensive care unit and will need further observation and follow-up with subsequent detailed neurologic testing.

Conclusion

We propose that the post anesthetic status epilepticus in our patient is due to acute changes in ionized calcium level induced by Propofol itself, which may account for the refractory nature of the seizure and the immediate response to calcium infusion. We are reporting this case highlighting the role of propofol on calcium homeostasis and clinical significance of this complication. In the mean time calcium bolus therapy should be considered for Propofol induced status epilepticus when standard regimens fail

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