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Intraoperative refractory status epilepticus caused by propofol -a case report-

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Case Report

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Background: Status epilepticus, when continued despite the administration of two antiepileptic drugs, is called refractory status epilepticus (RSE). The seizure-like phenomenon due to propofol is widely reported in the literature. However, RSE caused by propofol is rare and is a diagnostic dilemma.
Case: A 44-year-old male patient presented with RSE during the intraoperative period and was under general anesthesia on propofol infusion. The seizure was resistant to benzodiazepines and phenytoin. Thereafter, the seizure subsided after the discontinuation of propofol infusion, and the patient was shifted to fentanyl and dexmedetomidine infusion for the maintenance of anesthesia. The postoperative follow-up was uneventful.
Conclusions: This article focuses on the management of intractable intraoperative seizure and highlights the need for the exploration of seizure characteristics caused by propofol.

Keywords: Anesthesia; Intraoperative complications; Myoclonus; Propofol; Status epilepticus; Tonic-clonic seizure.

Propofol is the most popular drug used for the induction and maintenance of anesthesia, but causes excitatory activities, such as myoclonus, opisthotonus, and rarely, generalized seizures [1]. Prolonged non-resolving seizure activity is termed status epilepticus (SE) and is a medical emergency with significant associated morbidity and mortality. Pharmacological management is done with benzodiazepines and antiepileptic drugs, along with prompt resuscitation and source control. SE, when continued despite the administration of two antiepileptic drugs, is called refractory status epilepticus (RSE). The management of RSE includes the induction of general anesthesia with propofol, thiopentone, midazolam, or ketamine. However, management becomes intricate when RSE is caused by propofol. We report here a case of intraoperative RSE caused by propofol.

The patient has provided written informed consent for publication of this case report. This manuscript adheres to the applicable Enhancing the QUAlity and Transparency Of health Research (EQUATOR) guideline.

Case Report

A 44-year-old male patient (weight 60 kg) was posted for C2–C5 astrocytoma excision under general anesthesia. The surgery was performed at All India Institute of Medical Sciences Patna, India in 2019. The patient did not have any coexisting disease or history of seizure. Anesthesia was induced with injection of propofol, fentanyl, and vecuronium followed by tracheal intubation. The propofol infusion at a rate of 75–100 μg/kg/min was

started for the maintenance of anesthesia as motor and somatosensory evoked potential monitoring was planned for the patient. The bispectral index (BIS), invasive blood pressure, and central venous pressure were also monitored in addition to standard monitoring. Furthermore, the patient was made prone for surgery. Thirty minutes after the start of propofol infusion, as the surgeon was dissecting the superficial muscular layers after skin incision, the patient developed generalized tonic–clonic seizure (GTCS) involving all four limbs and truncal muscles. A sudden increase in blood pressure, heart rate, end tidal CO_2, and BIS were also noted. The injection of 2 mg midazolam was then immediately given intravenously (IV). Although the intensity of seizure decreased, GTCS continued, for which a repeat dose of midazolam was given, but in vain. As the seizure was not controlled, a loading dose of 15 mg/kg phenytoin was given IV over 20 minutes. Nonetheless, the seizure continued with a seizure-free interval of 5 minutes. The injection of 250 mg thiopentone was then administered IV as a last resort for treating SE, which successfully aborted the episode for approximately 20 minutes, only to reappear again. Meanwhile, investigations such as electrolytes and arterial blood gases (ABG) were done to rule out aggravating factors. ABG indicated metabolic acidosis with hyperlactatemia, and electrolytes were within the normal range. A provisional diagnosis of propofol-induced seizure was made, and propofol infusion was discontinued. Anesthesia was then maintained on fentanyl, dexmedetomidine infusion and isoflurane to maintain a minimum alveolar concentration of 0.5–0.8, and surgery was allowed to proceed. The rest of the intraoperative and postoperative periods were uneventful, and the postoperative computerized tomography of the brain and electroencephalogram were within normal limits. The patient was symptom-free after three months of follow-up.

Discussion

Propofol is widely used as an induction agent for general anesthesia, and its common side effects are hypotension, respiratory depression, and local intravascular pain at the injection site. Neurological complications caused by propofol are widely reported and include GTCS, focal motor seizures, increased tone with twitching and rhythmic movements, opisthotonus and involuntary movements, collectively termed as seizure-like phenomenon (SLP). The mechanism of SLP due to propofol is mostly unknown, but potentially due to the imbalance between the activity of excitatory and inhibitory neurons in the GABA pathway [2]. Propofol-induced SLP does not have any fixed pattern of occurrence with respect to timing, duration, clinical presentation, age group, and the health of the patient involved [1]. In addition, no clear consensus exists regarding the prevention and management of such adverse events.

Walder et al. [1], in a systemic review, analyzed 81 cases of SLP of which one of the principal findings was the predominance of SLP during induction, emergence, or delay after anesthesia and sedation. Only two cases of its occurrence arose during maintenance [3,4]. The lower incidence of SLP during maintenance of anesthesia resulted from masking by neuromuscular blockage (NMB), a steady state level of propofol concentration, and less cerebral excitation [1]. Our case was unique as it occurred during the maintenance phase and was presented as SE, which was refractory to treatment by two antiepileptic drugs. Only a few reported cases of propofol-induced SE have been available, most of which emerged in the postoperative period. Additionally, a report from Japan stated that prolonged GTCS was initiated 10 minutes after propofol infusion after the brachial plexus block [5]. One case of propofol-induced RSE during general anesthesia has also been reported in a patient with benign epilepsy with centrotemporal spikes, which lasted for 14 hours [6].

RSE is a condition where SE continues despite the administration of two antiepileptic drugs (e.g., benzodiazepines and phenytoin) and is associated with a high risk of complications. Complications of RSE include excitotoxic CNS injury, hyperthermia, pulmonary edema, arrhythmias, cardiovascular collapse, metabolic derangement, acute kidney and liver injury, rhabdomyolysis, and fractures [7]. Moreover, RSE has a high-mortality rate, and less than one-third of patients return to their premorbid level of functioning [8].

Seizures in the intraoperative period are difficult to diagnose when NMB is used, but suggestive signs include tachycardia, hypertension, increased end tidal CO_2, pupillary dilatation, increased oxygen consumption, and increased muscle tone [7]. Management includes the administration of antiepileptic drugs and the correction of precipitant factors. In our case, the seizure was apparent because we did not use NMB in the maintenance of anesthesia. The treatment of RSE includes administering general anesthesia with propofol, thiopentone, midazolam, or ketamine. However, our patient was already on high-dose propofol infusion when he developed RSE. As no precipitating factors were found, we opted to discontinue propofol and started dexmedetomidine and fentanyl for the maintenance of anesthesia, which stopped the seizure episodes.

Apart from being used as an induction agent for general anesthesia, propofol is also widely utilized in the treatment of seizure due to its anticonvulsive properties. Nevertheless, rare case reports of the pro-convulsant effects of propofol [1–6] emphasize the need for the exploration of seizure characteristics caused by

propofol.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Abhyuday Kumar (Conceptualization; Validation; Visualization; Writing – original draft)
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