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Case Report

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Status Epilepticus During Recovery from General Anesthesia

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ABSTRACT

Propofol is an anesthetic agent commonly used for sedation and induction and/or maintenance of general anesthesia and presents an inhibitory effect on the excitatory neurotransmitters through GABA receptors. Although propofol is an agent that can be used to treat status epilepticus because of its anticonvulsant property, it may cause epileptiform convulsions, as reported in the literature. In this case report, a young patient's epileptiform convulsions after administering a single dose of propofol injection for general anesthesia are presented. Due to uncontrolled epilepsy episodes following extubation, the patient was taken to intensive care. The patient regained consciousness, and epileptic attacks were controlled on the 4th day of intensive, was taken to the neurology service. We consider that this case is noteworthy concerning the association between propofol and epilepsy in anesthesia. Thus, this study aimed to draw attention to propofol in patients with a history of epilepsy.

Keywords:

Status epilepticus, General anesthesia, Propofol.

Introduction

Propofol is an intravenous sedative-hypnotic agent commonly used for short and/or long-term sedation purposes and induction and/or maintenance of general anesthesia 1980s [1]. It shows an inhibitory effect through GABA receptors. Although propofol is also defined as an anticonvulsant agent and used in the treatment of status epilepticus, sometimes, despite being rare, it may cause central nervous system excitation [2]. There are cases in the literature revealing that propofol may cause seizure or seizure-like phenomena. In most cases, a history of an epileptic disease does not exist [3]. The patients' neurological side effects are often observed for a short period, although some cases last for weeks [4].

This case report presents an otherwise healthy young male patient with long-lasting generalized tonic-clonic seizure following general anesthesia. Once the patient had epilepsy-like symptoms after local anesthesia, it was planned to have a dental operation under general anesthesia.

Case Report

A 23-year-old male patient was admitted to our outpatient clinic for tooth extraction. He had a history of seizure-like convulsions after being injected 40 mg of articaine for local anesthesia while having his tooth pulled two months ago. He defined loss of consciousness and two convulsions five minutes apart that lasted for one minute and 40 seconds immediately after the injection. While the brain CT was normal, an epileptic focus was detected in the EEG taken while the patient was resting and awake. Following the neurological examination, Levetiracetam 500 mg (b.i.d) was started. Given that these convulsions could be a possible allergic reaction against local anesthetics, the tooth extraction operation was planned to be administered later under general anesthesia according to anesthesia and allergy departments' common suggestion. Medical treatment was continued during the 2-months until the planned operation, and the patient had no epileptic seizures. After 1 mg midazolam for premedication, 2 mcg.kg^{-1} fentanyl, 2.5 mg.kg^{-1} propofol, and 0.9 mcg.kg^{-1} rocuronium were administered for induction, and the patient was intubated after two minutes on the day of surgery. Anesthesia was maintained with 50% oxygen/air mixture in 6% desflurane. Intraoperative blood pressures varied within the 90/65 mmHg and 120/80 mmHg range. Heart rate was 95-110 pulse-minute^{-1} range. The saturation was approximately 98-99% and end-tidal carbon dioxide pressure varied within the 30-35 mmHg range.

The operation took one hour and was completed without any complications. Following the procedure, the patient was extubated following i.v. 4 mg.kg^{-1} sugammadex. One minute after extubation, he started shivering and, in two minutes, had a generalized tonic-clonic seizure, which lasted for 50 seconds despite i.v. 1 mg midazolam. After four minutes, the patient once again had a generalized tonic-clonic seizure, so i.v. 5 mg diazepam was administered immediately, and the episode lasted for one minute. The patient lost consciousness, and there was no response to a painful stimulus. The patient had a third generalized tonic-clonic seizure, which lasted for 10-15 seconds within an hour following the second seizure. He underwent another neurology consultation, after which Phenytoin 1250 mg was started. During a 3-hour watch, the patient was unconscious, there was no response to a painful stimulus, but his vitals were stable. Blood tests revealed: glucose: 134 mg.dl^{-1}, Hgb: 10.3 g.dl^{-1}, leukocyte: 4,150 /mm^3, thrombocyte: 1,89,000/mm^3, BUN: 5.7 mg.dl^{-1}, Cr: 0.85 mg.dl^{-1}, Na: 139 mEq.liter^{-1}, K: 4.21 mEq.liter^{-1}, Ca: 8.5 mg.dl^{-1}, Cl: 105.9 mEq.liter^{-1}, blood ammonia levels: 55.7 ug.dl^{-1}, AST: 17 U.L^{-1}, ALT: 21 U.L^{-1}. There was no pathology in the patient's brain CT examination.

During the observation period, the patient was unconscious and again intubated and taken to the ICU. In the ICU, the patient was sedated with 3 mg.kg.hour^{-1} propofol infusion for 24 hours. As his epileptic seizures continued, 300 mg topiramate was administered as loading treatment. Along with levetiracetam treatment, 100 mg zonisamide (oral) was ordered for daily medication on the first day of ICU. The patient had five seizures on the second day of ICU, and all of them lasted for around 15 seconds. The convulsions continued following the extubation; accordingly, 2 mg.hour^{-1} Midazolam infusion was started. He had two more seizures under infusion treatment. On the third day of the ICU, the number of seizures decreased to two seizures per day. However, as the seizures did not stop, MRI was ordered, and no acute pathology was detected. Midazolam infusion was ceased, and 2 mg.day^{-1} clonazepam drops were started. The patient was unconscious for the following four days at the ICU. On the fourth day of the ICU, the patient regained consciousness, and the seizures were taken control. Thus, the patient was taken to the neurology service. As his epileptic seizures did not continue, the patient was discharged with medical treatments (i.e., levetiracetam, zonisamide, clonazepam) following the neurology service's first day of follow-up. Allergy tests to propofol, lidocaine, rocuronium and fentanyl revealed that the patient had no allergy to these agents.

Pharmacogenetic tests were conducted to understand whether there was a drug metabolism-related abnormality. Especially P-glycoprotein DNA variants might implicate a possible role in propofol metabolism [5,6]. CYP2C19 gene*2-*3-*17 haplotypes, CYP3A4 gene *1B haplotype and CYP2D6 gene *4 haplotype and P-glycoprotein (MDR1) gene c.3435C>T variant was investigated using peripheral blood DNA of the patient.

DNA variant analysis

Genomic DNA was isolated from a peripheral blood sample with silica-colon extraction (Qiagen, Germany) method. Target DNA variants were determined using the real-time quantitative PCR method with hybridization probes (LightSnip Kit, Roche, Germany). Melting curve analysis of probes was performed with LightCycler 480 SW1.5 (Roche, Germany) software. Target gene variants were as follows: CYP2C19 gene*2-*3-*17 haplotypes, CYP3A4 gene *1B haplotype, CYP2D6 gene *4 haplotype and P-glycoprotein (MDR1) gene c.3435C>T variant.

Test results showed that the patient had a heterozygous haplotype of P-glycoprotein (c.3435C>T) and CYP3A4*1B variants. The patient needed another operation for a patella fracture due to a traffic accident approximately one year later. Anesthesia was induced by pentothal 5 mg.kg^{-1}, rocuronium 0.6 mg.kg^{-1}, fentanyl l 1 mcg.kg^{-1} and was maintained with 2% sevoflurane in 40% O_2/air and 0.1 mcg.kg^{-1}.min^{-1} remifentanil. Intraoperative hemodynamics and vital signs were normal. After three hours of surgery, he was transferred to the intensive care unit intubated. The patient was sedated with midazolam and fentanyl in the intensive care unit and extubated after two hours. One day later, he was transferred to the orthopedic service without any problem. The patient's consent was obtained for this case study.

Discussion and Conclusion

Our patient with no history of systemic disease had epileptiform convulsions starting with articaine local anesthesia and induced by propofol injection for general anesthesia.

Articaine (4-methyl-3-[2-(propylamino)-propanamide]-2-thiophene-carboxylic acid, methyl ester hydrochloride) is a relatively new amide local anesthetic popularly used for dental procedures. It contains a thiophene ring, allowing more excellent lipid solubility and potency by causing a more significant portion of an administered dose to enter the neurons. It is a unique amide anesthetic containing an ester group, allowing inactivation by hydrolyzation with unspecific blood esterases inactivated into an inactive metabolite by serum esterases. This is a fast process decreasing the risk of systemic toxicity and overdose, even after repeated injection making Articaine one of the safer local anesthetics. Controversy exists concerning its clinical safety, although there is no conclusive evidence demonstrating neurotoxicity in dental procedures [7].

Propofol is a commonly used sedative-hypnotic medication worldwide with anticonvulsant features [1]. The frequent side-effects based on propofol administration are hypotension, pain, itch and paresthesia at the administration area. Although the central nervous system's effects are less than 51 in the literature, only 0.1% of the patients may develop convulsions and epileptiform behaviors. While presenting this case, we would like to show that propofol used in treating status epilepticus may sometimes, although rare, cause a seizure-like phenomenon. In this specific case, the patient was administered propofol; and following extubation, the patient had a generalized tonic-clonic seizure. These epileptiform behaviors might be caused or deepen the existing epileptic attack by propofol. These excitatory findings arise from propofol may come up during postoperative recovery after analgesic consumption, as well as during anesthesia induction [8]. However, we consider that the reason for these epileptic episodes may happen after desflurane-based anesthesia.

The mechanisms of the side effects of propofol have not been clarified in the literature. Anticonvulsant and proconvulsant effects of propofol are mostly related to the dose. High doses of the medication reduce the cortex and subcortex's influence, consequently generating an anticonvulsant effect. On the other hand, only the inhibitory subcortex is affected with low doses, but if the excitability of cerebral cortex neurons increases, the convulsant effect emerges [9].

There is no fixed treatment procedure for the treatment of these side effects. Under the consideration of literature cases, some seizures have not treated with benzodiazepines, while others did not respond to this treatment [10]. In our case, the patient has not also responded to benzodiazepine infusion for a long time.

We should note that although propofol can be a part of the treatment for status epilepticus because of its anticonvulsant property, propofol may also induce convulsions and epileptiform seizure-like phenomena. This agent, commonly used in anesthesia, may rarely trigger seizures, even in totally healthy patients.

Authors' contributions

BD contributed to this study with data gathering, preparation of the manuscript. IOA contributed to the study design, revision

and corresponding the article. AT contributed to the study conduct genetic analysis, reviewed the final version of the manuscript and agreed to its content before submission.

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