Sedation induced by antiepileptic drugs polytherapy: A note of caution during anesthesia

Sir,

Sedation is a common complaint among patients with epilepsy taking antiepileptic drugs (AEDs). This side-effect is compounded in patients taking multiple AEDs.1-3 An 18-year-old male presented with history of seizures (since day 3 of life) refractory to multiple AEDs. He was taking twice daily doses of valproate 500 mg, clonazepam 20 mg, oxcarbazepine 450 mg, and levetiracetam 1500 mg; and zonisamide 100 mg in the morning and 200 mg at bedtime. He had no other co-morbidities. The patient was scheduled for vagal nerve stimulation under general anesthesia for diffuse, bilateral, non-localizing seizure foci. In the preoperative period, the patient was oriented to time, place, and person despite periods of mood swings, during which he became restless and aggressive. Baseline laboratory parameters including liver function tests were within normal limits. The patient was advised to continue AEDs on the morning of surgery. On arrival at the operating room (OR), he was deeply sedated and responded only to painful stimuli. The baseline vitals were BP 129/64 mmHg, HR 88/min, and SpO₂ 99% on room air. The bispectral index (BIS) value was found to be between 77 and 80. Anesthesia was induced with fentanyl 120 µg and propofol 100 mg, and tracheal intubation was facilitated with rocuronium 50 mg. The maintenance of anesthesia was done with O₂: air (FiO₂ 0.5), sevoflurane (0.8–1 Minimum alveolar concentration [MAC]) along with continuous infusions of fentanyl (60 µg/h), and rocuronium (12 mg/h). However, the BIS value started decreasing progressively below 40 [Figure 1]. Accordingly, the sevoflurane dial concentration was tapered, and to our surprise, even at zero end-tidal concentration of sevoflurane and a MAC of 0, the BIS value consistently remained between 40 and 45 with no change in hemodynamic parameters. As a result, sevoflurane was avoided. Infusions of fentanyl and rocuronium were discontinued 45 min prior to completion of surgery. At the end of surgery (160 min), BIS value reached between 50 and 55. After confirming return of spontaneous respiration, neuromuscular reversal agent was administered. However, the patient was not...
able to follow the verbal commands even though gag and cough reflexes were intact, and spontaneous movement of all four limbs was present. Trachea was extubated at a BIS value of 65. The patient was shifted to the ICU and closely monitored. He showed gradual improvement in sensorium over the next 1 hour and started obeying verbal commands. On interrogation, the patient could not recall any intraoperative event.

Through this correspondence, we wish to highlight certain important issues with multiple AED therapy. First, many AEDs have sedation as an important side-effect, particularly at high doses. Our patient received five AEDs on the morning of surgery, and by the time he reached the OR, he was deeply sedated. As informed by his parents, it was a regular phenomenon, and after morning doses, he frequently slept till mid-afternoon. Second, loss of verbal responsiveness as end point of induction with propofol was not possible here. That is why a fixed dose of propofol was administered. Third, we also bring forth the importance of BIS monitoring in such cases to titrate drug doses. Had we not applied BIS monitoring, we would have unnecessarily administered higher concentrations of sevoflurane than required thereby causing further delay in anesthetic recovery. Fourth, one of the classical extubation criteria of obeying to commands by the patient at the end of the surgery was not followed. However, adequate return of spontaneous breathing and airway reflexes along with spontaneous movement of all four limbs were ensured. Moreover, the intraoperative period was uneventful, and no neurological worsening was expected. Finally, the patient could not recollect any intraoperative event in the postoperative period suggesting absence of awareness. Thus, patients taking multiple AEDs should be evaluated thoroughly during pre-anesthetic check-up. The modification of anesthetic drugs and doses should be done, accordingly.

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Conflicts of interest
There are no conflicts of interest.

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