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Flumazenil Reversal of Benzodiazepine Sedation before Electroconvulsive Therapy

To the Editor:—Benzodiazepines have been avoided as premedication for patients undergoing electroconvulsive therapy (ECT) to ensure development of a seizure and one of adequate duration. Premedication with midazolam or florazepam followed by flumazenil reversal, ECT, and successful seizure development is described in two patients.

Case 1. A 32-yr-old man weighing 85 kg with no significant medical history except for diagnosed chronic schizophrenic disorder was admitted for repeat ECT. His medication included 300 mg clozapine twice daily and 80 mg fluoxetine daily. He was very uncooperative and suspicious of people. ECT could not be done because of worsening anxiety and agitation upon arriving at the ECT treatment area, which resulted in him refusing treatments. Previous ECT treatments required premedication with ketamine, but this left him sedated without anxiolysis.

It was decided to premedicate this patient with lorazepam, which was administered in 2-mg increments intravenously until he was sedated and not resisting but responsive to verbal command. A total of 17 mg lorazepam was given, and he was brought into the treatment room and prepared for ECT. Flumazenil was titrated in 0.1-mg increments intravenously until the patient showed signs of increased responsiveness to verbal questioning (0.2 mg total given). The patient was then given 50 mg methohexital followed by 50 mg succinylcholine. ECT was performed, and a 29-s seizure resulted. Blood pressure increased from 140/88 to 180/100 mmHg and heart rate from 80 to 114 beats/min during the seizure. He was spontaneously breathing, arousable, but very sedated after the treatment.

The patient appeared less anxious and less resistant to having ECT 2 days later and for the duration of the treatment course.

The next five ECT treatments consisted of giving 7–20 mg intravenous midazolam and 0.2–0.5 mg flumazenil before each treatment. Adequate seizures of 25–33 s resulted, except for one treatment resulting in a 14-s seizure when 10 mg midazolam and 0.5 mg flumazenil were used with the same maximal electrical stimulus. The last three ECT treatments consisted of giving 4–6 mg oral lorazepam at least 1 h before ECT and 0.2–0.4 mg flumazenil. Seizures of adequate duration resulted.

Case 2. A 35-yr-old woman weighing 70 kg with a history of hypothyroidism, peptic ulcer disease, and recent exacerbation of schizoaffective disorder was to undergo ECT. She took synthroid daily and was euthyroid by lab results. She had paranoid hallucinations and appeared uncooperative and easily agitated.

This patient received 2 mg lorazepam orally 1 h before arriving in the ECT room. She was minimally sedated, more cooperative, and allowed an intravenous to be placed without resistance. Glycopyrolate, 0.2 mg, followed by 0.2 mg flumazenil were given. When clinical signs of increased alertness and wakefulness were seen (within 1 min of the flumazenil dose), 50 mg methohexital and 50 mg succinylcholine were given. A short seizure of inadequate duration

resulted. Another 0.2 mg flumazenil was given 2 min later followed by an additional 40 mg methohexital and 40 mg succinylcholine, and ECT was attempted again. An acceptable seizure of 43 s resulted, and the patient was soon after awake and not agitated. Blood pressure increased from 120/84 to 160/90 mmHg and heart rate from 100 to 120 beats/min during the treatment.

Flumazenil, a specific benzodiazepine receptor antagonist, has been shown to reliably reverse benzodiazepine-induced sedation and psychomotor impairment without risk of re sedation.¹ Surprisingly, clinical studies have shown that flumazenil in relatively large doses exhibits anticonvulsant effects in epileptic patients.² It is suggested that flumazenil is a partial agonist at the anticonvulsant receptor and a pure antagonist at the sedative site of action.³

ECT with adequate seizure duration was possible in these two patients, except for one time in the first case when a relatively larger dose of flumazenil (0.5 mg) was used and another time in the second case when reversal seemed inadequate and a repeat dose of flumazenil was needed.

In conclusion, flumazenil may be used to reverse benzodiazepine sedation before ECT so that a seizure can occur, but flumazenil dosing may be important. The minimum and maximum dose of flumazenil allowing an adequate seizure needs to be determined and is probably influenced by the benzodiazepine dose and patient characteristics. Benzodiazepine premedication for anxious patients undergoing ECT may be an option now that flumazenil is available.

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