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Flumazenil before Electroconvulsive Therapy: Outstanding Issues

To the Editor:—We were very interested to read Hanania's report of flumazenil administration before electroconvulsive therapy (ECT).¹ In his two cases, flumazenil, given immediately before ECT, reversed the sedative effects of benzodiazepine premedication; seizures of acceptable duration followed. This report raises several issues that deserve further consideration, regarding the seizures and the therapeutic outcome of ECT.

Regarding the seizures, the effects of flumazenil are unclear. In Hanania's cases, flumazenil was given before any ECT stimulus was delivered. We do not know what the outcome would have been without flumazenil in these two patients. Furthermore, in one case, extra flumazenil was given after an unsuccessful ECT attempt; however, Hanania does not note whether the stimulus current was increased at the same time, as is usually done when the first seizure is inadequate. So, we cannot surely attribute the subsequent success to the extra flumazenil. On the other hand, acute benzodiazepine administration has been shown to raise seizure threshold and shorten seizure duration.² (In this context, it is interesting that flumazenil did not cause unacceptably long seizures.) We may guess that flumazenil led to better seizure outcomes than otherwise might have occurred after benzodiazepine administration, but this remains to be demonstrated.

Clinically, of course, the most important issues concern the effects of flumazenil and benzodiazepines on the therapeutic outcome of ECT. Several questions arise here. First, do benzodiazepines affect clinical outcome, independent of seizure duration? Second, do acute *versus* chronic benzodiazepines have different effects? Third, does flumazenil reverse benzodiazepines' effects on ECT outcome? Finally, does flumazenil have relevant psychoactive effects of its own?

Several authors have raised the question of benzodiazepine interference with therapeutic effects of ECT. In one study in humans, the authors determined that unilateral ECT was less effective in patients who were receiving chronic benzodiazepines, despite adequate seizures.² A study in mice investigated behavioral responses to serial electroshocks. Behavioral changes that usually followed the shocks did not occur when diazepam was given, despite apparently identical seizures. This was noted whether diazepam was given before or after the shocks, suggesting that diazepam's antitherapeutic effects are independent of its effects on the seizures.³

The question of chronic *versus* acute benzodiazepine administration in this setting remains largely unaddressed. Hanania's patients received lorazepam only once, immediately before ECT. In contrast, the patients in the human study cited above received chronic ben-

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zodiazepine treatment. Because long-term psychoactive effects of medications often require chronic treatment, we might suppose that one-time dosing is relatively benign. However, the mouse study suggests that the presence of benzodiazepines after ECT, even from one dose of a long-acting agent, may alter the behavioral response.

The effects of flumazenil on ECT outcome remain unexplored. Of note, some authors have implicated benzodiazepine receptors and enhancement of the effects of γ -aminobutyric acid in recovery from depression.⁴ Will flumazenil reverse benzodiazepine effects on ECT outcome? Will it turn out to have its own clinical effects in patients receiving ECT or in other depressed patients? Answering these questions may clarify the mechanism of ECT therapeutic effects and illuminate the biochemical features of depression as well.

In the meantime, we may consider benzodiazepine sedation and flumazenil reversal in ECT patients who will not otherwise accept treatment. However, we should be prepared for the possibility of a reduced clinical antidepressant response.

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In Reply:—Doering and Ball raise many of which we can answer based on the whether the stimulus current had been inadequate duration occurred. Both overcome the effects of benzodiazepines parameters on the MECTA SR1 electrocine. Thus, there was no potential for rent. This suggests that, in the case where seizure probably was due to additional seizures of adequate duration is relevant. Second, they ask whether the fact efficacy when benzodiazepines and flumazenil we have no matched controls one known to us as responding well to ECT this course of ECT using the benzodiazepine comparable to his past responses. The by us for the first time, had an adequate seizure. The possibility that benzodiazepines could interfere with the therapeutic effect only a controlled trial could answer.

Flumazenil reversal of benzodiazepine seizure outcomes than otherwise might diazepam pretreatment because a threshold and shorten seizure duration. A controlled trial can confirm this.

It is known that, in larger doses, flumazenil, but its effect on seizure duration

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To the Editor:—Painful tonic convulsions in 1920, consists of ipsilateral tonic hemifacial spasm.¹ Fifty-five cases have been reported. In 7 of the 55 cases, it is to be caused by a brain tumor.² We report a 32-yr-old man was suffering from ipsilateral trigeminal neuralgia and to have an undiagnosed brain tumor. After decompression of the 5th and 7th cranial nerves, the patient had a presumed psychosomatic disorder. After treatment with imipramine he experienced severe lancinating pain in the face. Diagnosis of trigeminal neuralgia was made after a series of treatments with pranoprofen and diclofenac. After 1 yr, his pain increased