CASE REPORT

Benzodiazepine Withdrawal Seizures In A Chinese Lady

Michael T.H. Wong*, MBBS, MRCPsych
Lecturer
K.F. Chung, MBBS
Lecturer
Department of Psychiatry
University of Hong Kong

Keywords: Benzodiazepine, Withdrawal Seizure.

Introduction

Seizure as a symptom of withdrawal from benzodiazepines is uncommon but well recognized. In one series, none of the 22 patients undergoing withdrawal from benzodiazepines developed seizure[1]. In another series, no seizure was observed in 57 benzodiazepine-dependent patients undergoing abrupt discontinuation from benzodiazepine[2]. In fact, most of the cases were described in case reports. It was found that factors like duration of dependence, short half-life, high dosage, abrupt discontinuation and concurrent multiple drug use were important for the development of seizure. In the following report, three episodes of drug withdrawal in a Chinese lady dependent on benzodiazepines were described. Generalized tonic-clonic seizures were present as withdrawal symptoms but only in two of these episodes. Several clinical and pharmacological features are discussed to highlight how they interact and give rise to benzodiazepine withdrawal seizure. The present report also discusses how a change in the availability of benzodiazepines with the tightened legislation contributed to the occurrence of the withdrawal seizures.

Case Report

C, a 31-year-old divorced Chinese lady suffering from chronic primary insomnia, started taking a benzodiazepine hypnotic seven years ago when her husband deserted her. Her work as a nightclub hostess finished at 3am and she took flunitrazepam (Rohypnol) 2-4mg to make herself fall asleep 'quick and smooth'. Her tolerance to flunitrazepam increased gradually through these years. She needed to take flunitrazepam 8-12mg to induce sleep. Besides she also took dextromethorphen hydrobromide (Romilar), an anti-tussive tablet, 15-30mg, or 2-3 bottles of beer (Carlsberg) every now and then, in addition to flunitrazepam, to get herself to sleep. She did not experience any tolerance, withdrawal symptoms or craving for alcohol or the cough tablets however. There was no history of psychiatric illness, personality disorder, substance misuse or epilepsy in her family. She enjoyed good health all along. She received an education up to primary level only but was regarded by family members as intelligent and independent. She was outgoing, optimistic and hardworking. She had good social support from her brothers and mother, the latter actually helped in looking after her 3 children.

Before her first episode of withdrawal seizure, she felt fed up with her lifestyle as a nightclub hostess. She quit her job and stopped all her medication and alcohol straight away. She became tense, anxious, tremulous and unable to fall asleep. She had a generalized tonic-clonic seizure while she was having a barbecue picnic with her family on the seventh day after she stopped her benzodiazepine hypnotic. She was incontinent of urine but not of stool. She was violent and delirious on admission

* *Address for correspondence: Alcohol & Substance Misuse Clinic, Department of Psychiatry, The University of Hong Kong, Queen Mary Hospital, Hong Kong.*

(Continued on page 2156)

and required restraint and sedation. She became emotionally stable after 1 week and the EEG before discharge from hospital was normal.

She stopped substance misuse for 1 year during which she cohabitated with a married man and gave birth to a child. She started taking benzodiazepines again when she found out that the man decided not to divorce his wife. She could not fall asleep at night unless she took alprazolam (Xanax) 1.25-1.5mg. She also had craving for the drug during the day time when she felt frustrated or bored. This continued for 6 months when she decided to stop all her medication. She consulted a drug misuse counselling center and was advised to undergo in-patient detoxification bearing in mind her previous history of withdrawal seizure. She was later admitted to a mental hospital. She refused gradual tapering of her drug and insisted on a 'cold turkey' detoxification. She failed to get any sleep during the first 72 hours and experienced fatiguability, anxiety and blurring of vision. There was no muscle twitching or seizure. She was successfully detoxified in 12 days. She was calm and relaxed with no craving on discharge.

She stopped substance misuse for another year, but when she found her new boyfriend and cohabitant secretly having affairs with other women she started taking benzodiazepines again. She took brotizolam (Lendormin) up to 2 mg per day. She would crave for the drug during the day when frustrated and would become anxious and tremulous if she resisted to take the drug. Her tolerance gradually increased over 6 months during which she had episodes of taking brotizolam 5 mg without any sign of intoxication. After a while, she was unable to buy the medication when the Government classified it as a dangerous drug. She experienced insomnia, craving for the drug, anxiety and muscle twitching. On the fourth day, she developed a generalized tonic-clonic seizure. Blood assay for brotizolam was negative. EEG on admission showed generalized spikes. She slept well and remained calm throughout the detoxication and was discharged after one week. EEG done after discharge was normal.

Discussion

Seizures following abrupt discontinuation of benzodiazepines are uncommon but well recognized. A few factors such as the use of higher than therapeutic dosage for long periods of time[3,4] and abrupt withdrawal[5] contributed to withdrawal seizures in this patient. The regular use of alcohol may also have contributed to the withdrawal seizure although reports have only shown the association in patients who are dependent on alcohol[6]. In addition, the concurrent use of other sedative hypnotics or other psychotropic drugs that lower seizure threshold, such as neuroleptic and tricyclic antidepressants[7], may explain the withdrawal seizure in this patient as she belonged to the group of patients who might have multiple psychotropic drug misuse; but it was not always possible to get a positive confirmation in the history.

It is interesting that she stopped benzodiazepines abruptly for 3 times and had a seizure on only 2 occasions. There were at least two possible reasons. Firstly, she used flunitrazepam and brotizolam up to 10 times of the therapeutic dosage resulting in withdrawal seizure but she took alprazolam within the therapeutic range, the abrupt discontinuation of which did not result in a withdrawal seizure. Secondly, it was shown that maintenance of alertness and relaxation could sometimes inhibit a seizure[8]. The patient was admitted to hospital and psychologically prepared for the withdrawal of alprazolam which may contribute to the absence of withdrawal seizure.

Another interesting feature was that the withdrawal seizures occurred at Day 7 for flunitrazepam and at Day 4 for brotizolam upon discontinuation. Most reports found that withdrawal seizures usually occurred within 1 to 3 days of discontinuing benzodiazepines[3,4,9]. It was especially unusual since brotizolam and its metabolites had an elimination half life of only 3.6 to 7.9 hours[10]. However, some reports also noticed that withdrawal seizures might occur after a week or more following discontinuation[3,11] of benzodiazepines.

In 1990, the Dangerous Drug Ordinance in Hong Kong classified 3 kinds of widely abused benzodiazepines as dangerous drugs and one of them is brotizolam. Before the enforcement of legislation, brotizolam was easily available over-the-counter. The reduced availability of benzodiazepines and the adverse publicity on their effects will increase the worries about their long term effects among people who are dependent on benzodiazepines. They may abruptly stop the drug and have the risk of withdrawal seizures especially among those taking high doses as described in this report. The author hopes to draw the attention of medical practitioners to the risk among patients dependent on benzodiazepines. Patients should be helped to undergo detoxification in the proper manner. This involves gradual withdrawal combined with supportive counselling. Anxiety management may be needed for patients who cannot give up the drug with simple measures alone. Underlying psychiatric problems should be given specific treatment. In some patients, with high risk of complications as discussed above, an in-patient detoxification programme is indicated. ■

References

1. Petrusson H. & Lader M.: Dependence on Tranquilizers. Institute of Psychiatry Maudsley Monograph Number 28. Oxford University Press. 1984.
2. Rickels, K., Schweizer, E., Case, G., Greenblatt, D.J.: Long-term therapeutic Use of Benzodiazepine. I. Effect of Abrupt Discontinuation. II Effect of Gradual Taper. Archives General Psychiatry 1990; 47: 899-915.
3. De la Fuente, J.R., Rosenbaum, A.H., Martin, H.R. *et al*: Lorazepam-related withdrawal seizures. Mayo Clinic Proceedings. 1980; 55: 190-193.
4. Howe, H.G.: Lorazepam withdrawal seizures. British Medical Journal. 1980; 280: 1163-1164.
5. Robinson, G.M. & Sellers, C.M.: Diazepam withdrawal seizures. Canadian Medical Association Journal 1982; 126: 944-945.
6. Clare, A.W.: Diazepam, alcohol, and barbiturate abuse. British Medical Journal. 1971; 4: 340.
7. American Psychiatric Association: Benzodiazepine dependence, toxicity, & abuse - a task force report of the American Psychiatric Association. Washington, American Psychiatric Association, 1990; p19.
8. Fenwick, P.B.C.: Behavioral treatment of epilepsy. Postgraduate Medical Journal. 1990; 66: 336-338.
9. Tien, A.Y. & Gujavarty, K.S.: Seizure following withdrawal from triazolam [letter]. American Journal of Psychiatry 1985; 142: 1516-7.
10. Reynolds, J.E.F.: Martindale, the Extra Pharmacopoeia. 29th editions. London, the Pharmaceutical Press. 1989.
11. Kahan, B.B. & Haskett, R.F.: Lorazepam withdrawal and seizures. American Journal of Psychiatry 1984; 141: 1011-1012.

WORLD LEADERS IN MEDICAL SCIENCES TO CONVENE IN HONG KONG

Medical Update Conference 1992 — will bring a unique grouping of world leaders in all fields of medicine from Australia plus a number of Hong Kong's most distinguished medical authorities to discuss the latest developments with their colleagues in Hong Kong for four days, starting on August 15, 1992 at the Shangri-La Hotel, Kowloon.

A separate conference on Practice Management — of special value to support staff of Hong Kong's General Practitioners — will run concurrently with the ESMA Medical Update Conference.

Enquiries from Hong Kong can be Faxed on International Dialling to: Dr. Edward P. Kremer, Conference Convener, 61-2-365 2390.