

## Case Report

# Severe benzodiazepine withdrawal syndrome followed by anesthesia in elderly patient: A rare case report

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**Benzodiazepine dependence is a potentially clinically serious condition and its withdrawal syndrome is complex and often protracted in time course. However, the relationship between anesthesia and benzodiazepine withdrawal syndrome is unclear. Here, we presented a 79 year-old-female who had the history of major depression and had taken hypnotic benzodiazepines for five years. The patient received total hip replacement under spinal anesthesia and during the operation, the hypnotic benzodiazepines were discontinued. One day later, the patient was suddenly dropped to coma. Brain magnetic resonance (MR) imaging demonstrated no significant finding except to brain-tissue loss over the bilateral anterior frontal lobes. Accordingly, tracheostomy was performed and ventilator dependent. Interestingly, forty days later, the patient's consciousness became alert. To increase physicians' awareness that old age, anesthesia, and cortical dysfunction may exacerbate benzodiazepine withdrawal syndrome, we presented our experience in treating one patient who rapidly stopped the hypnotic benzodiazepines.**

**Key words:** Benzodiazepine withdrawal syndrome, anesthesia.

## INTRODUCTION

Benzodiazepine withdrawal symptoms are a normal response in individuals who have chronically used benzodiazepines, and a side effect and result of drug tolerance. Symptoms typically emerge when dosage of the drug is reduced. The symptoms include insomnia, headache, nausea and vomiting, and nightmares. However, an abrupt or over-rapid discontinuation of benzodiazepines may result in a more serious and very unpleasant withdrawal syndrome that may additionally result in convulsions, catatonia, suicide, coma, hyperthermia, and delusions. Here, we reported 79 year-old-female who had the history of major depression and had taken hypnotic benzodiazepines for five years. The patient received total hip replacement under spinal

anesthesia and during the operation, the hypnotic benzodiazepines were discontinued. One day later, very serious withdrawal syndrome happened, the patient suddenly dropped to coma.

## CASE REPORT

A 79 year-old-female had the history of major depression and had taken hypnotic benzodiazepines for five years. However, the patient was sustained severely, left hip pain and diagnosis was fracture of femoral neck, left hip with displacement. The patient received total hip replacement under spinal anesthesia and during the operation, the hypnotic benzodiazepines were stopping. Unfortunately, one day after the operation, the patient was suddenly dropped to coma. The laboratory examinations revealed no remarkable contribution. On neurological examination it show deep coma (Glasgow coma scale equal E1M1Vt), absent of bilateral babinski's signs, and decreased deep tendon reflex. Brain computed topography (CT) revealed no significant finding except to brain-tissue loss in the bilateral anterior frontal lobes. Brain magnetic resonance (MR) imaging demonstrated brain-tissue loss over the bilateral anterior

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frontal lobes and a recent lacunar infarction in the right centrum semiovale. Electroencephalogram (EEG) revealed cortical dysfunction. The psychologists suggest hypnotic benzodiazepines and flumazenil without improvement. However, forty days later, the patient's consciousness became alert (Glasgow coma scale equal E4M6Vt). Now, the patient regularly received rehabilitation, and can walk by herself.

## DISCUSSION

Long-term use of hypnotic benzodiazepines is higher in older adults than younger people throughout North America, Australia and Europe (Barbui et al., 1998). It is estimated that about 15% of over 65-year-olds adults regularly take sleeping pills and, in the United Kingdom, older adults received 80% of all the prescriptions written for hypnotic benzodiazepines (Jorm et al., 2000). Hypnotics are commonly given to over 65-year-olds adults in repeat prescriptions, although benzodiazepines are not nowadays recommended for long-term used. Ticehurst (1995) concluded that after tobacco and alcohol, benzodiazepine consumption is associated with the greatest risk of abuse and dependence in the elderly. This reflects a substantial decrease in benzodiazepine anxiolytics but relatively change a little in benzodiazepine hypnotics especially among old patients (Rumble and Morgan, 1994), although there has been a reduction in scripts for benzodiazepines since the mid-eighties. Holden et al., (1994) revealed patients over 65 are significantly less likely to stop benzodiazepine than younger patients by a large-scale audit of benzodiazepine prescribing and withdrawal in general practice. Moreover, it may be higher incidence in elderly patients than younger patients, but it need more research to demonstrate the hypothesis.

Some of the benzodiazepine withdrawal symptoms are identical to the symptoms for which the medication was originally prescribed. It is very important to determine the difference between relapse and rebound during the withdrawal phase and can often lead to a misdiagnosis. Therefore, many experts suggest that after withdrawal from long term or even fairly short term use of benzodiazepine drugs, at least six months should have elapsed prior to re-evaluating the symptoms and updating a diagnosis. GABA receptors are the most common receptor system in the central nervous system and use of benzodiazepines has a profound effect on almost every aspect of brain and body function, either directly or indirectly. Benzodiazepines cause a decrease in norepinephrine, serotonin, acetylcholine and dopamine. These neurotransmitters are needed for coordination, normal memory, emotional responses, mood, muscle tone, endocrine gland secretions, heart rate and blood pressure control. With chronic benzodiazepine use, tolerance develops rapidly to most of its effects, so that

when benzodiazepines are withdrawn, various neurotransmitter systems go into overdrive due to the lack of inhibitory GABA-ergic activity. Withdrawal symptoms then emerge as a result, and persist until the nervous system physically reverses the adaptations (physical dependence) which have occurred in the central nervous system. Therefore, the cortical dysfunction may exacerbate the benzodiazepine withdrawal symptom, but it need more study to prove the hypothesis.

Benzodiazepine withdrawal symptoms include insomnia, headache, nausea and vomiting, and nightmares. However, an abrupt or over-rapid discontinuation of benzodiazepines may result in a more serious and very unpleasant withdrawal syndrome that may additionally result in coma, convulsions, catatonia, suicide, hyperthermia, and delusions.

## Conclusion

The severe syndrome of benzodiazepine withdrawal syndrome may be coma. However, to the best of our knowledge the relationship between anesthesia and benzodiazepine withdrawal syndrome is unclear. In our patient, over-rapid discontinuation of benzodiazepines during anesthesia is followed by benzodiazepine withdrawal syndrome. Moreover, old age, and cortical dysfunction may exacerbate the symptom, but more study should be performed to prove the hypothesis. To increase physicians' awareness small dosage of hypnotic benzodiazepines should be maintained if elderly patient with cortical dysfunction who was chronic to hypnotic benzodiazepine use will received anesthesia.

## REFERENCES

- Barbui C, Gregis M, Zappa M (1998). A cross-sectional audit of benzodiazepine use among general practice patients. *Acta Psychiatr. Scand.* 97(2):153-6.
- Jorm AF, Grayson D, Creasey H, Waite L, Broe GA (2000). Long-term benzodiazepine use by elderly people living in the community. *Aust. N. Z. J. Pub. Health* 24(1):7-10.
- Ticehurst S (1995). Alcohol and drug abuse. In Linsey J (ed.), *Neurotic Disorders in the elderly*. Oxford University Press. Oxford. pp. 56-71.
- Rumble RH, Morgan K (1994). Longitudinal trends in prescribing for elderly patients: two surveys four years apart. *Br. J. Gen. Pract.* 44(389):571-5.
- Holden JD, Hughes IM, Tree A (1994). Benzodiazepine prescribing and withdrawal for 3234 patients in 15 general practices. *Fam. Pract.* 11(4):358-62.