CASE REPORT

Hazards of Deliriogenic Medications Used in a High Risk Patient: A Case Report

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Abstract

Although disturbance of consciousness in delirium patients have been well established, but sudden drop of Glasgow Coma Scale (GCS) level to three is frightening and mysterious. We are reporting a case of a delirious elderly man with multiple medical illnesses presented with acute precipitous decrement of GCS with pin point pupils bilaterally after given a course of benzodiazepines and regained full consciousness spontaneously 32 hours later. We discussed the use of deliriogenic medications in the context of delirious elderly gentleman with multiple medical illnesses. We also looked into the possible differentials of sudden drop of conscious level with bilateral pin point pupils.

Keywords: Benzodiazepine, Coma, Delirium, Elderly, Pin Point Pupils

Introduction

Delirium is a common and serious neuropsychiatric problem for elderly especially those with dementia or those with concurrent medical illness¹. Delirium is characterized by acute onset of altered level of consciousness, orientation and cognition. The incidence of delirium is from 14% to 56%, while the hospital mortality rate is from 25% to 33%². Infections (43%) and cerebrovascular attacks (25%) were found to be the most important primary causes of delirium in the elderly³.

Many medications can cause delirium and benzodiazepine is one of it. A recent retrospective descriptive analysis of community pharmacies in the United States found that 8.7% of adult ages 65-80 years used benzodiazepines⁴.

Disturbance of consciousness in delirium patients have been well established. However, it is rare and interesting to look into the possible reason of a delirious elderly gentleman with multiple medical illnesses who regained full consciousness spontaneously after 32 hours of unconsciousness with GCS of three. This case report describes a delirious elderly gentleman with multiple medical illnesses such as ischemic heart disease, Parkinson’s disease, dementia and depression, who was
on regular benzodiazepine (clonazepam), found to be unconscious with GCS three and bilateral pin point pupils, regained full consciousness spontaneously after 32 hours.

Case Report

Mr. X was a 65 years old Chinese gentleman. He was a non smoker and non alcoholic. He had coronary artery bypass grafting (CABG) 15 years ago. He was diagnosed with Parkinson’s disease 10 years ago and also suffered from depression and dementia as the complication of Parkinson’s disease for the past 5 years. He was on multiple medications (Escitalopram, Memantin, Rivastigmine, Sinemet, Madopar, Pramipexol and Entacaptone). He was an independent gentleman with good function of activities of daily living. He was started on regular benzodiazepine, clonazepam 2 mg nocte, by the psychiatrist 2 months before admission due to his sleep difficulties at night.

Two weeks prior to admission, he started to develop some abnormal behaviour. He was noted to be talking irrelevently and talking to himself. He had paranoid delusion whereby he believed people were trying to kill him. He became easily irritable, restless and had poor sleep. He was brought for psychiatric consultation and was commenced on atypical antipsychotic, tablet Quetiapine XR 50 mg nocte.

His abnormal behaviors became worse; hence he was brought to hospital for further management. At the hospital emergency department, a Computerized Tomography (CT) brain was done. He was given a total of Intravenous Midazolam 9mg for sedation to proceed with CT brain. CT brain result did not reveal any abnormalities. His vital signs were stable. In the ward, he was diagnosed with acute delirium secondary to urinary tract infection. He also had acute urinary retention secondary to benign prostate hypertrophy. Electrocardiogram (ECG) and blood investigations including Full Blood Count, Random Blood Sugar, Renal Profile, and Liver Profile were all normal. He was not in sepsis as his vital signs remained stable, and there were no hyper or hypothermia detected in the ward. In addition to the antibiotics that was started to treat the urinary tract infection, his previous medications were continued including clonazepam 2mg nocte.

On day 3 of admission, patient was found unconscious with GCS three and bilateral pin point pupils. His vital signs were stable and he was able to maintain his respiration with normal arterial blood gases under room air. He was immediately given intravenous Flumazenil for possible clonazepam overdose in view of the low GCS and pin point pupils bilaterally. However, patient did not show any improvement despite the repeated administration of 3.0mg intravenous Flumazenil in total. Urgent CT brain was done and showed no abnormalities. Electrocardiogram (ECG) and blood investigations repeated were all normal. All his medications were withheld. He was transferred to medical ward for further management by the medical and anesthesiology team. He was planned for electroencephalography (EEG), lumbar puncture and magnetic resonance imaging (MRI) brain. However, approximately 32 hours after the last ingestion of clonazepam 2mg, patient woke up spontaneously. He was weak but appeared conscious and alert. He was able to speak relevantly and moving all his 4 limbs.

What could have happened that led to the episode of 32 hours of unconsciousness with GCS of 3?
Discussion

The onset of delirium usually depends on a combination of predisposing, non-modifiable factors such as serious medical illness and co-morbidities, baseline cognitive impairment or dementia, advanced age and male sex\(^1\). Delirious patients were also more likely have a surgical/trauma diagnosis, history of tobacco or alcohol use\(^5\). Primary central nervous system disease such as Parkinson’s disease can predispose to delirium, and demented patient has a 2 to 5 fold increased risk for delirium\(^6\).

Regular dosing with benzodiazepines has been found to produce more sedation and confusion in elderly\(^8\). Older people maybe at greater risk for adverse effect such has reduced clearance of sedative hypnotics or increased sensitivity to peak drug effects\(^7\). Benzodiazepines are not recommended for the first line treatment of delirium\(^8\). Even without delirium, benzodiazepines used should be limited to a period of 2 to 3 weeks with tapering of the dosage during withdrawal\(^9\).

Previous studies suggested that benzodiazepines with long-acting are more likely than short-acting agents to cause adverse events\(^10\). Long-acting benzodiazepines have active metabolites that accumulate extensively during multiple dosages\(^9\). Clonazepam has a long half-life of 5-30 hours\(^11\). It can take 3 to 4 half lives for a drug to be clear from the body. Thus, the half-life of long-acting benzodiazepines tends to be prolonged in this elderly man.

The differential diagnosis of coma with small pupils includes non-toxicological causes such as pontine haemorrhage, metabolic encephalopathy, and toxicological causes organophosphate poisoning as well as benzodiazepines, antipsychotic and opiates use, abuse or overdose\(^12,13\).

The benzodiazepines level in this patient was not measured. Perhaps the clonazepam level can aid us with the diagnosis and to understand the incident better. Besides, EEG would be useful to rule out seizures as one of the possible differential diagnosis.

In conclusions, clinicians should be more cautious in prescribing medications to elderly patient with multiple medical conditions.

References


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