

Oxcarbazepine may induce psychotic symptoms in Parkinson's disease

(Case report)

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ABSTRACT

Although both idiopathic Parkinson's disease (PD) and epilepsy have a relatively high prevalence in the elderly population and PD appears more frequently in people with epilepsy, there are no studies investigating efficacy and tolerability of antiepileptic drugs (AED) in PD.

We present a case of a 71-year-old man with PD who experienced several seizures. The initiated oxcarbazepine (OXC) AED treatment provoked severe, long-lasting psychotic state. The patient had previously suffered from similar psychotic episodes during dopamine-agonist therapy. Because recent animal studies proved that OXC and its active metabolite exert important dopamine and serotonin promoting effects in the limbic area, we assume that in our case the OXC-induced psychosis was mediated by the dopaminergic system. We conclude that OXC should be used with care in case of a constellation of PD and epilepsy because of its possible psychiatric side-effects. The dopaminergic effect of OXC and its active metabolite might also play an ambivalent, but important role in the treatment of alcohol addiction and bipolar disorder; therefore, further studies are required to investigate its psychopharmacological aspects.

INTRODUCTION

Although both idiopathic Parkinson's disease (PD) and epilepsy [1] have a relatively high prevalence in the elderly population and PD appears more frequently in people with epilepsy [2], there are no studies investigating efficacy and tolerability of antiepileptic drugs (AED) in PD.

We present a case of a 71-year-old man with PD who experienced several seizures. The initiated oxcarbazepine (OXC) AED treatment provoked severe, long-lasting psychotic state. The patient had previously suffered from a similar psychotic episode during levodopa and dopamine-agonist therapy. We conclude that OXC might have some possible psychiatric side-effects in case of a constellation of PD and epilepsy; therefore, it should be used with caution.

CASE REPORT

The 71-year-old male patient first noticed rest tremor and clumsiness in his left extremities in 1988. Based on the clinical features, idiopathic PD was suspected and bromocriptine therapy was introduced resulting in marked clinical improvement lasting for years. At that time this type of dopamine agonist did not produce any side-effects. By 1995 his symptoms aggravated to such an extent that levodopa/benserazide treatment was initiated replacing bromocriptine. Between 2000 and 2006 two different dopamine-agonists (ropirinole and later pramipexole) were tried out to in adjacent to the levodopa, but each time the patient developed severe psychotic symptoms: agitation and visual hallucinations. Therefore, levodopa/carbidopa/entacapone combination was initiated to outweigh the clinical progression, without any serious side-effects. In 2005 the severe levodopa

complications (fluctuations and dyskinesias) required neurosurgical treatment. Because of the previous psychotic symptoms in the history, the brain atrophy observed on MRI and the mild cognitive decline measured on neuropsychological tests, right pallidotomy was performed instead of deep brain stimulation resulting in prominent improvement of the left Parkinsonian symptoms. After pallidotomy, the patient used 150 mg levodopa, 37.5 mg carbidopa and 200 mg entacapone combination (Stalevo 150 mg) tablets four times daily.

In 2007, the patient experienced four generalized tonic-clonic seizures within 2 days witnessed by his relatives. Cardiological examination, including Holter-ECG and echocardiography, did not any reveal pathological alterations capable of producing syncope. The EEG performed 3 days after the seizures did not show epileptiform discharges.

Brain MRI revealed numerous bilateral lacunar infarcts in the territory of periventricular white matter and basal ganglia. Based on the presence of recurrent unprovoked seizures and the fact that asymptomatic cerebral infarction is a well-known risk factor for epilepsy [1], we diagnosed the patient's seizures as symptoms of a localization-related epilepsy and carbamazepine (CBZ) was initiated. Because CBZ therapy was associated with an intolerable dizziness, we changed to OXC monotherapy 3 days later.

At the daily dose of 900 mg OXC, severe agitation and inexplicable fearfulness developed. Visual hallucinations including the appearance of already dead relatives, bugs, animals were also prominent symptoms. According to the family, these symptoms were quite similar to the ones previously induced by ropirinole or

pramipexole. Because the discontinuation of OXC resulted in a prompt elimination of psychiatric symptoms, we considered them as OXC-induced side-effects.

DISCUSSION AND IMPLICATIONS FOR CLINICAL CARE

Due to its favorable pharmacokinetic and side-effect profile, OXC is a well-tolerated AED with relatively few interactions in the treatment of localization-related epilepsy, moreover it can be relatively safely used in elderly people.[3] Besides, OXC seems to be effective in affective and other psychiatric disorders [4] as a mood-stabilizing agent.[5]

Currently there is no in vivo human study investigating the dopaminergic effects of OXC. A recent animal study demonstrated that OXC dose-dependently reduced the haloperidol-induced catalepsy in rats and increased the intensity of apomorphine-induced stereotypy, suggesting that OXC probably exhibited antidepressant-like effect by the enhancement of dopaminergic neurotransmission.[6] Another animal investigation also proved that OXC and its active metabolite (10,11-dihydro-10-hydroxycarbamazepine) exert important dopamine and serotonin promoting effects in the limbic area that, at least partly, contribute to the anticonvulsant mechanism of action by hippocampal D(2) and 5-HT(1A) receptor stimulation.[7]

To our knowledge, no previous study reported psychosis as a side-effect of OXC. In the lack of human data, our case indirectly indicates that OXC may provoke psychotic symptoms in PD patients probably through the similar mechanism as dopamine-agonists. Besides OXC, we could not identify any other trigger provoking psychotic state in our case. Because the routine laboratory parameters, including

serum sodium level, were in the normal range, hyponatremia was not feasible in the background of the psychotic state either.

The fact that the initiation and the termination of OXC treatment had an immediate effect on the psychotic symptoms suggests that OXC is strongly involved in the provocation of psychotic symptoms. Because previous dopamine-agonist (ropirinole and pramipexole) and OXC medication resulted in clinically similar psychosis and the OXC probably alters dopaminergic neurotransmission, we assume that the OXC-induced psychosis was mediated by the dopaminergic system.

Our case suggests that OXC might have considerable dopamine-mediated effects in certain humans, which has to be considered during its prescription in both epilepsy and psychiatric disorders. The dopaminergic effect of OXC and its active metabolite might presumably play also an ambivalent, but important role in the treatment of alcohol addiction [8] and bipolar disorder [5, 9]; therefore, further studies are required to investigate its psychopharmacological aspects.

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