CASE REPORT

Duloxetine Induced Discontinuation Syndrome: A Case Report On Drug Safety

Pharmacology Section

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ABSTRACT

Introduction: Discontinuation symptoms are those which are experienced on stopping prescribed drugs that are not drugs of dependence, with predictable onset, duration and cessation of action. The symptoms can be suppressed by the reinstitution of the discontinued medication. Antidepressant discontinuation symptoms can cause morbidity, they can affect compliance, they can prevent the cessation of antidepressant therapy and can be misdiagnosed, thus leading to inappropriate treatment. The alertness of clinicians regarding the possibility of the antidepressant-induced discontinuation syndrome is necessary for its prevention and management. Hence, we wanted to assess the causality of a suspected case of discontinuation reaction with duloxetine.

Case report: Suspected adverse drug reaction (ADR) data which were collected retrospectively from the case records of patients attending the Psychiatry Outpatients Clinic of a teaching hospital in Pondicherry was analysed for causality by using Naranjo's scale. A 50 year old female who was diagnosed with mixed anxiety and depressive disorder with somatoform disorder, was prescribed duloxetine for six months along with zolpidem. Later on, zolpidem was changed to lorazepam. On stopping the drug after a gradual taper over eight weeks, she developed a feeling of tension and irritability, insomnia, indigestion, dizziness and a crawling sensation in the scalp on the next day. On re-administration of duloxetine, the symptoms disappeared within a day. Naranjo's score was 6 (probable) for the ADR.

Discussion: The ADR fulfils the diagnostic criteria for discontinuation reaction for the onset, duration, type of symptoms, risk factors and the response to the reinstitution of the withdrawn drug.

Conclusion: This is a probable case of duloxetine induced discontinuation reaction which appeared even though a gradual taper was done over eight weeks before stopping treatment. The current guidelines require a taper over four weeks only. A high index of suspicion is helpful in identifying antidepressant induced discontinuation symptoms for their proper management and prevention in future.

Key Words : Duloxetine, discontinuation symptoms

KEY MESSAGES: Duloxetine may cause discontinuation symptoms even if a gradual taper is done over the recommended four-week period. The risk is increased if co-existing anxiety, treatment beyond eight weeks and the concurrent administration of centrally acting drugs is present. The discontinuation symptoms need to be identified early for proper management. The prolongation of symptoms due to misdiagnosis causes morbidity and may hamper the compliance with future drug treatment.

INTRODUCTION

Discontinuation symptoms are those which are experienced on stopping prescribed drugs that are not drugs of dependence and they may be new symptoms or those which are similar to the original symptoms of the illness. The onset, duration and cessation of action are predictable and the symptoms can be suppressed by the reinstitution of the discontinued medication. These may manifest as gastrointestinal symptoms, irritability, increased dreaming, ataxia, sweating or paraesthesias. [1] About one third of the patients who are on antidepressants, suffer from discontinuation symptoms. [2] Antidepressant discontinuation symptoms can cause morbidity, they can affect the adherence to antidepressant treatment, they can prevent the cessation of antidepressant therapy and can be misdiagnosed, thus leading to inappropriate treatment. [3] The alertness of clinicians regarding the possibility of antidepressant-induced discontinuation syndrome is necessary for its prevention and management. Hence, we wanted to assess the causality of a suspected case of discontinuation reaction with duloxetine.

CASE REPORT

We report here, a suspected case of Discontinuation Syndrome with the use of the antidepressant, Duloxetine, which was detected during a retrospective adverse drug (ADR) monitoring study conducted in the Psychiatry unit of a teaching hospital in Pondicherry.

A 50 year old female was diagnosed in the outpatients clinic of the Psychiatry Department as a case of Mixed anxiety and depressive disorder with somatoform disorder. She was prescribed Duloxetine at a dose of 40mg for 124 days, followed by a 30mg dose for 48 days and a 20mg dose for seven days, after which the drug was stopped. On the withdrawal of Duloxetine, she developed a feeling of tension and irritability, insomnia, indigestion, dizziness and a crawling sensation in the scalp, one day after the stoppage of the drug. Concurrently, she was being administered zolpidem as an anxiolytic, which was later changed to lorazepam. Duloxetine was re-started and the symptoms disappeared over the next day.

We applied the Naranjo's ADR Causality Assessment scale[4]and found that it could be categorized as Probable only, with a score of six.

DISCUSSION

Duloxetine is known to cause discontinuation symptoms on withdrawal,[5] with an onset within seventy two hours of stoppage of the drug. They often occur on abrupt stoppage or missed doses, or even during the tapering of the drug. [6],[7] Increased risk is seen in patients who are on treatment for more than eight weeks, patients with anxiety symptoms at the start of antidepressant treatment and patients receiving other centrally acting drugs. [8],[9],[10] The symptoms are manifested within 24 hours. Duloxetine was continued for 180 days (six months) along with lorazepam and zolpidem, which are both centrally acting drugs. Anxiety was present at the start of the treatment. The common manifestations of the discontinuation reaction of duloxetine are dizziness, nausea, headache, paresthaesia, vomiting, irritability, and nightmares. [5] In our patient, affective (irritability), gastrointestinal (indigestion), neurological (dizziness, insomnia) and neurosensory (crawling sensation in the scalp, that is, paraesthaesia) components were observed. The discontinuation symptoms usually resolve fully within twenty four hours if the original antidepressant is recommenced, [4] which happened in our patient as well. The discontinuation symptoms with duloxetine can be avoided by careful tapering of the doses over four weeks. But in our patient, they appeared even though a gradual taper was done over a period of eight weeks.

The confounding factors in the causality assessment were the possibility of relapse of depression and/or anxiety. Considering the symptoms that distinguish the antidepressant discontinuation syndrome from the relapse of depressive illness and anxiety (e.g., dizziness, "electric shock" sensations, "rushing" sensations in the head) and the complete resolution of the symptoms in one week (not characteristic of depressive relapse), [11] we made a diagnosis of discontinuation syndrome. Depressive relapses typically occur after two weeks or more after the cessation of the medication and are most often marked by the gradual worsening of depression, insomnia, and psychomotor symptoms.

Although discontinuation syndrome is not dangerous and is normally mild and self resolving, it is uncomfortable and distressing to the patients. The symptoms are occasionally severe and prolonged, wherein they interfere with daily functioning and may affect the future compliance with antidepressants. The treatment approach is reassurance in mild cases and the reintroduction of duloxetine or another drug in the same class, that is, selective noradrenaline reuptake inhibitor (SNRI) with a longer half life in severe cases, followed by gradual tapering and monitoring. To improve compliance, the patients should be informed about the possibility of experiencing discontinuation symptoms on the stoppage of the drug and the clinician should stress that such drugs are not addictive.

CONCLUSION

This is a probable case of duloxetine induced discontinuation reaction which appeared even though a gradual taper was done over eight weeks before stopping the treatment. The current guidelines require a taper over four weeks only. A high index of suspicion is helpful in identifying the antidepressant induced discontinuation symptoms for their proper management and prevention in future.

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