

Bleeding in a Depressed dementia Patient Related with Mirtazapine replacing Duloxetine

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Antidepressants are widely used to treat depression in dementia since it is a prevalent and significant comorbidity [1]. There is no evidence to support the theory that mirtazapine, rather than duloxetine, may be a more effective treatment for depressive patients with dementia in some older people. All age groups may tolerate mirtazapine [2], and an overdose on its own is generally safe and does not cause delirium in any of the patients. To date, there have been five cases documented of mirtazapine-induced delirium; one case involved a depressed patient with early Lewy body type senile dementia, and two significant cases involved depressed individuals with slight memory impairment or a small lacuna of the left basal ganglia, the latter two [3-6] experiencing hyponatremia. In the absence of hyponatremia, we described a case of delirium in a depressed patient with Alzheimer's dementia that was linked to mirtazapine replacing duloxetine. Due to a case that has been documented, an 86-year-old woman with Alzheimer's disease experienced delirium following her administration of duloxetine.

A 69-year-old woman named Ms. Z was admitted to our department due to depression. She went to a mental health clinic because of low mood, waist pain, and backache. Major depressive illness was the diagnosis made. For eight months, she had been treated with 60 mg of duloxetine each day (up to 90 mg). Three months ago, she ceased medication due to improvement in her symptoms, although she still had lethargy and palpitations. For two months, she had been experiencing palpitations, sleepless-

ness, abrupt weight loss, decreased appetite, dejection, retardation, bad memory, guilt, and feelings of worthlessness. She had also occasionally entertained thoughts of suicide. The results of the brain CT scan after admission were consistent with cerebrovascular illness and indicated "right basal ganglia ischemic focus or lacunar infarction" (these findings are not regarded abnormal in a lady of this age). Major depressive disorder was identified as the diagnosis. Duloxetine 60 mg per day was administered to the patient for 12 days, and then 90 mg per day. There were no improvements seen; instead, the patient's anxiousness was getting worse and she had trouble falling asleep. Day 14 saw the beginning of 30 mg of mirtazapine daily and a reduction of 30 mg of duloxetine. The drug duloxetine was stopped on day 15. On the other hand, extreme anxiety was noted. Even after mirtazapine was increased to 45 mg daily on day 18, the patient continued to experience palpitations, sleeplessness, and chest discomfort despite having normal blood pressure and heart rate. Thus, lorazepam 2 mg or alprazolam 0.8 mg per day were paired with mirtazapine, respectively, while clonazepam 1 mg was administered intravenously. The patient's mental state significantly changed on day 22, and she appeared to be experiencing a disruption in consciousness. Mirtazapine was stopped for the patient after severe dizziness and visual hallucinations were noticeable at night. The patient was diagnosed with drug-induced delirium. A brain MRI scan on day 28 revealed "dual basal ganglia ischemic focus or lacunar infarction," which is broadly in line with the admission diagnosis. Olanzapine 2.5 mg was administered at night to treat the patient's delirium since they were unable to sleep and were wandering the ward [8]. By day 34, her delirium had disappeared, but her dementia was still evident in her impaired memory and visuospatial skills. According to her daughter, the patient actually experienced memory problems a year ago. The diagnosis of dementia, namely Alzheimer's disease, was changed after the subject's minimal state examination resulted in an 18/30 score and the inability to draw clock face components. The patient's anxiousness was treated with venlafaxin 75 mg daily after she complained of palpitations. The patient returned home on day 42, feeling less anxious. The subject provided written informed consent.

The topic states that depending on when delirium first appears and when medications are taken, drugs like duloxetine and mirtazapine, which are processed by the cytochrome P450 (CYP) enzyme system in the liver, may directly cause delirium [9]. The main isoforms involved in metabolising mirtazapine, a weak inhibitor of CYP isozymes, in vitro have been shown to be CYP2D6 and, to a lesser extent, CYP1A2. This drug has little inhibitory effects on the different CYP isoforms and seems to have a low risk of drug pharmacokinetic interactions [10]. It has been demonstrated that taking fluvoxamine 50 mg daily, a strong inhibitor of several CYP isoforms, and mirtazapine 30 mg daily together caused increases in plasma levels that were three and four times greater. Therefore, the metabolism of mirtazapine may be mediated via the inhibitory impact on CYP2D6. Duloxetine has a clinically negligible inhibition on CYP1A2, which is the primary enzyme involved in its extensive hepatic metabolism. Furthermore, duloxetine is a mild CYP2D6 inhibitor. Numerous drug interaction studies have assessed the possibility of duloxetine to alter other medications. For instance, duloxetine 60 mg twice daily for three weeks enhanced the C_{max} and AUC of desipramine [12,13]. This example suggests that delirium happens when the daily dose of mirtazapine (45 mg) is administered and the daily dose of duloxetine (30 mg) is reduced. It follows that the use of the serotonin and norepinephrine reuptake inhibitor duloxetine and the noradrenergic and selective serotonergic antidepressant mirtazapine causes elevated blood concentrations of mirtazapine, improving the reuptake of norepinephrine and serotonin [9]. The pathophysiology of delirium has been linked to a central increase in serotonin and norepinephrine [14], however the precise mechanism causing delirium has not been fully elucidated. It's still possible that the patient's heightened sensitivity to serotonin and norepinephrine's actions in their brain contributed to the delirium that developed.

Considering the prevalence and favourable tolerability of mirtazapine in older and co-occurring depression patients [2,15], one should be mindful of the possibility of infrequent but severe delirious episodes. It is advised to start treatment with a comparatively low dosage. Furthermore, in patients whose physical conditions make them more susceptible to this adverse effect, the replacement of a robust CYP2D6 inhibitor, such as duloxetine, with mirtazapine should be done gradually to prevent medication interactions.

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