Major depressive disorder with mania precipitated by antidepressant use (SNRI – serotonin and noradrenaline reuptake inhibitors)

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Abstract

Psychosis/mania is a serious drug-induced adverse effect that can occur with venlafaxine (serotonin noradrenaline reuptake inhibitor – SNRI) therapy in susceptible patients. Venlafaxine use is favoured in major depression, due to its side-effect profile and quick response. Mania precipitated by venlafaxine use in a patient diagnosed with major depression is reported here. These patients should therefore be managed under close supervision.

Keywords: major depressive disorder, mania, venlafaxine

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Introduction

Major depressive disorder (MDD) is diagnosed when a person experiences one or more major depressive episodes, without manic, hypomanic or mixed episodes.[1] Depression is associated with morbidity, mortality and functional disability. Females are at a higher risk than males.[2] The highest rate of depression occurs between the ages of 18–29, and is influenced by both genetic and environmental factors. Depressed patients have irregularities/decrease in monoamine neurotransmitters (norepinephrine-NE, serotonin-5HT and dopamine-DA) of unknown cause.[3] Antidepressant (AD) usage leads to an almost immediate blockade of neurotransmitter uptake (NE, 5HT and DA), but clinical response can take a few weeks.

Venlafaxine usage in patients with MDD has increased due to its favourable adverse effect profile and quick response. However, there is published evidence that it has precipitated mania in certain individuals. The UK National Institute for Health and Care Excellence (NICE)[4] recommends that a single AD be initiated at a low dose and titrated upwards slowly to avoid situations like this. The frequency of monitoring should also be increased, and lastly a different AD can be considered. Extra care must be taken when switching ADs.

Presented here is a 19-year-old Caucasian male that developed this adverse effect whilst on venlafaxine, which highlights the extra vigilance needed when prescribing venlafaxine for MDD.

Case history

RD, a first-year university student, presented at hospital with psychosis after five weeks of AD treatment. RD was referred to the hospital via his university counsellor, whom he had been seeing for a period of two months. The counsellor's report stated that he had symptoms of a depressive episode (difficult to complete tasks, loss of hope, low mood, struggled to concentrate, suicide ideation and possible self-harm), which was progressively worsening, with no improvement.

He was diagnosed with MDD and started treatment (fluoxetine 20 mg po 24 h). He was then prescribed lorazepam two weeks later for the anxiety. There is no family history of mood disorders or mental illness. RD is an avid church-goer and denies having used any substances (drugs, smoking and alcohol).

During the four weeks after initiation, his dose was titrated up as there was no improvement (fluoxetine 40 mg po 24 h). At the end of week four, the medication was changed to venlafaxine (this dose was also titrated up, as there was still no improvement). RD's condition was worsening, with increased suicidality, low mood and severe overall impairment in functioning. The fluoxetine was concurrently tapered off. The lorazepam dose was subsequently increased as RD became more aggressive and anxious.

During week six, he received venlafaxine (112.5 mg po 24 h) for two days, when family members noted a drastic change in his behaviour (burying items in the garden, not sleeping, irritability and aggressiveness). He was admitted as he was floridly psychotic which was due to venlafaxine use (which was discontinued). To manage his mood fluctuations, he was prescribed sodium valproate (mood stabiliser). The eventual mania was then controlled with the addition of quetiapine. For the purpose of the drug-related problem detected, there will be no further discussion on the other medicines prescribed. See Table I for a summary of his medication history.

Discussion

The British Association for Psychopharmacology guideline,[5] states that once moderate/severe depression is diagnosed, patients

Table I: Medication history

Date started	Indication	Medication	Dose/Route/Interval	Date treatment discontinued	Reason for initiation/ discontinuation
29/09/15	MDD	Fluoxetine	20 mg po 24 h	*20/10/2015*	***Increased dose – still depressed***
13/10/15	Anxiety	Lorazepam	0.5 mg po 24 h	*13/11/15*	
20/10/15	MDD	Fluoxetine	40 mg po 24 h	*27/10/15*	***Decreased dose – still depressed, change to 2nd antidepressant***
27/10/15	1. MDD	Fluoxetine	20 mg po 24 h for 3 days, then stop	*30/10/15*	***Tapering off – 2nd antidepressant introduced***
	2. MDD	Venlafaxine	37.5 mg po for 7 days, then increase to 75 mg po for 7 days	*09/11/15*	***Titrating dose upwards***
09/11/15	MDD	Venlafaxine	112.5 mg po 24 h for 14 days	*11/11/15*	***Patient appearing manic – decision to decrease dose and wean off***
11/11/15	MDD	Venlafaxine	75 mg po 24 h	*13/11/15*	***Patient was overtly psychotic – antidepressant stopped***
13/11/15	1. Anxiety	Lorazepam	0.5 mg po mane, 0.5 mg po midday, 2 mg po nocte	*16/11/15*	***Unable to contain patient, dose increased***
	2. Mood disorder (mania)	Sodium valproate	500 mg po 12 h	*On-going whilst in hospital*	***Added for mood stabilising benefit***
16/11/15	1. Anxiety	Lorazepam	0.5 mg po mane, 0.5 mg po midday, 3 mg po nocte	*On-going whilst in hospital*	
	2. Mood disorder (mania)	Quetiapine	100 mg po nocte	*19/11/15*	***Antipsychotic added due to mania – used with valproate for mood stabilising properties***

should be initiated on an AD, preferably the selective serotonin reuptake inhibitors (SSRIs), as it is usually better tolerated. The patient should be reviewed every one to two weeks after initiation of treatment.

Non-adherence and sub-therapeutic dosing results in treatment failure. Doses need to be titrated upwards slowly. In some instances, the diagnosis needs to be reviewed. At four weeks of treatment, if there is some improvement, treatment should be continued. If not, a longer trial should be considered. Thereafter, a dose increase can be trialled and lastly a new AD can be introduced if still no improvement.

RD's initial SSRI was titrated upwards, and, with no improvement, it was changed to venlafaxine (SNRI), during week five, instead of a longer trial of the SSRI. With psychiatric patients, therapy is often individualised. There was also a short period where RD was subsequently on an SSRI and SNRI.

It is important to rule out bipolar disorder prior to venlafaxine usage due to the possible precipitation of mania in patients. Venlafaxine is a new generation dual-action AD that inhibits the reuptake of 5-HT and NE similarly to the tricyclic antidepressants (TCAs). The dose of 75 mg will produce an SSRI effect, dual action starts at doses of 150 mg, and with doses higher than 150 mg it starts to inhibit DA reuptake as well.

Schueler et al. performed a meta-analysis that compared venlafaxine and duloxetine to SSRIs.[6] Venlafaxine was more effective for response but not for remission, and had a large number of drop-outs due to adverse effects. In a retrospective cohort study by Patel et al. to investigate AD therapy causing an onset of mania/ bipolar disorder it was concluded that it increased the risk for patients with depression.[7]

Tondo et al. showed that acute mania was precipitated by the use of TCAs and SNRIs (venlafaxine), with an estimated rate of 12.5% for those treated with AD,[8] whilst Patel's study demonstrated an overall incidence of mania of 10.9 in 1 000 persons-years. Ghaemi et al. looked at randomised controlled studies of AD that caused acute mania and they concluded that there was significant risk of mania and worsening of bipolar with ADs.[9] Vieta et al. found that venlafaxine had a 12% chance of inducing acute mania and paroxetine 2%.[10] Evidence thus shows that venlafaxine and AD usage have been linked to precipitation of psychosis.

Both fluoxetine and venlafaxine are serotonin agonists, and a combination of these drugs can lead to either serotonin syndrome or mania. Serum levels of venlafaxine can increase when administered together with fluoxetine.[11] There was also a point when RD was on fluoxetine and venlafaxine simultaneously, which could have contributed to precipitating mania. Fluoxetine has a long half-life and has the potential to cause drug-drug interactions with newly initiated drugs. ADs can take four to six weeks to reach maximum effect.[12] He should therefore have been on fluoxetine for a longer period prior to changing ADs, whilst the pharmacokinetic profile of fluoxetine should have also been taken into consideration, to minimise any potential drug-drug interactions.

Conclusion

This case illustrates that the use of venlafaxine in MDD can precipitate mania. It is imperative that patients be screened appropriately prior to initiation of ADs and should be closely monitored; they should be encouraged to report adverse effects. Caution must be taken when switching ADs in the absence of a therapeutic response from the initial AD. Upward titration

of necessary doses and tapering off of the unnecessary drug should be done under supervision of the healthcare professional. Pharmacists should become more involved in the patient's clinical care to identify patients at risk and prevent potential adverse effects. This case report shows that there should be heightened vigilance when prescribing venlafaxine for MDD.

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