Original Article

Case Reports Of Escitalopram Induced Switch-Dose Independent

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Abstract

Objective

A couple of studies have recorded that treatment with SSRIs for various psychiatricillnesses can get a switch in the mood like emergent manic or hypomanic symptoms.Escitalopram, being one of the mainline prescriptions among the serotonin reuptake inhibitors (SSRIs) for its tolerability and less side effect delivering nature additionally have been accounted for to have mood switching nature. This impact remains unknown whether it is dose related.

Method

In the current report, we displayed about five such instances of treatment-induced hypomania or mania with escitalopram as a commonly prescribed drug for MDD and Anxiety spectrum disorders. There was no significant family history of bipolarity or high-risk factor for bipolarity in the patient itself.

Results

In each of the five cases, manic/hypomanic symptoms arose in less than 6 weeks justafter the initiation of escitalopram in varying doses from 5mg to 20 mg/day. In addition, hypomanic episodes dialed back on reducing escitalopram. Activating symptoms were not seen after the discontinuance of escitalopram treatment.

Conclusion

Our case series shows that escitalopram may provoke treatment-induced mania/hypomania in a dose-independent manner. indeed, Treatment at lower dosages needs to be cautious and psychoeducation about the activating effects couldpick all the more such events in clinical settings. Accordingly helps in the discontinuance of medication and/or substitute measurements perceived.

Introduction

Beginning with first-line management of SSRIs as prescription of choice for variousmental disorders such as MDD, OCD, and Anxiety spectrum disorders. several studies reported the mood-switching tendency of SSRIs. however, higher on the instance is with activating SSRIs such as fluoxetine, and sertraline with dose independence and chronicity. the major guidelines [1,2] warrant the activating side effects of SSRIs and it grades them as the least mood-switching drug in comparisonwith other classes of anti-depressants such as TCAs, and SNRIs.[3]

Regardless of the significance of the activating phenomenon, the researchers postulated focal serotonergic and

catecholaminergic hypotheses [6,7] for the accompanying reasons. In the first place, more elevated levels of urinary noradrenaline and dopamine have been related to switching to hypomania and mania.The elevated levels of specific monoamine metabolites in the CSF were related to enacting effects.[8] on the contrary, direct pharmacological treatment brought about raised catecholamine levels to mimic mood switches. At last, a few hereditary polymorphisms associated with serotonergic and catecholaminergic pathways havebeen proposed as putative risk factors for treatment-induced Mania/hypomania.[9] Albeit a few examinations have distinguished different risk factors for switching with antidepressant treatments,[5,10,11] others have different opinions on these data.[12,13]Eminently, past studies have reported that antidepressants result in long-term side effects invariably, and with individual and family history of bipolarity there is an increased risk of mood cycling.

Major depressive episodes occur in patients with both MDD and bipolar disorder. However, it is often challenging to distinguish between the two because the clinicalfeatures of MDD and Bipolar disorder show a hairline of demarcations. Around 20%–70% of bipolar disorder clinically presents as depression, majority diagnosed as bipolar depression and hypomanic episodes are missed due to the productivity

caused by illness itself.[14] Therefore, careful use of antidepressants while managing patients with major depressive episodes might be a relieving factor.

Escitalopram, one of the FDA-endorsed SSRIs, is the S-enantiomer of citalopram. Itacts explicitly on 5HTT receptors, with less troublesome effects than other SSRIs. less reported mood switches have been documented,[15,16] it stays obscure whether thiseffect is dose-dependent. Subsequently, the current work shows the dose- independent properties of escitalopram in developing mania/hypomania. There are negligible articles reporting activating effects of escitalopram on the dose- independent pattern. Making our case reports on the focus of antidepressant-inducedmood switching.

Case presentation

We presented five patients with no foundation of bipolarity who developed manic- hypomanic switching with escitalopram on independent doses within 6 weeks of treatment initiation. The singular narratives are summed up beneath. Tables 1 and and 2

Table 1 Case histories

Case	Diagnosis	Duration of illness	Personal and family history of bipolar	Comorbidity with medical illnesses
A. Female, age 20	Moderate depression	3 months	No	No
B. Male, age 37	Generalised anxiety disorder	8 months	No	Gastritis
C. Female, age 52	Recurrent depressive disorder	4 years	No	Diabetes andHypertension
D. Female, age 19	Pathological grief reaction	1 year	No	Hypothyroid
E. Female Age 27	Acute stress disorder	1 Month 10 days	No	Bronchial asthma

BRIEF HISTORY OF PATIENTS

Patient A

Patient A was a 20-year-old female nursing student presenting with a 2-month history of low mood, anhedonia, decreased appetite, insomnia, decreased interaction with friends, and Lack of concentration with premorbid internalizing traits not on any medications. No Individual or family history of bipolarity or history of medical comorbidities. with normal blood indices. Diagnosed with Moderate depression based on the Diagnostic and Statistical Manual of Mental Disorders (DSM- 5)[35] following which she was prescribed escitalopram at a dosage of 5 mg/day. After1st week she reported no improvement in her depressive symptoms. However, as thiseffect was insufficient, the dose was increased to 10 mg/day. The patient was broughtto OPD on the 4th day of dose increment with overfamiliarity, an urgency to talk, appeared very cheerful, excessive grooming and feels energetic throughout the day.Symptoms of hypomania reduced within a month as escitalopram was tapered off. The patient and attender refused mood stabilizers. Hence, started on Tablet Quetiapine 25mg increased to 50mg/day due to reporting of sedating effect taperedto 25mg/day and maintained for 2 months without manic/hypomanic symptoms. There was a loss to follow up.

Patient B

Patient B was a 37-year-old man presenting with a 4-month history of free-floating anxiety, negative thoughts, worrying about minor matters, palpitation associated with sweating, and increased frequency of urination and defecation. he had previously been diagnosed with the recurrent acid peptic disease currently asymptomatic not on medication. he had no history of manic or depressive episodesand had no family history of bipolar disorder. His blood parameters were normal. He was diagnosed with Generalized anxiety disorder based on DSM V criteria, following which he was prescribed escitalopram at a dosage of 5 mg/day along withTab. clonazepam 0.5mg Hs in 1st week. On 1st follow-up increased to 10mg for 2 weeks along with Tab clonazepam 0.25mg. as there was a mild improvement with his symptoms. during 3rd follow-up increased to 15mg and clonazepam was stopped,7th day after which his wife reported that he exhibited manic symptoms such as irritability, uninterruptable pressured speech, authoritative behavior, increased motor drive, hypersexuality, reckless behavior, flight of ideas, excessive energy formore than 2 days. Abrupt discontinuation of escitalopram was done. As the patient and attender are not willing for admission. Treatment was initiated on an OPD basis with weekly follow-up and started on sodium valproate 250mg once daily and increased on the 4th day to 500mg after a month 750mg was maintained as there wasa significant improvement. and he has exhibited no manic/hypomanic symptoms during follow-up.

Patient C

Patient C was a 52-year-old post-menopausal woman presenting with a 2-year history of depressed mood, anhedonia, easy fatigability, loss of appetite, and decreased productivity with a history of diabetes and hypertension for 7 years on regular medication Tab metformin 500mg BD and Tab. Amlodipine 5mg OD. H/o 2 previous depressive episodes which lasted for 2 months of duration with no treatment history, no features suggestive of hypomania or mania, and no family history of any mental illness. Her thyroid gland was functioning normally. Blood parameters are within normal limits except for elevated ESR. Started on escitalopram 5mg for 7 days, but the patient reported on the 8th day with irritability,restlessness, increased energy, cracking jokes, cheerfulness, distractibility, anddecreased need for sleep. When escitalopram was tapered off, her hypomanic symptoms significantly improved. The patient is currently stable on the treatment ofTab Quetiapine 300mg/night, and she has exhibited no hypomanic symptoms duringfollow-up.

Patient D

Patient D was a 19-year-old unmarried female presenting with 1 year history of lowmood, insomnia, irritability, lack of concentration, crying spells, low appetite, anhedonia followed by father's sudden demise. She is also a known case of hypothyroidism on Tab. Levothyroxine 50mcg currently her TSH values were normal. There is no history of depressive or manic or hypomanic episodes in the past. She was started on Tab. Escitalopram 5mg for 7 days and reviewed on 8th dayas she was responding the dose increased to 10mg for 14days. Reviewed her on 22nd day. as her affect improved since last visit the dose adjusted to 15mg. While on 15mgshe reported feeling talkative, excessive

happiness, increased motor activity, doesn't feel tired, increased appetite. Following which she was started on Tab.olanzapine 5mg and tapered Escitalopram to 5mg and stopped her symptoms reduced by the end of 2nd week and Tab.olanzapine increased to 10mg and maintained for 6 months. the patient is maintaining well without any manic/hypomanic symptoms.

Table 2 Course of escitalopram treatment-emergent mania

Case	Duration of escitalopram treatment				Days after discontinuation of escitalopram mania/hypomania symptoms resolved	Medications following switch	Follow-up results
	5mg/day	10mg/day	15mg/day	20mg/day			
A.	7 days	4 days of treatment before mania	-	-	Within 1 month	Quetiapine 25mg/day for 2 months was tapered slowly and stopped. The patient refused a mood stabilizer.	2 months, no hypomanic switch, loss to follow-up
B.	7days	14days	7days	-	Within 3 weeks	Sodium valproate 750 mg/day at night	5 months, no manic switch.
C.	7 days	Reported on 8th day	-	-	Within 2 weeks	Quetiapine 300mg/day	4 months,no hypomanic switch.
D.	7 days	14days	10th day	-	Within 2 weeks	Tab olanzapine 5mg/day	6 months,no hypomanic switch
E.	7 days	14days	14days	9th day	Within 3 weeks	Tab Quetiapine 200mg/day	3months no hypomanic switch

Patient E

Patient E was a 27-year-old female she is supervisor by profession diagnosed with acute stress disorder following termination from job. She presented with 1-month complaints of low energy, low mood, loss of appetite, crying spells, trying to isolateherself from family and friends with poor sleep. She is a known case of Bronchial asthma currently on maintenance dose of steroids. With no significant family historyof bipolar or any psychiatric illness. She was started on Tab Escitalopram 5mg for 7days increased to 10mg for 14days and during 3rd visit increased to 15mg as she wasnot responding well. While she was on 20mg escitalopram on the 8th day of dose shereported feeling energetic, developing new interests, being argumentative on small matters, increased productivity and decreased need for sleep. Tapered escitalopramto 5mg and stopped along with Tablet Quetiapine 100mg symptoms reduced by 3rd week. She was maintained on 100mg of quetiapine for 3 months with no symptomsof mania or hypomania.

Discussion

The present case series demonstrates that escitalopram-induced mania/hypo-mania is a dosage-independent phenomenon. Indeed, in patients A, B, D, E mood switchingappeared shortly after the few weeks of initiation of escitalopram treatment and subsequent upward titration with proper gaping. Furthermore, manic/hypomanic episodes subsided as the dosages of escitalopram were reduced within a month. Notably, in Patient C, mood switching occurred rapidly within the first week of commencement of treatment at a low dose of escitalopram 5mg.

Late reports cited that antidepressants incited a switch among patients with MDD.[18,19]Without a doubt, patient switched symptoms can be sorted under disorders in DSM-5.[20] Hence, In addition, our patients continued with standard treatments with a mood stabilizer or antipsychotics for bipolar disorder as per CANMET rules.[2]Regardless, a couple of past studies have recommended that a single episode of switch related to anti-depressants doesn't need mood stabilizers.[18,21]. Further explanations on antidepressant-induced switches requiring mood stabilizers should be perceived.

According to Akiskal's classification unipolar depression gets rapid response with antidepressant's and switched to bipolar (Switching from "unipolar" to bipolar II)[2.] Escitalopram displays better tolerability and efficacy than citalopram or potentiallyany antidepressants in patients with unipolar depression. Although it is less side effect producing than other SSRIs Escitalopram-induced mania/hypomania has beenrecorded in a couple of case reports.[16] the percentage of SSRI-induced switch is around 3-6% in a person diagnosed with bipolar depression.[5,6] some studies cite thatit's difficult to diagnose bipolar depression in absence of genetic or family history orin the absence of risk factors for bipolar disorder .[24] even though our case series of patients who experienced treatment-induced switch were 4 females of different agegroup out of which 3 had co-morbidities[26]. Patient 'C' is of post-menopausal age group and almost all Patients (A, D, E) were in 20's age group and Patient 'B' is a male with no other complications except for gastritis has also been reported with mood switch.[17,25].

Scott et al[26] have proposed a basic relationship between thyroid disorder andbipolarity in the family for the switch phenomenon, which matches with patient D (hypothyroidism). One of our patients has hypothyroid as comorbidity as referencedto this article. Likewise, a couple of distributions cited that newer antidepressants have revealed that treatment-induced switch may be dose-dependent, which doesn'tfit with our case reports. Around half of the patients with bipolar disorder take antidepressants without any mood stabilizers and still doesn't switch.

Although the way that escitalopram efficacy and tolerability have been assessed because of monotherapy or adjunctive treatment for bipolar depression,the escitalopram dose used in the related article correlates with our patient profiles, suggesting that escitalopram-induced switches are real. A further review ought to bedone on wide treatment groups to know the genuine reality.

Our patient profile is not extensive. we just featured the perspectives in our cases which most likely actuated the switch phenomenon.[7] For example, SSRIs can quickly show improvement because of polymorphisms (5-HTTLPR) in the serotoninreceptor gene which was related to treatment responsiveness as per speculation [27]. indeed, even its viewed as 5HTT restricting potential is impacted by polymorphismof the HTR2A receptor and CYP450 gene independently[28].

It is that, no bipolar risk factors were found in our cases even with a lower dose of 5mg Escitalopram can prompt a switch. We can't close it as a dose-related incidentaleffect because our 5 patient profiles responded differently at various dosages within6-week period which is considered to be the normal adaptability time for any antidepressants to act on receptors. Four cases show a switch with up-titration and another with a fundamental dose of Escitalopram 5mg. Future multicentric analysiscan be done like, pharmacogenomics and genetic imaging studies on multiethnic groups to perceive the connections between dose-related or unrelated switches in regards with escitalopram.

Conclusion

Our case series shows that escitalopram may answer distinctively in different peopleeven with no bipolar risk factors. Even though escitalopram is seen as safer and hasfewer side effects providing the drug in comparison with various SSRIs, treatment at lower doses and with careful vertical titration may be vital in patients with suspected bipolarity or co-morbidities. Hereby concluding it with no small case reporting can make an impact on this topic and further supportive studies are neededto conclude it.

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