Original Research Article

Development of untoward withdrawal symptoms due to abrupt discontinuation of antidepressants: A comparative study of duloxetine and desvenlafaxine

Tarun Yadav[1], Prerana Gupta[2*]

[1]PG Resident (Year 2), [2]Associate Professor, Department of Psychiatry, Teerthanker Mahaveer Medical College and Research Centre, Moradabad , Uttar Pradesh, INDIA.
Email: preranagupta1978@gmail.com

Abstract

Background: About 20 % of patients develop antidepressant discontinuation syndrome following an abrupt stoppage or marked reduction in the dose of an antidepressant taken continuously for one month. It is important to recognize these symptoms in the initial stage itself in order to avoid the problems in further management. **Aims and Objectives:** Aim of the study was to compare the development of untoward withdrawal symptoms due to abrupt discontinuation of Desvenlafaxine and Duloxetine by the patients themselves either willfully or accidently **Materials and Methods:** We had taken patients who were already on duloxetine and desvenlafaxine at prescribed dose for at least 1 month and now discontinued on their own for 1 day or more and reported with some untoward symptoms were included in the study. **Sample:** Total number of patients were 50. 25 consecutive patients who stopped duloxetine for 1 day or more and fulfilled all the inclusion criteria. 25 consecutive patients who stopped desvenlafaxine for 1 day or more and fulfilled all the inclusion criteria. **Results:** The results of this systemic review indicate that withdrawal symptoms occur after abrupt discontinuation of Desvenlafaxine and Duloxetine.88% of sample on duloxetine and 80% of sample on desvenlafaxine reported lethargy after discontinuing medicines.92% of the patients on duloxetine and 84% patients on desvenlafaxine reported fatigue on stopping the drugs.80% of sample on duloxetine and 62% of the sample on desvenlafaxine reported headache.80% of sample on duloxetine and 72% on desvenlafaxine reported vertigo on sudden stoppage of the drugs.Lethargy and fatigue were the most common withdrawal symptoms. However, no significant difference was found for the comparison of Lethargy, Fatigue, Headache/ Achiness, Achiness and Sweating between Duloxetine and Desvenlafaxine. Both the SNRIs were seen to be equal in causing withdrawal symptoms insomnia, nausea, vomitting, dizziness and vertigo. No significant difference was found for the comparison of light headedness, burning sensation, tingling, electric like / shock-like sensations and anxiety between Duloxetine and Desvenlafaxine. **Conclusions:** We concluded that both drugs cause similar withdrawal symptoms. The withdrawal symptoms were independent of the dose prescribed. The clinicians need to be aware of this abrupt withdrawal and should counsel the patient well in advance about the severity of withdrawal symptoms while prescribing either of the drugs.

Key Words: Antidepressant Withdrawal, Duloxetine, Desvenlafaxine.

[*]**Address for Correspondence:**
Dr. Prerana Gupta, Associate Professor, Department of Psychiatry, TMMC and RC, Moradabad, UP, India.
Email: preranagupta1978@gmail.com
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INTRODUCTION

About 20% of patients develop antidepressant discontinuation syndrome following an abrupt stoppage or marked reduction in the dose of an antidepressant taken continuously for one month.[1] Cessation of antidepressant therapy may increase the risk of relapse of depression or anxiety. Unlike the symptoms of antidepressant discontinuation syndrome, symptoms of relapse usually take more than few days to appear and to disappear following reintroduction of the antidepressant.[2]

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Withdrawal symptoms have been reported after reduction and/or discontinuation of antidepressant drugs including selective serotonin reuptake inhibitors (SSRI) and serotonin – noradrenaline reuptake inhibitors (SNRI). Withdrawal symptoms can have either an early or a late onset, may have a short or long duration, and can be easily misinterpreted as signs of an impending relapse. SNRI have been reported to produce similar types of discontinuation/withdrawal symptomologies.[3-5] Such a review appears to be important in view of the fact that SNRIs are increasingly prescribed6 and usually considered the first choice in the treatment of mood and anxiety disorders, both for their efficacy and for their presumed high levels of safety and tolerability.[7] They are indicated and administered in clinical conditions such as chronic pain, functional medical disorders, and menopausal symptoms.[7] The aetiology of antidepressant discontinuation syndrome is not fully understood but it tends to occur after the abrupt discontinuation of an antidepressants, though may also occur even with a tapering dose of these medicines. It is known to occur with MAO (inhibitors), SSRI, SNRI, and atypical antidepressants. The syndrome can occur by missing even a single dose of medications with short half-lives, such as paroxetine and venlafaxine. Symptoms can last for weeks, sometimes longer. It is important to recognize these symptoms in the initial stage itself in order to avoid the problems in further management.[8]

AIM

Aim of the study was to compare the untoward withdrawal symptoms due to abrupt discontinuation of Desvenlafaxine and Duloxetine by the patients themselves either wilfully or accidently.

OBJECTIVES

- To Study the withdrawal symptoms from the discontinuation of desvenlafaxine.
- To Study the withdrawal symptoms from the discontinuation of Duloxetine.
- To compare the withdrawal symptoms arising from the discontinuation of desvenlafaxine and duloxetine.

MATERIALS AND METHODS

We had taken patients who were already on duloxetine and desvenlafaxine at prescribed dose for at least 1 month and now discontinued on their own for 1 day or more and reported with some untoward symptoms were included in the study.

Sample size: Total number of patients was 50. 25 consecutive patients were those who stopped duloxetine for 1 day or more and fulfilled all the inclusion criteria. 25 consecutive patients were those who stopped desvenlafaxine for 1 day or more and fulfilled all the inclusion criteria.

Tools: Patients were interviewed based on a structured proforma with a list of commonly occurring withdrawal symptoms from desvenlafaxine and duloxetine.

Inclusion Criteria:

- Patient taking duloxetine or desvenlafaxine continuously for atleast 1 month.
- Patient discontinued duloxetine or desvenlafaxine for 1 day or more.
- Patient willing to participate in the study.

Exclusion Criteria:

- Patient having any major medical / surgical illness.
- Patient taking any drug/drugs other than duloxetine or desvenlafaxine.

RESULTS

Table 1: Sex Wise Distribution of Sample

Sex	Duloxetine	Desvenlafaxine	Total
Male	11	11	22
	44%	44%	44%
Female	14	14	28
	56%	56%	56%
Total	25	25	50
	100%	100%	100%

Table 2: Religion Wise Distribution Of Sample

Religion	Duloxetine	Desvenlafaxine	Total
Hindu	15	11	26
	60%	44%	52%
Muslim	10	13	23
	40%	52%	46%
Sikh	0	1	1
	0%	4%	2%
Total	25	25	50
	100%	100%	100%

Table 3: Distribution Of Sample According To Marital Status

Marital Status	Duloxetine	Desvenlafaxine	Total
Married	25	23	48
	100%	92%	96%
Unmarried	0	2	2
	0%	8%	4%
Total	25	25	50
	100%	100%	100%

Table 4: Distribution Of Sample As Per Family Type:

Family Type	Duloxetine	Desvenlafaxine	Total
Joint	15	6	21
	60%	24%	42%
Nuclear	10	19	29
	40%	76%	58%
Total	25	25	50
	100%	100%	100%
Chi Square value=6.650, p value=0.010			

Table 5: Distribution Of Sample As Per Socioeconomic Status

Socio Economic Status	Duloxetine	Desvenlafaxine	Total
Lower Class	25	22	47
	100%	88%	94%
Middle Class	0	2	2
	0%	8%	4%
Upper Middle Class	0	1	1
	0%	4%	2%
Total	25	25	50
	100%	100%	100%
Chi Square value=3.191, p value=0.203			

Table 6: Distribution Of Lethargy, Fatigue, Headcahe, Achiness, Sweating Between Duloxetine And Desvenlafaxine

		Duloxetine	Desvenlafaxine	Total	Chi Square value	p value
Lethargy	No	3	5	8	0.595	0.440
		12%	20%	16%		
	Yes	22	20	42		
		88%	80%	84%		
Fatigue	No	2	4	6	0.758	0.384
		8%	16%	12%		
	Yes	23	21	44		
		92%	84%	88%		
Headache	No	5	7	12	0.439	0.508
		20%	24%	24%		
	Yes	20	18	38		
		80%	72%	76%		
Achiness	No	8	9	17	0.089	0.765
		32%	36%	34%		
	Yes	17	16	33		
		68%	64%	66%		
Sweating	No	14	14	28	0.000	1.000
		56%	56%	56%		
	Yes	11	11	22		
		44%	44%	44%		

Table 7: Distribution Of Insomnia, Nausea, Vomitting, Dizziness And Vertigo Between Duloxetine And Desvenlafaxine

		Duloxetine	Desvenlafaxine	Total	Chi Square value	p value
Insomnia	No	6	11	17	2.228	0.136
		24%	44%	34%		
	Yes	19	14	33		
		76%	56%	66%		
Nausea	No	16	12	28	1.299	0.254
		64%	48%	56%		
	Yes	9	13	22		
		36%	52%	44%		
Vomiting	No	18	21	39	1.049	0.306
		72%	84%	78%		
	Yes	7	4	11		
		28%	16%	22%		
Dizziness	No	7	8	15	0.095	0.758
		28%	32%	30%		
	Yes	18	17	35		
		72%	68%	70%		
Vertigo	No	5	7	12	0.439	0.508
		20%	28%	24%		
	Yes	20	18	38		
		80%	72%	76%		

Table 8: Distribution Of Irritability, Aggression, Agitation, Mania And Jerkiness Between Duloxetine And Desvenlafaxine

		Duloxetine	Desvenlafaxine	Total	Chi Square value	p value
Irritability	No	9	7	16	0.368	0.544
		36%	28%	32%		
	Yes	16	18	34		
		64%	72%	68%		
Agitation	No	13	12	25	0.080	0.777
		52%	48%	50%		
	Yes	12	13	25		
		48%	52%	50%		
Aggression	No	7	9	16	0.368	0.544
		28%	36%	32%		
	Yes	18	16	34		
		72%	64%	68%		
Mania	No	25	25	50	0.000	1.000
		100%	100%	100%		
	Yes	0	0	0		
		0%	0%	0%		
Jerkiness	No	22	20	42	0.595	0.440
		88%	80%	84%		
	Yes	3	5	8		
		12%	20%	16%		

DISCUSSION

56% of the sample in both duloxetine and desvenlafaxine group was females. (table 1) 60% of sample on duloxetine were Hindus and 40% were Muslims (table 2). 44% of sample on desvenlafaxine were hindus, 52% were Muslims and 4% were Sikhs.(table 2). All the patient son duloxetine were married while 2 patients on desvenlafaxine were unmarried (table 3).15 patients taking duloxetine lived in a joint family while 10 resided in a nuclear family (table 4). 19 patients taking desvenlafaxine were living in a nuclear family whereas only 6 were in a joint family system (table 4). All the patients taking duloxetine belonged to a low socioeconomic status while 22 patients on desvenlafaxine belonged to low socioeconomic status (table 5). Most of the discontinuation of the drugs was cited due to inability to buy the drugs as most of our sample belonged to a low socio-economic status. 3 patients on duloxetine and 5 patients on desvenlafaxine reported wilful stoppage of drug as they didn't want to continue the treatment further. Studies have shown that one third of patients discontinue within one month and 50 % of patients discontinue within

3 months of start of antidepressants[3]. The results of this systemic review indicate that withdrawal symptoms occur after abrupt discontinuation of Desvenlafaxine and Duloxetine. 88% of sample on duloxetine and 80% of sample on desvenlafaxine reported lethargy after discontinuing medicines (table 6). Lethargy or flu like syndrome has been very frequently reported as the most prominent symptom in both SSRI and SNRI withdrawal syndromes.[4] Withdrawal symptoms are usually mild and self-limiting.4 92% of the patients on duloxetine and 84% patients on desvenlafaxine reported fatigue on stopping the drugs (table 6). 80% of sample on duloxetine and 62% of the sample on desvenlafaxine reported headache (table 6).Headache is the second most common withdrawal symptom reported in many studies.3,4 80% of sample on duloxetine and 72% on desvenlafaxine reported vertigo on sudden stoppage of the drugs.(table 8). Lethargy and fatigue were the most common withdrawal symptoms. The distribution of Lethargy, Fatigue, Headache/ Achiness, Achiness and Sweating was compared between Duloxetine and Desvenlafaxine using the Chi-square test. No significant difference was found for the comparison of Lethargy, Fatigue, Headache/ Achiness, Achiness and Sweating between Duloxetine and Desvenlafaxine ($p>0.05$) (figure 1). Both the SNRIs were seen to be equal in causing withdrawal symptoms like insomnia, nausea, vomiting, dizziness and vertigo (table 8, figure 3). No significant difference was found for the comparison of light headedness, burning sensation, tingling, electric like / shock-like sensations and anxiety between Duloxetine and Desvenlafaxine. The distribution of Irritability, Agitation, Aggression, Mania and Jerkiness was compared between Duloxetine and Desvenlafaxine using the Chi-square test. No significant difference was found for the comparison of Irritability, Agitation, Aggression, Mania and Jerkiness between Duloxetine and Desvenlafaxine (Figure3). However many studies have reported that desvenlafaxine carries a significantly higher risk of Antidepressant discontinuation syndrome.[2-4] Desvenlafaxine also causes a more severe form of Antidepressant Discontinuation Syndrome which is characterized by early onset withdrawal symptoms which can be linked to the short half –life of the drug2.Duloxetine carries a low risk in comparison but this advantage wanes with higher doses(120 mg/day).[2] Most Desvenlafaxine treated patients experienced discontinuation symptoms to the rate of 75%.4 The incidence of discontinuation symptoms after treatment with duloxetine ranged from 9.1% to 16.5%4In this study the most common symptoms were dizziness and headache.4 Withdrawl symptoms in Desvenlafaxine typically appeared 24-48 hours after discontinuation and waned after 3 weeks.4 In our study, 100% of the sample on Desvenlafaxine and duloxetine experienced withdrawal symptoms.100 % of the sample reported the withdrawal symptoms within 24 hours of discontinuation.

CONCLUSIONS

We concluded that both drugs cause similar withdrawal symptoms. The withdrawal symptoms were independent of the dose prescribed. The clinicians need to be aware of this abrupt withdrawal and should counsel the patient well in advance about the severity of withdrawal symptoms while prescribing either of the drugs. In our country where sudden stoppage of drug is common phenomenon, both these drugs seem to be causing same withdrawal effects. So our study has important clinical implications in the prescription of SNRIs drugs in Depression.

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