A Novel Ten-Step Titration of Patients Discontinuing SSRI's Shows a Reduction in Severity and Frequency of Withdrawal Side Effects.

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Purpose

SSRI discontinuation syndromes are well recognized in the clinical literature and also in the product monographs for Paxil®, Effexor®, Celexa® and Cipralex® published in the Compendium of Pharmaceuticals and Specialties (CPS). All contain warnings against abrupt discontinuation. While all SSRI monographs recommend a gradual reduction in dose, no protocol is provided. Furthermore, SSRIs are available in a limited number of strengths, which does not allow for a gradual reduction in dose. Bogetto et al.[1], in 2002, described a four step, 25% decrement taper, in which patients experienced the discontinuation syndrome, and Keuthen et al.[2], in 1994, reported several cases using 16-20% decrement tapers in which patients also experienced the syndrome. We devised a more gradual 10-step protocol, 10% decrement per week, for 10 weeks. The objective of this study was to determine whether a 10-step tapering protocol was effective in reducing side effects associated with discontinuing SSRI therapy.

Methods

This is a retrospective study of randomly selected patients from our pharmacy database. Most of these patients had previously attempted to discontinue their SSRI using available commercial strengths. On a subsequent discontinuation they received a personalized treatment protocol reducing their SSRI dosage in approximately 10% decrements over a period of 10 weeks, irrespective of the dose of the SSRI patients were taking at the time of initiation of discontinuation.

Patients were asked if they were willing to answer questions about their treatment and consented to having the results presented in a report. Patients were asked to score the following side effects noted to be associated with SSRI discontinuation; irritability, dizziness, confusion, headache, nervousness, trouble sleeping, nausea, moodiness and crying [3]. For each of these symptoms a patient could select none (0), mild (1), moderate (2) or severe (3). Patients were then asked to rate the same side effects for their previous attempt to discontinue their SSRI treatment without our 10-step tapering protocol.

Results

We contacted 20 patients and 19 agreed to participate. Of these, 13 patients had tried to discontinue using existing product strengths (standard treatment) but experienced side effects and subsequently used our gradual stepwise treatment service. Six patients used our titration service without first attempting to discontinue their SSRI using the available commercial strengths.

The reduction in discontinuation symptom scores with the gradual stepwise reduction, in the 13 patients who used both methods, was shown to be statistically different at a p-value <0.0005 based on a Wilcoxon Signed Rank Test (Figure 1).

Summary statistics for individual symptoms by treatment group are presented in Table 1. All nine symptoms were impacted when the 10-step tapering protocol was used. Table 1 shows the mean symptom scores for the 13 patients using a standard taper and the 10-step tapering protocol. The data in Table 1 is shown graphically in Figure 2.

Furthermore, 53 per cent of patients using gradual stepwise reduction reported no discontinuation symptoms compared to 100 per cent of those using a standard treatment discontinuation protocol (Table 2).

Moderate to severe symptoms were reported more frequently across every symptom type for standard treatment than for the 10-step taper (Figure 3).

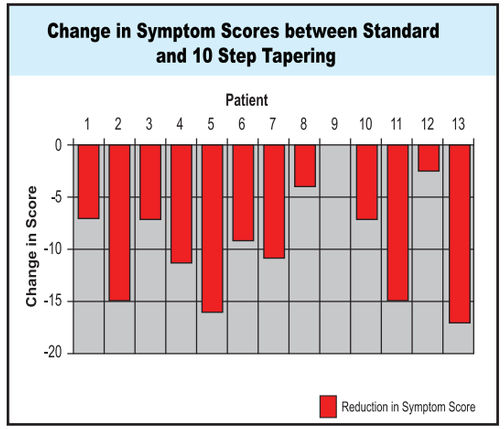

Figure 1. Change in symptom scores between standard and 10-step tapering.

The reduction in discontinuation symptom scores in the 13 patients using the 10-Step Tapering method verses the Standard Treatment Taper was significant at a p value = 0.0005. The p value calculation was based on the Wilcoxon Sign-Ranked Test.

	Treatment	
	Standard (N=13)	10-Step Tapering (N=13)
Symptom (Score 0,1,2,3)	Mean (std deviation)	Mean (std deviation)
Moodiness	2.08 (±0.95)	0.38 (±0.65)
Nervousness	1.92 (±1.04)	0.46 (±0.66)
Crying	1.69 (±1.38)	0.38 (±0.65)
Irritability	1.54 (±1.13)	0.46 (±0.66)
Trouble sleeping	1.46 (±1.27)	0.31 (±0.63)
Dizziness	1.15 (±1.28)	0.31 (±0.63)
Nausea	1.00 (±1.22)	0.15 (±0.55)
Confusion	0.85 (±0.9)	0.31 (±0.63)
Headache	0.69 (±0.95)	0.23 (±0.6)
Total Score(Max = 27)	**12.38 (±6.31)**	**3.00 (±5.26)**

Table 1. Summary statistics of individual symptoms by treatment

Mean treatment scores were reduced for all symptom types when 10-step tapering was used.

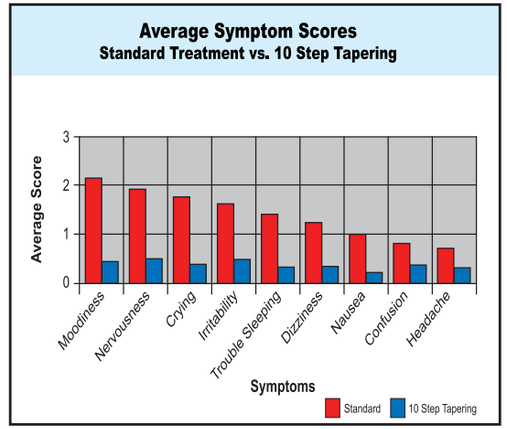

Figure 2. Average score across symptom type in 13 patients using both standard treatment taper and 10-step taper.

Average symptom scores were higher across every symptom in the standard treatment taper.

	Treatment			
	Standard		10 Step Tapering	
	n	%	n	%
Patients With Symptoms	13	100 %	6	46 %
Patients With No Symptoms	0	0 %	7	53 %

Table 2. Frequency of discontinuation symptoms with 10-step tapering.

All of the patients experienced symptoms using standard tapering protocols but 53% of patients were symptom free when the 10-step tapering protocol was used.

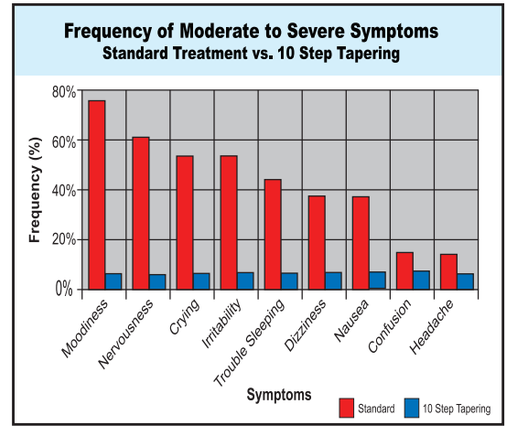

Figure 3. Frequency of moderate to severe symptoms across both tapering protocols.

Moderate to severe symptoms were reported more frequently across every symptom for the standard treatment tapering than for the 10-step taper.

Discussion

This study shows that a 10-step, gradual reduction in the SSRI dose can reduce discontinuation symptoms in patients that had previously experienced difficulty in stopping their SSRI treatment. A prospective double blind study confirming the difference between the two approaches would provide further support for this patient centered approach to SSRI discontinuation.

References

1. Bogetto, F., et al. (2002). "Discontinuation syndrome in dysthymic patients treated with selective serotonin reuptake inhibitors: a clinical investigation." CNS Drugs 16(4): 273-83.

2. Keuthen, N.J., et al. (1994). "Medication withdrawal symptoms in obsessive-compulsive disorder patients treated with paroxetine." J Clin Psychopharmacol 14(3): 206-7.

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