Physicians' Knowledge of Antidepressant Withdrawal Effects: A Survey

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Background: While the incidence of discontinuation events in controlled studies of serotonin reuptake inhibitors ranges between 34.5% and 86%, only a small number of discontinuation reactions are reported to national data bases of spontaneously reported adverse drug reactions. It was hypothesized that the disparity was due to lack of knowledge amongst physicians about the potential for antidepressant discontinuation reactions. ***Method:*** Therefore, a questionnaire was mailed to 100 psychiatrists and 100 general practitioners (GPs) in northeast England to assess the knowledge base and to validate this assumption. ***Results:*** Fifty psychiatrists (50%) and 53 GPs (53%) responded to the questionnaire. Of the respondents, 36 (72%) of the psychiatrists and 16 (30%) of the GPs were aware that patients may experience antidepressant discontinuation events; 33 (66%) psychiatrists and 22 (42%) GPs had had experience with patients who had discontinuation symptoms; and 10 (20%) psychiatrists and 9 (17%) GPs said they always caution patients about the possibility of discontinuation events. ***Conclusion:*** According to the results of the survey, a sizable minority of physicians denied being confidently aware of the existence of antidepressant withdrawal symptoms. Education about discontinuation reactions, including the hallmark features, symptoms, and course, is needed for both psychiatrists and family practice physicians.

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Withdrawal symptoms have been well-described for tricyclic antidepressants, primarily through the work of Dilsaver and colleagues.[1] As the use of the serotonin reuptake inhibitors (SRIs) increased, anecdotal case reports of discontinuation reactions appeared in the literature,[2–4] and several investigators began to study this phenomenon. In 1993, Black et al.[5] evaluated patients who were abruptly terminated from fluvoxamine treatment and found that 12 (86%) of 14 subjects developed new symptoms after discontinuation. At the end of a placebo-controlled clinical trial assessing the efficacy of paroxetine in the treatment of obsessive-compulsive disorder (OCD),[6] 5 (38.5%) of 13 subjects reported the onset of new adverse events during medication taper or within 2 to 14 days after their last dose. Similarly, 19 (34.5%) of 55 patients enrolled in a double-blind, placebo-controlled paroxetine study[7] reported the onset of new adverse events during the 2 weeks after treatment was discontinued.

While reports of SRI discontinuation phenomena have also been published in postmarketing studies based on information from the national data base of spontaneously reported adverse drug events in the United Kingdom[8,9] and Australia,[10] the incidence in these reports appears to be far lower than the 34.5% to 86% of patients reported to experience discontinuation events in controlled studies. This low incidence suggests either underreporting of discontinuation symptoms, lack of recognition of the phenomenon, or both.

We hypothesized that if doctors are not aware of the likelihood that patients will experience symptoms when SRIs are discontinued, they would be unlikely to recognize these symptoms and report them to national surveillance units. This report describes the results of a survey of physicians and psychiatrists undertaken to ascertain the general level of knowledge about antidepressant discontinuation events and, in particular, SRI discontinuation symptoms.

METHOD

We designed a questionnaire (Appendix 1) to elicit information on physicians' awareness of and experience with antidepressant discontinuation events. The 2-page questionnaire was mailed to 100 psychiatrists and 100 general practice physicians in northeast England, who were asked to respond anonymously. Percentages were calculated for each question on the basis of the total number of physicians who answered the question, i.e., blank responses were ignored.

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Table 1. Physicians' Knowledge of and Experience With Antidepressant Discontinuation Events*

	TCA		MAOI		SSRI	
Discontinuation Events	N	%	N	%	N	%
Knew of reports						
Psychiatrists	37	74	39	78	47	94
General practitioners	31	58	25	47	36	68
Have seen patients						
Psychiatrists	21	42	17	34	33	66
General practitioner	20	38	3	6	22	42

*Responses from a survey of 100 psychiatrists (N = 50) and 100 general practitioners (N = 53). Abbreviations: MAOI = monoamine oxidase inhibitor; SSRI = serotonin selective reuptake inhibitor; TCA = tricyclic antidepressant.

Table 2. Physicians' Response to Antidepressant Discontinuation Events*

	Psychiatrist		General Practice Physician	
Response	N	%	N	%
Always or usually advise patients	26	52	27	51
Would report to national surveillance bureau	20	40	26	49
Would write letter to journal	1	3	0	0

*Responses from a survey of 100 psychiatrists (N = 50) and 100 general practitioners (N = 53).

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RESULTS

A total of 50 psychiatrists, including 44 consultants in psychiatry and 6 psychiatry trainees, and 53 GPs responded to the questionnaire, although not all the respondents answered every question. Interestingly, 72% of the psychiatrists (N = 36) as opposed to 30% of the GPs (N = 16) said they were confidently aware of the possibility that patients might experience symptoms when they stop antidepressant treatment. In addition, 11% of the GPs (N = 6) and none of the psychiatrists reported that they were unaware of the risk of discontinuation events after antidepressant treatment.

Most physicians (both psychiatrists and general practice physicians) knew of reports about, and a sizable minority had seen, patients with discontinuation symptoms (Table 1). Almost all the psychiatrists (94%; N = 47) knew of reports of discontinuation events associated with serotonin selective reuptake inhibitors (SSRIs), a larger number than knew of reports about monoamine oxidase inhibitor (MAOI) (78%; N = 39) or tricyclic antidepressant (TCA) discontinuation (74%; N = 37). More GPs (68%; N = 36) also knew of reports of SSRI discontinuation events than of MAOI (47%; N = 25) or TCA (58%; N = 31) discontinuation symptoms. In terms of having experience with discontinuation symptoms after antidepressant treatment, 66% of psychiatrists (N = 33) had seen patients with SSRI discontinuation events, 34% (N = 17) had experience with MAOI discontinuation, and 42% (N = 21) had experience with TCA discontinuation. This is opposed to 42% (N = 22) of GPs who had experience with SSRI discontinuation, 6% (N = 3) who had seen patients with MAOI discontinuation symptoms, and 38% (N = 20) who had seen patients with TCA discontinuation events.

While most physicians said they would advise patients about the possibility of discontinuation events, few said they would report these symptoms to a national surveillance bureau or write a letter to a journal (Table 2). Fifty-two percent of the psychiatrists (N = 26) and 51% of the general practice physicians (N = 27) said they always or usually give advice to patients about possible discontinuation symptoms. However, only 1 psychiatrist (3%) and no GPs said they would be likely to write a letter to a journal reporting such symptoms. Fewer than half of both psychiatrists (40%; N = 20) and general practice physicians (49%; N = 26) said they would report discontinuation symptoms to a national adverse drug event monitoring bureau.

DISCUSSION

A sizable minority of psychiatrists and a majority of GPs said they were not confidently aware of adverse events associated with antidepressant discontinuation. This has important implications since physicians who have not heard about these phenomena will not be able to recognize or treat them. While many physicians reported that they generally would advise patients about the possibility of discontinuation events, less than half said that they would record these events with a national surveillance bureau, which may account for the discrepancy between the incidence in postmarketing surveillance data[8–10] and the studies of antidepressant discontinuation[5,6,10,11] Additionally, routinely educating patients about the possibility of antidepressant discontinuation symptoms may be justified since patients often become noncompliant and abruptly stop taking their medication.

One strategy for reducing the likelihood of discontinuation events would be to inform psychiatrists and primary care physicians about the hallmark features, symptoms, and course of these phenomena. In turn, they could take the time necessary to educate their patients on the benefits of good compliance and, equally important, the consequences of intermittent noncompliant behaviors (e.g., missed doses, late refills) that would lead to withdrawal reactions. In addition, physicians must become comfortable with implementing appropriate tapering schedules when discontinuing the shorter acting SRIs such as paroxetine, venlafaxine, and fluvoxamine. Fluoxetine, on the other hand, which has an extended half-life, is much less likely to cause discontinuation-emergent symptoms and, for the most part, tapering is not required for fluoxetine.

Drug names: amitriptyline (Elavil and others), fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft), venlafaxine (Effexor)

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Appendix 1. Survey of Knowledge of Antidepressant Withdrawal Effects

The purpose of this questionnaire is to survey the knowledge and experience of doctors and pharmacists of withdrawal effects with antidepressants. You are asked to complete the questionnaire by ticking the appropriate boxes **without using any reference source.** Thank you for your cooperation.

What is your area of practice:
Consultant/lecturer psychiatry ❑ Nonconsultant psychiatrist ❑ General practitioner ❑ Hospital pharmacist ❑ Community pharmacist ❑

1) Are you aware of any adverse effects which are likely to occur on cessation of treatment with antidepressants?
Confidently aware ❑ Heard reports, but unsure about likely effects ❑ Not aware of any reports ❑

2) Which, if any, antidepressants have been reported to be associated with withdrawal symptoms?

Tricyclic antidepressants	yes ❑	no ❑
MAOIs	yes ❑	no ❑
SSRIs	yes ❑	no ❑
Other	yes ❑	no ❑

If you have answered yes, please explain by giving some examples. _____

3) Have you had experience of withdrawal effects with antidepressants in any of your patients?

Tricyclic antidepressants	yes ❑	no ❑
MAOIs	yes ❑	no ❑
SSRIs	yes ❑	no ❑
Other	yes ❑	no ❑

If you answered yes, please state which antidepressant and number of occurrences. _____

Please indicate which bodily systems were involved:
CNS ❑ GI ❑ Respiratory ❑ Cardiovascular ❑ Musculoskeletal ❑
Other ❑ (describe briefly) _____

4) What dose of antidepressant would you consider stopping abruptly for the following antidepressants and indicate your usual practice regarding tapering the dose before stoppage? (Complete the table for your usual antidepressants only.)

Antidepressant	Daily dose at which you abruptly stop	Taper usually	
Amitriptyline	_____ mg/day	yes ❑	no ❑
Dothiepin	_____ mg/day	yes ❑	no ❑
Lofepramine	_____ mg/day	yes ❑	no ❑
Citalopram	_____ mg/day	yes ❑	no ❑
Fluoxetine	_____ mg/day	yes ❑	no ❑
Fluvoxamine	_____ mg/day	yes ❑	no ❑
Paroxetine	_____ mg/day	yes ❑	no ❑
Sertraline	_____ mg/day	yes ❑	no ❑

5) Do you advise/inform patients and carers of possible withdrawal symptoms on cessation of antidepressant treatment?
Always ❑ Usually ❑ Sometimes ❑ Never ❑

6) If you came across a case of antidepressant withdrawal phenomena would you…

a) Report to the CSM (or government drug surveillance unit)	yes ❑	no ❑
b) Write a letter to a medical journal	yes ❑	no ❑