IJPP
International Journal of
Pharmacy Practice

IJPP 2007, 15: 291–293

Received January 25, 2007
Accepted June 7, 2007
DOI 10.1211/ijpp.15.4.0006
ISSN 0961-7671

Patients' concerns about and problems experienced with discontinuation of antidepressants

ECG van Geffen, M Brugman, R van Hulten, ML Bouvy, ACG Egberts and ER Heerdink

Division of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences (UIPS), Faculty of Science, Utrecht, The Netherlands

ECG van Geffen, PhD student
M Brugman, research student
R van Hulten, researcher
ML Bouvy, researcher
ACG Egberts, professor in clinical pharmacoepidemiology
ER Heerdink, assistant professor of pharmacoepidemiology

Science Shop for Medicines, Department of Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands

ECG van Geffen, head of science shop for medicines
M Brugman, research student

SIR Institute for Pharmacy Practice and Policy, Leiden, The Netherlands

ML Bouvy, researcher

Correspondence: Dr. E.R. Heerdink, Division of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences (UIPS), Faculty of Science, PO Box 80082, 3508 TB Utrecht, The Netherlands. E-mail: e.r.heerdink@uu.nl

Acknowledgements: We would like to thank the pharmacists who staff the telephone medicines information service for collecting and providing the data.

All authors declare that there are no conflicts of interest. The study was funded by the Utrecht Institute for Pharmaceutical Sciences. We received no other funding.

Abstract

Objective Clinical trials and epidemiological studies have shown that premature discontinuation is a major problem during antidepressant therapy. Unfortunately, there is little information on how patients perceive treatment with antidepressants in clinical practice, and it is unclear whether patients perceive discontinuation as a problem. The objective of this study is to assess whether concerns and problems experienced with drug discontinuation occur more frequently in patients using antidepressants than in patients using benzodiazepines, antipsychotics or non-psychiatric medication.

Method All calls to a national telephone medicines information service received between 1990 and 2004 were examined using retrospective examination. Calls about discontinuation were identified and classified either as a general question about discontinuation, or as a problem experienced with discontinuation. These calls were grouped into the following main classes: antidepressants, antipsychotics, benzodiazepines or non-psychiatric medicines.

Key findings Of all 39 786 registered phone calls, 6159 (15,5%) related to antidepressants, 1658 (4.2%) to antipsychotics and 3916 (9.8%) to benzodiazepines. Patients calling about antidepressants called about discontinuation three times as often (odds ratio (OR) 2.8; 95% confidence interval (CI) 2.6–3.0), and reported a problem with discontinuation five times more often (OR 5.4; 95% CI 4.6–6.3), compared to patients who called about non-psychiatric medicines. The proportion of questions about discontinuation and problems experienced with discontinuation was also higher in patients calling about benzodiazepines and antipsychotics compared to patients calling about non-psychiatric medication.

Conclusion Patients perceive discontinuation of antidepressants, as well as discontinuation of antipsychotics and benzodiazepines, as a problem. Discontinuation seems a general problem for all psychiatric medicines, and needs more attention in the communication between patients and healthcare providers.

Introduction

Clinical guidelines recommend that patients treated with antidepressants should continue their therapy for at least 6 months after remission of symptoms.[1] However, clinical trials and epidemiological studies have shown that premature discontinuation is a major problem during antidepressant therapy. About one-third of the patients abruptly discontinue antidepressant treatment within the first 2 months, and as many as half of patients discontinue treatment within the first 6 months.[2,3] Dosing lapses and partial non-adherence also often occur.[4,5] In addition, one in five patients who stop therapy, abruptly discontinue their antidepressant instead of tapering, which increases the risk of unwanted withdrawal symptoms.[6]

Unfortunately, there is little information on how patients perceive treatment with antidepressants in clinical practice, and it is unclear whether patients perceive discontinuation as a problem. Information received directly from the patient may improve the understanding of patients' behaviour towards discontinuation of antidepressant use. The analysis of calls received by a specialist helpline confirmed the high prevalence of discontinuation symptoms with antidepressants.[7] A national telephone medicines information service in The

Netherlands has been shown to be a useful tool in identifying problems related to the daily use of medicines.[8] We used calls from this telephone information service with the objective to assess whether concerns and problems experienced with drug discontinuation occur more frequently in patients using antidepressants than in patients using benzodiazepines, antipsychotics or non-psychiatric medication.

Methods

In 1990 a national telephone medicines information service was started by consumer organisations and the Royal Dutch Association for the Advancement of Pharmacy, supported by the Dutch Ministry of Health. Through this service, patients or their carers can consult a pharmacist anonymously. Pharmacists are requested to complete a standard form for each call, registering the sex and age of the caller, drug names involved and a short description of the call itself. The forms are stored in a database. All calls registered between the beginning of the information service in 1990 and November 2004 were included in the study. Ethical approval was not required for this study.

Calls about discontinuation were identified with a free-text search using keywords (or parts thereof) for discontinuation (e.g. 'tapering', 'reduce', 'discontinuation symptoms', 'withdrawal', 'stopping'). These calls were reviewed by two of the authors (EvG and MB) independently, in order to classify the call as either a general question about discontinuation, or a problem experienced with discontinuation. In case of disagreement about the classification, the call was assessed by four of the authors to reach agreement. Questions about discontinuation include questions on whether, when and how to discontinue the medicine, and what to expect during discontinuation of the medicine. Problems experienced with discontinuation include the following: the occurrence of discontinuation symptoms following dose reduction or abrupt discontinuation, or recurrence of previous symptoms of the disease. All calls were grouped into the following main classes: antidepressants, antipsychotics, benzodiazepines, or non-psychiatric medicines. The total number of calls about antidepressants, antipsychotics and benzodiazepines was related to the mean number of users during the study period in The Netherlands, obtained through the Drug Information System of the Health Insurance Board (www.gipdatabank.nl). Antipsychotics and benzodiazepines were included to assess whether discontinuation is a specific problem for antidepressants or a general problem for all psychiatric medicines. The calls about discontinuation and the problems with discontinuation were compared between antidepressants, antipsychotics, benzodiazepines and non-psychiatric medicines, expressed as an odds ratio (OR) and 95% confidence interval (CI). Chi-square test was used to compare proportions of calls and problems with discontinuation between antipsychotics, benzodiazepines and antidepressants. Antidepressants were classified further into tricyclic antidepressants (TCAs), serotonin reuptake inhibitors (SSRIs) and other antidepressants. The calls about discontinuation and the problems with discontinuation were compared between TCAs, SSRIs and other antidepressants expressed as an OR and 95% CI. Chi-square test was used to compare the proportions of calls and problems with discontinuation between TCAs and SSRIs, male and female, and age categories.

Results

Between 1990 and November 2004, the national telephone service registered 39 786 phone calls. Of these, 6159 (15.5%) calls related to antidepressants. Of all calls about antidepressants, most callers were women (72%) and were aged between 21 and 40 years (55%) and 41 and 60 years (43%). Table 1 shows the total number of calls about discontinuation and the number of problems experienced with discontinuation for the different classes of medicines. Related to the total number of users during the study period in The Netherlands, antidepressant and antipsychotic users called four times as often to the telephone service as did benzodiazepine users. Relatively, there were three times as many calls about discontinuation of antidepressants and five times more problems experienced with discontinuation of antidepressants, compared to calls about non-psychiatric medicines. The proportion of calls about discontinuation and problems experienced with discontinuation was also higher in patients calling about

Table 1 Calls to a national telephone information service between 1990 and 2004 related to drug discontinuation

	Total number of calls	Calls about discontinuation			Problems with discontinuation		
		n	% of total	OR (95% CI)	n	% of total	OR 95% CI
Non-psychiatric medicines	28053	1982	7.1	Reference	292	1.0	Reference
Antidepressants	6159	1072	17.4	2.77 (2.56–3.00)	329	5.3	5.37 (4.57–6.30)
Antipsychotics	1658	255	15.4	2.39 (1.93–2.46)	68	4.1	4.07 (3.11–5.32)
Benzodiazepines	3916	755	19.3	3.14 (2.87–3.44)	239	6.1	6.18 (5.19–7.36)
Classes of antidepressants[a]							
TCA	1315	273	20.8	Reference	77	5.9	Reference
SSRI	3612	606	16.8	0.77 (0.66–0.90)	189	5.2	0.89 (0.68–1.17)
Other antidepressants	1038	170	16.4	0.75 (0.60–0.92)	60	5.8	0.99 (0.70–1.40)

[a]Totals do not add up to 6159 due to unknown type of antidepressant used.

benzodiazepines and antipsychotics compared to patients calling about non-psychiatric medication. Patients calling about antidepressants called more often about discontinuation ($P=0.05$) and experienced more problems with discontinuation ($P=0.04$) than patients calling about antipsychotics. Compared to patients calling about benzodiazepines, the antidepressant users less often called about discontinuation ($P=0.02$), but did not differ in the proportion of problems experienced with discontinuation ($P=0.11$). Regarding the two major classes of antidepressants, patients taking TCAs more often called about discontinuation compared to patients taking SSRIs ($P=0.001$), but did not differ in the number of problems experienced with discontinuation ($P=0.39$). The relative number of calls about and problems with discontinuation remained constant through time for the major classes of antidepressants as well as the individual antidepressants.

Compared to men, women more often called about discontinuation (18.9% versus 14.5%; $P<0.001$) and experienced more problems with discontinuation (5.8% versus 4.4%; $P=0.03$). There was no difference in the number of calls about discontinuation ($P=0.09$) and the number of problems experienced with discontinuation ($P=0.80$) for the different age categories.

Discussion

Patients calling about antidepressants called about discontinuation three times as often, and reported a problem with discontinuation five times more often, compared to patients who called about non-psychiatric medicines. A higher proportion of concerns about discontinuation and problems experienced with discontinuation was also seen in patients calling about antipsychotics and benzodiazepines compared to patients calling about non-psychiatric medication. Our findings show that patients perceive discontinuation of antidepressants, as well as discontinuation of antipsychotics and benzodiazepines, as a problem. Long-term use of these psychiatric medicines, together with the high rates and burden of adverse effects, is likely to be an important factor in the explanation of this general issue of discontinuation. In addition, most patients consider psychiatric medicines to be addictive, and want to take these medicines for as short a time as possible.[9,10] Moreover, most psychiatric medicines need to be tapered, which patients are often not aware of.[6]

The strength of our study is that we received daily life experiences direct from patients. Information from clinical trials may not reflect experiences of patients in the real-world setting, and automated prescription data as used in epidemiological studies may not provide the insight needed to understand patients' behaviour. Moreover, patient experiences provide information of which doctors and other healthcare providers may not be aware, because patients who have stopped the medicine are often not under the direct care of a doctor, and a considerable number of patients do not inform their doctor about stopping the medicine.[11,12] The use of calls from a telephone medicine information service also has its limitations. First, the nature of the illness may have introduced a response bias. Patients taking psychiatric medicines may be more likely to contact an information service line than patients taking non-psychiatric medication. Second, the calls represent only a small proportion of all medicine users, which means that the results may not be representative for all users. On the other hand, in this way only issues that are considered relevant and important by medicine users are revealed. In addition, we had no absolute evidence for the appropriate assessment of a problem in all cases, assessed as either the occurrence of discontinuation symptoms or recurrence of symptoms. Although our procedure required confirmation of assessment of the call by the other authors, a thorough assessment was not always possible. Nevertheless, these limitations do not undermine our conclusion. Insight in the issue of discontinution of medicines can be improved by getting information directly from the patient. Discontinuation seems a general problem for all psychiatric medicines, and needs more attention in the communication between patients and healthcare providers.[13]

References

1 National Institute for Clinical Excellence. Quick reference guide: depression; the management of depression in primary and secondary care (Clinical Guideline 23). London: National Institute for Clinical Excellence; 2004. www.nice.org.uk/pdf/CG023quickrefguide.pdf (accessed 21 July 2007).

2 Lin EHB, Von Korff M, Katon W et al. The role of the primary care physician in patients' adherence to antidepressant therapy. Med Care 1995;33:67–74.

3 Meijer WEE, Heerdink ER, Leufkens HMG et al. Incidence and determinants of long-term use of antidepressants. Eur J Clin Pharmacol 2004;60:57–61.

4 Meijer WEE, Bouvy ML, Heerdink ER, Urquhart J, Leufkens HMG. Spontaneous lapses in dosing during chronic treatment with selective serotonin reuptake inhibitors. Br J Psychiatry 2001;179:519–22.

5 Bambauer KZ, Adams AS, Zhang F et al. Physicians alerts to increase antidepressant adherence. Arch Intern Med 2006;166:498–504.

6 van Geffen ECG, Hugtenburg JG, Heerdink ER, van Hulten RP, Egberts ACG. Discontinuation symptoms in users of selective serotonin reuptake inhibitors in clinical practice: tapering versus abrupt discontinuation. Eur J Clin Pharmacol 2005;61:303–7.

7 Taylor D, Stewart S, Connoly A. Antidepressant withdrawal symptoms:telephone calls to a national medication helpline. J Affect Disord 2006;95:129–33.

8 Egberts ACG, Smulders M, De Koning FHP, Meyboom RHB, Leufkens HMG. Can adverse drug reactions be detected earlier? A comparison of reports by patients and professionals. BMJ 1996;313:530–1.

9 Croghan TW, Tomlin ME, Pescosolido BA et al. American attitudes toward and willingness to use psychiatric medications. J Nerv Ment Disord 2003;191:166–74.

10 Pound P, Britten N, Morgan M et al. Resisting medicines: a synthesis of qualitative studies of medicine taking. Soc Sci Med 2005;61:133–55.

11 Demyttenaere K, Enzlin P, Dewé W et al. Compliance with antidepressants in a primary care setting, 1: beyond lack of efficacy and adverse events. J Clin Psychiatry 2001;62(suppl. 22):30–3.

12 Maddox J, Levi M, Thompson C. The compliance with antidepressants in general practice. J Psychopharmacol 1994;8:48–53.

13 Young HN, Bell RA, Epstein RM, Feldman MD, Kravitz RL. Types of information physicians provide when prescribing antidepressants. J Gen Intern Med 2006;21:1172–7.