Determinants for successful smoking cessation with bupropion in daily practice

• Marcel L. Bouvy, Henk Buurma and Antoine C.G. Egberts

M.L. Bouvy (correspondence): SIR Institute for Pharmacy Practice Research, T. Mansholtstraat 5b, 2331 JE Leiden, The Netherlands (e-mail sir@stevenshof.nl)
H. Buurma: SIR Institute for Pharmacy Practice Research, Leiden, The Netherlands
A.C.G. Egberts: Department of Pharmacoepidemiology & Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences, Utrecht, The Netherlands, and Hospital Pharmacy Midden Brabant, TweeSteden and St. Elisabeth Hospital, Tilburg, The Netherlands

Abstract
Objective: to describe the patterns of use of bupropion in daily clinical practice and factors which determine successful smoking cessation.
Methods: Retrospective follow-up study in 36 pharmacies in the Netherlands. Patients who received at least one prescription for bupropion between January and April, 2000 were included. The pharmacists noted several characteristics relating to the patient, use of bupropion and co-medication. Patients were interviewed by telephone about their current and former smoking habits, the success of their smoking cessation and their experiences with bupropion.
Main outcome measure: Abstinence rate and factors determining successful abstinence after six months.
Results: 322 patients with a least one prescription for bupropion were identified. In 93.5% of patients bupropion was prescribed by the general practitioner. Half of the patients were dispensed 30 or fewer tablets. Pharmacists interviewed 215 (66.8%) patients by telephone. Of these patients 58 (27.0%) still did not smoke six months after the prescription for bupropion. The number of tablets used, lack of co-morbidity, less than two previous attempts to stop smoking and private-insurance were associated with a higher rate of successful abstinence.
Conclusion: Most patients do not use bupropion in accordance with the recommended period and did not receive the same degree of additional support provided in clinical trials. Nevertheless 27.0% of patients reported to have stopped smoking six months after the prescription for bupropion. This self-reported abstinence rate is only slightly lower than is reported in literature. This might be partly related to the fact that we did not validate smoking cessation by carbonmonoxide monitoring. Bupropion is not reimbursed in the Netherlands. It is difficult to assess whether patients' self-payment has led to the selection of motivated patients, or has been a barrier to finishing using bupropion.

Introduction

Smoking is responsible for a large proportion of annual mortality and constitutes the major preventable health risk in western society[1]. Nevertheless the number of smokers in Western societies does not decrease.

Without intervention the estimated rate of smoking cessation is estimated at a rate of approximately 7% over an average 10-month period[2].

Supportive counselling by professionals, like physicians, has shown to be an effective aid in smoking cessation[3]. A combination of counselling with nicotine replacement therapy (NRT) or antidepressants increases the success of abstinence[3,4]. It is not clear whether the effects of antidepressants such as bupropion and nortriptylin are drug-specific or an antidepressant class effect. Currently, bupropion is the most extensively investigated antidepressant for this indication[5,6]. It has been approved for use as a seven-to-nine week course aid in smoking cessation in several western countries since 1999.

The patients included in clinical trials with bupropion were highly selected and well-motivated by telephone calls, repeat visits and supportive educational materials.

Studies have shown that certain patient groups, such as patients with low economic status and women, might have more difficulties in maintaining long-term smoking abstinence[8–12]. Therefore the effects of bupropion in daily clinical practice need to be evaluated.

The objective of this study was to describe usage patterns of bupropion in daily practice, and the factors determining successful abstinence from smoking.

Methods

We performed a retrospective follow-up study among 36 pharmacies in the Netherlands. Pharmacists selected all patients who received at least one prescription for bupropion between 1 January and 30 April of 2000. Bupropion has been available in The Netherlands since December 1999 and is not reimbursed. The pharmacists noted characteristics relating to the patient (age, gender and number of bupropion tablets dispensed by the pharmacy, the prescriber of bupropion, co-medication and insurance status (a proxy for socio-economic status) on a standard case report form.

Cardiovascular co-medication was defined as at least two prescriptions for cardiovascular drugs (ATC-code C or B01AC) in the year preceding the prescription for bupropion. Antidepressant co-medication was defined as at least two prescriptions for antidepressants (ATC-code N06A) in the year preceding the prescription for bupropion. Pulmonary co-medication was defined as at least two prescriptions for pulmonary drugs (ATC-code R03) in the year preceding the prescription for bupropion.

Subsequently, the pharmacists conducted a structured telephone interview among their patients including questions about their current and former smoking habits, nature and success of current and former smoking cessation attempts and their experiences with bupropion. The telephone interview was conducted at least 6 months after the start of bupropion, with a maximum of 12 months.

The data were analysed using SPSS 10.1. We calculated crude independent rate ratio's for all available variables comparing patients with successful and unsuccessful abstinence. Logistic regression analysis was performed to adjust for potential confounders such as age and gender and all variables with inde-

pendent *P*-values < 0.15; using the indicator method for missing values.

Results

The participating pharmacists identified 322 patients (169 male (52.5%), 153 female (47.5%) with a prescription for bupropion). The average age was 46.6 years [range: 21-81]. In 93.5% of the patients bupropion was prescribed by the general practitioner (Table 1).

Half of the patients collected only one box of bupropion (30 tablets corresponding to a use of 2–3 weeks). Nine patients (2.8%) collected more than 150 tablets, corresponding to twice the recommended period.

9.6% of patients were likely to suffer from cardiovascular disease, 22.7% from pulmonary disease and 12.1% from depression (derived from the chronic use of low dose aspirin or anticoagulants, inhaled pulmonary medication or antidepressants).

The participating pharmacists phoned all patients. One hundred two (31.6%) patients were ex directory or were repeatedly not at home when called. Five (1.6%) patients did not want to co-operate with the interview.

The only statistically significant difference between patients with and without questionnaires was the lower use of cardiovascular drugs in the group without questionnaires. There was a strong tendency towards a lower number of dispensed tablets in patients without a questionnaire.

Of the 215 patients interviewed 58 (27.0%) self reported that they still did not smoke six months after the first prescription for bupropion. Almost half (*n* = 101; 47.0%) of patients reported (mostly minor) adverse events. Of the patients with self reported successful abstinence experienced 41.4% adverse events *versus* 49.0% of the patients who did not succeed.

Seventy (32.6%) patients reported having visited the prescriber to discuss smoking cessation after the first prescription for bupropion. In most cases this was restricted to one extra visit. Of the interviewed patients 19 (8.8%) visited the prescriber more than 2 extra times in relation to the smoking cessation attempt. Written manufacturer's material was used by

Table 1 *Basic characteristics of patients*

	All patients N = 322		With questionnaire N = 215		Without questionnaire N = 107	
Gender						
Female	153	47.5%	107	49.8%	46	43%
Male	169	52.5%	108	50.2%	61	57%
Age						
< 40	91	28.3%	60	27.9%	31	28.4%
40–49	105	32.6%	72	33.5%	33	30.3%
> 9	126	39.1%	83	38.6%	44	40.4%
Number of dispensed tablets						
< 31	161	50.0%	98	45.6%	63	58.9%
31–90	83	25.5%	60	27.9%	23	21.5%
> 90	78	24.2%	57	26.5%	21	19.6%
Concomitantly used medication						
Cardiovascular agents	31	9.6%	27	12.1%	4	4.6%
Pulmonary disease	73	22.7%	49	22.4%	24	22.9%
Depression	39	12.1%	28	13.1%	11	10.8%
Any of above	120	37.3%	84	38.8%	36	33.9%
Prescriber						
General practitioner	301	93.5%	202	94.4%	99	90.8%
Specialist	19	5.9%	13	5.6%	6	6.4%
Unknown	2	0.6%			2	1.8%
Insurance						
National Health service	169	52.5%	111	51.4%	58	54.1%
Private	151	46.9%	103	48.1%	48	44.0%
Unknown	2	0.6%	1	0.5%	1	0.9%
Number of cigarettes per day						
< 16			25	11.6%		
16–25			84	39.1%		
> 25			100	46.5%		
More than two previous attempts?			69	32.1%		

Table 2 *Determinants for successful abstinence*

	Unsuccessful at 6 months (n = 157)	Successful abstinence at 6 months (n = 58)	Crude risk ratio	Adjusted risk ratio[a]
Gender				
Female	82 (52.2%)	25 (43.1%)	0.7 [0.4–1.3]	0.7 [0.3–1.4]
Male	75 (47.8%)	33 (56.9%)	ref.	ref.
Age category				
< 40	42 (26.8%)	18 (31.0%)	1.3 [0.6–2.7]	0.5 [0.2–1.3]
40–49	53 (33.8%)	19 (32.8%)	1.1 [0.5–2.2]	0.8 [0.3–2.1]
> 49	62 (39.5%)	21 (36.2%)	ref.	ref.
Prescriber				
GP	145 (92.4%)	57 (98.3%)	ref.	ref.
Specialist	12 (7.6%)	1 (1.7%)	0.2 [0.0–1.7]	0.3 [0.0-3.6]
Number of tablets				
< 31	84 (53.5%)	14 (24.1%)	ref.	ref.
31-90	43 (27.4%)	17 (29.3%)	**2.4 [1.1–5.3]**	**2.9 [1.2–7.0]**
> 90	30 (19.1%)	27 (46.6%)	**5.4 [2.5–11.6]**	**4.9 [2.1–11.5]**
Number of cigarettes				
< 16	18 (11.5%)	7 (12.1%)	0.9 [0.5–2.5]	0.7 [0.3–1.6]
16–25	62 (39.5%)	22 (37.9%)	1.0 [0.4–2.5]	1.1 [0.3–3.6]
> 25	71 (45.2%)	29 (50.0%)	ref.	ref.
More than two previous attempts	56 (35.7%)	13 (22.4%)	0.5 [0.2–1.0]	0.5 [0.2–1.0]
Ever used nicotine replacement	78 (49.7%)	35 (60.3%)	1.4 [0.7–2.8]	
Adverse drug reactions	77 (49.0%)	24 (41.4%)	0.7 [0.4–1.2]	
Counselling				
>2 extra visits after first prescription	11 (7.5%)	8 (13.8%)	2.0 [0.8–4.8]	2.5 [0.8-8.3]
Use of manufacturer's booklet	90 (58.8%)	36 (62.1%)	1.2 [0.6–2.2]	
Use of toll free phone number	19 (12.1%)	9 (15.5%)	1.2 [0.6–2.2]	
Concomitantly used medication				
Antidepressants	23 (14.6%)	5 (8.6%)	0.5 [0.2–1.5]	0.3 [0.1–1.1]
Pulmonary	41 (26.1%)	8 (13.8%)	0.5 [0.2–1.0]	0.5 [0.2–1.3]
Cardiovascular	22 (14.0%)	5 (8.6%)	0.6 [0.2–1.6]	0.6 [0.2–1.9]
Any of above	68 (43.3%)	16 (27.6%)	**0.5 [0.3–1.0]**	**0.4 [0.2–0.9]**
Insurance				
National Health Service	91 (58.0%)	20 (34.5%)	ref.	ref.
Private	65 (41.4%)	38 (65.5%)	**2.7 [1.4–5.2]**	**2.4 [1.1–5.1]**

a Logistic regression with age and gender and all variables with univariate *P*-values < 0.15; using indicator method for missing values; statistical significant (*P* < 0.05) associations are in bold.

126 (60.0%) of the interviewed patients. Twenty-eight (13.3%) patients used a toll-free phone number, which was mentioned in the patient information leaflet provided by the manufacturer

Several characteristics were clearly and independently associated with abstinence after six months. Patients who used more than 30 tablets (31–90 tablets OR 2.6 [95% CI 1.0–6.2], > 90 tablets OR 3.6 [95% CI 1.4–8.8] or had private health insurance (OR: 2.4 [1.1–5.1]) had higher probability for successful abstinence. Patients who concomitantly used antidepressant, pulmonary or cardiovascular drugs were less likely (OR 0.5 [95%CI 0.2-1.0] to be abstinent after six months. Patients who had attempted to stop smoking more than twice in the two years preceding the use of bupropion showed a tendency to be less likely (OR 0.5 [95% CI 0.2–1.0] to be abstinent after six months.

Discussion

The overall probability of successful (self-reported) smoking cessation in this group of bupropion users in daily practice was 27.0% after six months. This abstinence rate at six months is only slightly lower than

that reported in two randomised clinical trials. In our study abstinence was determined by questioning users by telephone. It is suggested that self-reporting overestimates smoking cessation rates[7]. When this overestimation were 30%, the remaining abstinence rate of 18% is still high.

A limitation of our study is the response rate for the telephone interview, although based upon the characteristics that were known from the non-responders, these patients did not seem to be very different from the respondents. We are therefore in the opinion that this will not have strongly influenced our findings.

Another limitation of our study is that a proper control group (e.g., NRT users) was lacking. In designing our study we expected a much lower abstinence rate in daily practice compared to that reported in clinical trials, given the inclusion of highly selected patients in these trials and the use of other motivational measures besides bupropion, which are difficult to establish in daily practice.

The high success rate in this study might be explained by the selection of motivated patients, because self-payment was needed. An indicator for some selection of motivated persons is the relative high prevalence of male patients with private insurance in the study. It would be interesting to see whether the high abstinence rate seen in our study alters when the drug is reimbursed. Patients could also be extra motivated because our study period partly coincided with extra media attention in relation with a 'millennium attempt' to have a record number of people give up smoking.

Selection of motivated patients could also explain the fact that so many patients reported success in spite of lack of counselling. Patients did not receive the same support given in clinical trials with bupropion. Only 17% of patients visited their physician more than once after the prescription for bupropion. Although manufacturer's materials were used by 60% of the interviewed patients, most patients did not use this material extensively. A toll-free phone number that was installed by the manufacturer was only used by 13% of patients.

It is interesting that most patients did not use bupropion in accordance with the recommended period of 7–9 weeks (90–120 tablets). Half of the patients used less than 30 tablets, implying a period of less than 2 weeks. Another 25% of patients used the drug less than 7 weeks (no more than 90 tablets). This high early discontinuation is only partly related to adverse drug reactions. Adverse drug reactions were not a determinant for unsuccessful smoking cessation. Most patients who did not stop smoking successfully also discontinued using bupropion. Therefore, there is a clear association between the number of tablets used and successful abstinence.

Apart from the number of tablets used we found several other determinants, which were associated with successful abstinence. Patients with private insurance were twice as likely to succeed than patients with National Health Service. An income threshold determines type of insurance. Therefore, it seems likely that these differences in insurance are a proxy of differences in socio-economic status. Differences in prevalence of smoking and successful abstinence between different educational groups have been described several times[8–10].

Attention should be given to this phenomenon since it will only widen existing social differences in the total tobacco-related morbidity[11].

It should also be mentioned that patients with private insurance were already over-represented in this study. Approximately 65% of the Dutch population are in the National Health Service, while in this study only 46.9% were in the National Health Service.

Another determinant that was associated with successful abstinence was the absence of depression, pulmonary or cardiovascular disease. This means that patients who are in greatest need of smoking cessation have more difficulty in successful smoking cessation. This also implies that counselling is even more important in those groups.

A recent study showed that the effectiveness of NRT decreased after this therapy became available over the counter (OTC). OTC availabilty might lead to less counselling and decreased effectiveness[12].

Patients who attempted to stop smoking more than twice in the two years preceding the use of bupropion had a lower success rate. This probably means that this is a group of patients who also need more attention.

Several other determinants, such as male gender, prescription by a GP and more than two extra physician visits related to smoking cessation showed a tendency for successful abstinence. A higher success-rate in males is also reported in the literature. Women are less likely than men to maintain long-term smoking abstinence following an unaided quitting attempt[13]. Worries about weight control could play a role in women's problems with smoking cessation[14].

Conclusion

The first users of bupropion showed a relative high self-reported abstinence rate. We found several determinants for successful abstinence. These determinants indicate that patients who have the highest need to stop smoking have the lowest success rates.

References

1 Lancaster T, Stead L, Silagy C, Sowden A. Effectiveness of interventions to help people stop smoking: findings from the Cochrane Library. BMJ 2000; 321: 355–8.

2 Baillie AJ, Mattick RP, Hall W. Quitting smoking: estimation by meta-analysis of the rate of unaided smoking cessation. Aust J Public Health 1995; 19: 129–31.

3 Law M, Tang JL. An analysis of the effectiveness of interventions intended to help people stop smoking. Arch Intern Med 1995; 155: 1933–41.

4 Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation (Cochrane Review). Cochrane Database Syst Rev 2000; 4.

5 Hurt RD, Sachs DP, Glover ED, Offord KP, Johnston JA, Dale LC, et al. A comparison of sustained-release bupropion and placebo for smoking cessation. N Engl J Med 1997; 337: 1195–202.

6 Jorenby DE, Leischow SJ, Nides MA, Rennard SI, Johnston JA, Hughes AR et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. N Engl J Med 1999; 340: 685–91.

7 Muir J, Lancaster T Fowler G, Neil A. Community based heart health promotion project in England. Self reporting overestimates smoking cessation rates. BMJ 1998; 316: 704–5.

8 Osler M, Gerdes LU, Davidsen M, Bronnum-Hansen H, Madsen M, Jorgensen T et al. Socioeconomic status and trends in risk factors for cardiovascular diseases in the Danish MONICA population, 1982–1992. J Epidemiol Commun Health 2000; 54: 108–13.

9 Crampton P, Salmond C, Woodward A, Reid P. Socioeconomic deprivation and ethnicity are both important for anti-tobacco health promotion. Health Educ Behav 2000; 27: 317–27.

10 Connor SK, McIntyre L. The sociodemographic predictors of smoking cessation among pregnant women in Canada. Can J Public Health 1999; 90: 352–5.

11 Cavelaars AE, Kunst AE, Geurts JJ, Crialesi R, Grotvedt L, Helmert U et al. Educational differences in smoking: international comparison. BMJ 2000; 320: 1102–7.

12 Pierce JP, Gilpin EA. Impact of over-the-counter sales on effectiveness of pharmaceutical aids for smoking cessation. JAMA 2002; 288: 1260–4.

12 Ward KD, Klesges RC, Zbikowski SM, Bliss RE, Garvey AJ. Gender differences in the outcome of an unaided smoking cessation attempt. Addict Behav 1997; 22: 521–33.

13 Wee CC, Rigotti NA, Davis RB, Phillips RS. Relationship between smoking and weight control efforts among adults in the united states. Arch Intern Med 2001; 161: 546–50.