Differences in health status between long-term and short-term benzodiazepine users

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SUMMARY

Background: *Despite generally accepted advice to keep treatment short, benzodiazepines are often prescribed for more than six months. Prevention of long-term benzodiazepine use could be facilitated by the utilisation of risk indicators for long-term use. However, the characteristics of long-term benzodiazepine users described in the literature are based on studies in which long-term users were compared with non-users. Thus these characteristics may be imprecise.*

Aim: *To study the characteristics of long-term benzodiazepine users by comparing their demographic data and health status (mental and physical) with those of short-term users.*

Design of study: *Cross-sectional comparison of short-term and long-term benzodiazepine users.*

Setting: Patients from 32 GP practices of the Nijmegen Health Area, The Netherlands.

Method: *The characteristics of 164 short-term and 158 long-term benzodiazepine users in general practice were compared, using interview data and morbidity, referral and prescription data from GP records.*

Results: *Long-term benzodiazepine users were (a) older, (b) had a more severe history of mental health problems for which they had received more serious treatment, (c) used more psychotropic drugs, (d) had a higher hospital specialist consultation frequency, (e) had more diagnoses of the following: diabetes, asthma, chronic obstructive pulmonary disease, hypertension, a serious skin disorder, and (f) reported a lower perceived general health status. There were no sex differences.*

Conclusion: *Specific risk characteristics of long-term benzodiazepine users can be used to develop a risk profile for the management of benzodiazepines in general practice. We believe that (somatic) secondary care also contributes to benzodiazepine use. It may be worthwhile to coordinate care for benzodiazepine users between GPs and hospital specialists.*

Keywords: *benzodiazepines; prescription failure; health status.*

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Introduction

LONG-TERM benzodiazepine use is a precarious theme in general practice. The guidelines[1-3] recommend short intervention (maximum of 8 to 12 weeks), nevertheless 1.7% to 4.9% of the population receive benzodiazepine prescriptions for more than six months.[4-12] Apparently, despite the fact that the initial benzodiazepine prescription is the result of carefully weighing benefits against risks, some patients end up as long-term users.

Specific patient characteristics could be responsible for long-term use, and this is supported by the literature. Based on the comparison of long-term users with non-users, the following health status factors were related with long-term benzodiazepine use: older age, psychological problems (more), physical disease (more), and sex (female).[8,11,13-21] It is unclear however, if this refers specifically to long-term benzodiazepine users or to benzodiazepine use in general. Only a few studies have compared long-term with short-term benzodiazepine users: they were older, had poorer health, more depression, a higher daily benzodiazepine use and got their prescription more often from a hospital physician.[22,23]

An alternative explanation for long-term use that is patient-unrelated would be prescription failures. A minimal failure to discontinue initial benzodiazepine use (for example, in 1% of prescriptions) would cumulate in a prevalence of long-term use of 1 per 1000 patients per year (under a prescription rate of 10%[12,24]). Prescription failure is plausible, given that most repeat prescriptions are provided without a doctor–patient encounter[25,22] As a consequence a proportion of the original short-term benzodiazepine users become long-term users. Further insight into benzodiazepine use is needed to develop a tool for prevention of long-term use. Therefore, this study compared the physical and mental health status of long-term and short-term benzodiazepine users.

Method

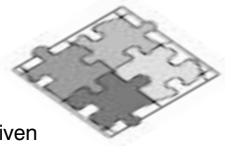
Design

The design of this study was a cross-sectional comparison of short-term and long-term benzodiazepine users in general practice. Data were used from the practices of the Nijmegen Health Area Project-2, a study on psychopathology in the general population.[26] Benzodiazepine users were identified from the practices' prescription files.

Definition criteria for benzodiazepine users

Under the Dutch health insurance guidelines, benzodiazepines (defined according to the standardised classification system for drugs of the WHO using the Anatomical Therapeutic Chemical classification — index groups N05BA, CD, CF and CG;[27] N = nervous system N05 = psycholep-

HOW THIS FITS IN



What do we know?

Long-term use of benzodiazepines is common, but should be discouraged, given the harmful side effects. Benzodiazepine use is particularly common among the elderly, women patients with psychological problems, and chronic physical diseases. However, it is unclear whether this profile singles out the group at risk for long-term use.

What does this paper add?

This paper reports a comparison of long-term users with short-term users. The findings are that patients — in particular those who use other psychotropic drugs or are under regular hospital care of specialists of physical diseases, and those with poor quality of life and high medical consumption — are using benzodiazepines on a long-term basis. The involvement of secondary care is remarkable. Insight into this profile can help GPs to forestall benzodiazepine use or wean patients off them at an early stage.

tics, N05B = anxiolytics, N05C = hypnotics and sedatives, N06 = psychoanaleptics) have to be prescribed by a medical practitioner. Short-term benzodiazepine users were defined as having prescriptions for less than or equal to 90 days (the maximum prescription advice of the WHO) with the exclusion of patients who finished taking the drug at the beginning of the measurement period or who started at the end of that period, because of uncertainty about their user pattern. Long-term benzodiazepine users were defined as having prescriptions for more than or equal to 180 days. Patients with 91 to 179 days' use were excluded from this study.[24]

Practices and patients

General practitioners (GPs) had to be using a computerised patient and medication registration system. In total, 64 practices were approached and 32 agreed to participate. Practices' main reason for non-participation was involvement in other research; details of approach and representativeness of the general practices and the population samples have been described elsewhere.[24,26] The general practice patients' lists comprised 80 315 persons aged between 18 and 74 years, of whom 4% were short-term and 2% long-term benzodiazepine users.[24] An equal number of short-term and long-term benzodiazepine users were recruited from each practice to eliminate effects related to a GP's work style. This resulted in the selection of 164 short-term users and 158 long-term benzodiazepine users for the study. There were no sex differences between the groups selected for this study or between all the short and long-term benzodiazepine users at the practices. With respect to age, the short-term benzodiazepine user participants were older than all the short-term users at the practices (participants aged over 45 years = 63.4%, versus practices = 53.8%).[24]

Variables

Health status was measured using:

1. the 24-item chronic diseases list of the CBS in the past year based on the Health Survey of Statistics Netherlands,[28] the Short Form 36-item Health Survey (SF-36),[29,30] the General Health Questionnaire (GHQ_{30}),[31,32] and the Four Neurotic Symptoms (4-NS) questionnaire,[33] and
2. a structured interview concerning the patient's history of mental health problems and details about treatment, hospitalisation for psychiatric diseases, drug and alcohol abuse and treatment. Patients were also asked about their use of over-the-counter (OTC) psychotropic drugs in the past four weeks and the frequency with which they had consulted a hospital specialist (excluding visits to an ophthalmologist). The GP records provided data on the number of consultations and the psychotropics prescribed during the past year. The psychotropics were defined using Anatomical Therapeutic Chemical classification codes[27]: N05 and N06, (N06 = psychoanaleptics) with the exception of the benzodiazepines named earlier.

Analyses

The recruited sample was split in two parts so that the risk profile found in the first part (split 1) could be validated in the second part (split 2).[34] To detect differences of at least 16% between long-term and short-term benzodiazepine users, two groups of 95 subjects were necessary (if $\alpha = 0.05$ and $\beta = 0.20$) or the first split. All subjects were stratified for each practice. Subsequently univariate procedures (χ^2-test, *t*-test) on single variables were used to select significant variables for the logistic regression, resulting in a risk profile. The goodness-of-fit method was used,[34] testing observations from the second split (subsample of 69 short-term and 63 long-term benzodiazepine users) with the findings of the first split. Analyses were done with the SAS statistical software package.

Results

The long-term users were older (mean age = 56.8 years versus 48.5 years), but there was no sex difference between the two groups. Many long-term and short-term users had a history of mental health problems (48% and 42%, respectively). However, more long-term benzodiazepine users had been treated by a psychiatrist and had a history of alcohol abuse. As a large proportion of the patients with alcohol problems also had psychiatric problems, we regarded these two aspects as a history of treatment in secondary health care — 35.8% long-term users, 14.7% short-term users. In contrast, more short-term benzodiazepine users had been treated for psychological problems in primary care — 27.4% versus 12.6%.

Long-term benzodiazepine users had received more antidepressants and antipsychotics (32.6% versus 13.7%) in the past year and visited a hospital specialist more often (mean number of visits = 2.4 versus 1.3). Both groups reported one or more chronic disease in more than 80% of cases, but among long-term benzodiazepine users there was significantly more diabetes, asthma or chronic obstructive pulmonary disease (COPD), hypertension or a serious skin disorder (combined in 50.5% versus 24.2% of short-term

users). Therefore 'chronic diseases' were taken as one category in the logistic regression risk profile.

Long-term benzodiazepine users had poorer perceived general health (mean GHQ score = 56.8 versus 65.9), physical functioning (mean SF-36 score = 78.3 versus 85.8) and mental health (mean 4-NS score = 64.3 versus 71.4). Otherwise, the scores on SF-36 GHQ_{30} and 4-NS were elevated in both groups. Also, reported OTC psychotropic use and the GP consultation frequency were similar.

All the above-named significant variables of the first split were entered into the logistic regression. Controlling for redundancy in logistic regression eliminated perceived general health and physical functioning. We controlled for confounding of age, but all the variables were independent. Because the outcome of the second split logistic regression was comparable with that of the first (AUC1 = 0.77 ± 0.7; AUC2 = 0.80 ± 0.8) Table 1 gives the logistic regressions of both splits combined — older age, a history of psychiatric treatment, and chronic illness were independently related to long-term benzodiazepine use.

Discussion

The study provided the profile of long-term benzodiazepine users; they were older, had a more severe psychiatric history, had frequent prescriptions of psychotropics, and poorer mental health status, with more common chronic diseases and more visits to medical specialists.

Not included in the analysis were socioeconomic status, coping behaviour or GPs' work style. In fact the long-term users we studied were long-term users despite the efforts of their GP to use benzodiazepines in a more appropriate, short-term or intermittent way. As we did not study the GP–patient interaction in benzodiazepine use and prescribing we are not able to comment on this in depth.

Our findings differ from others with respect to sex as well as showing some unexpected similarities,[8,11,14-21] in all probability due to our comparison with short-term benzodiazepine users rather than non-users. In particular this was the case for the elevated scores on SF-36 and GHQ_{30},[29,31] indicating that long- and short-term benzodiazepine users have many psychiatric symptoms and a broad range of dysfunctions. The relationship between long-term benzodiazepine use and common chronic diseases was interesting. A possible explanation for this is that these are all diseases with highly protocolised[35-38] treatments that require frequent visits to primary and secondary care physicians. As the second split confirmed the findings of the first split, we are confident that these characteristics are indeed specific for long-term benzodiazepine users.

Frequent visits to a physician in themselves increase the chance of starting prescriptions for drugs like benzodiazepine. Moreover, treatment started in secondary care may be continued in primary care. This is in line with the reported role of (somatic) hospital specialists[23] as well as the described role of follow-up prescriptions in general practice.[22,25]. Given the disadvantages of long-term benzodiazepine use (cognitive[39] and sedative[3,20-23] effects) and their consequences[40] and given that stopping benzodiazepine therapy is a problem for many patients,[41-43] it is important to prevent long-term use.

Recapitulating, we found specific risk indicators for long-term benzodiazepine use, and so patient-unrelated prescription failures are an improbable cause of long-term use. Many of the risk indicators we found suggest the involvement of secondary care, which can only be dealt with by accurate communication and coordination of the various disciplines by the GP. More research will provide greater insight into the role of these indicators in creating long-term benzodiazepine users. Further exploration of differences between short- and long-term benzodiazepine users is desirable (for example, coping). The findings of this study will be used in developing GP support to counter long-term benzodiazepine use in a more effective way.

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Table 1. Logistic regression of the health status factors of long-term benzodiazepine users compared with short-term users (first split and second split combined, missing n = 3).

Logistic regression risk profile	Odds ratio (OR)	Confidence interval (CI)	*P*-value
Intercept	–	–	<0.001
Age >50 years	3.18	1.84–5.50	<0.001
Frequency of consulting specialist in past half year >1	1.56	0.93–2.59	0.09
History of treatment in secondary care (psychiatrist) and/or treatment for alcohol abuse	2.80	1.49–5.29	0.001
Diabetes mellitus or asthma or COPD or hypertension or a serious skin disorder	2.33	1.38–3.93	0.001
Mental Health (SF-36)	1.93	1.15–3.22	0.012
Prescribed psychotropics (antidepressives and antipsychotics)	2.52	1.32–4.81	0.005
Concordant		75.9%	
Discordant		21.1%	
C		0.774	

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