Singapore Med J 1999; Vol 40(3):138-143

Long-term Benzodiazepine Users – Characteristics, Views and Effectiveness of Benzodiazepine Reduction Information Leaflet

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ABSTRACT

Objective: The authors looked at the clinical characteristics of long-term benzodiazepine users and how they viewed their use of benzodiazepine. We also examined the effectiveness of a self-help leaflet on reducing benzodiazepine use.

Method: One hundred and nine long-term benzodiazepine users (daily use for more than 1 year) were assessed. Their perceived beneficial and undesirable effects of benzodiazepine and intention to reduce benzodiazepine use were studied and their history of benzodiazepine use was obtained. Psychiatric diagnosis and medical history were reviewed. A self-help leaflet was provided to 56 users whose anxiety symptoms were assessed to have been under control. We re-examined these 56 users 3 months later on their use of benzodiazepine and anxiety levels.

Results: The 109 long-term benzodiazepine users used a therapeutic dose of benzodiazepine (median: 10 mg diazepam equivalent) regularly for a median of 9 years (range: 1 – 40). Most of the users found benzodiazepine helpful and only 11% of them reported undesirable side effects. Half of the 109 subjects refused to reduce the dosage. Most of the subjects still experienced significant anxiety despite the use of benzodiazepine. Fourteen of the 56 subjects provided with a self-help leaflet were able to reduce a median of 2.5 mg of diazepam equivalent when re-examined after 3 months.

Conclusion: The results are compared with previous studies in Western societies and are discussed in the light of clinical management of patients with anxiety disorders.

Keywords: benzodiazepine, drug long-term use, drug dependence, patient information

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INTRODUCTION

There has been a continuous debate on the use of benzodiazepine (BZ)[1], especially on when and for how long BZ should be prescribed. Most guidelines of good clinical practice endorsed by professional bodies recommend a short-term use of BZ in the treatment of anxiety disorders and insomnia, and regular evaluation of continuous BZ[2-5]. The concerns of BZ use of the public and amongst clinicians have resulted in a downward trend in BZ prescription in most countries in the last 15 years[1,6]. In Hong Kong, BZ prescription fell by 50% between 1991 and 1994 after an introduction of a stricter legislative control on its prescription in 1992[7]. Nevertheless, the amount of BZ consumed is still large and a significant part of which is taken up by long-term users[8-10].

Long-term BZ users (daily use of more than 1 year) in Western societies are predominantly elderly female with significant psychiatric and physical distress[11-13]. In the 1979 US National Survey, Mellinger and co-workers[11] reported that 61% of long-term anxiolytics users (most of the anxiolytics reported were BZ) were women and 71% of the users were aged 50 years or older. Two recent UK studies on long-term BZ users in general practice[12,13] have shown that 75% – 80% of the users were women and about 75% of them were older than 50 years of age. When compared with BZ non-users, long-term BZ users generally have higher levels of anxiety and depressive symptoms[11,12], more physical health problems[11,12] and more frequent medical consultations[11].

Long-term users generally found BZ helpful and with little undesirable side effects[14] although half of them still expressed a desire to stop taking the drug[14,15]. The characteristics and views of long-term BZ users in a Chinese population have yet to be studied. The present survey looks at such a group of Chinese patients in a psychiatric clinic in Hong Kong.

Most of the long-term BZ users experienced withdrawal symptoms when the drug was discontinued, even by slow tapering[16]. Both psychological and drug treatments[17] are reported to be useful in helping patients to withdraw from BZ. The use of a letter or a short interview asking patients to reduce their BZ dosage is found to be cost-effective[18-20]. The present research studied the effectiveness of a similar approach in cutting BZ use in a psychiatric clinic. A major concern of BZ dose reduction is a relapse of anxiety in long-term BZ users. In this study, we also examined the levels of anxiety symptoms experienced by subjects before and after BZ dose reduction.

METHODS

Subjects

BZ is classified as a dangerous drug under the Drug and Poison Ordinance in Hong Kong. All BZ prescriptions are monitored through a register maintained in each pharmacy. The study was conducted in a general psychiatric out-patient clinic in Hong Kong from July 1995 to April 1996. The psychiatric clinic has about 2,500 patient visits each month. Fourteen doctors worked in the clinic on a part-time basis during the study period. The patients were seen by the same doctor when they visited the clinic. The main form of treatment is pharmacotherapy. The doctors' psychiatric experiences ranged from 1 to more than 10 years. About half of the them were specialists and the others were psychiatric trainees. Through the pharmacy register of the clinic, all patients who were prescribed with BZ regularly for more than 12 months were identified. Patients who were not taking BZ daily and those prescribed with psychotropic medications in addition to BZs were excluded.

Assessment

The author (KFC) interviewed the subjects and obtained their demographic data, habits of taking tobacco, coffee, alcohol and abusive substance, type, dosage and duration of BZ use, perceived beneficial and undesirable effects of BZ, ways of managing their problems apart from the use of BZ and history of reduction or stoppage of BZ use. The author (KFC) also asked whether their doctors had advised them to reduce or stop BZ, whether they would like to reduce or stop BZ gradually and at their own pace and the reasons for such thoughts. Questions on their perception of BZ were standardised and open ended to avoid any suggestive answers. Multiple choices were given if the subjects did not volunteer any answer. In addition, the author (KFC) examined the patients and reviewed their medical records to arrive at the primary DSM IV psychiatric diagnosis when BZ was first prescribed. The author (KFC) then administered the Hamilton Anxiety Rating Scale (HARS)[20], a 14-item physician-rated checklist, to assess the severity of subjects' anxiety and depressive symptoms during the week before the interview. Each item in HARS could be rated from O point to 4 points (ie., none, mild, moderate, severe, grossly disabling). The subjects were also asked about their medical history including hospitalisations due to physical illnesses during the year before the study, visits to doctors for physical symptoms in the one month before the study and details of physical illnesses that required regular medications. At the beginning of the interviews, the subjects were assured that answers provided would not affect their drug prescriptions.

Intervention

Subjects were considered to be clinically stable and suitable for dose reduction if their HARS total scores were not more than 5 points and the scores for each of the items ie. anxious mood and depressed mood were none or mild. A research assistant used about 15 minutes to explain to the suitable subjects ways to reduce BZ gradually and the subjects were given an information leaflet (a copy of which is obtainable from the authors) to bring home. The author (KFC) re-examined all of the subjects 3 months after the first interview to ascertain the dosage of BZ use during the 3 months' interval and also reassessed the subjects using HARS. When HARS was administered, the author was aware of whether the subjects were able to reduce their BZ dosage or not.

Data analysis

We analysed the data by SPSS for Windows[21] and used unpaired t-test to compare means of parametric data. Chi-square test (χ^2) with Pearson's continuity correction or Fisher's exact test for small numbers were used for categorical data.

RESULTS

A total of 142 patients were identified as long-term regular BZ users of whom 33 refused to participate in the study. Characteristics and pattern of BZ use of the remaining 109 subjects (77%) are shown in Table I. There were no significant differences between the subjects who consented and those who refused to participate in the study, in terms of women : men ratio (1.9 vs 1.4, $\chi^2 = 0.62$, df = 1, p = 0.43), age (55.5 $\pm$ 12.8 vs 54.6 $\pm$ 10.5, t = 0.39, df = 140, p = 0.70), years of BZ use (11.0 $\pm$ 8.2 vs 11.1 $\pm$ 6.9, t = 0.08, df = 140, p = 0.94), and dosage of BZ use in mg diazepam equivalent (16.5 $\pm$ 18.3 vs 14.9 $\pm$ 17.0, t = 0.44, df = 140, p = 0.66).

Patients' view of benzodiazepine and ways of managing their daily lives other than relying on benzodiazepine

Most of the subjects viewed BZ to be helpful (Table II). Only 12% of the subjects complained about undesirable effects of BZ. The majority of the subjects (59.6%) could not suggest any alternative which would help them to cope with their daily lives besides BZ use. Some of the patients suggested the following: taking of health food or vitamins (12.8%), physical exercise (11.9%), going out or chatting with friends (11%) and relaxation (7.3%).

Attempts to stop or reduce BZ use

Forty-two subjects (38.5%) had attempted to stop taking the drug at least once in the past but only 12 of them were able to stop BZ for more than 1 month. Seventy-two respondents (67.2%) had previously tried to reduce the dosage of BZ for at least once but only 47 of them managed to reduce BZ for more than 2 weeks and only 37 of them continued with the reduced dosage until the time of the survey.

Psychological ill health

The primary DSM IV psychiatric diagnosis of the subjects at the time when BZ was first prescribed is listed in Table III. Fifty-two subjects (47.7%) experienced significant anxiety during the week before

Table I – Characteristics of 109 long-term benzodiazepine users

Ratio of women : men	**1.9 : 1**
Age (mean, SD, range)	55.5, 12.8. 26 – 81
Years of education (median, range)	4, 0 – 16
Married (n, %)	82, 75.2
Regular tobacco use (n, %)	11, 10.1
Regular coffee use (n, %)	8, 7.3
History of substance abuse (n, %)	3, 2.8
History of regular alcohol use (n, %)	1, 0.9
Ratio of subjects taking one, two and three BZs	86 : 21 : 2
Years of BZ use (median, range)	9, 1 – 40
Proportion of subjects who have been started on BZs before being seen in the clinic * (n, %)	47, 47.5
Dosage of BZ in mg diazepam equivalent # (median, range)	10, 1.7 – 110
Type of commonly used BZ (% of subjects)	
diazepam	30.3
lorazepam	23.9
bromazepam	20.2
alprazolam	16.5

* 10 subjects replied that they did not know or could not remember.

\# Diazepam 5 mg equivalent to alprazolam 0.25 mg, bromazepam 1.5 mg, chlordiazepoxide 15 mg, clorazepate dipotassium 7.5 mg, flunitrazepam 1 mg, flurazepam 7.5 mg, lorazepam 0.5 mg, lormetazepam 0.5 mg, midazolam 7.5 mg, nitrazepam 5 mg, temazepam 10 mg, triazolam 0.125 mg.

Table II – Patients' view of benzodiazepine

	Number (%) of responses* (n = 109)
Beneficial effect:	
Help with sleep	60 (55.0)
Produce calming effect	42 (38.5)
Reduce worry and tension	25 (23.9)
Reduce physical discomfort	22 (20.2)
Give more confidence	9 (8.3)
Give greater happiness	7 (6.4)
Don't know but cannot live without the drug	7 (6.4)
Undesirable effect:	
Poor memory	4 (3.7)
Drowsiness	3 (2.8)
Weakness	2 (1.8)
Others	4 (3.7)

* Patients could give more than one reply.

Table III – Psychological ill health

	Number (%)
Primary DSM IV psychiatric diagnosis at the time when benzodiazepine was first prescribed (n = 103)	
Generalised anxiety disorder	57 (55.3)
Adjustment disorder with anxiety	10 (9.7)
Panic disorder	7 (7.0)
Major depressive disorder	6 (5.8)
Anxiety disorder NOS	5 (5.0)
Dysthymia	4 (3.9)
Others	14 (13.6)
Common anxiety symptoms by using Hamilton Anxiety Rating Scale (n = 109)	
Anxious mood	52 (47.7)
Insomnia	50 (45.9)
Muscle pain, twitching or stiffness	40 (36.7)
Tension headache, dry month or flushing	39 (35.8)
Difficulty in concentrating and poor memory	34 (33.0)

the survey. Only 25 subjects (22.9%) were free of anxiety symptoms when they were assessed with the HARS. Some common anxiety symptoms reported by the subjects were as shown in Table III.

Physical ill health

Seventeen of the respondents (17.5%) were admitted to hospitals due to physical illnesses during the year before the study. Half of the subjects had visited doctors for physical symptoms in the month prior to the study. Forty-eight respondents (49.5%) reported current physical illnesses that required regular medications. Musculoskeletal (20%), endocrine or metabolic (11.3%), gastrointestinal (8.2%) and ear, eye and nose (8.2%) disorders were the more common physical illnesses of the subjects.

Patients' willingness to reduce or stop benzodiazepine

Most of the subjects' doctors (69.7%) had advised them to stop or reduce BZ use. When the subjects were asked at the interview whether they would like to reduce or stop BZ use, nearly half (48.6%) of them refused the suggestion despite an assurance that dose reduction would be gradual and according to their own pace. Those subjects who agreed to reduce BZ were worried of BZ's side effects (18.3%) and of the long-term reliance on its use (18.3%). Reasons for refusal to reduce BZ given by the subjects included poor current health condition (18.3%), fear of relapse (13.8%) and worries that stopping the drug could affect their work performance (11%). There were no significant statistical differences between those who agreed and those who refused to attempt BZ dose reduction with respect to women : men ratio (1.7 vs 2.1, $\chi^2 = 0.35$, df = 1, p = 0.55), years of BZ use (10.2 ± 8.1 vs 11.8 ± 8.2, t = 0.99, df = 107, p = 0.32), BZ dosage in mg diazepam equivalent (16.4 ± 17.6 vs 16.6 ± 19.3, t = 0.06, df = 107, p = 0.96), presence of undesirable side effects (7/56 vs 11/53, $\chi^2 = 1.35$, df= 1, p = 0.25) and total HARS score (5.5 ± 5.6 vs 6.7 ± 6.8, t = 1.05, df = 107, p = 0.3). The differences between those 2 groups were that a greater proportion of the subjects who agreed to BZ dose reduction had previously managed to reduce BZ for longer than 2 weeks (32/56 vs 14/51, $\chi^2 = 9.6$, df = 1, p = 0.002) and that subjects who agreed to BZ dose reduction were younger (52.9 ± 12.2 vs 58.3 ± 13.0, t = 2.2, df = 107, p = 0.03).

Effectiveness of information leaflet about benzodiazepine withdrawal

Sixty three out of the 109 subjects (57.8%) with their HARS total scores of not more than 5 points and the scores for each of the items ie. anxious mood and depressed mood rated none or mild, were considered to be clinically stable and suitable for dose reduction. Only 56 (88.9%) amongst the 63 subjects consented to a second interview 3 months later. No significant statistical differences were found between the 7 subjects who refused to attend the second interview and those who consented in terms of age (58.6 ± 12.1 vs 56.1 ± 12.4, t = 0.49, df = 61, p = 0.62),

Table IV – Differences between subjects who are successful and unsuccessful in benzodiazepine reduction

	Reduced dosage of BZ (n = 14)	Same dosage of BZ (n = 42)	c^2	t	p
Ratio of women : men	1.8 : 1	1.1 : 1	0.60		0.44
Age (mean ± SD)	57.4 ± 12.4	55.7 ± 12.5		0.45	0.65
Years of education (mean ± SD)	4.9 ± 3.8	4.3 ± 4.3		0.46	0.65
Years of BZ use (mean ± SD)	13.3 ± 11.0	11.2 ± 7.9		0.78	0.44
Dosage of BZ in mg diazepam equivalent (mean ± SD)	19.7 ± 18.5	14.0 ± 15.6		1.13	0.26
Subjects who have generalised anxiety disorder as primary psychiatric diagnosis : those who have other diagnoses	6 : 8	22 : 20	0.38		0.54
Subjects who agreed to attempt reducing BZ : those who refused	11 : 3	20 : 22	4.07		0.04
Subjects who have previously reduced BZ > 2 weeks : those who have not	6 : 8	21 : 21	0.21		0.64
Subjects who have physical illnesses: those who do not have	6 : 8	22 : 19	0.49		0.49

women : men ratio (6.0 vs 1.2, Fisher's exact test p = 0.13), BZ dosage in mg diazepam equivalent (27.2 ± 25.8 vs 15.4 ± 16.4, t = 1.7, df= 61, p = 0.10), duration of BZ use (7.1 ± 7.6 vs 11.8 ± 8.7, t = 1.4, df = 61, p = 0.17) and total HARS scores (2.4 ± 2.1 vs 1.5 ± 1.7, t = 1.3, df = 61, p = 0.20). None of the 56 subjects received any psychotherapy during the 3 months' interval and 14 of them (25%) were able to reduce BZ use. The differences between the 14 subjects who managed to reduce BZ and the 42 subjects who maintained the same dosage of BZ during the 3 months' study interval were, as shown in Table IV. The percentage of subjects who agreed to BZ reduction at the first interview was significantly higher for the group of 14 subjects than the group of 42 subjects (Table IV). The 14 subjects were able to reduce a median of 2.5 mg diazepam equivalent per day (range: 0.48 – 7.5). The median percentage reduction of dosage between the first and the second interview was 19 (range: 6 – 50). Amongst the 23 subjects who did not report any anxiety symptom during the first interview, only 4 of them managed to reduce the use of BZ in the 3 months' interval. Amongst the 14 subjects who reduced BZ use during the 3 months' interval, their total HARS scores before dose reduction did not differ significantly with their scores when they were reassessed (1.9 ± 1.9 vs 2.1 ± 1.9, t = 1.47, df = 13, p = 0.17).

DISCUSSION

The present study looked at a group of long-term BZ users who took BZ as the only psychotropic medication. The selection of this sample allowed us to study patients' perception of BZ more accurately because patients using BZ with other psychotropic medications may not distinguish BZ from the other drugs prescribed.

A majority of long-term BZ users in the present study were women in their late middle age. The demographics of the patients are similar to long-term BZ users in studies done in UK and US[11-13]. The major differences between our Chinese sample and the long-term BZ users in Western population[12,13,23] are that patients in the current sample have used BZ for a longer duration and very few of them have any history of regular alcohol or abusive substance use.

The subjects in our study have generally a favorable opinion of BZ. Most of our patients considered BZ to be helpful in reducing anxiety and improving sleep. Few subjects experienced undesirable side effects of BZ. Nevertheless, a lower percentage of our Chinese sample could suggest other alternatives that would help them to cope with their daily lives when compared with a UK sample[14].

We found that a majority of long-term users have attempted to stop or reduce their BZ use. This finding has also been reported in a previous study[14]. The subjects' attempts to stop taking BZ corresponded with the general public's uneasiness about tranquilizers use[24].

More than two-thirds of the 109 subjects were diagnosed to have an anxiety disorder at the time when BZ was first prescribed. Only 25 subjects were free of anxiety symptoms and nearly half of the sample (52 subjects) complained of anxious mood, insomnia or other physical symptoms of anxiety when assessed by the HARS despite continuous BZ use. The finding suggests that alternatives should be explored for better control of anxiety for long-term BZ users especially in cases where further increment of BZ dosage is not preferred. Half of the subjects have current physical illnesses that require medical treatment and they are frequent consumers of health services. This pattern is also observed in long-term BZ users in another study[13].

Although most of the subjects (76 subjects) have been advised by their doctors to reduce or stop BZ use, nearly half of them (53 subjects) refused to attempt dose reduction when asked during the interview. The proportion of subjects who rejected BZ reduction is comparable to previous studies in UK[12,14]. A higher percentage of subjects who agreed to reduce their BZ use have previously reduced BZ for longer than 2 weeks compared to those who rejected the idea. This suggests that past successful experience of dose reduction may reinforce dose reduction attempts. Some of the patients could not maintain the dose reduction period for more than 2 weeks partly due to severe withdrawal reactions on

abrupt BZ withdrawal[25]. In order to minimize severe withdrawal reactions that may jeopardize patients' future attempts of dose reduction, it is suggested that clinicians should advise their patients that BZ has to be reduced gradually when the drug is first prescribed. We also found that subjects who agreed to reduce BZ were younger in age than those who rejected the idea.

The effectiveness of the information leaflet in reducing BZ use is moderate in our sample. Amongst a group of long-term BZ users with stable clinical conditions, 25% of them were able to reduce their dosage within a period of 3 months by 2.5 mg diazepam equivalent (ie., about 20% of their initial dosage). Most of the subjects in our study have been advised by their doctors to reduce BZ before. When the subjects were asked to reduce their BZ use in this study, and at the same time given an information leaflet, some of them were able to achieve further BZ reduction. Although the proportion of subjects who managed to reduce BZ use (25%) is relatively low when compared with the reported figures in previous studies (18% – 62%)[17-19] and the average BZ dosage reduced is minimal, repeated advice to patients who are clinically stable is important. We also found that the fundamental factor for successful BZ reduction is the subjects' own willingness to attempt although a small percentage of subjects (3 out of 25 subjects) who rejected the idea managed to reduce BZ in the 3 months' interval.

We did not find that the anxiety levels of the subjects worsened upon BZ reduction. This finding suggests that long-term BZ users who are clinically stable and willing to reduce BZ use should be encouraged to do so. Patients who managed to reduce their BZ use have no sign of relapse in the following 3 months.

The limitation of this study is the selection of our sample of long-term BZ users from one psychiatric clinic only. However, half of our patients were originally long-term BZ users of other medical practice and were referred to our clinic from a wide spectrum of general practitioners and specialists. Our finding that the use of an information leaflet is effective in reducing BZ use is also limited by the lack of a control treatment group and the short follow-up period. It is doubtful whether the 14 subjects would have managed to reduce BZ use without the provision of the information leaflet and the 15 minutes' explanation. We have subsequently reviewed the records of the 14 subjects during the 1 year period before the survey. We found that 11 of the 14 subjects had been prescribed with the same dosage of BZ for more than 1 year and the other 3 subjects received a reduced dosage of BZ during the period. Although most of the 14 subjects might have had the motivation to reduce BZ use, no actual dose reduction took place before the study. The implication behind such findings is that the use of the information leaflet and the 15 minutes' explanation might have facilitated BZ reduction, in particular for users who have had an initial motivation to reduce BZ use.

In conclusion, the present study found that the characteristics and views of long-term BZ users in Hong Kong have both similarities and differences when compared with that in Western societies. Half of our patients refused to even attempt BZ reduction. Twenty-five percent of subjects whose anxiety symptoms were assessed to have been under control were able to reduce BZ dosage by encouragement and the provision of an information leaflet. There is no sign of relapse in patients who managed to reduce BZ use during the study period. For patients who are reluctant to change their BZ dosage, the chance of BZ reduction or withdrawal is remote.

ACKNOWLEDGEMENT

This study was supported by the Health Services Research Fund, Hospital Authority, Hong Kong.

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