

Health of long term benzodiazepine users

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Abstract

The physical and psychological health of long term (over one year) users of benzodiazepines in one general practice was assessed by patients' self reporting of illness and by general practitioners' records. Of 3741 patients registered with the practice, 82 had been prescribed a benzodiazepine, and 64 of these agreed to enter the study. All but five of these patients were over 40 years of age, nearly a third (19) were given a diagnosis related to depression by interviewers, and between a third and a half reported a current physical illness.

Long term treatment with benzodiazepines is not necessarily optimum management but may reflect the realities of general practice.

Introduction

The use of benzodiazepines and other tranquillisers has caused considerable concern among the public and the medical profession,^{1,2} mainly because of the large, regular increases in the number of prescriptions for these drugs in the late 1960s and early 1970s.^{3,5} The evidence clearly shows that this was due primarily to a steep increase in the extent of long term use of tranquillisers.⁶

There have, however, been few systematic investigations of the health of long term users. We decided to study the psychological ill health and self reported physical ill health of a population of long term (one year or more) benzodiazepine users in a south London general practice.

Method

The study was conducted in a two partner practice based in a health centre in inner south London. The number of patients on the age-sex register at the end of December 1985 was 3741. The general practitioners identified the patients who had received benzodiazepine prescriptions continuously for one year or more by means of an audit of their repeat prescribing. These patients were asked to consent to an interview, which was mostly conducted (by EKR and MBK) in the patient's home.

Basic sociodemographic data were collected, and information about health was elicited by means of three schedules. Firstly, the patients were asked questions about their past and present use of medicines, using a schedule modified from Murray.⁷ Secondly, the Clinical Interview Schedule was administered.⁸ This is a widely used semistructured interview designed to identify and quantify psychological ill health in community and general practice samples. Included in this schedule is a section concerned with past and current general medical history, and from this information about self reported physical ill health was collected. Thirdly, each patient was asked to complete the Symptom Rating Test, which is a 30 item self report questionnaire which is designed to elicit the experience of psychological symptoms during the preceding week.⁹ Finally, information on physical ill health was extracted from the general practitioners' records.

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Results

Eighty two patients (20 men and 62 women, comprising 2.2% of the practice population) who were long term benzodiazepine users were identified by the general practitioners. Sixty four (78%) agreed to be interviewed. Of the 18 who were not interviewed, four had moved away, two were not interviewed on the advice of the general practitioner, one was dead, eight could not be contacted (after repeated efforts), and the remaining three refused to participate.

TABLE 1—Self reported consumption of other drugs

	No (%) of men	No (%) of women
No of other drugs:		
None	4 (25)	15 (31)
One	6 (38)	14 (29)
Two	3 (19)	11 (23)
Three	1 (6)	7 (15)
Four	2 (12)	1 (2)
Total No of patients interviewed		
	16 (100)	48 (100)
Type of drug:		
Psychotropic:		
Antidepressants	2	8
Major tranquillisers	0	6
Non-psychotropics:		
Cardiovascular drugs	6	16
Analgesics	6	5
Gastrointestinal preparations	3	6
Hormones, metabolic	1	6
Vitamins, minerals	1	4
Anti-rheumatic drugs	0	4
Other	4	6
Total No of drugs		
	23	61

CHARACTERISTICS OF THE PATIENTS

Sixteen patients were men and 48 were women. Only five were under 40 years of age, and 26 (41%) were 70 years or over. Six had never married, 28 were currently married, and the remaining 30 were widowed, divorced, or separated. Forty seven (73%) were working class (based where possible on their own occupations, classified according to the scheme of Goldthorpe and Hope¹⁰), and 25 (40%) lived alone.

Benzodiazepine use—The median duration of treatment with benzodiazepines was five years, range one to 25 years. Most of the patients (51; 80%) claimed that they had been started on the drugs by their general practitioner; 53 (83%) said that they were taking the drugs at least once each day; a further five reported that they took the drugs "several times each week." None reported consumption at dosages above those recommended in the *British National Formulary*. Five men and five women were taking two benzodiazepines concurrently. Altogether, nine different benzodiazepine preparations were being prescribed for the patients: the most common were temazepam (25 patients), diazepam (14), nitrazepam (12), and lorazepam (11). Over half of the patients (39; 61%) thought that the drugs had been prescribed in the first place for insomnia.

Concurrent use of other drugs—Table 1 shows that most of the long term benzodiazepine users were also taking other drugs; about one fifth were taking three or more other drugs. Two men and 14 women were taking other psychotropics (table 1): 10 men (63%) and 19 women (30%) were taking one or more of a wide range of non-psychotropic drugs. Of these, drugs used to treat cardiovascular disorders were the most common, followed by analgesics and gastrointestinal preparations.

PSYCHOLOGICAL ILL HEALTH

Two men and eight women reported that they had seen a psychiatrist during their treatment with benzodiazepines, four women the previous year.

Fifty four patients (12 men and 42 women) completed the Symptom Rating Test. Table II gives the results and the results of other studies for comparison. For the total score as well as all four subscale scores the results from the sample in this study lay between those from clinical samples (psychiatric outpatients) and those from community samples but were closer to the latter. The proportion of patients who scored >12 was substantially lower than that found by Murray in her self selected sample of long term tranquilliser users and that obtained by Williams *et al.*, in their study of new recipients of psychotropic drug prescriptions in general practice.^{7,12}

Two men and 20 (42%) women—that is, 34% overall—were classified as cases according to the Clinical Interview Schedule (Overall Severity Rating >2). Table III shows that 19 of these 22 cases were allotted an ICD diagnosis relating to depression (ICD numbers 296.1, 300.4, and 309.0), while only

one patient was allotted an anxiety related diagnosis (ICD 300.2). In addition, one man was allotted an ICD diagnosis of postconcussional syndrome (ICD 310.2), although not rated as a case on the Clinical Interview Schedule.

PHYSICAL ILL HEALTH

Six (38%) men and 19 (30%) women had consulted a hospital physician or surgeon during the year before the survey. Each patient was asked to state current and past physical illnesses. Table IV shows that only two men and seven women claimed never to have been ill, while about a third of them reported three or more past illnesses. Just over half of the men and just over a

TABLE II—Symptom Rating Test (mean and SD) total and subscale scores

	Total	Anxiety	Depression	Somatic	Inadequacy	No (%) scoring >12
This study:						
Men (n=12)	13.9 (9.6)	4.3 (3.2)	3.8 (3.6)	2.7 (2.3)	3.3 (3.0)	7 (44)
Women (n=42)	20.1 (16.4)	5.9 (5.3)	5.4 (5.2)	4.2 (3.6)	4.7 (4.7)	25 (52)
Kellner and Sheffield ⁹ :						
Outpatients sample 1	51.1 (25.1)	11.7 (6.6)	11.6 (5.8)	6.9 (5.5)	13.6 (6.6)	—
Outpatients sample 2	49.8 (27.2)	11.3 (6.1)	11.6 (6.6)	5.7 (5.0)	13.4 (8.5)	—
"Normals" sample 1	9.0 (8.3)	1.5 (1.9)	1.5 (2.1)	1.6 (1.8)	2.3 (2.8)	—
"Normals" sample 2	11.9 (13.6)	2.4 (2.9)	2.5 (2.9)	1.6 (2.3)	3.2 (4.2)	—
Cochrane ¹¹ :						
Out/day patients	24.6 (12.0)	—	—	—	—	—
Community sample	8.0 (9.0)	2.5	2.0	1.4	2.1	—
Murray ⁷ :						
Self selected long term psychotropic drug users	—	—	—	—	—	152 (83)
Williams <i>et al.</i> ¹² :						
New users of psychotropic drugs	—	—	—	—	—	—
Men	—	—	—	—	—	49 (84)
Women	—	—	—	—	—	86 (91)

TABLE III—Psychiatric morbidity

	No of men	No of women
Psychiatric cases according to Clinical Interview Schedule	2	20
ICD diagnosis:		
296.1 manic-depression psychosis, depressed	—	1
300.2 phobic state	—	1
300.4 neurotic depression	1	16
301.5 hysterical personality	1	—
307.8 psychalgia	—	1
309.0 brief depressive reaction	—	1
Not psychiatric cases, according to Clinical Interview Schedule	14	28
Total No of patients interviewed	16	48

ICD=International Classification of Diseases.

TABLE IV—Self reported physical ill health

	Past		Current	
	No (%) of men	No (%) of women	No (%) of men	No (%) of women
No of physical illnesses reported:				
None	2 (12)	7 (15)	7 (44)	30 (63)
One	4 (25)	11 (23)	9 (56)	12 (25)
Two	5 (32)	13 (27)	0	5 (10)
Three	3 (19)	10 (21)	0	1 (2)
Four	1 (6)	6 (12)	0	0
Five	1 (6)	1 (2)	0	0
Total No of patients interviewed	16 (100)	48 (100)	16 (100)	48 (100)
Nature of illnesses reported:				
gastrointestinal	12	19	0	2
musculoskeletal	5	18	2	6
cardiovascular	5	13	4	5
respiratory	3	9	0	2
other	7	37	3	10
Total No of illnesses reported	32	96	9	25

TABLE V—Physical ill health recorded in the general practitioners' records

	No (%) of men	No (%) of women
No of physical illnesses recorded:		
None	5 (31)	18 (38)
One	8 (50)	22 (46)
Two	3 (19)	4 (8)
Three	0	4 (8)
Total No of patients interviewed	16 (100)	48 (100)
Nature of illness recorded:		
Gastrointestinal	4 (30)	1 (2)
Musculoskeletal	1 (7)	11 (27)
Cardiovascular	3 (21)	8 (19)
Respiratory	3 (21)	8 (19)
Malignant	1 (7)	5 (12)
Other	2 (14)	9 (21)
Total No of illnesses recorded	14 (100)	42 (100)

third of the women reported a current physical illness. Gastrointestinal, musculoskeletal, and cardiovascular disorders were predominant.

Table V shows the major physical illnesses recorded in the general practitioners' notes. About a third of the patients had no such illnesses recorded, but just under a fifth had records of two or more illnesses. The few reported illnesses in the men precluded a reliable analysis of the nature of the illnesses, but musculoskeletal, cardiovascular, and respiratory disorders predominated in the women.

Discussion

These results are derived from patients of one general practice so the findings may not be generalisable to other settings. Furthermore, much of the information is based on recall and self report. Despite these limitations we believe that the findings are a useful

addition to the knowledge of long term benzodiazepine use: in particular, this is the first study of long term benzodiazepine users (as far as we know) in which a standardised assessment of psychiatric morbidity has been carried out.

We found that 2.2% of the practice population had received prescriptions for benzodiazepines continuously for one year or more. Table VI shows the results of some other recent studies that estimated the extent of long term tranquilliser use, and our findings are not dissimilar. Thus, it can be estimated that between 825 000 and 1 650 000 people in the United Kingdom (1.5% and 3% of 55 million) are long term (one year or more) users of benzodiazepines and other tranquillisers.

TABLE VI—Extent of long term use of tranquillisers in recent studies

Stoll and Lader ¹³ Community survey	"Use of tranquillisers for one year or more"	1.5% of men
Mellinger and Balter ¹⁴ Community survey, USA	"Use of anti-anxiety agents for 12 months or more"	1.6% of population
Balter <i>et al</i> ¹⁶ Community survey, several countries	"Regular daily use of anti-anxiety/sedative drugs for 12 months or more"	UK: 3.1% of population USA: 1.8% of population Europe: 1.6% of population
Salinsky and Dore ¹⁶ General practice, UK	"Taking benzodiazepines regularly during the day for more than a year"	1.6% of registered patients
Present study General practice, UK	"Prescription of benzodiazepines for one year or more"	2.2% of registered patients

Previous studies have shown that sex and age are related not only to the use of benzodiazepines and other psychotropic drugs in general but to prolonged use in particular.^{3,17,21} Our findings confirmed this: the ratio of women to men was 3/1 compared with 1.6/1 in the study by Williams *et al* of new users of psychotropic drugs in six south London general practices and with Cooperstock's observation of a "consistent 2/1 ratio of women to men in the receipt of prescriptions for psychotropic drugs."^{12,18} Similarly, the long term benzodiazepine users in the present study were predominantly elderly, whereas the mean age of new recipients of psychotropic drugs in Williams's study was 47 years.¹²

There is evidence that long term users of benzodiazepines and other tranquillisers report high levels of emotional distress. Mellinger *et al* studied 68 respondents from a community survey who reported regular (daily for one year or more) use of anxiolytics.²¹ Half of these long term users had high scores on the measure of emotional distress on the questionnaire, the PSYDIS,²² compared with a fifth of the non-users. The authors noted, however, that "the long-term users did not differ much from the other users in this respect," 45% of whom were also high scorers.

The Symptom Rating Test scores in the present study confirm the association between long term tranquilliser use and emotional distress, as the levels were higher than those previously reported from normal samples. The scores, however, were substantially below those previously reported from samples of neurotic outpatients, and the proportion that scored >12 was lower than among the new psychotropic drug users studied by Williams *et al* or the self selected sample of long term psychotropic drug users studied by Murray.^{12,7}

As far as we know this is the first study in which a standardised assessment of the mental state was carried out. We found that two of the men and 20 of the women—34% of the patients overall—were rated by the interviewing psychiatrists as cases. While in absolute terms this shows substantial psychiatric morbidity, it is not very different from what would be found in an unselected series of general practice attenders. For example, Marks *et al* obtained a case rate of 39% in their study of patients attending 91 general practitioners in Manchester,²³ and Skuse and Williams recorded a rate of 34% in a south London general practice,²⁴ in both cases using the Clinical Interview Schedule as the case criterion.

A notable finding was that when the interviewing psychiatrists assigned an ICD diagnosis according to the International Classification of Diseases to the 22 patients who were classified as cases most were assigned a diagnosis related to depression. There is evidence that the use of tranquillisers in the treatment of depressed people in the community is widespread. For example, Weissman and Klerman followed up 150 depressed women who had responded to tricyclic antidepressants and who had received eight months of maintenance treatment as part of a controlled clinical trial.²⁵ Followed up one and four years after the maintenance treatment had ended, these women were more likely to have received a minor tranquilliser than an antidepressant when they sought medical help. Furthermore, when Gullick and King studied patients who were attending a marital and sexual counselling centre they noted that those with major depressive disorder were more likely to have received a minor tranquilliser than an antidepressant.²⁶ Similar findings were obtained by Weissman *et al* in their community survey of depression and its treatment in the United States.²⁷ Despite this widespread application it now seems clear that the benzodiazepines are generally devoid of antidepressant effects, although alprazolam is claimed to elevate mood.²⁸⁻³⁰

There is evidence that de novo prescription of benzodiazepines and other psychotropic drugs frequently occurs in response to a physical rather than psychological disorder.^{31,32} It is not surprising, therefore, that we found that long term users reported extensive physical ill health and consumption of non-psychotropic medication. This supports previous work. For example, Murray and her colleagues interviewed 22 patients who had been prescribed psychotropic drugs continuously for six months or more and found that "chronic physical complaints were common in the sample (diverticulitis, arthritis, hypertension, migraine) and 13 people were long-term users of non-psychotropic prescribed drugs."³³ Furthermore, Mellinger *et al* found that physical health distinguished between long term users and other users of tranquillisers more sharply than did any other factor they studied (including emotional distress).²¹ They noted that "at least one-third of the long-term users reported four or more health problems—a rate twice that found among the other anxiolytic users and seven times that of the non users." These differences persisted when age was controlled for, and they also observed that much of the difference between the long term users and the others could be accounted for by cardiovascular disorders and arthritis.

The findings give little support to the popular stereotype of the long term tranquilliser user as being a young woman with a host of social difficulties. Instead, the long term users we studied, although mostly women, were predominantly elderly and were experiencing appreciable ill health. It was not clear, however, that the nature of the ill health (depression and a range of physical illnesses) was such that chronic treatment with tranquillisers was necessarily the best form of management. These findings, if replicated, have important implications for the prevention and management of long term use of tranquillisers.

We are indebted to Dr M Courtenay and Dr H Dawson for allowing access to their patients, and for their kind help at every stage of the project.

The study was conducted as part of the research programme of the General Practice Research Unit, funded by the Department of Health and Social Security and directed by Professor Michael Shepherd. We also thank him for his helpful comments on an earlier version of the paper.

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(Accepted 17 November 1987)

SHORT REPORTS

Ultrasound guided core biopsy in AIDS: experience in six patients

Ultrasound guided biopsy with use of a special Tru-Cut needle fired by a spring loaded device (Biopty gun) is a safe, quick, and effective way of obtaining specimens for histological examination. We report using this technique in six patients with the acquired immune deficiency syndrome (AIDS) who had various lesions which presented problems in diagnosis and management.

Patients, methods, and results

The six patients were male homosexuals known to be positive for the human immunodeficiency virus (HIV) at the time of biopsy. The table gives their clinical details. Biopsy was performed by using the Biopty gun described by Lindgren (Radioplast Biopty, Henleys Medical Supplies Ltd, London).¹ This mechanical device uses a special Tru-Cut needle which obtains a core biopsy sample (1 mm diameter, 17 mm long) within a fraction of a second of releasing a trigger mechanism. It allows for exact guidance of an 18 gauge needle by a single operator because it leaves a free hand for holding the ultrasonic probe. Specimens obtained with this device are better than those obtained manually.¹

Two specimens were taken from each patient under local anaesthesia except in case 5; a single specimen was taken from this man because he was thrombocyto-

penic. Specimens were subjected to microbiological examination in all cases and histological examination in all except case 2.

Adequate tissue was obtained in every case. The management was directly influenced by the biopsy results in all six patients (table). There were no serious complications. In the man with thrombocytopenia (case 5) a self limiting retroperitoneal haematoma occurred and was monitored at the time by ultrasonography. The patient quickly recovered.

The biopsies were performed after other investigations had failed to provide a definitive diagnosis. Postmortem examination was not performed in the single patient who died.

Comment

Infection with HIV produces a range of disease, AIDS being the most severe. There are numerous causes for enlargement of lymph nodes in patients positive for HIV, including Kaposi's sarcoma, lymphoma, and infections such as tuberculosis. Enlargement of lymph nodes also occurs in persistent generalised lymphadenopathy, which lies between the asymptomatic carrier state and AIDS. Persistent generalised lymphadenopathy may occur alone or may be seen with other clinical and laboratory abnormalities, when it is known as AIDS related complex.

Other reports have suggested that routine biopsy is usually unhelpful in HIV positive patients with simple lymphadenopathy and rarely alters management.^{2,3} Many patients with lymphadenopathy in AIDS or AIDS

Clinical details of patients studied (male homosexuals positive for HIV)

Case No	Age (years)	No of months HIV positive	Clinical data	Ultrasonographic findings	Biopsy site(s)	Results	Subsequent management and outcome
1	34	8	Fevers, anorexia, weight loss, intermittent diarrhoea	Enlarged small bowel lymph nodes	Mesenteric lymph node	Mycobacterium laden macrophages; <i>Mycobacterium avium-intracellulare</i> cultured	Quadruple antituberculous treatment and prednisolone with relief of symptoms
2	52	3	Diarrhoea and rectal bleeding due to intestinal Kaposi's sarcoma; enlarged peripheral lymph nodes; mass in right iliac fossa	Mild hepatosplenomegaly; diffuse thickening of small bowel and mesenteric lymphadenopathy; hypochoic lesion within right iliacus	Right iliacus lesion (fine needle aspiration unsuccessful)	<i>Escherichia coli</i> cultured	Antimicrobial treatment; there was disappearance of lesion on follow up scans
3	37	7	Cutaneous and buccal Kaposi's sarcoma; fever, cough, and hepatosplenomegaly	Hepatosplenomegaly and para-aortic lymphadenopathy	Para-aortic lymph node	Kaposi's sarcoma	Chemotherapy; this did not prevent disease progression
4	27	2	Neurosyphilis and severe anaemia; sudden severe pain and swelling in thigh adductor muscle	Severe hepatosplenomegaly and pelvic lymphadenopathy; enlarged and hypochoic thigh adductor muscle	Pelvic lymph node; thigh adductor muscle	High grade T cell lymphoblastic lymphoma from both sites	Chemotherapy; patient died soon after
5	41	28	Cutaneous Kaposi's sarcoma; fever, cough, splenomegaly	Massive splenomegaly and abdominal lymphadenopathy	Para-aortic lymph node	Lymphocyte depletion; no malignant cells or organisms seen	Chemotherapy with resolution of fever, splenomegaly, and abnormal nodes
6	35	0	Herpes zoster, oral candidiasis, peripheral lymphadenopathy; low back pain, leg weakness, numbness with lower motor neurone signs	Splenomegaly and abdominal lymphadenopathy; soft tissue mass related to lumbar spine	Bone and soft tissue	High grade B cell lymphoma	Radiotherapy and chemotherapy recently started