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Main Section

OUTCOME PREDICTORS OF BENZODIAZEPINE WITHDRAWAL

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Abstract. Psychological treatment that reduces anxiety has been found to be beneficial to benzodiazepine withdrawal. High drop-out and relapse rates, however, have also been reported. They might be due to a heightened anxiety level maintaining the drug-taking habit or to the addictive potency of the drug, which is not addressed by the intervention strategies. In the present study, initial assessment data were compared among treatment refusers, drop-outs and completers – successful as well as unsuccessful ones – of a psychological treatment programme in support of benzodiazepine withdrawal. Treatment refusers showed a more negative current mood state than those consenting to treatment. Internal locus of control was predictive of premature termination and unsuccessful completion of the treatment trial. Neither medication-related variables nor anxiety or depression were found to influence the success of treatment. Perceived control over medication intake is thought to reduce compliance with the treatment regimen – a pattern that may be consistent with the addiction hypothesis.

Keywords: Addiction, benzodiazepine withdrawal, locus of control, treatment failure.

Introduction

Over one million people in the U.K. and in Germany are taking benzodiazepines (BZ) on a long-term basis, i.e., for periods of one year or more (Ashton & Golding, 1989; Remien & Raber, 1993). At least 50% of them are estimated to be dependent on BZ (Rickels, Schweizer, Case, & Greenblatt, 1990) and experience withdrawal symptoms upon discontinuation of their medication. Among the pharmacological strategies supporting BZ withdrawal were the substitution of clonidine and buspirone, which failed to alleviate withdrawal symptoms (Schweizer & Rickels, 1986; Ashton, Rawlins, & Tyrer, 1990; Goodmann, Charney, Price, Woods, & Heninger, 1986; Joyce, Moodley, Keshavan, & Lader, 1990). Propranolol substitution attenuated some of the withdrawal symptoms but resulted in a high drop-out rate (Tyrer, Rutherford, & Huggett, 1981; Cantopher, Oliveri, Cleave, & Edwards, 1990). The most promising results are so far shown by carbamazepine in terms of abstinence rate, yet the patients still experienced

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comparably intense withdrawal symptoms (Schweizer, Rickels, Case, & Greenblatt, 1991). The few reported follow-up data indicated that none of the pharmacological substitutes proved successful in aiding BZ withdrawal.

Among psychological techniques employed so far are biofeedback-supported relaxation training and stress management counselling (Nathan, Robinson, Cherek, Sebastian, & Hack, 1986), stress management training (Onyett & Turpin, 1988), anxiety management training (Higgitt, Golombok, Fonagy, & Lader, 1987) and cognitive behaviour therapy techniques (Sanchez-Craig, Cappell, Busto, & Kay, 1987; Otto et al., 1994). These strategies have been found to be of some benefit in BZ withdrawal, with abstinence rates of up to 70% at follow-up. High drop-out and relapse rates have, however, also been noted.

The scrutiny of predictors of withdrawal outcome could lead to an improvement of the intervention strategies. Most reports of predictive factors were provided by pharmacological treatment studies, but with inconsistent results. There is an indication that slow tapering of BZ leads to higher success rates, presumably because it produces less intense withdrawal symptoms (Tyrer et al., 1981). Drugs with a short half-life tend to produce more withdrawal symptoms than those with a long half-life (Rickels et al., 1990). The half-life of the drug did not, however, affect outcomes, if withdrawal was carried out gradually (Schweizer, Rickels, Case, & Greenblatt, 1990). Low initial dose and shorter duration of intake were reported to be predictors of withdrawal success by Rickels et al. (1990), but not by Ashton (1987). Age of the patients, although covarying with duration of BZ use, failed to be a reliable predictor of short-term outcome (Cantopher et al., 1990; Schweizer, Case, & Rickels, 1989); nonetheless, younger patients were able to maintain their abstinence for longer periods than older patients (Holton, Riley, & Tyrer, 1992).

Psychological factors predictive of relapse have been marginally more consistent. High anxiety scores (Ashton et al., 1990; Rickels et al., 1990) and depression scores (Schweizer et al., 1991) were associated with poor outcome. Holton et al. (1992) assessed the long-term outcome of 41 patients five years after a withdrawal programme. Poor outcome was associated with female sex, shorter medication intake, a higher age, more anxiety, the lack of a clear-cut withdrawal syndrome during discontinuation of BZ, and a high level of neuroticism six months after the end of the withdrawal programme. Conversely, Golombok et al. (1987) followed up 46 patients for one to five years after detoxification of BZ and reported a better outcome for women and no effect of withdrawal intensity or psychiatric history on long-term outcome.

In summary, hardly any consistent predictors of withdrawal success have been identified so far; differences in patient samples, in assessment methods, withdrawal programmes and in follow-up periods may account for the rather contradictory findings. To date, predictors have been investigated mainly in pharmacological treatment programmes. It can be expected that different predictors affect the success of psychological treatment supporting withdrawal. So far, both pharmacological and psychological treatment aimed at the reduction of anxiety states (Sartory & Maurer, 1991). It is, however, conceivable that the drug-taking habit is maintained by other factors. Lader (1984) remarked earlier on the addictive powers of BZ, a notion that has been given scarce attention. Classifying prolonged BZ use as an addiction would entail different assessment and treatment strategies from the ones used so far.

The current data are derived from a treatment trial that evaluated the efficacy of two treatment approaches during outpatient BZ withdrawal (Elsesser, Sartory, & Maurer, 1996). A standard anxiety management training was administered to one group of patients, whereas the other group received complaints management training. Withdrawal complaints were monitored closely in both groups and addressed directly during complaints management training. In this treatment condition, patients were instructed in the use of a range of techniques that matched, and conveyed control over, the reported symptoms. Patients were, for instance, trained in Valsalva if they reported tachycardias, in breathing techniques for hyperventilation, and in cued relaxation if they reported insomnia. The treatment was thus more specific to the reported symptoms than anxiety management training during which patients are instructed to counteract all anxiety-related symptoms with relaxation. At the end of treatment, 78% of patients in the complaints management group and 50% of the anxiety management group were abstinent. Patients were also less depressed and anxious in the former group than in the latter. At a follow-up six months later, the groups no longer differed in their abstinence rate (67% and 61%, respectively). There was no difference between the two treatment conditions in terms of number of drop-outs; namely eight in the anxiety management group and nine in the complaints management group. The two groups were therefore combined for the sake of the present data analysis. Initial assessment data were compared between patients who completed the BZ withdrawal trial, drop-outs and those who refused to enter treatment after having been informed about it. Successful completers were additionally compared with unsuccessful ones. Two variables were thought to merit special attention as predictors of withdrawal success: (i) heightened anxiety was thought to lead to premature termination of withdrawal, if psychological treatment failed to induce its sufficiently rapid attenuation; pre-treatment anxiety was therefore considered as a predictor of drop-out; and (ii) a long duration of intake may be indicative of the presence or extent of BZ-addiction, which was not addressed in the treatment regimen and might therefore have lead to its failure.

Method

Subjects

Forty-four chronic BZ users, 25 (57%) of whom were female, entered the study. Patients were referred to the outpatient treatment centre of the Psychology Department or responded to newspaper advertisements and articles. Criteria for inclusion were: at least three months of regular BZ use, at least one prior unsuccessful withdrawal attempt, and no current abuse of substances other than BZ. The mean age of the patients was 49.95 years ($SD = 14.38$) with a range of 27 to 81 years. The mean duration of BZ use was 12.17 years ($SD = 7.67$) with a range of 0.5 to 31 years. Twelve different kinds of BZ were used by patients, most frequently bromazepam (39%) and lorazepam (25%), followed by flurazepam and oxazepam (9% each). Eight patients took different kinds at the same time. The mean daily dose (expressed as diazepam equivalent doses) was 29.31 mg ($SD = 51.85$). Excluding two of the patients who took extremely high doses (200 mg and 300 mg), the daily average dose was 18.54 mg ($SD = 11.69$) which is within the therapeutic range. Upon presentation in the treatment centre, patients were assessed

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and informed about the treatment programme. At this stage, eight patients declined the offer of treatment; all other patients entered treatment. All patients gave their informed consent.

Design

Patients were divided into those who refused treatment (refusers, $N = 8$), those who terminated treatment prematurely (drop-outs, $N = 17$) and those who completed treatment (completers, $N = 19$). Furthermore, completers were divided into those who completed treatment unsuccessfully (unsuccessful completers: $N = 7$; among them, six patients reduced their daily dose of BZ by an average of 70% but failed to reach abstinence and one patient raised his dose by 7%), and those who reached abstinence by the end of the treatment (successful completers: $N = 12$). BZ were gradually withdrawn during the first four weeks, starting with a reduction of the initial daily dose by 50% during the second treatment week and by 75% during the third treatment week; patients were to be abstinent by the fourth week. Psychological treatment was administered for eight weeks and assessments (measurement occasions) were carried out every two weeks. Initial assessment data are presented for all patients and also data from the second assessment from the patients still remaining in the programme. Finally, assessment data from the end of treatment are reported only for completers.

Measurements

Initially, patients were interviewed as to their medication history, withdrawal attempts and current reasons for taking BZ; the following measures were taken during all assessment occasions: BZ-intake: Patients kept a daily record of all medication intake. Urge to use BZ: Patients kept a daily record of their urge to take BZ on a scale of 0 (no urge) to 100 (extreme urge). Spielberger Anxiety Index, Trait form (STAI) (Spielberger, Gorsuch, & Lushene, 1970): Scores range from 20 (no anxiety) to 80 (high anxiety). Erlanger Depression Scale (EDS) (Lehrl & Gallwitz, 1977): This questionnaire consists of a 9-item self-rated inventory with a score range from 0 to 32. A total score of 17 is considered indicative of depression and one of 25 of severe depression. Complaints Inventory (Beschwerden-Liste, von Zerssen, 1976b): This contains a list of 24 bodily complaints whose presence can be indicated on a 4-point-scale in terms of ''not at all'' (0) to ''severely'' (3). Scores can range from 0 to 72 (the higher the score the more severe the complaints). Mood-Scale (Befindlichkeits-Skala, von Zerssen, 1976a): It consists of 28 pairs of adjectives (e.g., happy–sad, fresh–tired). Patients decide which of the two apply to their current state. Scores can range from 0 to 56 (higher scores indicate a more disturbed mood). IPC-Questionnaire of locus of control (Krampen, 1981): The questionnaire (24 items) consists of the scales: ''perceived mastery over one's personal life'' (I); ''belief in external control by powerful others'' (P); and ''belief in chance'' (C). The C-scale is also termed fatalism-scale. Withdrawal Symptom List: This list contains 33 frequently reported withdrawal symptoms whose presence can be indicated on a 5-point-scale in terms of hardly noticeable to severe.

Table 1. Characteristics of the refusers, drop-outs and completers before treatment. Completers are additionally divided into successful and unsuccessful completers

Variable	Refusers ($N = 8$)	Drop-outs ($N = 17$)	Completers ($N = 19$)	Unsuccessful completers ($N = 7$)	Successful completers ($N = 12$)
Age	50.62 (13.41)	54.53 (15.11)	46.05 (13.78)	44.43 (14.60)	47.00 (13.85)
Sex (M/F)	4/4	8/9	7/12	4/3	3/9
Years of BZ-use	10.52 (9.77)	11.97 (8.54)	13.03 (6.10)	10.71 (3.82)	14.37 (6.90)
Daily dose of BZ*	53.50 (100.34)	21.77 (13.83)	25.47 (43.26)	44.88 (69.68)	15.55 (4.88)
	18.28 (11.73)[1]		16.71 (8.99)[1]	19.03 (14.58)[1]	
BZ half-life (short/long)	5/3	14/3	18/1	7/0	11/1
Withdrawal attempts (1/>1)	3/5	5/11	9/10	2/5	7/5

* Diazepam equivalent dose.
[1] One refuser and one unsuccessful completer took extremely high doses of BZ (300 and 200 mg). Therefore *M* and *SD* excluding these two patients are reported additionally.

Results

Comparison between completers, drop-outs and refusers: pre-treatment scores

Among the frequently indicated reasons for currently taking BZ, 44% of patients named anxiety, 23% insomnia, 16% dependence, and 15% stress and depression. Pre-treatment characteristics of the treatment refusers, drop-outs, successful and unsuccessful completers are presented in Table 1. Group comparisons were carried out by means of *t*-tests and χ^2-tests.

Completers were marginally younger than drop-outs ($t(32) = 1.71$; $p < .10$). There were no significant group differences with regard to sex, years of daily use of BZ, daily dose of BZ, BZ-half-life, and number of withdrawal attempts.

Table 2 shows the pre-treatment assessment scores of refusers, drop-outs and completers. Comparing refusers with the other groups showed that the former reported

Table 2. Pre-treatment assessment scores: Means and standard deviations of refusers, drop-outs and completers

	Refusers ($N = 8$)		Drop-outs ($N = 17$)		Completers ($N = 19$)	
Variable	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)
Trait Anxiety (STAI)	54.43	(12.07)	48.94	(12.69)	54.17	(12.35)
Depression (EDS) (total score)	14.25	(7.48)	11.25	(6.35)	13.63	(6.64)
Mood (adjectives)	37.25	(11.72)	25.23	(15.92)	24.19	(14.27)
Bodily complaints	35.56	(11.61)	29.88	(12.53)	34.81	(15.69)
IPC-Internal	33.00	(4.34)	38.65	(5.67)	35.28	(6.02)
IPC-Power	24.00	(4.50)	24.12	(6.93)	22.89	(6.87)
IPC-Chance (fatalism)	22.62	(6.32)	29.06	(8.13)	25.11	(6.63)
Withdrawal symptoms (total score)	81.62	(25.43)	70.59	(25.51)	70.50	(20.93)

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Table 3. Pre- and post-treatment assessment scores: Means and standard deviations of successful and unsuccessful completers

	Pre-treatment				Post-treatment			
	Unsuccessful completers ($N = 7$)		Successful completers ($N = 12$)		Unsuccessful completers ($N = 7$)		Successful completers ($N = 12$)	
Variable	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)	*M*	(*SD*)
Trait Anxiety (STAI)	51.83	(12.70)	55.33	(12.56)	54.00	(13.35)	46.58	(13.50)
Depression (EDS) (total score)	12.28	(5.76)	14.42	(7.23)	11.71	(8.67)	7.92	(7.09)
Mood (adjectives)	21.57	(11.75)	25.86	(15.99)	23.50	(17.54)	18.25	(15.39)
Bodily complaints	34.57	(10.90)	34.96	(18.38)	26.65	(14.59)	26.33	(18.90)
IPC-Internal	39.00	(4.86)	32.91	(5.61)	39.14	(5.34)	32.92	(6.20)
IPC-Power	23.00	(7.89)	22.82	(6.54)	24.14	(6.09)	23.58	(6.89)
IPC-Chance (fatalism)	25.00	(6.93)	25.18	(6.78)	24.43	(6.45)	23.25	(5.89)
Withdrawal symptoms (total score)	70.28	(22.30)	70.64	(21.13)	77.71	(22.26)	61.45	(30.04)

significantly more negative mood adjectives than completers ($t(24) = 2.26$; $p < .05$). None of the other psychological variables yielded significant results. Comparing drop-outs with completers showed that the former had a marginally higher mean score on the IPC-Internal-scale than completers ($t(33) = 1.70$; $p < .10$). When comparing drop-outs with only successful completers (Table 3), this difference became significant ($t(26) = 2.63$); $p < .01$). Drop-outs reported a higher level of perceived internal control than successful completers.

Comparison of successful and unsuccessful completers

Table 3 shows the means and *SD*s of psychological variables of successful and unsuccessful completers at the beginning and end of treatment. Similar to patients who dropped out, unsuccessful completers reported a higher degree of perceived internal control than successful completers at pre-treatment ($t(16) = 2.36$; $p < .05$) and post-treatment assessment ($t(17) = 2.22$; $p < .05$). Furthermore, successful completers reported a significantly lower urge to take BZ ($M = 22.57$; $SD = 31.91$) than unsuccessful completers ($M = 71.30$; $SD = 16.90$; $t(17) = 3.72$; $p < .01$) at the end of treatment.

Relationship between variables pre-treatment

Duration of BZ-use was positively correlated with age ($r = .52$, $df = 40$) and marginally associated with perceived external control by powerful others ($r = .26$, $df = 40$). Age was also correlated with fatalism ($r = .39$, $df = 39$). Number and extent of BZ-withdrawal symptoms were not correlated with age, dose or duration of use but with anxiety, depression and bodily complaints ($r = .55$ to $.71$, $df = 39$) and negatively with perceived internal locus of control ($r = -.34$, $df = 40$). All psychological variables were significantly interrelated.

Discussion

The most pronounced predictor of early termination or unsuccessful completion of the treatment programme was perceived internal controllability. In comparison with

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successful completers, drop-outs and unsuccessful completers evidenced significantly higher internality. It is conceivable that the standardized withdrawal regime constituted too directive an intervention for patients with high internal control prompting their early termination or non-compliance with the treatment regimen. Using an ideosyncratic withdrawal regimen together with anxiety management training, Higgitt et al. (1987) reported a lower drop-out rate than the one found in the present study. An internal locus of control may also be indicative of a sense of control over the drug-taking habit, and therefore engender less of a need to comply with treatment instructions.

In the present study no significant differences were found between drop-outs and completers with regard to demographic characteristics. Drop-outs were only marginally older than completers. In contrast, other studies reported a better outcome for older patients (Cantopher et al., 1990) or no effect of age on treatment success (Schweizer et al., 1989). Both studies employed slower taper rates compared to the present withdrawal regimen. It is conceivable that an increasingly slower reduction of BZ dose may be required with increasing age.

The half-life of the drug and the initial dose – the latter of which was within the therapeutic range for most patients – were not related to withdrawal success, nor were they shown to be predictors in previous studies using gradual withdrawal. The duration of BZ intake also failed to affect withdrawal outcome. Since the average consisted of 10 to 14 years, this result is consistent with the observation by Schweizer et al. (1990) who suggested a duration threshold of one year, beyond which further BZ intake has little influence on the withdrawal experience.

Consistent with the results of Higgitt et al.'s (1987) treatment programme, we found no difference in pre-treatment anxiety or depression between completers and drop-outs. Higher anxiety and depression before treatment were identified as predictors of unsuccessful withdrawal (Ashton et al., 1990; Cantopher et al., 1990; Schweizer et al., 1991) in the case of pharmaceutically-supported BZ withdrawal. In fact, the patients of these three studies reported only slightly elevated anxiety and/or depression, whereas the present sample showed severe impairment. It can be concluded that psychological treatment programmes are effective in long-term users, independent of the severity of their initial symptoms.

A number of factors are likely to maintain the urge to take BZ, of which anxiety is clinically the most obvious one. Addiction is, however, also likely to be one of the factors contributing to the continued BZ use (Lader, 1984). In the present study seven patients reported being dependent on BZ: two of them refused treatment, four dropped out, and one completed treatment unsuccessfully. A high sense of internal control is also likely to be consistent with addiction to the drug. Neither assessment nor treatment of long-term BZ use as yet takes this factor into account. Drop-outs were also marginally older than completers, and may therefore have been less capable of learning new coping strategies.

It is conceivable that long-term use of BZ is maintained by multiple factors, namely its, at least initial, anxiety-relieving properties, addiction to the drug, and the increasing loss of other coping strategies. It might therefore be clinically appropriate to assess not only emotional and affective disorders of the long-term users, but also dependency and addiction to BZ-use, as well as coping strategies. If dependency is evident, elements

from treatment approaches in addictive disorders will need to be recruited for the intervention programme. A lack of alternative coping strategies or slowness in their acquisition during treatment may necessitate an individualized and equally slow withdrawal regimen. Only two of our patients showed clear evidence of BZ abuse, taking diazepam equivalent doses of 200 and 300 mg daily. One of them refused treatment and the other was an unsuccessful completer. Although no firm conclusions can be drawn from so small a number, in-patient withdrawal is likely to be necessary for habitual users of a high BZ-dose.

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