

ORIGINAL ARTICLE

Benzhexol-dependence resulting from self-medication for intermittent explosive disorder

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Abstract

Objective. Recent observations in Iraq during the period of sanction suggest the existence of benzhexol prescribing linked to its calming effects on explosive behaviours. This inspired our group to research the existence of this practice and the characteristics of those involved in it. **Method.** All patients from the psychiatric service in Merjan Hospital, Al Hilla City, Babylon Governate, Iraq, who had a prescription for benzhexol between January 1991 and December 2000, were identified. All participants received their diagnosis based on the clinical criteria of the DSM-IV, after taking a comprehensive medical and psychiatric history, mental state examination and collateral information from family members. The patients were evaluated by the same qualified consultant psychiatrist at the initial assessment and all through the period of follow-up. **Results.** In the 10-year period under study, 354 patients were prescribed benzhexol. A total of 190 patients diagnosed as intermittent explosive disorder (IED) and 164 suffering from severe mental disorders or personality disorders were excluded from the study. The average age of the IED group was 29.5 years. On direct questioning, the main reason patients gave most frequently for using benzhexol was to control the aggressive outbursts ($N=92$, 48.4), to get high ($N=49$, 25.8), to relax ($N=26$, 13.7), to get rid of boredom ($N=23$, 12.1). In total, the whole group were prescribed benzhexol, at an average dose of 12.5 mg/day (range 2–20 mg/day). At the time of final assessment the mean dose of prescribed benzhexol had fallen slightly to 12 mg/day (2–20 mg/day), with 10 patients being benzhexol free. Of the 190, three patients had a diagnosis of obsessive compulsive disorders, 36 patients had a diagnosis of benzodiazepines dependence, and a further five had a diagnosis of alcohol dependency syndrome. Eighty percent felt satisfied with the effect of the drug and 95 were not motivated to stop it. **Conclusions.** There are a significant number of patients who are routinely prescribed benzhexol as a replacement therapy. The main original reason for starting it is to control outbursts and improves their reaction to stress situations. This growing issue raises the need for awareness, by both public and medical practitioners, of the potential adverse effects of benzhexol and its untoward consequences.

Key Words: *intermittent explosive disorder, benzhexol, drug abuse*

Introduction

Intermittent explosive disorder falls in the recognised category of impulse-control disorders. This disorder is characterized by frequent and often unpredictable episodes of extreme anger or physical outbursts. Between episodes, there is typically no evidence of violence or physical threat. Often genuine regret is expressed after the outburst [1]. Most patients are young men and history will often involve frequent traffic accidents, moving violations and possibly sexual impulsivity. This disorder is a controversial category because some clinicians be-

lieve that it is only a symptom of other diagnoses rather than a disorder on its own [1]. The degree of aggressiveness expressed during the episode is grossly out of proportion to any precipitating psychosocial stressor [2]. Depending on how it is defined, intermittent explosive disorder affects between 5.4 and 7.3% of adults in their life times [3]. These patients often need psychological treatment along with medications. Studies suggest that patients with intermittent explosive disorders respond to treatment with antidepressants and mood stabilizers [4–6]. In addition, it is agreed that as much as 50% of the mentally ill population also has a

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substance abuse problem [7]. The drugs most commonly used are alcohol, cannabis, cocaine and opioids. Prescription drugs, such as sleeping medication, may also be abused [7,8]. However, opiates, cannabis and cocaine misuse was almost unknown in Iraq before the US invasion in 2003 [9]. Drug abuse at that time, which was the sanction period against Iraq, was mainly benzodiazepines and anticholinergic drugs [9]. Recent observations suggest the existence of anticholinergic abuse among drug abusers [10,11] and schizophrenic patients [12–14] linked to their hallucinogenic and euphoric effects. In this study, for the first time, we report abuse of benzhexol as a self-medication for intermittent explosive disorder started by the patients and prescribed as a replacement therapy by the psychiatric service in Iraq during the period of sanction.

Clinical setting

The psychiatry in- and out-patient facilities in Al-Hilla City are in Merjan General Hospital. It has an open referral policy completely free of charges, with 400 beds, including 20 psychiatric beds. It serves a population of the whole Babylon Governorate (1,200,000 people). As a result of the impact of the sanction on the mental health service, the members of the multi-disciplinary team can offer only very limited varieties of treatment modalities.

United Nations sanctions against Iraq were imposed by the United Nations in 1990 following Iraq's invasion of Kuwait in 1990, and continued until the US-led invasion of Iraq in 2003. They were perhaps the toughest, most comprehensive sanctions in history, and have caused much controversy over the humanitarian impact, culminating with two senior UN representatives in Iraq resigning in protest of the sanctions. The sanctions resulted in high rates of malnutrition, lack of medical supplies, and diseases caused by the lack of clean water [15]. Sanctions, following on the effects of war, have seriously hampered the Iraqi health care system in many ways: cutting imports of drugs and equipment; slowing resumption of local drugs production; causing an exit of foreign medical and nursing staff. Moreover, they have restricted contacts between Iraqi doctors and outside experts. Iraqi spending on medicines fell to about \$3 per capita in 1995/1996 [16].

Methods

Participants and procedure

Three hundred and fifty-four patients from the out-patient psychiatric service in Merjan hospital, Al

Hilla City, Babylon Governorate, Iraq, who had a prescription for benzhexol between January 1991 and December 2000, were identified. Of these, 164 who had a diagnosis of severe mental disorders, personality disorders, or on antipsychotic medications were excluded. Thus, 190 participants were included in the study. All participants received their diagnosis based on the clinical criteria of the DSM-IV, after taking a comprehensive medical and psychiatric history, mental state examination and collateral information from family members. The patients were evaluated by the same qualified consultant psychiatrist (AY) at the beginning and all through the period of follow-up.

All subjects met the criteria of intermittent explosive disorder and also met inclusion criteria for replacement therapy: (a) use of benzhexol regularly on a daily basis for the preceding 12 weeks; (b) failure to succeed with abstinence during the normal program (antidepressants, antipsychotic and counselling) with treatment exposure of at least 4 weeks; (c) severe subjective benzhexol craving and feeling dyscontrol over urges to use it.

Analyses were performed using the Statistical Package for Social Sciences (SPSS, version 14). Descriptive statistics were used to summarize socio-demographic and clinical characteristics of the sample. The Merjan Hospital Local Ethics Committee approved this study.

Results

In the 10-year period under study, 354 patients were prescribed benzhexol. Patients were excluded from the study if they had a diagnosis of severe mental disorders, personality disorder or were prescribed antipsychotic medications for any reasons. Thus, this sample was limited to patients with pure intermittent explosive disorders (IED) with exclusion of potentially confounding influencing factors. Monthly clinical assessment was performed before repeating the benzhexol prescription.

Table I. Demographic characteristics.

	N = 190	%
Gender (male/female)	183/7	96.3/3.7
Employment (employed/unemployed)	58/132	30.5/69.5
Marital status (single/married/divorced/widow)	63/121/4/2	33/63.6/2.1/1.1
Education (illiterate/primary/secondary/university)	19/85/82/4	10/44.7/43.2/2.1
Residence area (rural/urban)	41/149	21.6/78.4

Table II. Length of contact with psychiatric service in IED group.

Time in contact with service	Number	%
74+ months	127	66.8
60–73 months	41	21.6
36–59 months	3	1.6
<12 months	19	10

Demographic details of cases

The mean age at first presentation to the service was 29.5 (range 19–52 years). The subjects were mostly males (183 male). Table I shows some of the important demographic data.

Contact with the psychiatric service

The 190 cases remained in contact with the team for an average of 88 months (range 1–120). Table II shows that 168 (88.4%) remained in contact with the service for more than 5 years.

Drug use problem

At initial assessment, 190 subjects were using benzhexol, at an average dose of 20 mg/day (range 5–25 mg/day). A total of 105 were first introduced to the use of benzhexol while in the army doing military service, with a further 85 admitting to buying street benzhexol following friends' advice. Other drugs used at the time of the assessments were benzodiazepines (36) and alcohol (5). Of the whole sample, none admitted to ever using illicit drugs (opioids, cocaine, or cannabis). On direct questioning, the main reason patients gave most frequently for using benzhexol was to control aggressive outbursts ($N=92$, 48.4%), to get high ($N=49$, 25.8%), to relax ($N=26$, 13.7%), to relieve boredom ($N=23$, 12.1%).

Treatment

During the review period, the preferred treatment tactics for patients using benzhexol was benzhexol replacement therapy, with the option of slowly withdrawing the drug if the patient wished. Of the 190 cases, 63 (39.4%) began a reducing regime, which ten (5.3%) had completed by the time of final assessment, and 53 (27.9%) came back to the service after stoppage for an average of 6 weeks, asking to go back to the maintenance benzhexol as they could not cope without it. The patients reported that the discontinuation of benzhexol produced anxiety and angry feelings.

In total, the whole group were prescribed benzhexol, at an average dose of 12.5 mg/day (range 2–20 mg/day). At the time of final assessment the

mean dose of prescribed benzhexol had fallen slightly to 12 mg/day (2–20 mg/day), with ten patients being benzhexol free. Benzodiazepines were prescribed to 36 patients, at an average initial dose of 25.0 mg diazepam per day. All of them agreed to begin a reducing regime of benzodiazepine in which 29 had completed within the first year of benzhexol replacement therapy. At final assessment the average dose of benzodiazepine was 9.2 mg. Five patients were taking alcohol before use of benzhexol and were maintained on benzhexol throughout the follow-up at an average dose of 15 mg/day. By final assessment, and based on self-reports, three patients had reduced their alcohol intake to zero, with the other two admitting to reducing the amount greatly after been stabilized on benzhexol. All patients refused to be transferred to other anticholinergic medications.

Benzhexol was supplied in tablet form, and its effect benzhexol was self-reported by the patients after 15–20 min of taking it, and it would last for 24 h. There was no report of toxic psychosis among the whole group. Patients and their families reported a reduction in frequency and severity of explosive attacks and nearly half (61, 46.2%) of the unemployed managed to be engaged in a form of work. Eighty percent (152 patients) felt satisfied with the effect of the drug and nearly 95 (180 patients) were not motivated to stop it.

Psychopathology in IED patients

At initial assessment, of the 190 patients in the IED group, three patients had a diagnosis of obsessive compulsive disorders, 36 patients had a diagnosis of benzodiazepines dependence, and a further five had a diagnosis of alcohol dependency syndrome. There were several different impulsive behaviours among the group, which are summarized in Table III.

Discussion

The occasional abuse of anticholinergic drugs for their psychotropic effect has attracted attention in recent literature as case reports [17–22], studies [10–14], or audits [23]. Marken et al. [24] reviewed 110 published cases of anticholinergic abuse. They divided the abusers into three groups: first subjects

Table III. Impulsive behaviour in IED group.

Domestic violence (mainly toward partner)	142 (74.7%)
Damage to furniture	149 (78.4%)
Street fighting	135 (71.1%)
Self cutting	55 (28.9%)
History of truancy at school	48 (25.3%)

with substance dependence and no medical indication for anticholinergic use; secondly, substance abusers with valid indication for anticholinergic prescriptions; finally, those who are not known to abuse other substances but overuse their prescribed anticholinergic medication. In our study it is reasonable to presume that the use of benzhexol in intermittent explosive disorder patients could have been suggestive of their desire to control violent uncontrolled behaviour. The other group of substance abusers used benzhexol for recreation purposes (to get high). The specific mode of action is unknown, but it is positively thought that these agents partially block central (striatal) cholinergic receptors, thereby helping to balance cholinergic and dopaminergic activity in the basal ganglia [25]. In addition, case reports and clinical studies showed that patients experience a buzz (euphoria), and are relaxed, energetic, and sociable while ingesting these compounds [26]. Furthermore, preclinical studies found these compounds to inhibit dopamine uptake like cocaine, but with less effectiveness than cocaine in producing behavioural effects related to drug abuse [27,28]. Among all the anticholinergic drugs, benzhexol (trihexyphenidyl) is the most stimulating [29], which can explain the its preference by most of our sample.

We have to evaluate the results of this work within its limits of being retrospective observational work. Our findings suggest that benzhexol treatment for patients suffering from comorbid intermittent explosive disorder and benzhexol dependency could be parallel to methadone for opiate dependence. It could be a form of a replacement therapy as an answer for benzhexol self-medication for intermittent explosive disorder. Harm reduction was evident when explosive behaviour was reduced, use of other illicit drugs diminished (but did not necessary disappear), and many patients returned to gainful employment. Even so, the benefits usually only last while the maintenance treatment continued. Benzhexol should not be seen as a pharmacological alternative to psychological intervention of intermittent explosive disorder, which should be a prime objective.

There was a high level of engagement with the service, as most the groups stayed in contact for years. This could gradually help in initiation of other psychological interventions for intermittent explosive disorder. However, observational studies in these areas are difficult to interpret and caution should be taken in premature clinical use of benzhexol in intermittent explosive disorder patients.

Consistent with the experience of other authors [17,20] a recognizable withdrawal syndrome followed discontinuation of the benzhexol. However,

contrary to the experience of others [30], a small number of the sample managed to be completely detoxified from benzhexol. Furthermore, although benzhexol maintenance prescribing for IED patients is a new and controversial treatment, note that the patients maintained on the drug reported good outcomes from their intermittent explosive symptoms. Meanwhile, this group of patients manifested at least four criteria of substance dependence according to the DSM-IV [2]. These criteria include: withdrawal syndrome, the substance was often taken over a longer period than was intended, there was unsuccessful efforts to cut down substance use in most patients, and, finally, a great deal of time was spent to obtain a steady supply of the substance. However, there was no report of tolerance once the patient reached the needed dose.

Substantial methodological limitations, particularly the lack of double-blind placebo for a randomly assigned control, preclude any current generalizations from these findings.

In summary, benzhexol dependence is common in intermittent explosive disorders as a direct result of self medication or routine prescribing by the psychiatric service. Further research is needed to explore the potential superiority of benzhexol over other medications in its potential to improve violent impulsive behaviours and the underlying biological correlates and path mechanisms need evaluation. For the clinician, greater awareness of benzhexol dependence can lead to routine enquiry and thereby appropriate management. This could result in improved treatment adherence and improved quality of life of these patients.

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