Patterns of use of benzodiazepines in psychiatric patients

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الخلاصه

تعتبر العقاقير المهدئة بأنواعها من العقاقير الواسعة الاستخدام في منتجات الأمراض النفسية و العقلية و كذلك في الوحدات النفسية في المستشفيات العامة بسبب ما تمتاز به هذه العقاقير من تأثيرات واسعة الطيف في تخفيف الألم و علاج الصرع و التأثير المنوم لها.

تهدف الدراسة لحساب دواعي استعمال العقاقير المهدئة و توضيح التأثيرات الجانبية و مخاطر سوء استخدامها في المستقبل.

تمت هذه دراسة مقطعية شملت 300 مريضاً مصاباً بأمراض نفسية و عقلية مختلفة عند دخولهم في كل من مستشفيات: ابن رشد، الرشاد والديوانية التعليمي/الوحدة النفسية خلال الفترة من الأول من ايار لعام 2011 إلى العشرين من اذار لعام 2012.

أثبتت هذه الدراسة بأن نسبة 66% من المرضى الذين شملتهم الدراسة هم من الذكور و أن أعلى نسبة استخدام للعقاقير المهدئة لدى المرضى المصابين بالاضطرابات الوجدانية (الاكتئاب) بنسبة 38%. و كذلك أثبتت أعلى نسبة استخدام لهذه العقاقير في الدخول الأول للمرضى المصابين بالأمراض النفسية.

استنتج بالاثبات في هذه الدراسة بأن استخدام العقاقير المهدئة و تأثيرها على المرضى ذات طابع معقد يعتمد على عوامل كثيرة منها التكوين و الطباع و الحالة النفسية و الوزن و الجسم و الصحة و الجنس و كذلك الثقافة و المجتمع الواحد.

نلمس الفوارق في مفعول العقار الواحد. العلاج بالطرق العضوية (العقاقير) له ثلاث مقومات و هو المفعول الكيميائي للعقار و المفعول النفسي لعلاقة المريض بالطبيب و المفعول الايحائي (placebo) لأن اتجاه المريض إلى الطبيب لطلب العون و الخلاص يجعل من الماء أو الهواء مشحوناً بمفعول طبي، فكيف بالعقار؟

Abstract

Background: The benzodiazepine has been one of the most commonly used drugs in psychiatry and general medicine because benzodiazepine have multifaceted actions like pain killing, antiepileptic and others therefore increasing the abuse of these drugs.

Objectives (Aims): The aim of the study is to show the indications for benzodiazepine as in psychiatric patients, and to clarify some of the risks and hazards of their use in general.

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Methods: This is a cross sectional study that enrolled 300 patients who had been admitted in three centres including Ibn-Rushid Teaching Hospital For Mental Illness, Al-Rashad Mental Hospital and Al-Diwaniyah Teaching Hospital, Psychiatric Unit, during period between 1st of May 2011-20st of March 2012 because of different psychiatric illness.

Result: This study revealed that 66% patients are male and the majority of patients for whom benzodiazepines were prescribed during their stay in hospital are depression (38%). Also this study revealed majority of patients whom benzodiazepines were prescribed for first admission to psychiatric hospitals or psychiatric unit in general hospital.

Conclusion: This study proved that the effect of drug benzodiazepine up on an individual is complex interacting. There are many variables involved such as their pharmacological actions, unwanted effects and interactions with other drugs. We should not prescribe drugs in divided daily dose in those instances where once-daily dose offers advantages.

Introduction

The benzodiazepine has been one of the most commonly used drugs in psychiatry and general medicine as a whole since the introduction of the first item in 1960 which was the Chlordiazepoxide, and because of the euphoria which occurred to physicians after testing its efficacy in treating anxious people, it was increasingly introduced in almost every prescription[1, 2].

The benzodiazepines are minor tranquillizers which recently appeared to have multifaceted actions like pain, killing action, antiepileptic action, sedative action, hypnotic action, accentuation of anaesthetics and muscle relaxant action.

They appear to act through specific receptors in the central nervous system. These receptors appear to have their highest density in the Limbic system, the part of the brain involved in the control of affect and visceral function, they are part of the macromolecular complex that also contains the receptors for gama - aminobutyric acid (GABA), the principle inhibitory

neurotransmitter in the brain, and the chloride channel through which GABA acts to hyperolarize neuron, i.e. decrease their likelihood of firing. The benzodiazepine are present in the brain they bind to their receptors and facilitate the action of GABA, resulting in increased chloride conductance and therefore greater inhibitory effect on the nervous system.

Benzodiazepine have experimentally been shown to suppress neuronal activity in the Limbic system including the hippocampus, amygdala, hypothalamus and the septal region, leading to the hypothesis that these areas are involved in the aetiology of anxiety.[3, 4]

The first report of dependency liability to benzodiazepine came from Hollister et al[5, 6]. only one year after the introduction of chlodiazepoxide, since then there has been steadily increased number of papers concerned with the abuse of these drugs.[4, 7]

Methods

The study is a prospective one, and was conducted on psychiatric admissions in the years 2011-2012 in three centres including Ibn-Rushd Teaching Hospital for Mental Illness, Rashad Hospital and Al-Diwaniyah Teaching Hospital- Psychiatric Unit.

The total number of patients collected for whom benzodiazepine were prescribed was 300. Females constituted 34% of the sample (102), and males constituted 66% (198). The age range was distributed throughout three categories, 15-30 years, 31-50 years and 51 and over.

The data were gathered and classified according to the variables and factors listed in the appendix page.

Results

Data for benzodiazepine prescription by age and sex are presented in Tables (1) and (2) respectively:

Age range in years	Number of patients	Percentage
15-30	176	58.7%
31-50	100	33.3%
51-over	24	8%

Chi-square (x^2)= 115.5   Degree of Freedom (df)=2   P-value (p.v) = 0.0001

Table (1): Number of patients to age range

Regarding sex differences males were exceeding females by 2:1 approximately

Sex	Number of Patients	Percentage
Females	102	34%
Males	198	66%

Chi-square (x^2)= 30.72   Degree of Freedom (df)=1   P-value (p.v) = 3 (non specific)

Table (2): Number of Patients according to Sex

Taking occupation into consideration, it seems that there is a correlation between young ages, males and certain occupation such as in the case of students, peoples in military services and civil services, as shown in Table (3).

Occupation	Number of Patients	Percentage
Military	62	20.7%
Students	60	20%
Civil Services	59	19.7%
Private Jobs	36	12%
House Wives	42	14%
Without Job	24	8%
Retired	17	5.7%

Chi-square (x^2)= 46   Degree of Freedom (df)=6   P-value (p.v) = 2 (non specific)

Table (3): Number of Patients According to Occupation

There were certain diagnosis which showed higher frequencies with certain age groups as it is shown down in (Table 4).

Diagnosis	No. of Patients within Age of 15-30 Years	No. of Patients within Age of 31-50 Years	No of Patients within Age of 51 Years over	Total Number of Patients	Statistic Value		
					x^2	d.f	p.value
Depression	62	38	15	115	28.2	2	5
Alcoholism	20	19	5	44	9.59	2	0.008
Anxiety	14	9	1	24	9.7	2	0.004
Anxiety-depression	14	12	0	26	28	2	3
Conversion Reaction	20	4	0	24	8.6	2	0.01
Schizophrenia	15	7	3	25	3.5	2	0.1
Acute Psychological Disturbance	3	1	0	4	2	2	0.36
Post-Psychotic Depression	0	1	0	1	6	2	0.04
Personality Disorder	3	0	0	3	1	2	0.6
Obsessive Compulsive Neurosis	1	1	0	2	5.4	2	0.05
Acute Grief Reaction	5	2	0	7	1	2	0.5
Brief Reactive Psychosis	13	5	0	18	14.3	2	0.007
Drug Abuse	6	0	0	6	12	2	0.002
Mania	0	1	0	1	2	2	0.3
TOTAL	176	100	24	300			

Table (4): Number of Patients with their Age Range according to Clinical-Diagnosis

From Table (4) it has been found that depression, alcoholism, anxiety and conversion reaction constituted the majority of patients for whom benzodiazepines were regularly prescribed during their stay in hospital.

The duration of stay of patients in hospital for each diagnosis encountered in the study is shown down in Table (5).

Diagnosis	Range of Number of Days of Stay in Hospital
Depression	17-23
Alcoholism	20-28
Anxiety	12-16
Anxiety-Depression	15-19
Conversion Reaction	7-9
Personality Disorder	6-11
Obsessive-Compulsive Neurosis	12-15
Acute Grief Reaction	7-10
Drug Abuse	10-13

Table (5): Duration of Stay in Hospital in Days according to Diagnosis for which Benzodiazepines are prescribed in Regular Oral Intake

Concerning the marital status of the patients included in the sample, it appeared that most of the patients were in a single status followed by the married as it is shown down in Table (6)

Marital Status	Number of Patients	Percentage
Single	147	49%
Married	126	42%
Divorced	13	4.3%
Widow	12	4%
Separated	2	0.7%

Chi-square (x^2)= 330.03   Degree of Freedom (df)=4   P-value (p.v) = 0.0001

Table (6): Number of Patients according to Marital Status

Data concerning with the number of admission to psychiatric hospitals or units in which benzodiazepines were prescribed in each admission with the same or almost the same diagnosis, are listed down in Table (7).

Number of Admissions	No. of Patients
First Admission	176
Second Admission	61
Third Admission	36
Fourth Admission	18
Fifth Admission	9
TOTAL	300

Chi-square (x^2)= 306.63   Degree of Freedom (df)=4   P-value (p.v) = 0.0001

Table (7): Number of Patients in the Sample according to Number of Admissions.

As regards to the level of education, it appeared that those patients who were at secondary school level and primary school level were more frequently repeated in the sample, next were those with intermediate school level, and the least represented were those of college level and graduates and the illiterate as shown down in Table (8).

Level of Education	Number of Patients
Illiterate	33
Primary School	70
Intermediate School	60
Secondary School	73
College	29
Graduate	35

Chi-square (x^2)= 39.68   Degree of Freedom (df)=5   P-value (p.v) = 1.7 (non specific)

Table (8): Number of Patients according to the Level of Education.

The benzodiazepine preparations or items, found to be prescribed more commonly for psychiatric inpatients as it is shown down in Table (9)

Benzodiazepine item	Number of Patients
Chlordiazepoxide (Librium)	141
Diazepam (Valium)	77
Clonazepam (Klonopin)	49
Lorazepam (Ativan)	16
Alprazolam (Xanax)	11
Temazepam (Restoril)	9
Bromazepam (Lexotan)	4

Chi-square (x^2)= 347.05   Degree of Freedom (df)=6   P-value (p.v) = 0.0001

Table (9): Benzodiazepine Item Most Commonly Prescribed for Psychiatric Inpatients

Concerning the clinical symptomatology in psychiatric patients for whom different items of benzodiazepine have been used are listed down in Table (10).

Clinical Situation	Benzodiazepine
1. Short-term treatment: a- Treatment of insomnia	Diazepam Clonazepam Lorazepam
b- Acute anxiety or agitation	Diazepam
c- Delirious states (alcohol withdrawal)	Diazepam
2. Long-term treatment: a- Long treatment of anxiety:	Chlordiazepoxide Diazepam
b- Treatment of sleep latency insomnia	Clonazepam Diazepam
c- Adjunctive use with antidepressants	Chlordiazepoxide Diazepam Lorazepam Alprazolam
d- Treatment of alcohol abuse:	Chlordiazepoxide Diazepam
e- Neuroleptic induced akathesia	Diazepam

Discussion

From the study, it was found that benzodiazepines were used as adjunctive to antidepressants in patients diagnosed as depression with anxiety and those with depression only. For the latter group probably the benzodiazepines were given to treat insomnia. They were prescribed also for alcoholics, those with anxiety and other neurotic disorders (Table (4)). In all the conditions where benzodiazepines were prescribed on regular daily regimen, the doses were tapered gradually. (Table 5)

The most common benzodiazepine prescribed was surprisingly chlordiazepoxide, next was diazepam (Table 9). I think there is some bias in this result or they may be a tendency by physician to avoid stereotype of prescribing diazepam.

Depending on clinical circumstance, the rate of onset of action may be an important variable in choosing benzodiazepine item, for example, rapid onset is important for patients who have trouble falling asleep, but a more slowly acting drug might be useful when insomnia comes later in the night.

Alprazolam was found to be used as a hypnotic more than other items, next was diazepam and loranzepam.

Taking occupation into consideration, it appeared that a high correlation between young ages, males and certain occupation such as in the case of students (20%), people in military service (20.7%), and civil services (19.7%). These sectors of the society were probably under higher stress.

People in single status were more represented in the sample (49%), next were the married (42%) and about a quarter of the latter group were originally with psychiatric illness before marriage.

The level of education of patients as listed down in (Table 8), it was shown that people of higher social and educational status were less presented in the sample because probably such people are still avoiding the stigma of mental hospital, and because younger and lower educated people could not deal well their social problems, besides they could not consult privately.

When duration of benzodiazepine use was considered the pattern emerged was related to the duration of stay in hospital and type of diagnosis labeled to the inpatients. The duration of stay in hospital in days ranged from 28 days for alcoholics to 7 days for patients with conversion reaction (Table 5).

In Table 7, it is shown that some patients with more than one admission, and benzodiazepines were prescribed for them in each admission, a majority of such patients i.e., with more than one admission were alcoholics, however it was not possible to know whether such patients continued to use benzodiazepines throughout the period between admissions or not, because such information was not supported in the case notes.

Concerning the age, among the 24 patients in the study who fell in the age group (over 51 years), only two of them were above

60 years of age and for both chlordiazepoxide was used in a dose of 15mg per day, all others were treated with the same dose regime as the younger age group, which ranged between 30-60mg of chlordiazepoxide per day.

Conclusion

The prescribing of drugs in general and benzodiazepines in particular, is a complex social process, much more than one might readily imagine. The following points may be considered useful in minimizing the hazards of such drugs as the benzodiazepines:

1. There is a considerable evidence that psychotropic drugs in general, and benzodiazepines in particular are overprescribed, especially by general practitioners. Their unwanted effects contribute to a serious public health hazards, such drug abuse, increased social hostility in situations where people are grouped together, and a frustrating stimulus is introduced. [8,5]. In addition, the problem of cost, as overprescribing throws heavy demands upon an already restricted national budget, so one should adopt more thoughtful prescribing policies.[9, 7]

2. The effect of a drug a benzodiazepine, upon an individual is a complex interaction that depends on the drug, the patient's pathophysiological state, psychological and social factors. There are so many variables involved such as their pharmacological actions, unwanted effects and interactions with other drugs, the patients' medical and psychiatric history and those factors that will influence the outcome of treatment. [10,11]

3. We should learn more about normality and social problems, and resist offering chemical solutions to non-medical problem. [12, 13]

4. Unless there are definite indications for immediate symptomatic relief, a planned withholding of drugs will often be rewarded by a significant favourable response to the initial interview, or even a spontaneous recovery. [14, 11]

5. In administering a drug, we should tailor the dose to the patients clinical needs. And we should not prescribe drugs in

divided daily doses in those instances where once-daily dose offers advantages. [15, 13]

6.   We should avoid drug combinations wherever possible. [16, 17]

7.   A drug should be given in adequate dose for a sufficient length of time to produce its desired effect, and before changing a drug, a more detailed assessment will often be more rewarding.[18, 6]

8. It is only in a very small minority of patients that drug treatment will need to be continued indefinitely. In the vast majority, we should have a target for discontinuing treatment constantly in mind.[19]

Reference

1. Ashton, H. (1984), British Medical Journal, 288, 1135-1140.

2. Balter, M.B. (1984), Current Medical Research Opinion, 8 (Supp-4_, 5-50.

3. Blackwell, B. (1973), Rational Drug Use in Psychiatry (Ed.F.J.Ayd).

4. Coleman, V. (1975), The Medical Men: Drug Makers, Doctors And Patients, Temple Smith, London.

5. Dunloo, Sir Derrick M. (1971), The Use Of Abuse Of Psychotropic Drugs, Scot, Med. J., 16, 345-349.

6. Edwards, J.G. (1974), Doctors, Drugs and Drug Abuse, Practitioner, 212, 815-822.

7. Edwards, J.G., (1977), Unwanted Effects Of Psychotropic Drugs, Practitioner, 218, 556-562.

8. Gatley, M.S. (1968), To Be Taken As Directed, J.R., Coll. Gen. Pract. 16, 39-44.

9. Greenblatt, D.J., et al (1975), Archives Of General Psychiatry, 32, 518-521.

10. Salzman, C., Schader, R.I., and Sweet, C.P. (1974), Chlordiazepoxide-Induced Hostility In A Small Group Setting, Archs. Gen. Psychiat. 31, 401.

11. Stimon, G.V. (1976), Doctor-Patient Interaction And Some Problems For Prescribing. J.R. Coll. Gen. Practitioner, 26, Supplement No. 1, 88-96.

12. Trethowan, W.H. (1975), Pills For Personal Problems, Br. Med. J., 4, 749-751.

13. Tyrer, P., Murphy, S. (1987), British Journal Of Psychiatry, 151: 719-23.

14. Winolur, A., et al (1984), Am. J. Psychiatry, 141: 1427.

15. S.M. Lawrie: Companion To Psychiatric Study, 7th Ed., 2004, Page: 369-399.

16. Theodore A. Stern, JohnB. Herman: Psychiatric Update And Board Preparation, Substance Misuse, (2000), Page: 85.

17. Louis Appleby, David M. Forhow, Tim Amos: Post Graduate Psychiatry, 2nd Ed, 2001, Page: 331.

18. Mihael Gelder, Philip, Philip Cowen: Shorter Oxford Textbook, 4th Ed, 2004, Page 708.

19. Kaplan and Sadock's: Synopsis of Pschiatry, 11th Ed, 2009, Page: 785

Patterns of use of benzodiazepines in psychiatric patterns

Number: Age: Sex:

     Marital Status:

Education:

     Date of admission

Presenting admissions:

Previous admissions:

History of Alcohol &/or Drugs Use:

Associated physical illness:

Occupation:

Diagnosis:

Treatment: Type of benzodiazepine

               Oral / Injection

Pattern: Continuous (   )   Intermittent (   )

           Basic   (   )   or   Additional   (   )