USE AND ABUSE OF BENZODIAZEPINES AMONG RISK GROUPS IN BASRAH

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Introduction

Benzodiazepines are widely used and prescribed among all the psychotropic drugs (1). They are used as anxiolytics , sedatives and hypnotics, anticonvulsants, and muscle relaxants(2,3).

It is apparent now that the benzodiazepine drugs, produce both physical and psychological dependence, which occurs even when they are used for a relatively short time of few weeks, and even in therapeutic doses(4).

The dependence on benzodiazepines can be initiated by a medical prescription, specially in patients with an underlying psychiatric disturbances(5).

The non-medical use of these drugs usually occurs in young age groups, and often associated with the consumption of other drugs of abuse(6).

Various factors contribute to the abuse of benzodiazepines including psychological , neuro-chemical , pharmacological , and environmental (7,8,9).

The prevalence of drug abuse among health professionals is higher than the general population , probably due to the stress at work, increase self medication and easy excess to various drugs (10, 11).

In view of the above mentioned, we tried to investigate the problem of use and abuse of various benzodiazepines among selected risk groups, including medical students, health care professionals and psychiatric patients. The probable precipitating factors will also be considered.

Subjects Materials And Methods

Subjects were selected from various risk groups and categorized into five groups which include :

Group 1 : Patients attending the psychiatric outpatient clinics at the two major hospitals in Basrah i.e saddam's and Basrah teaching hospitals. These patients complaining of various psychiatric illnesses and their age ranging between 15 to 65 years . Total number of (175).

Grup 2: Health workers at the above two hospitals including doctors, pharmacists, laboratory workers, nurses and hospital cleaners. Total number of (180), with similar age ranges.

Group 3 Medical students from college of medicine, University of Basrah. This include second and fifth year students (76 students).

Group 4 :Technical institute students in the medical or nursing department in Nasiriya(130 students).

All the subjects were interviewed either during the day or at the night working shifts. Specially designed questionnaire form were introduced to all subjects . illiterate patients were directly asked the questions by the same investigator and the form were filled for them.

Urine samples: urine was collected from all the subjects at the time of interview, 10 ml was stored in refrigerator for not more than 2 days.

A modified Thin layer chromatography (TLC) method used for the detection of benzodiazepines in the urine. The urine was hydrolized by concentrated acid and boiling for the extraction of the conjugated form (12,13). Then the urine is extracted by petrolium spirit and 5 µl of the extract was applied to the TLC plate. The spot was then located by Dragendorff reagent and UV light.

Statistical analysis:

Chi-square test to examine the difference between two or more parameters. Z-test for differences between proportions

Results

Self reported questioners resulted in more and statistically significant benzodiazepines users as compared to thin layer chromatography method.

The psychiatric patients group was among the highest in the use or abuse of benzodiazepines, the lowest rate of use occur among the second year medical students (table-1).

The highest percentage of denial occurs among 5^{th}. Year medical students (39%), followed by the 2^{nd}. Year medical students(25%), while the least percentage occur among the patients group(2.3%)(fig.1).

There was a significant association between the use of benzodiazepines and the abuse of other drugs of dependence namely alcohol and smoking. Smoking rate was high among students, while alcohol intake was high among patients . Lower rate of abuse of both substances was detected in the non-benzodiazepines user group (table2).

Diazepam was the most popular drug used by various risk groups. Bromazepam and clonazepam use was reported only by the patients group (table-3) .

As regard to the predisposing factors, psychiatric complains represent the major factor for the use of benzodiazepines, which include anxiety, fear and insomnia, while there are no differences in depression symptoms between user and non-users. (table-4, and, fig.2).

Hospital pharmacy was the main source for obtaining drugs by the medical students (67%), private pharmacy in 23%, and 10% of the students obtain the drug by other means as from friends, relatives or from the market (table-5).

The performance of medical students in the mid-year examination in the last academic year showed higher percentage of examinations failure among users of BNZ's as compared to the non-users(table-6).

The nursing occupation represent the major risk factor for use of BNZ's (37.3%), followed by medical assistants (21.4%), while physicians represent the least percentage (2.4%). This is similar to the percentage among pharmacists.

As regard to the working site, medical units takes the lead(42,.1%), followed by the laboratory(19.1%) and the cleaners were the least(7.1%).

Discussion and conclusions

The abuse of benzodiazepines is a common problem world wide, many studies showed high prevalence of the problem in most western countries (14), its also an existing problem in the third world countries (15,16).

The world wide excessive exposure of people to benzodiazepine drugs is probably due to the wide prescription of these drugs for the relief of stress and other psychological disturbances (2, 1). In comparison with other drugs of abuse the BNZ's are also cheap, widely distributed and can easily be obtained from various sources(17).

Our study population is selected at risk group, therefore it shows high prevalence of use of these drugs. The percentage of the population at large is probably lower than this figure.

The abuse of no-prescription (hard) drugs of abuse is not detected in this study.

The majority of the risky population in our study are abusers of BNZ's with higher percentage among psychiatric patients, followed by medical staff and medical students. The rate of abuse by medical staff is in agreement with other studies(18, 7). The abuse of drugs among medical staff may be multifactorial, the stress at work, frequent self medication easy excess and knowledge of medication effects may all contribute(10).

The finding among medical students again agreed with the published studies(19). Medical undergraduate education is characterized by various psychological changes (20). There are numerous studies which revealed high rate of psychological disturbances among medical students at various stages of their training including anxiety and depression(21).

Self-reported questionnaire alone, might no detect all people abusing drugs. This is demonstrated by the denial of drug use by various groups, to avoid the social embarrassments and or possible legal action against them. As expected denial was higher among the medical students, followed by the medical staff, with the lowest figure among the patients group, as probably they have no reason to deny their intake of drugs.

The confirmation of drug intake by more than one method is recommended. Screening for benzodiazepines by thin layer chromatography method is supported by various studies. It is easy reliable, low cost and requires minimal instrumentation (22,23). However the test of a single urine sample collected randomly has

shortcomings in the detection of drugs ingestion. This can be affected by the time of drug ingestion , urine secretion , amount of drug or metabolites excreted in the urine and the possibility of sample adulteration(22,24)

There was a significant association between the use of BNZ's , smoking and alcohol abuse. This is probably due to the synergistic CNS effects of these drugs, this association of abuse was detecteed by many studies(25,26).

Diazepam is the most popular drug used, followed by lorazepam and chlordiazepoxid, while promazepam and clonazepam represent only small percentage. This is probably related to the prevalence of diazepam and familiarity with its use, that resulted in high rate of consumption(27). This could berelated to the stronger dependence liability of diazepam among the other member of the BNZ's group(WHO). The world health organization expert committee on drug dependence rescheduled some of the benzodiazepine as flunitrazepam into schedule(III) instead of schedule(IV)of the drugs of dependence(28) . Several epidemiological studies, which have been adjusted for drug availability, suggest that the rate of abuse odf diazepam exceeds those of most of the other benzodiazepines. However diazepam is particularly important in developing countries due to its wide clinical uses and the alternatives may be unavailable or unaffordable. Diazepam is included in the WHO Model list of essential drugs(29). The committee decided that rescheduling of diazepam to a higher level of control is not currently warranted. However it is recommended that WHO continue to keep diazepam under surviellance(30).

The major source for obtaining BNZ's by the medical students was the hospital pharmacy, followed by private pharmacies .

Psychological complains were common among students using benzodiazepines, this is supported by various other studies(31, 19, 20). The psychological complains were found to be increased as the student study level(21, 32, 20). This could partly be explain the high percentage among 5th year medical students as compared to the 2nd year students .

The therapeutic use following medical consultation is the major reason for initiating the use of benzodiazepines among stuidents. Over prescribing for medical students should be avoided as this might initiate a life long habit taking drugs by the future doctors (6). There was An association between the intake of benzodiazepines and high rate of failure in the examination among students , this could be explained by the effect of these drugs on the various mental processes as memory, concentration and alertness , although the rule of the underlying psyhchological and or social problems can not be excluded(33, 34).

In conclusion the problem of chronic use of benzodiazepine is existed in our at risk population. It is often associated with smoking and alcohol abuse , and precipitated by psychological stress and social factors. Study of this problem in the population at large is recommended . The use of questionnaire form in such studies should be supported by an analytical method , which will increase the sensitivity. Health education directed to the risk groups is recommended as well as education of the prescribers and dispensers of these drugs.

References

2. Melander,A., Henricson,K., Stenberg,P, et.al. : Anxiolytic hypnotic drugs1. Salzman,C. : Benzodiazepines treatment of panic, agarophobic symptoms: use dependence, toxicity and abuse. J.Psychiatr.Res., 1993, 1; 97-110

; relationship between prescribing, abuse and suicide. Eur.J.Clin.Pharmacol., 1991,41; -529

3. Buchanan,N. : Clobazam in the treatment of epilepsy; A prospective follow up to 8 years . J.R.Soc.Med., 1993, 86; 378-380

4. Loudon,J.B.: Drug treatment in comparison to psychiatric studies. Edited by Kendell,R.E.and Zelley ,A.K., 5th edition, Churchill Livingstone .1993; 8117-844

5. Hollister,L.E.: Drug abuse in : Basic and Clinical Phamacology, Edited by Katzung,B.G. 4th edition . Lange Medical Books, 1989,383-394

6. Woods,J.H, Katz,J.L. and Wigner,G.: Benzodiazepines; use, abuse and consequences. Pharmacol. Rev., 1992, 44 ; 151-347

7.Tyrer,P.: ABC of sleep disorders,withdrawal from hypnotic drugs. Br.Med.J., 1993, 306; 706-708

8. Barnac,C., whithworth,A.B. and Ficischacker,W.W.: Are patterns of benzodiazepines use predictable? A follow up study of benzodiazepines users. Psychopharmacology. 1993,111; 301-305

9. Cowleg,D.S., Roy-Byme ,P.P., Greenblatt, D.J., et.al.,: Personality and benzodiazepines sensitivity in anxious patients and control subjects. Psychiatric Res. 1993, 447;151-162

10. Hughes,P.H. Donmez,L, and Dinc, G.: Prevalence of substance abuse among U.S. physicians. JAMA, 1992,267; 2333

11. Sanz,Y.F., Lopez-Corbalan,J.C., Gath,M.B. et.al., Abuse of psychoactive drugs among health professionals. Rev.Esp-Anesthesiol.Ream. 2000, 46;354-358

12.Vu,D.T. and Vernay,A.: Validation of a method for detecting benzodiazepines in the urine by acid extraction of their benzophenones by thin layer chromatography. Ann.Biol.Clin., 1985, 43; 261-265

13. Wollf,K., Shanab,M.A., Sanderson,M.J., et.al., Screening for drugs of abuse: effect of heat-treating urine for safe handling of samples. Clin.Chem. 1990,36;908-910

14. Pelissolo, Bisserbe,J.C. Petursson,H.et.al. : Dependence on benzodiazepines. Encephale, 1994, 20;147-157.

15. **Deshpande,S.N. and Nagpal,R.S.: Benzodiazepines abuse among female patients in India. Addict.Behav. 1993,18;595-596**

31. **Pederson ,W and Lavik,N.J.: Adolescent and benzodiazepines prescribed use, self-medication and intoxication. Acta.Psychiatr.Scand., 1991, 84; 94-98**
32. **Guthrie,E., Black,D., Bagalkote,H.et.al., Psychological stress and burn out in medical students: a five-year prospective longitudinal study. J.R. Soc.Med., 1998, 91; 237-243**
33. **Roth, T., Hauri, P., Zorick, F., et.al., The effects of medazolam and temazepam on sleep and performance when administered in the middle of the night . J.Clin. Psycho-Pharmacol., 1985, 5;66-69**
34. **Rodrigo, E.K., King,M.B. and Williams, B.: Health of long term benzodiazepine users . B.M.J., 1988, 296; 603-606**

Risky groups	No. studied	% positive by reportintg	% positive by TLC
Psychiatric patients	**175**	**74.3**	**41.7**
Medical staff	**180**	**70.0**	**59.4**
2nd year medical students	**65**	**36.9**	**24.6**
5th year medical students	**76**	**47.4**	**50.0**
Medical institute students	**130**	**66.9**	**46.2**
Total	**626**	**64.4**	**47.0**

Table: 1 Results of reported and TLC measured use and abuse of benzodiazepines

Risky groups	BNZD's users			BNZD'sNon-users		
	Smoking	Alcohol	No.smoking or alcohol	Smoking	alcohol	No.smoking or alcohol
	No. %	No. %	No. %	No. %	No. %	No. %

Psychiatricp atients	**70**	**53.8**	**30**	**23.1**	**30**	**23.1**	**7**	**15.6**	**6**	**13.3**	**32**	**71.1**
Medical staff	**71**	**56.3**	**20**	**15.9**	**35**	**27.8**	**8**	**14.8**	**5**	**9.2**	**41**	**75.9**
2nd year medical students	**15**	**62.5**	**2**	**8.3**	**7**	**29.9**	**3**	**7.3**	**1**	**2.4**	**37**	**90.2**
5th year medical students	**20**	**55.6**	**5**	**13.9**	**11**	**30.6**	**4**	**10**	**0**	**-**	**36**	**90**
Medical institute students	**44**	**50.6**	**6**	**6.9**	**37**	**42.5**	**6**	**13.9**	**3**	**6.9**	**34**	**79.1**
Total No.	**220**	**54.6**	**63**	**15.6**	**120**	**29.8**	**28**	**12.6**	**15**	**6.7**	**180**	**80.7**

Table 2 : Smoking and alcohol abuse among BNZD's users or non-users by questionaries

Type of Benzodiazepine	Total cases No.	%	TLC –ve No.	%	TLC +ve No.	%
Diazepam	**171**	**42.4**	**90**	**52.6**	**81**	**47.4**
Chlordiazepoxide	**73**	**18.1**	**31**	**42.5**	**42**	**57.5**
Lorazepam	**83**	**20.6**	**33**	**39.8**	**50**	**60.2**
Bromazepam	**20**	**4.9**	**8**	**40**	**12**	**60**

Clonazepam	**3**	**0.7**	**0**	**-**	**3**	**100**
Denial but TLC +ve	**53**	**13.2**	**0**	**-**	**53**	**100**
Total	**403**	**100**	**162**	**40.2**	**241**	**59.8**

Table:3 Different benzodiazepines used by risky groups and their detection by TLC

Psychiatric patients	**Total cases**		**BNZD,Users**		**Non-users**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Anxiety	**77**	**28.4**	**56**	**72.6**	**21**	**27.3**
Fear	**31**	**11.4**	**23**	**74.2**	**8**	**25.8**
Insomnia	**46**	**16.9**	**33**	**71.7**	**13**	**28.3**
Depression	**4**	**1.5**	**2**	**50.0**	**2**	**50.0**
Suicidal ideas	**2**	**0.7**	**1**	**50.0**	**1**	**50.0**

Other complain	**3**	**1.2**	**1**	**33.3**	**2**	**66.7**
No. complain	**108**	**39.9**	**32**	**29.6**	**76**	**70.4**
Total	**271**	**100**	**147**	**54.2**	**124**	**45.8**

Table:4 Psychiatric complains among students group

The source	**Total cases**		**TLC negative**		**TLC positive**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Hospital	**118**	**67**	**28**	**23.7**	**90**	**76.3**
Private pharmacy	**41**	**23.3**	**11**	**26.8**	**30**	**73.2**
The market	**13**	**7.4**	**4**	**30.8**	**9**	**69.2**

Other sources	**4**	**2.3**	**1**	**25**	**3**	**7 5**
Total	**176**	**100**	**44**	**25**	**132**	**75**

Table: 5 Sources of obtaining BNZD's drugs by medical students

No. of failure subjects	**Total cases No. =271**		**BNZD's users No.=147**		**Non-users No.= 124**	
	No.	**%**	**No.**	**%**	**No.**	**%**
One	**90**	**33.2**	**59**	**40.1**	**31**	**26**
Two	**72**	**26.6**	**42**	**28.6**	**30**	**24.2**

Three	**29**	**10.7**	**19**	**12.9**	**10**	**8.1**
Four and more	**17**	**6.3**	**10**	**6.8**	**7**	**5.6**
No failure	**63**	**23.2**	**17**	**11.6**	**46**	**37.1**
Total	**271**	**100**	**147**	**54.2**	**124**	**45.8**

Table 6: performance of students in mid -year examination in the last academic year

Summary:

The problem of benzodiazepine abuse is common worldwide . We investigate this problem among selected at risk groups, which include various health care professionals, medical, students and psychiatric outpatients. They were randomly selected and classified into related groups. Use/ or abuse was assessed by a questionnaire form and TLC method for screening of urine samples for the presence of BNZD,S .

Psychiatric outpatients were the highest group in the use of benzodiazepines, while the lowest rate occurs among the 2nd year medical students. Denial of drug intake is more common among medical students and less among psychiatric patients.
There was a significant association between the use of benzodiazepines and other substances of dependence such as alcohol and smoking. Diazepam is the most common drug taken by the various groups. Neurotic symptoms such as anxiety, fear and insomnia were common among benzodiazepines abusers.
Nursing occupation represent a major risk factor for abuse of benzodiazepine.

Medical students using benzodiazepines have the high failure rate in examination as compared to non-users.
It is concluded that the problem of chronic use of benzodiazepineas is existed in our at risk population, usually precipitated by psychological stress.
Health education is recommended as well as the education of prescripers and

dispensers of these drugs.

تعاطى مركبات البنزودايزيبين بين مجاميع الخطورة

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الخلاصة

تعتبر مشكلة تعاطى مركبات البنزودايزيبين منتشرة على نطاق واسع في العالم .حاولنا في هذا البحث دراسة مدى توافر هذه المشكلة في مجموعات الخطورة المعرضة أكثر لإستعمال هذه الأدوية ، وتشمل المجموعات

العاملين الصحيين وطلبة الطب والمرضى المصابين بأمراض نفسية مختلفة من اللذين يراجعن العيادة الأستشارية . تم أختيار الأشخاص عشوائيا ، وصنفوا حسب عائديتهم الى مجاميع مختلفة. أجري التقييم بأستعمال إستمارة المعلومات الخاصة بالاضافة الى فحص عينات الأدرار لهؤلاء الاشخاص بواسطة طريقة فحص الكروماتوغرافي ذو الطبقة الرقيقة للكشف عن هذه الادوية، وكانت مجموعة المرضى المصابين بالأمراض النفسية هي أكثر المجاميع التي تستعمل مركبات البنزودايزيبين، بينما كانت أوطأ نسبة للأستعمال في مجموعة طلبة السنة الثانية في كلية الطب. ظهر ان نكران أستعمال هذة الأدوية أكثر شيوعا ضمن مجموعة طلبة الطب بصورة عامة ، بينما كانت أقل نسبة هي ضمن مجموعة الأمراض النفسية، وكانت هناك علاقة معتدة أحصائيا بين أستعمال مركبات البنزودايزيبين وأستعمال مواد أخرى تسبب الأعتماد مثل الكحول والتبغ. أن عقار الدايزيبام هو من أكثر المركبات شيوعا بين متعاطين هذة الأدوية ولمختلف المجاميع، لقد وجد أن بعض الأعراض النفسية العصابية مثل القلق والخوف وفقدان النوم أكثر شيوعا بين متعاطى مركبات البنزودايزيبين.

ويظهر أن العاملين في مهنة التمريض هم أكثر الأشخاص اللذين يستعملون هذه الأدوية وأن طلبة كلية الطب المتعاطين لمركبات البنزودايزيبين ، قد فشلوا في أداء الآمتحانات المقررة بنسبة أعلى من الطلبة اللذين لايتعاطون هذه المركبات.

يستنتج من هذه الدراسة أن مشكلة تعاطي مركبات البنزودايزيبين موجودة في مجاميع الخطورة التي تمت دراستها، ومما يزيد في حدوثها هو وجود أعراض أجهاد نفسي، وننصح بالتثقيف الصحي الموجة الى مجاميع الخطورة أعلاه، وكذلك زيادة تثقيف الأطباء والصيادلة ممن يصفون أو يصرفون هذه الأدوية للمرضى.