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ORIGINAL RESEARCH ARTICLE

STUDY OF ASSOCIATION BETWEEN CHARACTERISTICS OF PATIENT AND LIKELIHOOD OF BENZODIAZEPINE USE IN PSYCHIATRY OUTPATIENT DEPARTMENT AT TERTIARY CARE HOSPITAL OF KATHMANDU.

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ABSTRACT

Introduction: Benzodiazepines exert their pharmacological properties as hypnotics, anxiolytics, anticonvulsants and muscle relaxants. Benzodiazepines are clinically effective for a number of indication including the reduction of anxiety, the induction and maintenance of sleep, muscle relaxation. They have a range of well documented adverse effects that may outweigh the benefits in certain patient population including psychomotor impairment, development of tolerance and dependence, potential for abuse. **Methods:** It is a hospital based prospective cross-sectional study conducted in a psychiatry outpatient department of tertiary care hospital. All the patients attended to the outpatient department of psychiatry and prescribed with benzodiazepine were selected for study. Drug therapy details in medication chart review and clinical review in patients treated with benzodiazepines was analyzed to measure the utilization pattern of benzodiazepines in terms of patient characteristics (e.g. age, gender and marital status), occupation, education and diagnosis, number of prescription of benzodiazepines, their doses, frequency, routes of administration and duration of use in each patient. **Results:** Out of a total of 384 patients, 246 of the patients had been currently using at least one benzodiazepine. Prevalence of benzodiazepine use was 64%. There was statistically significant association between benzodiazepines use with gender distribution, occupation and education. The prevalence of benzodiazepines use is relatively higher than that reported in the developed countries. Clonazepam was the most widely used benzodiazepine followed by lorazepam. **Conclusion:** The study evaluated the association between characteristics of patient and likelihood of benzodiazepines use. This will definitely help to optimize the drug therapy, improve the quality of care and reduce the negative outcomes in the usage of benzodiazepines.

Key words: *Benzodiazepine, Patients, Psychiatry*

INTRODUCTION

The importance of mental health has been gaining attention from various corner of society. The focus should also be given to the role of drugs in the treatment and prevention of mental illness. Among various drugs used in psychiatry, benzodiazepines are one of the commonest group which are prescribed all over the world.[1]

Benzodiazepine drugs were first introduced into clinical practice fifty years ago as anxiolytics and hypnotic agents.[2] Benzodiazepines are clinically effective for a number of indications including the reduction of anxiety, the induction and maintenance of sleep, muscle relaxation, and the treatment and prevention of epileptic seizures.[3,4] Though there is widespread concerns on benzodiazepine use for three decades regarding their unfavourable side effects profile as well as their propensity for dependence and potential for abuse, these drugs are still widely prescribed in most industrialized countries.[5,6] Diazepam is reputedly one of the most

widely prescribed drugs of all time.[7] In addition, the benzodiazepines have questionable clinical effectiveness which leads to matter of concerns for health professionals and most importantly patients in prolonged use.[8]

Howeve, there are no such largescale studies on the rational use of benzodiazepines as individual based therapy. For that purpose, it is essential to know the association of drug usage and the population demographics. Though pharmacogenetic and pharmacogenomics data will be more appropriate for the individual tailored use of benzodiazepines, population demographics might be useful as the initiation towards the more scientific rationalized use of drug in the developing world like ours until the advancement of genomic research in our part of world.[9]

Population characteristics can yield data to complement prescribers since the prescription of drug is based on individual's requirement.[10] Population studies assist the actual benzodiazepine users, the time and rationale of the initial prescription, and the number of months or years of use. Long-term use of benzodiazepines leads to physical and mental problems, so it is recommended for short-term use only.[11] These factors lead to non-compliance in patients. It is therefore important to perform a study investigating the utilization patterns of benzodiazepines in different diseases in a given clinical setting. The estimation of beneficial and adverse effects of benzodiazepines should take into consideration their immediate and long-term consequences upon social, emotional and professional life. The establishment of significant association between several demographic pattern of patient and benzodiazepine use leads to the effective implentation of rational prescribing of benzodiazepines. The rational use of benzodiazepines has a long way to go which certainly includes training of prescribers, and informing and educating the patient as well as general population.

The present study aimed to assess the association between characteristics of patient and likelihood of benzodiazepines use at psychiatry outpatient department at tertiary care hospital of Kathmandu. In the wake of implementation of stricter and rational recommendation on the use of benzodiazepines, this study will help to define the boundary for the use of such drugs in individual patient.

Materials and Methods

The prospective cross-sectional study involving 384 patients based on non-probability sampling was conducted in the outpatient Department of psychiatry of tertiary care hospital from May 2016 to December 2016 after obtaining ethical approval from institutional ethical committee. Data has been recorded in customized proforma from the out-patient daily record sheets and reports. Outpatient department record sheets were analyzed for patient characteristics (e.g. age, gender and marital status), occupation, education and diagnosis, number of prescription of benzodiazepines, their doses, frequency, routes of administration and duration of use in each patient.

SPSS package version 20 was used for analysis. Results are expressed as mean standard deviation. The Chi-square test was carried out to determine the statistical significance of the differences between the prescription rates.

Observations and Results

During the study period, prescription of 384 patients attended at outpatient department of psychiatry were assessed. Among 384 patients, only 246 (64%) of them were prescribed benzodiazepines.

A. Age wise distribution

The mean age of the patient attending psychiatry OPD was 37.05 years, ranging from minimum of 13 years to a maximum of 82 years. The highest numbers of patients attended to the psychiatry outpatient department were between the age group 30-39 years old (105 patients i.e. 27.34%) which was followed by the age group 20-29 years old (102 patients i.e. 26.56%).

Although the highest number of patient attended were from the age group 30-39 years old, the highest prescribing rate of benzodiazepines were found among the age group between 50-59 years old. There was no statistically significant association were found between benzodiazepines use and age distribution (p-value = 0.958) [Table 1]. Benzodiazepines were not prescribed to the age group 80-89 years.

Table 1: Association between age and the likelihood of benzodiazepines prescription

Age group (years)	Number (%) of patients	Patients prescribed with benzodiazepines (%)	'p' value
10-19	28 (7.29)	12 (42.85)	0.958
20-29	102 (26.56)	54 (52.94)	
30-39	105 (27.34)	71 (67.61)	
40-49	77 (20.05)	56 (72.72)	
50-59	37 (9.63)	28 (75.67)	
60-69	23 (5.98)	17 (73.91)	
70-79	11 (2.86)	8 (72.72)	
80-89	1 (0.26)	0 (0)	
Total	**384**	**246**	

B. **Gender Distribution**

The number of female patients and male patients who attended the psychiatry OPD during study period were 207 (53.9%) and 177 (46.1%) respectively. The male to female ratio was 0.85. Out of 207 female patients, only 141 (68.1%) patients were prescribed benzodiazepines and out of 177 male patients, only 105 (59.3%) patients were prescribed benzodiazepines [Figure 1]. There was statistically significant association between benzodiazepines use and gender distribution (p-value < 0.005).

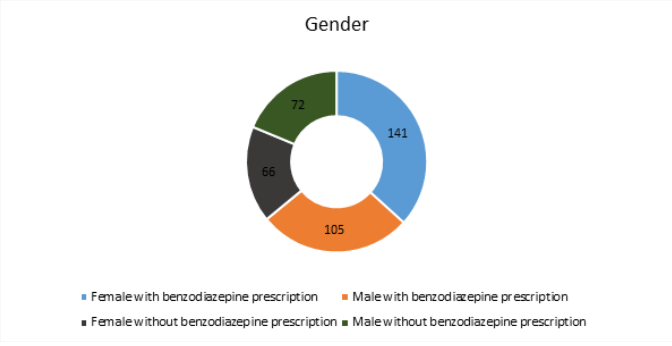

Figure 1: Gender distribution with and without benzodiazepine prescription

C. **Marital status**

Out of 322 married patients, 218 patients were prescribed benzodiazepines and out of 62 unmarried patients, 28 patients were prescribed benzodiazepines. There was no statistically significant association between benzodiazepines use and marital status ('p' value = 0.346) [Table 2].

Table 2: Association between marital status and the likelihood of benzodiazepines prescription.

Marital Status	Number (%) of patients	Patients prescribed with benzodiazepines (%)	'p' value
Married	322(83.85)	218 (67.70)	0.346
Unmarried	62(16.14)	28 (45.16)	

D. **Occupation Status**

Among 384 patients, all were engaged in various occupations. Most of the patients were housewives followed

by professionals, students, skilled labour and business man. 73.38% of housewives, 49 % of professionals, 45.2 % of students, 63.79% of skilled labour and 28% of business man attending OPD were prescribed benzodiazepines. Association between benzodiazepines use and occupation was statistically significant ('p' value=0.000) [Table 3].

Table 3: Association between occupation and the likelihood of BENZODIAZEPINESs prescription:

Occupation	Number (%) of patients	Patients prescribed with benzodiazepines (%)	'p' value
Business man	41 (10.7)	28 (68.29)	
Farmer	1 (0.3)	0 (0)	
Government officer	7 (1.8)	5 (71.42)	
Housewife	124 (32.3)	91 (73.38)	
Professional	78 (20.3)	49 (62.82)	0.000
Retired	13 (3.4)	8 (61.53)	
Skilled labour	58 (15.1)	37 (63.79)	
Student	62 (16.1)	28 (45.16)	
Total	**384**	**246**	

E. **Education status**

Among 384 patients who were attended at OPD during the study time, the education level was found from no formal education upto Ph.D. 68% of patients with secondary education need benzodiazepine, followed by 63 % patient with graduate level of education and 52% of patient with intermediate level of education. There was statistically significant association between benzodiazepines use and education parameter ('p' value = 0.001) [Table 4].

Table 4: Association between education and the likelihood of BDZs prescription.

Education	Number (%) of patients	Patients prescribed with benzodiazepine (%)	P – value
No formal education	15 (3.9)	10 (66.67)	
Primary	53 (13.8)	41 (77.35)	
Secondary	100 (26.0)	68 (68.0)	
Intermediate	89 (23.2)	52 (58.42)	0.001
Graduate	110 (28.6)	63 (57.27)	
Postgraduate	16 (4.2)	12 (75.0)	
Ph.D.	1 (0.3)	0 (0)	

F. **Distribution of psychiatric illness in relation with age and sex of patients prescribed with benzodiazepines**

Among 384 patients attended to the OPD, only 246 patients were prescribed with benzodiazepines which were prescribed for mainly anxiety, insomnia and depression. Most prominent psychiatric illness observed in the OPD was anxiety. Between the age group 10-19 years old and 60-69 years old, both male and female were suffering from depression. Similarly, between the age group 40-49 years old, 50-59 years old and 70-79 years old, both male and female were prone to anxiety. But between the age group 20-29 and 30-39 years old, most prominent psychiatric illness in male was observed depression whereas in female of 20-29 years old and 30-39 years old, it was insomnia and anxiety respectively.

G. **Commonly prescribed benzodiazepines**

Out of 246 benzodiazepines prescription, clonazepam, lorazepam and chlordiazepoxide were commonly prescribed during the study period. Out of three drugs, widely prescribed drug was clonazepam (88.6%) followed by lorazepam (4.5%) and chlordiazepoxide (2.4%). Least prescribed benzodiazepines were diazepam (1.6%), alprazolam (1.6%) and triazolam (1.2%).

Table 5: Commonly prescribed drugs, their dose, frequency, routes of administration and duration

Drug group	No. prescribed	Dose (mg)	Frequency	Route	Duration(days)
Clonazepam	218	0.25, 0.5	Bed time	Oral	7 to 14
Lorazepam	11	1	Twice a day	Oral	7 to 14
Chlordiazepoxide	6	10	Bed time	Oral	7

H. **Number of drugs used in patients along with benzodiazepine**

Out of 246 patients prescribed with benzodiazepines, 39.1% were prescribed with one drug i.e benzodiazepine only, 56.5% and 4% patients were co-prescribed with two drugs and three or more than three drugs respectively. [Figure 1]. The other commonly co-prescribed drugs along with benzodiazepines were antidepressants, antipsychotics, antihypertensives, oral ypoglycemics and few other systemic drugs.

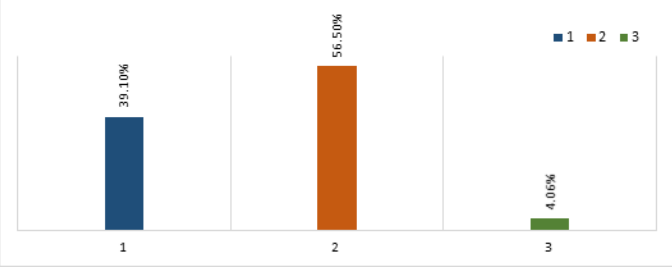

Figure 1: Number of drugs used in patients prescribed with benzodiazepines

Discussion

The present study was conducted to find out the characteristics of patient in psychiatry OPD and the utilization pattern of benzodiazepines among them. The observations from our study is able to delineate the fact that benzodiazepine use varied with patient characteristics. This study elucidated that the 64 % of patients attending Psychiatric OPD were prescribed benzodiazepines which is found to be higher than the similar type of studies conducted in France (7.5%), Lebanon (9.6%), Sydney (19.1%) and Chile (31.4%). [12-15]

Benzodiazepines prescription were common in middle age group patients as anxiety, depression and insomnia are more common in them.[3,4,16] Nepalese society is composed of various social relationships, families and relatives and depends upon the youths and adults. They express their high hopes from their adult siblings which results in anxiety and depression especially among the age group of thirty to thirty nine years.[17] As the people of this age group are considered to be of productive age, in case of failure of fulfilling the hopes of the family and society, these particular age groups are prone to develop psychiatric illness. However, benzodiazepines were prescribed comparatively less to elderly patient because prescription in such patients need extra precautions. Various studies showed that they have psychomotor impairment and excessive sedation with the use of benzodiazepines.[18-20]

Majority of patients attending psychiatry OPD were females and 68.1% of them were prescribed benzodiazepines, slightly higher than in males (59.3%). This may be due to the fact that females are more emotionally labile and more prone to develop insomnia and anxiety as compared to males.[21,22] The study revealed that the benzodiazepines were more commonly prescribed to housewives followed by other professionals. There was significant association between benzodiazepine use and occupation which is also supported by the results published in various

literatures.[23] Anxiety and depression is common in female housewives because of trends of female staying in home, vulnerable to stress, least contact with outer world and the male dominant culture of our society.[24,25] Similarly, psychosocial factors that women experience and hormonal factors may be linked to women for higher preponderance to anxiety and depression.[26] Hormone directly affect the brain chemistry that controls emotion and mood. Interestingly, there was no unemployed patients who opted to psychiatry OPD during our study period. This fact resembles the mental health unawareness among them as they might feel awkward to seek psychiatric care or they might not be aware about their abnormal mental conditions.

Marriage was found to be one of the factor that increases the likelihood of benzodiazepine use. As our study found that the higher number of married patients were attending psychiatry OPD and most of them were prescribed benzodiazepines. This finding is similar from the study conducted in United States, India and Pakistan.[27] This might be due to increase in responsibility and difficulty in adjusting in family life as well as higher likelihood of misunderstanding and family disputes. All of these condition are the major risk factors for developing psychiatric illness which ultimately require the prescription of benzodiazepines.[28, 29]

The larger number of patients attending psychiatry OPD and getting benzodiazepine as prescription were educated (96%). Most of the patients had completed secondary to tertiary level of education. The association of education and benzodiazepine use is directly related as educated people have higher ambitions, lots of future planning and have to face different obstacles which leads to stress and frustration turning to mental illnesses like anxiety, insomnia and depression later on. These conditions required treatment and benzodiazepine is one of the commonest drug used for treatment sooner or later.[23]

This study observed that the three common psychiatric illnesses in patient attending psychiatry OPD were anxiety, insomnia and depression similar to the study done by Rode SB et al.[30] All these three conditions are the indications for the use of benzodiazepines. Benzodiazepine is the first line agent in anxiety and insomnia and alternative agent in depression.[31, 32]

Among all benzodiazepines, most commonly used benzodiazepine was found to be clonazepam followed by lorazepam and chlordiazepoxide. The study conducted by Nomura K et al also found clonazepam as most commonly prescribed benzodiazepine.[33] Various studies showed that the most commonly used benzodiazepines were bromazepam, alprazolam and temazepam.[34-36] The variation in the use of benzodiazepine might be due to the differences in settings and protocols of treatment along with availability of the drug in such settings. The socio-demographic factors, ethnic factors, comorbid conditions, and the prevalence of mental illness might also play the determining role in selection of benzodiazepines.[34,35] The study also showed that benzodiazepine was not always used as single agent. Antidepressant, antipsychotics, antihypertensives, oral hypoglycemics, lithium etc were co-prescribed along with benzodiazepine in over half of the patient attending psychiatry OPD. The co-prescribed drugs also sometimes play determining role in benzodiazepine selection as there might be some drug-drug interactions or some synergism which might lead to either selection of appropriate drug or appropriate dose with least interaction or more favorable clinical responses.[37-39]

Conclusion

The age, gender, marital status, occupational status, educational status, psychiatric illnesses and other co-morbid conditions have determining role in prescription of benzodiazepines. The prevalence of benzodiazepines use is relatively higher than that reported in the developed countries. Sensitization of the medical community and the masses of this growing problem of benzodiazepine use and associated risks is necessary to control in the developing world. This study is limited to a single OPD of tertiary care hospital so it needs further multicentric study to justify and validate the results. It is high time to standardize the use of benzodiazepines in order to fulfill the rationality of prescription with safeguarding the mental health in wider sense.

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