



CODEN (USA): IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**Available online at: <http://www.iajps.com>

Review Article

**CHOICE OF BENZODIAZEPINES BY THE PSYCHIATRISTS
AND NEUROLOGISTS IN COMILLA AND FENI DISTRICT OF
BANGLADESH****Mehedi Hasan*¹, Mofazzal Hossain¹, Masiur Rhaman²**¹Department of Pharmacy, University of Information Technology and Sciences (UITS),
Baridhara, Dhaka, Bangladesh²Brand Management Department, SBMD, The ACME Laboratories Ltd., Dhaka, Bangladesh**Abstract:**

This prescription survey was carried out to find the most frequently used benzodiazepine class (e.g. Clonazepam, Diazepam, Bromazepam, Clobazam, Midazolam, Flurazepam and Alprazolam) and their rational use as anti-anxiety agents in the Comilla and Feni District of Bangladesh. All the prescriptions were collected in the June 2015, prescribed by psychiatrists throughout the month of May 2015. We have found prescription containing 21% Clonazepam, 12% Flurazepam, 6% Midazolam, 4% Alprazolam, 2% Bromazepam, 2% Diazepam and 2% Clobazam in Comilla district. 51% prescription did not contain any benzodiazepines. In Feni district, we have found 22% Clonazepam, 0% Flurazepam, 0% Midazolam, 11% Alprazolam, 6% Bromazepam, 0% Diazepam and 0% Clobazam in the prescription. 61% prescription in this district did not contain benzodiazepines. We found 1 prescription containing Midazolam and Flurazepam (both are benzodiazepines). In another prescription collected from Feni district we got 1 prescription containing Clonazepam and Alprazolam. But we recommend the citation of the chief complain or diagnosis in the prescription for better understanding and justification of using any drug especially when it is sedative, hypnotic or narcotic drug.

Keywords: Psychiatric diseases, benzodiazepines, Insomnia, Anxiety, Schizophrenia**Correspondence to Author:****Md. Mehedi Hasan**

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Please cite this article in press as Mehedi Hasan et al , Choice Of Benzodiazepines By The Psychiatrists and Neurologists In Comilla and Feni District Of Bangladesh, *Indo Am. J. Pharm. Sci.*, 2015;2(9).

INTRODUCTION

According to National Mental Health Survey in 2003-2005 about 16.05% of the adult population in Bangladesh is suffering from mental disorders. A small portion of patients are reporting to government facilities and they receive some psychotropic medicines from the facilities[1]. Benzodiazepines are the class of anti-anxiety agents (i.e. Clonazepam, Diazepam, Bromazepam, Clobazam, Midazolam, Flurazepam, Nitrazepam, Alprazolam, Chlordiazepoxide, Lorazepam etc.) used as the first-line therapy for treating anxiety disorders throughout the world. Diazepam, lorazepam, alprazolam and clonazepam remain in the top 200 most frequently prescribed medication in the USA [2].

Benzodiazepine Indications [3]

1. Benzodiazepines are indicated for the short-term relief (two to four weeks only) of anxiety that is severe, disabling, or causing the patient unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic, or psychotic illness.
2. The use of benzodiazepines to treat short-term 'mild' anxiety is inappropriate.
3. Benzodiazepines should be used to treat insomnia only when it is severe, disabling, or causing the patient extreme distress.

Prescribed use of the Following 4 Benzodiazepines [4]:

Clonazepam: Alone or as in an adjunct in the treatment of panic disorder, seizure disorder, periodic leg movement, neuralgia, anxiety.

Alprazolam: Treatment of anxiety disorder, panic disorder, with or without agoraphobia, and anxiety associated with depression.

Flurazepam: The short term management of insomnia.

Midazolam: Sedative-hypnotic; preoperative sedation and provides conscious sedation prior to diagnostic or radiographic procedures, ICU sedation (continuous IV infusion), intravenous anesthesia induction and maintenance.

Objective of the Study

This prescription survey was carried out to find the most frequently used benzodiazepine class (e.g. clonazepam, diazepam, bromazepam, clobazam,

midazolam, flurazepam and alprazolam) and their rational use as anti-anxiety agents in the Comilla and Feni District of Bangladesh. All the prescriptions were collected in the June 2015, prescribed by psychiatrists/neurologists during one month period (May 2015). Moreover, our other objectives were to find out whether more than one benzodiazepine generic is used in the same prescription or not, all the medications are given after proper diagnosis, what are the indications for prescribing clonazepam, diazepam, bromazepam, clobazam, midazolam, flurazepam and alprazolam, what are the most common chief complain by the patients, patients outside Dhaka are getting proper medication advice or not. This is the reason behind choosing Comilla and Feni as our survey area.

MATERIALS AND METHODS

We conducted a prescription survey to examine the use of benzodiazepine class drugs in the clinics, private chambers and Govt. hospitals situated in the Comilla and Feni District of Bangladesh. We collected 49 prescriptions from Comilla District and 17 prescriptions from Feni District of the country. All the physicians are specialist in psychiatry, neurology, neuro-medicine and neuro-surgery. Those prescriptions were given throughout the month of May 2015. We collected all the prescriptions in the month of June 2015.

Then we used MS word and MS Excel worksheet to find out the percentage of clonazepam, diazepam, bromazepam, clobazam, midazolam, flurazepam and alprazolam prescribed by the specialist physicians for the patients with anxiety, hypertension, insomnia, without diagnosis or without mentioning the chief complain in the prescription. At first, we found out the frequency of prescription containing different benzodiazepines in collected form Comilla district. Then we found out the prescription frequency containing different benzodiazepines in different psychological conditions. After that we identified how many prescriptions contain 2 benzodiazepine generics for a same patient and what could be the reason behind choosing two generic at the same time.

Limitations of the Study

We collected only one month data (prescription) from only two districts. It is not sufficient to make a decision for whole the country. The number of prescriptions collected might be more than we used in the survey.

RESULT AND DISCUSSION

Comilla District:

Among 49 prescriptions collected from the Comilla district we have got the following benzodiazepines containing prescriptions:

Generic drugs	No. of prescription (s)	Diagnosis
Clonazepam	10	Insomnia/Hysteria/No diagnosis
Diazepam	1	No diagnosis
Clobazam	1	No diagnosis
Bromazepam	1	No diagnosis
Midazolam	3	Bipolar Mood Disorder/Schizophrenia
Flurazepam	6	Insomnia/ without diagnosis
Alprazolam	2	No diagnosis
No benzodiazepines	25	Various diagnosis

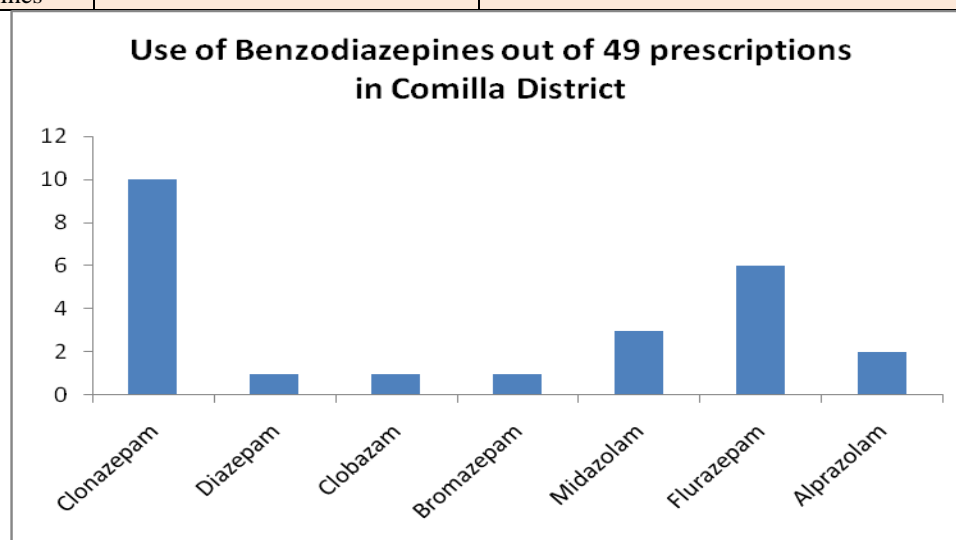


Fig 1: Use of Benzodiazepines in Comilla District

It is clear that the psychiatrists/neurologists/neurosurgeons prefer Clonazepam generic among all the benzodiazepines. They trust and recommend Clonazepam for patients with primary insomnia, secondary insomnia, hysteria etc. Moreover, it has been proved that physicians always prefer Clonazepam for patients with any type of sleep disorders, because we found 38 among 49 prescriptions where no diagnosis was mentioned. It might be happened that the chief complain of those patients were less sleep/irregular sleep.

Diazepam had been found in only one prescription without mentioning diagnosis or 'chief complain' by the patient. Clobazam has the same effect on prescription like diazepam. We found 1 prescription in the Comilla district that contains Clobazam. Sometimes it is prescribed without diagnosis and on

the basis of patients complains. In integration to that Bromazepam was found in 1 prescription among 49 prescriptions in the Comilla district. Midazolam had been found in 3 prescriptions with mentioning Bipolar mood disorder/Schizophrenia. 1 prescription had been given to the patient without diagnosis. Surprisingly, we found 1 prescription containing Midazolam and Flurazepam (both are benzodiazepines). We will discuss the justification of using midazolam and flurazepam as adjunct therapy. Flurazepam had been found in the 6 prescriptions among 49 prescriptions in the Comilla district. Physicians recommended the generic to the patients suffering from insomnia. Some prescriptions had been given without mentioning the diagnosis or chief complain. We identified 2 prescriptions containing Alprazolam for the patients without citation of the disease name or chief complain.

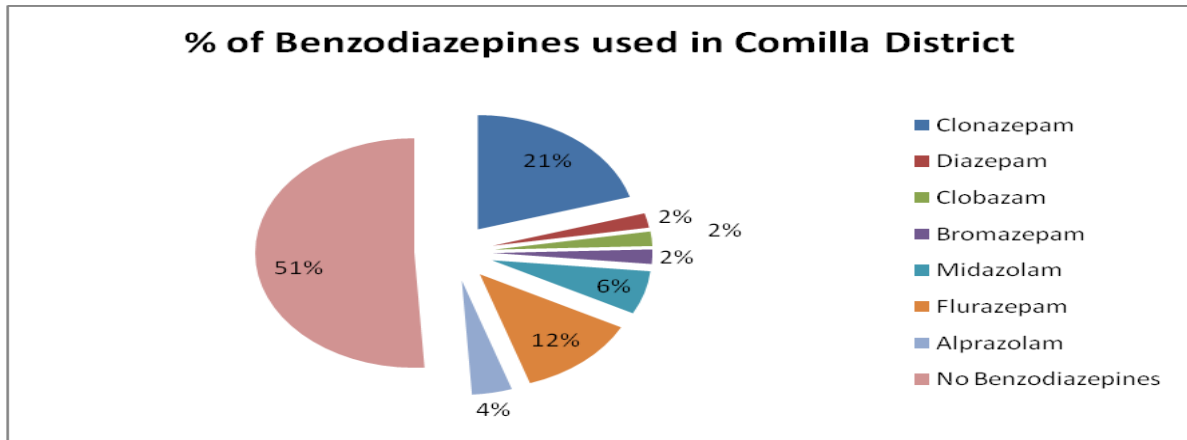


Fig 2: Frequency Distribution of Percentage of Benzodiazepines Used In Comilla District

Feni District:

Following are the result found from the Feni district containing benzodiazepines among 17 prescriptions:

Generic drugs	No. of prescription (s)	Diagnosis
Clonazepam	4	Insomnia/Hysteria/No diagnosis
Diazepam	0	No diagnosis
Clobazam	0	No diagnosis
Bromazepam	1	No diagnosis
Midazolam	0	Bipolar Mood Disorder/Schizophrenia/without diagnosis
Flurazepam	0	Insomnia/ without diagnosis
Alprazolam	2	No diagnosis
No benzodiazepines	11	Various diagnosis

From the result of Feni district we got similar finding that the psychiatrists/neurologists/neuro-surgeons prefer Clonazepam generic among all the benzodiazepines. They trust and recommend Clonazepam for patients with primary insomnia, secondary insomnia, hysteria etc. Moreover, it has been proved that physicians always prefer

Clonazepam for patients with any type of sleep disorders, because we found 11 prescriptions out of 17 prescriptions where no diagnosis was mentioned. It might be happened that the chief complain of those patients were anxiety/disruption of sleep.

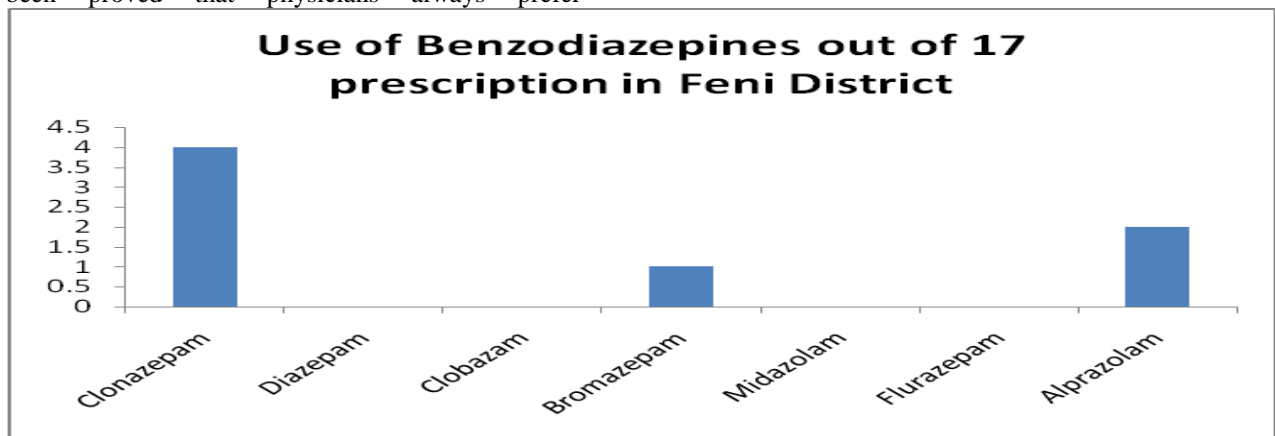


Fig 3: Use of Benzodiazepines in Feni District

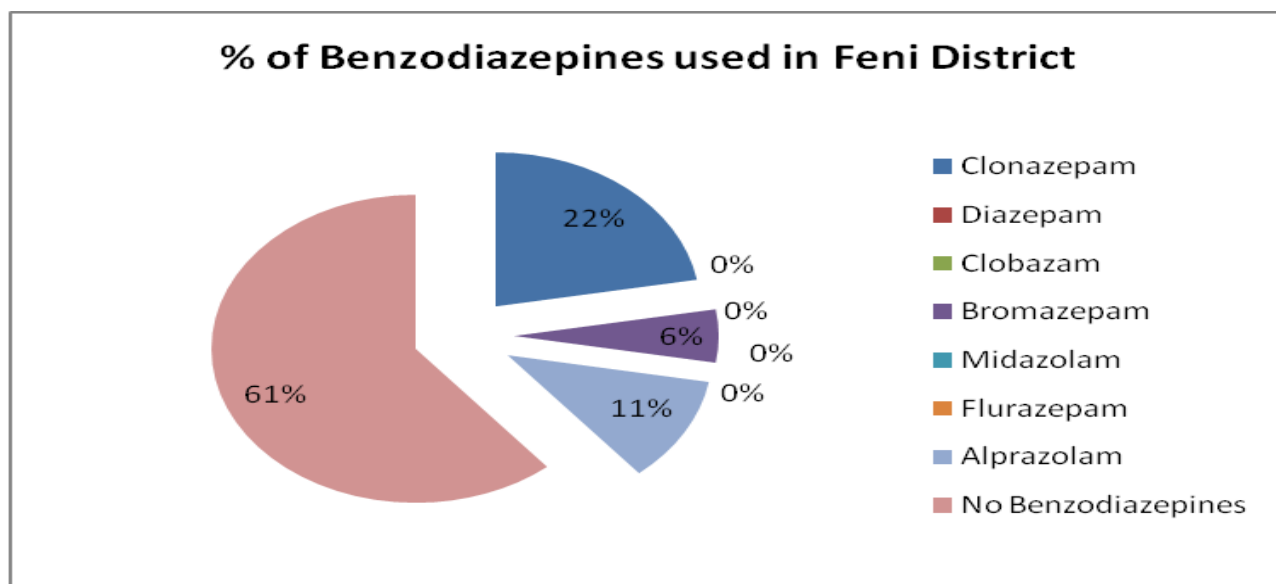


Fig 4: Frequency distribution of percentage of Benzodiazepines used in Feni district

There were no diazepam, clobazam, midazolam and flurazepam prescribed by the physicians in the 17 prescription collected from Feni. In addition to that Bromazepam had been found in 1 prescription among 17 prescriptions in the Feni district. We identified 2 prescriptions containing Alprazolam for the patients without citation of the disease name or chief complain. Exceptionally, we found 1 prescription containing Clonazepam and Alprazolam (both are benzodiazepines). We will discuss the justification of using Clonazepam and Alprazolam administration simultaneously.

Justification of Combined Use of 2 Benzodiazepines:

Flurazepam can be used as adjunct with Midazolam as flurazepam is used in the short-term management of insomnia, whereas midazolam exerts continuous sedation.

On the other hand, as per the indication approved by USFDA [8], Clonazepam can be used as an adjunct in the treatment of anxiety, panic disorder, periodic leg movement, neuralgia and anxiety with other benzodiazepines like Alprazolam which we found in 1 prescription in Feni district. We know that Diazepam is very effective as muscle relaxant so it may be found as adjunct therapy.

CONCLUSION

Finally in conclusion we can say that in both the district (Comilla and Feni) frequently prescribed benzodiazepine is Clonazepam as an anti-anxiety agent. Less frequently prescribed generic of this class are diazepam, clobazam and bromazepam. Flurazepam is the 2nd choice of physicians in the Comilla district and Alprazolam is the 2nd choice as per our study. Midazolam is the 3rd choice in Comilla, whereas Bromazepam is the 3rd choice by the neurologists/psychiatrists in Feni district.

A review paper found that long term use of flurazepam is associated with drug tolerance, drug dependence, rebound insomnia and CNS related adverse effects. Flurazepam is best used for a short time period and at the lowest possible dose to avoid complications associated with long term use. Non-pharmacological treatment options however, were found to have sustained improvements in sleep quality [5, 6, 7]. In our survey, we have got 12% prescription containing Flurazepam (2nd highest prescribed) in Comilla district.

Although, the administration of anti-anxiety agents is currently the most common treatment modality for insomnia, but long term use can cause many side effects as well as addiction. Therapy without involving drugs-including combinations of behavioral changes, sleep-restriction therapy, and patient education-provide longer-lasting benefits.

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