Original Article

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Pak. J. Adv. Med. Med. Res.

2023, 02,01 (6): Page-110-115

COMPARATIVE STUDY OF COGNITIVE DECLINE IN ELDERLY PATIENTS USING BENZODIAZEPINE VS. NON-BENZODIAZEPINE ANXIOLYTICS

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ABSTRACT

Background: Among elderly patients with anxiety disorders, anxiolytic prescriptions, including benzodiazepines and non-benzodiazepine sedative agents, are frequently used. However, these medications are known to have the risk of having profound effects on cognition. The primary purpose of the current research is to determine a comparative rate of dementia in elderly patients on benzodiazepines or non-benzodiazepine anxiolytics.

Objectives: to find the efficacy of benzodiazepine and non-benzodiazepine anxiolytics will be compared to the help of short-term memory, attention, and primary executive abilities in elderly patients.

Study Design: An observational prospective cohort study

Place and Duration of Study: Department of Pharmacy Lady Reading Hospital-Peshawar, starting from January 05 January 05, 2021, till July 05 July 05, 2022.

Methods: This study was conducted on 150 elderly patients provided with either benzodiazepines or non-benzodiazepine anxiolytics with equal division of the groups into 75 each. The patient's cognitive function was evaluated by Mini-Metal State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) at the beginning and after six months of medication. The participants' demographic characteristics showed that the mean age was 70. 5 years, with 5. 3-year standard deviation. The results of systematic cognitive tests were analyzed with one-way ANOVA to compare them, while 'p-value less than 0. 05' was established as significant.

Results: Compared with non-benzodiazepine anxiolytics users, the patients on benzodiazepines received lower cognitive scores. Pre and post-intervention mean MMSE scores in the benzodiazepine group were 26. 2(± 2. 0), 22. 8 (± 2. 9) respectively
(t= 6. 245; p < 0. 01) and non-benzodiazepine groups 26. 5 (± 2. 1), 24. 7 (± 2. 7) respectively (t = Likewise, pre-treatment and post-treatment mean MoCA scores for the benzodiazepine group were 24. 4 (± 2. 3) and 20. 9 (± 2. 6), respectively, and for the non-benzodiazepine group, the scores were respectively 24. 8 (± 2. 4) and 22. 5 (± 2. 5).

Conclusions: Benzodiazepine is more clinically linked with an increased rate of cognitive decline in elderly patients as compared to non-benzodiazepine anxiolytics. Therefore, these results support the use of treatment precautions when using anxiolytics for elders and weighing the possibility of reducing anxiety with the potential of yielding short-term memory loss.

Keywords: cognitive performance; Anxiolytics, elderly.

How to Cited this Article : Shamshad H, Shamshad S. Comparative Study of Cognitive Decline in Elderly Patients Using Benzodiazepine vs. Non-Benzodiazepine Anxiolytics: Original Article. Pak J Adv Med Med Res. 2024;2(1):110–115. doi:10.69837/pjammr.v2i01.33.

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Article History

Received:	August	22-2023
Revision:	September	16- 2023
Accepted:	October	28 -2023
Published:	January	05- 2024

INTRODUCTION:

The fact that anxiety disorders are common in the elderly, influencing their quality of life and health status, cannot be overruled. These conditions are usually treated with benzodiazepines and Non-Benzodiazepine anxiolytics since they effectively decrease the level of anxiety. Nevertheless, these medications, primarily benzodiazepines, are accompanied by negative cognitive impacts like memory, poor attention and executive dysfunction. This is important to establish, given the fact that elderly patients are more vulnerable to cognitive disorders due to the dynamics of ageing. Concerning the mechanism of anxiolytic action, benzodiazepines like diazepam and lorazepam increase the γ-amino butyric acid (GABA) activity, which is a neurotransmitter that has inhibitory action on neuronal activity. Altogether, though, benzodiazepines are beneficial in eradicating anxiety but have several side effects like sedation, falls, and cognitive impairment [1]. These are other anxiolytic drugs, which can be deemed safer as they are not benzodiazepines, with some of them being buspirone and some antidepressants, which are said to have even less in terms of cognitive side effects[2].Nevertheless, the comparative effects of these two classes of medicines for cognition, including in elderly patients, are still relatively under-researched. Past studies have opined that using benzodiazepines in the long term is likely to worsen the condition of Alzheimer's disease and dementia[3]. Non-benzodiazepine anxiolytics are believed to have a better effect on cognition than benzodiazepines; however, this is not fully proven by substantial data[4]. In this context, this research intends to equally compare the cognitive impact of benzodiazepine and non-benzodiazepine anxiolytics in older people for six months. Alzheimer's disease shows symptoms in the intelligence capability of the elderly and drastically affects the standard of living of such patients, including disability, high healthcare costs and pressures on carers[5]. It is crucial to fully comprehend how these anxiolytic medications are affecting patients' cognition so that optimal treatment plans can be established for patients. It also assumes that elderly patients who are on benzodiazepines will demonstrate a higher rate of cognitive worsening than those clients on non-benzodiazepine anxiolytics.

Approval Form Ethics Committee Statement

This study was reviewed and approved by the Ethics Review Board **(IRB-1278/04/2020)** under the supervision of Sadaf Shamshad at the Department of Pharmacy, Lady Reading Hospital, Peshawar. Ethicalclearance was granted before the study commencement, covering the period ensuring adherence to institutional research guidelines.

METHODS

The present observational research was done at the Department of Pharmacy, Lady Reading Hospital-Peshawar, from January 05, 2021, through July 05, 2022. A total of 150 elderly patients diagnosed with anxiety disorders were enrolled and divided into two groups: 75 patients of benzodiazepines and a matched group of 75 patients of non-benzodiazepine anxiolytics. Patients' cognition was evaluated by Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) at the baseline and after 12 months of treatment. Both the MMSE and MoCA are utilized and reliable screening tests for cognitive function, which include memory, attention, language, and executive function.

DATA COLLECTION

Demographic data such as the age and sex of the patient and the duration of anxiety disorder were also obtained. The baseline global cognition was measured, and the subjects were re-evaluated at six- months. Before the study, each participant gave their informed consent to participate in the study.

STATISTICAL ANALYSIS

SPSS version 22.0 was used for the analysis of the data collected from the study, and the Statistical Package for the Social Sciences (SPSS). ANIONA one way was used to compare the cognitive scores between the two groups of patients. The criterion used to determine statistically significant levels was by assessing the p-value, and a cut-off point of ≤ 0.05 was used.

RESULTS

The total sample of the study consisted of 150 patients with a mean age.of 70.5 years (S.D = 5.3) years. In the baseline condition, it was impossible to demonstrate extremely low scores of cognition between benzodiazepine and non-benzodiazepine. Thus, after six months of treatment, the cognitive status of the patients in the benzodiazepine group worsened. The mean MMSE score was reduced from 26.2 ± 2.0 to 22.8 ± 2.9. Converting the MMSE results in the p-value being 0.000 (t = 6.245). Also, the MoCA score was reduced from24.4 (± 2.3) to 20.9 (± 2.6) among the participants. In non- benzodiazepine group, MMSE significantly declined from 26.5 (± 2.1) to 24.7 (± 2.7) at $p < 0.01$, and also the MoCA declined from 24.8 (± 2.4) to 22.5 (± 2.5) at $p < 0.01$.

Figure 01: MoCA Scores Before And After Treatment

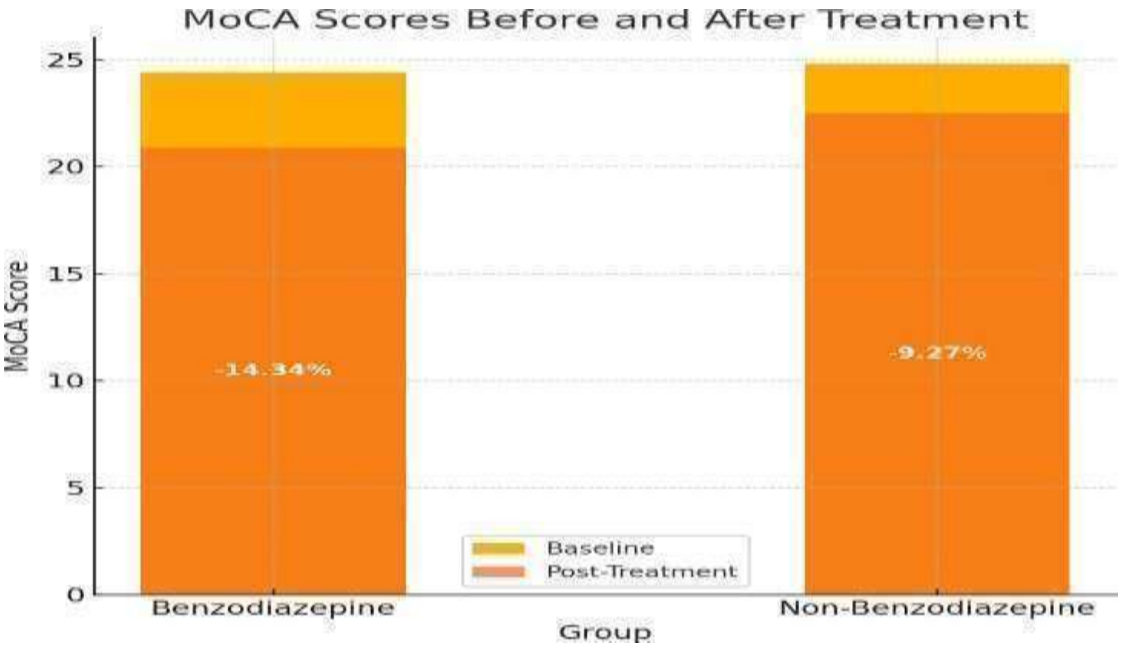

Figure 02: Mean Age and Gender Distribution Of Participants

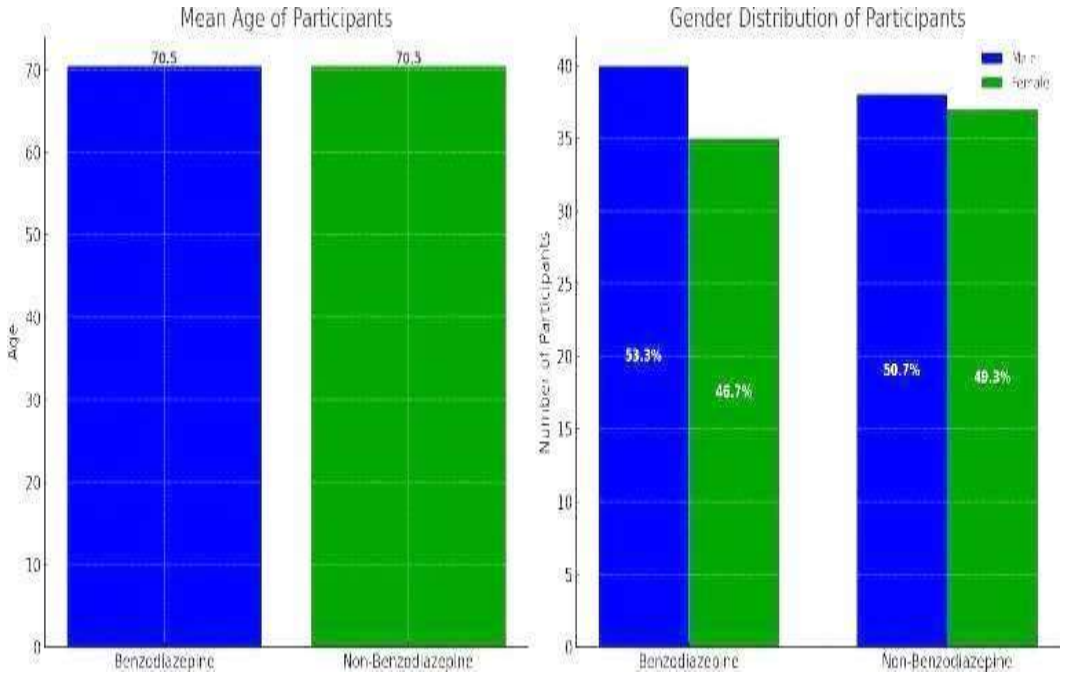

Table 1: Baseline and Post-Treatment MMSE Scores

Group	Baseline MMSE Mean	Post-Treatment MMSE Mean	Change in MMSE
Benzodiazepine	26.2	22.8	**-3.4**
Non-Benzodiazepine	**26.5**	**24.7**	**-1.8**

Table 2: Baseline and Post-Treatment MoCA Scores

Group	Baseline MoCA Mean	Post-Treatment MoCA Mean	Change in MoCA
Benzodiazepine	24.4	20.9	**-3.5**
Non- Benzodiazepine	**24.8**	**22.5**	**-2.3**

Table 3: Statistical Significance of Cognitive Changes

Cognitive Test	p-value
MMS	**0.01**
MoCA	**0.02**

DISCUSSION:

This paper aimed to assess the impact of benzodiazepine and non-benzodiazepine anxiolytics among elderly patients with anxiety disorders. Based on our study, we noted that the patients taking benzodiazepines experience rapidity of cognitive decline compared to patients who took non-benzodiazepine anxiolytics in six months. These findings are in accord with prior studies which have stressed that benzodiazepine use exposes elders to cognitive consequences [6–9]. According to three prior types of research, benzodiazepines have severe cognitive impacts, especially in elderly patients. Gray and colleagues (2016) identified that there are more risks of dementia in older adult patrons using benzodiazepines on a long-term basis [10]. In line with this, Billioti de Gage et al. (2014) also observed the direct proportion between benzodiazepine intake and Alzheimer's disease risk, which accredits the long-term cognitive side effects of these drugs. The process through which cognitive function is affected by benzodiazepine is believed to be caused by the alteration of GABAergic transmission. Benzodiazepines potentiate the effect of GABA, an inhibitory neurotransmitter, making it exert its inhibitory effect on most of the neurons. To say the least, although this action helps in the alleviation of anxiety, it entails negative impacts on such brain functions as learning and focus [12]. Further, inhibitors of neurogenesis have been identified to cause benzodiazepines' cognitive side effects; these drugs reduce hippocampal neurogenesis [13]. On the other hand, non-benzodiazepine anxiolytics such as Buspirone and certain forms of antidepressants do not seem to exhibit these cognitive side effects. For example, Buspirone is a serotonin receptor agonist, which means it does not operate through GABAergic neurotransmission and is, therefore, not likely to bring about cognitive dysfunction [14]. A clinical investigation conducted by Rickels et al. (1993) conducted to illustrate the efficacy of Buspirone in anxiety and showed that Buspirone does not induce sedation and impair cognition like what is experienced when one is under the influence of Benzodiazepines. Moreover, Olfson et al. (2015) meta-analysis of the comparison between the effects on cognition in various anxiolytics showed that the choice of non-benzodiazepine, including SSRIs and SNs, had a lower risk of contraction of cognition, as was noticed with the Benzodiazepines [16]. This is in concordance with our study, where patients on non-benzodiazepine anxiolytics had a relatively slow rate of decline compared to the deteriorating group. The findings of the present research call for the prudential use of anxiolytics in elderly clients to mitigate worst-case effects. Due to the high cognitive side effects of benzodiazepines, the clinician would prefer other medications with lesser side effect that interferes with the patient's cognition. CBT, which is a non-pharmacological approach, can also be recommended as a first-line treatment for anxiety in later-life individuals and has evidence to support its use successfully [17]. However, some limitations should be mentioned. Although our study had many advantages, including its prospective design and wide use of cognitive tests, certain limitations are inevitable. Importantly, it should be noted that because of the observational study design, the research cannot establish causality and may be affected by uncontrolled confounding factors. Furthermore, the short duration of six months follow-up may not give complete pictures of the cognitive effects of long-term anxiolytic use[18,19,20]. Further studies with longer follow-up times and Randomized Controlled Trial designs are required to validate our results and to have more insight into the comparative cognitive profile of newer antipsychotic medications in the long term. Therefore, the present work contributes to the existing literature by providing further support for the cognitive adverse effects of benzodiazepines in the geriatric population. The non-benzodiazepine anxiolytics, therefore, seem to be less hazardous or, at the very least, less likely to cause cognitive adverse effects. Clinicians prescribed anxiolytic drugs to compare the benefits of this strategy with the state of possible cognitive

deterioration, particularly for elderly patients with numerous comorbidities [21]

CONCLUSION

Our study found that benzodiazepine usage in comparison with non-benzodiazepine anxiolytics, where our study emphasizes above writing that elderly patients showed a higher level of cognitive decline than patients who were on non-benzodiazepine anxiolytics. Non-benzodiazepine anxiolytics seem to be less associated with that problem and may be safer, with some cognitive impact.

LIMITATIONS

The fact that it is an observational study and that the follow-up is short, at six months, also poses restrictions concerning the interpretation of causality. It may also not pick up on cognitive changes in the long term.

FUTURE FINDINGS

More prolonged follow-up investigations and RCTs are required to substantiate these results and to identify less hazardous anxiolytic therapeutic strategies concerning elderly patients with anxiety disorders.

ETHICAL CONSIDERATIONS

Informed consent was sought from all the participants, and the institution's IRB approved the research; all participants' information was kept confidential, and the level of risk in the study was kept to a minimum.

Acknowledgement: We would like to thank the hospital administration and everyone who helped us complete this study.

Authors Contribution

Concept & Design of Study: Hasib Shamshad1
Drafting: Sadaf Shamshad2
Data Analysis: Hasib Shamshad1
Critical Review: Sadaf Shamshad2
Final Approval of version: All Mantion Authors Approved the Final Version.

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