

Comparative Study of Cognitive Decline in Elderly Patients Using Benzodiazepine vs. Non-Benzodiazepine Anxiolytics

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Abstract

Background: Among elderly patients with the 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 serious effects on cognition. The main purpose of the current research is to determine a comparative rate of dementia in elderly patients on benzodiazepines or non-benzodiazepine anxiolytics.

Objectives: First of all, the efficacy of benzodiazepine and non-benzodiazepine anxiolytics will be compared with helping of short-time memory, attention, and main executive abilities in the elderly patients.

Study Design: A Observational prospective cohort study

Place and Duration of Study: Department of Pharmacy, Lady Reading Hospital-Peshawar, starting from: 05 January 2021 till: 05 July 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 patients' cognitive function was evaluated by Mini-Metal State Examination (MMSE), 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 years standard deviation. The results of systematically 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 score in the benzodiazepine group were 26. 2(\pm 2. 0), 22. 8 (\pm 2. 9) respectively ($t=$ 6. 245; $p <$ 0. 01) and non benzodiazepine groups 26. 5 (\pm 2. 1), 24. 7 (\pm 2. 7) respectively ($t =$ Likewise, pre-treatment and post-treatment mean MoCA scores for the benzodiazepine group were 24. 4 (\pm 2. 3) and 20. 9 (\pm 2. 6) respectively and for the non-benzodiazepine group the scores were respectively 24. 8 (\pm 2. 4) and 22. 5 (\pm 2. 5).

Conclusions: Benzodiazepine is more clinically linked with the 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.

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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 normally treated with benzodiazepines and Non-Benzodiazepine anxiolytics since they effectively decrease the level of anxiety. Nevertheless, these medications mostly the 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 aging. Concerning the mechanism of anxiolytic action, benzodiazepines like diazepam and lorazepam increase the γ -amino butyric acid (GABA) activity which is neurotransmitter that has inhibitory action on neuronal activity. Altogether though, benzodiazepines are beneficial in eradicating anxiety, but has 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 compared the cognitive impact of benzodiazepine and non-benzodiazepine anxiolytics in the elderly 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, the elderly patients who are on benzodiazepines will demonstrate a higher rate of cognitive worsening than those clients on non-benzodiazepine anxiolytics.

Methods

The present observational research was done at the Department of Pharmacy, Lady Reading Hospital-Peshawar from January 5, 2021 through July 5, 2022. A total of 150 elderly patients diagnosed with anxiety disorders were enrolled and divided into two groups: 75 patients of benzodiazepines and 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 6 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 age and sex of the patient and duration of anxiety disorder was also obtained. The baseline global cognition was measured, and the subjects were re-evaluated at six-months. Before the study each participant give 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 were by assessing p-value and a cut-off point of ≤ 0.05 was used.

Results

Total sample of the study consisted of 150 patients with 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 MMSE result p-value being 0.000 ($t = 6.245$). Also the MoCA score reduced from $24.4 (\pm 2.3)$ to $20.9 (\pm 2.6)$ among the participants. In non-benzodiazepine group, MMSE was significantly declined from $26.5 (\pm 2.1)$ to $24.7 (\pm 2.7)$ at $p < 0.01$, and also the MoCA was declined from $24.8 (\pm 2.4)$ to $22.5 (\pm 2.5)$ at $p < 0.01$.

Figure 01: MoCA Scores Before And After Treatment

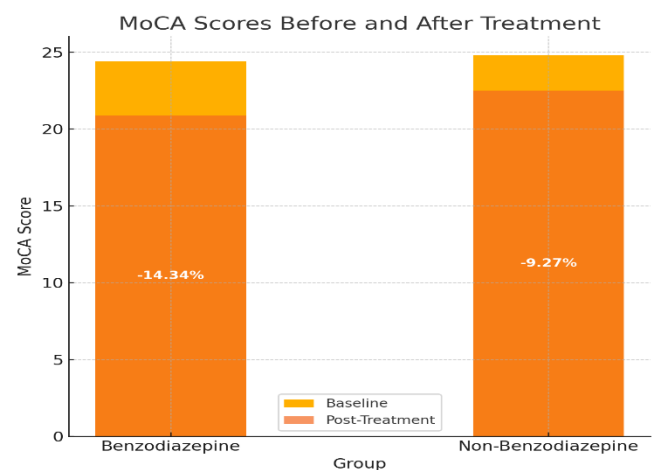


Figure 02 : Mean age and Gender Distribution Of Participants

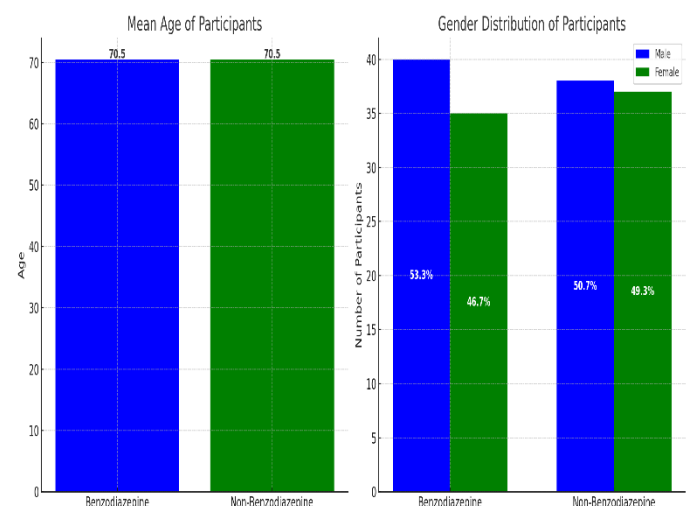


Table 1: Baseline and Post-Treatment MMSE Scores

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
MMSE	0.01
MoCA	0.02

Discussion:

This paper aimed at assessing 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 a period of six months. These findings are in accord with prior studies which have stressed that benzodiazepine use exposes elders to the cognitive consequences [6–9]. According to three prior researches, benzodiazepines have severe cognitive impacts especially in the elderly patients. Gray and colleagues (2016) identified that there are more risks of dementia in older adults patrons using benzodiazepines for 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 alteration of GABAergic transmission. Benzodiazepines potentiate effect of GABA, an inhibitory neurotransmitter, making it to 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 reduces 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 that means it does not operate through GABAergic neurotransmission and is, therefore, not likely to bring about cognitive dysfunctioning [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 patient on non-benzodiazepine anxiolytics had a relatively slow rate of decline compared to the deteriorating group. The findings of the present research call for prudential use of anxiolytics in elderly clients to mitigate worst-case effects. Due to the high cognitive side effect of benzodiazepines, the clinician would prefer other medications with lesser side effect that interferes with patient's cognition. CBT, which is non-pharmacological approach, can also be recommended as first-line treatment for anxiety in later life individuals, and has evidence to support its use successfully [17]. However, there are some limitations that 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 time and Randomized Controlled Trial designs are required to validate our results and to have more insight on 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 finding 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 the short six months follow up also pose restrictions concerning interpretation of causality and also may 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 research was approved by the institution's IRB; all participants' information was kept confidential and the level of risk in the study was kept to a minimum.

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Concept & Design of Study: Hasib Shamshad1

Drafting: Sadaf Shamshad2

Data Analysis: Hasib Shamshad1

Critical Review: Sadaf Shamshad2

Final Approval of version: Sadaf Shamshad2



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