

Original Research Article

Risk of dementia in patients taking beta blocker as antihypertensive treatment: a cross sectional study

Mervin K. Soman, Sankara Thiagarajan*, S. Priyanka, V. Subashini

Department of General Medicine, Saveetha Medical College and Hospital, Chennai, Tamilnadu, India

Received: 07 October 2019

Revised: 20 November 2019

Accepted: 28 November 2019

*Correspondence:

Dr. Sankara Thiagarajan,

E-mail: saran.param90@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Hypertension is considered to be the third most important disease in the list of diseases in the south Asian region. Several trials have shown active treatment of hypertension reduced the incidence of dementia. This study was adopted to understand the cognitive status of patients using beta blockers for hypertension for a period of more than 5 years.

Methods: The study was done during the period of August 2018 and September 2018. Patients taking beta blockers for atleast 5 years were included and was made to take the MMSE test which is scored out of 30 marks containing 11 questions, each of varying marks.

Results: In the study, 54 patients were included, 8 out of 54 patients taking beta blockers obtained a score of 30 which is 15% of the study population taking beta blockers, 15 out of 54 patients taking beta blockers obtained a score of 29 which corresponds to 28% of the study population, 21 out of 54 individuals taking beta blockers obtained a score of 28 which is 39% of the population taking it, 7 patients taking beta blockers obtained a score of 27 pertaining to 13% of the population. One patient obtained a score of 26 and two patients scored 25 out of 30. The average score obtained was 28.2963.

Conclusions: About 18.5% of the study population had scores below the average value of 28 in this study. This population is at higher risk of developing dementia in the future and need follow up.

Keywords: Atenolol, Beta blockers, Bisoprolol, Carvedilol, Cognition, Dementia, Hypertension

INTRODUCTION

Hypertension is considered to be the third most important disease in the list of diseases in the south Asian region.¹ In 2005, a study determined that 20.6% of Indian men and 20.9% of Indian women suffered from hypertension.² According to WHO studies, the percentage of Indian men suffering from hypertension had gone up to 33.2% in men and 31.7% in women. In total, the prevalence of hypertension in India was 32.5%.³ A review and meta-analysis study done in 2013 shows the prevalence to be 29.8%, in which the prevalence in rural population was shown to be 27.6 and in urban population it was shown to be 33.8. In this, only 25% of rural and 42% of urban

population undergo proper treatment for hypertension.⁴ In 2015 it was determined that one fourth of all men and one fifth of all women suffered from hypertension. This accounted to approximately 22% of the population. The prevalence of hypertension was only 18% in high income countries compared to the prevalence in low income countries which was 28%.⁵

According to world health organisation (WHO), the fraction of aged population is increasing in developing countries and dementia will become an epidemic. WHO has made a prediction that by 2025, 75% of the elderly population who belong to the developing countries would suffer from dementia. Also, the number of people

suffering from dementia will double every 20 years.⁶ Women have a higher risk of dementia compared to men in the age group 45-65.⁷

Beta blockers are a class of antihypertensive drugs which act on the beta receptors (either beta-1 or beta-2 or both) to reduce symptoms of hypertension in the patient by reduction of cardiac output and heart rate. Few beta blockers have additional alpha-1 blocking activity which cause vasodilation. CNS side effects of beta blockers are insomnia, hallucinations, depression and vivid dreams. This class of drugs are contraindicated in asthmatics, unstable heart failure, atrioventricular block and patients with sick sinus syndrome without a pacemaker. They also have the capability to block hypoglycaemic symptoms and cause glucose intolerance. Hence beta blockers are not used or used with caution in diabetic individuals.⁸

The Sys-Eur trial which started in 1988 showed that active treatment of hypertension reduced the incidence of dementia by 50%. It reduced from 7.7 to 3.3 cases per 1000 patient years. It was found that antihypertensive treatment in the elderly population having isolated systemic hypertension reduced the incidence of dementia. In this study, the drug nitrendipine was taken as first line medication. If necessary, the drug was replaced by enalapril as second line drug and/or hydrochlorothiazide as third line drug.⁹ The 1997 Rotterdam study showed that hypertension was related to onset of dementia. It proved that hypertension was a risk factor for dementia.¹⁰

Medical research council's treatment trial of hypertension (MRC) Project didn't show any difference in neuropsychometric test result in the 54-month long project. The drugs taken into account were beta blockers with or without diuretics. A similar study- systolic hypertension in the elderly program (SHEP) study also didn't get any major results regarding the effect of antihypertensive medications in preventing the onset of dementia.¹¹

Perindopril protection against recurrent stroke study showed positive results. This study was to determine the benefit of antihypertensive treatment among patients with a history of stroke. It was seen that there was a 19% decline in the risk of cognitive impairment when they were reviewed after 4 years. Perindopril and indapamide were the drugs utilised in this study.¹² Ertekin et al., have indicated that health related factors such as a family history of having dementia, Parkinson's disease and heart disease have also been associated with demential occurrence at latter part of life. He also have indicated that increasing age, members from low socio-economic status, poor education, and members from rural areas are associated with high risk of dementia.¹³ Heart outcome prevention evaluation (HOPE) study shows that 41% decline in cognitive impairment was seen when reviewed after 4.5 years. ACE inhibitor drug ramipril was used in this study.¹⁴

A recent study comparing ACE inhibitors and ARB drugs in Taipei showed that angiotensin receptor blockers are much better in preventing dementia than ACE inhibitors, but both drugs have the ability to prevent early onset of dementia.¹⁵ Having known all this, a methodical study was adopted to understand the cognitive status of patients using beta blockers for hypertension for a period of more than 5 years.

METHODS

The study was done in Saveetha Medical College Hospital during the period of August 2018 and September 2018. The study population was chosen among the hypertensive patients visiting Saveetha Medical College hospital, Thandalam. Proper informed consent was obtained from the patients prior to taking part in the study.

Research design

- Approval to conduct the study was obtained from institutional ethics committee.
- Patients who are eligible to take part in the study were invited.
- Proper explanation regarding the nature of study were given and the patient was given the choice of taking part in the study.
- Patients willing to take part were made to give a written informed consent.
- Detailed history of hypertension and mental illness was taken.
- Patient was made to take the MMSE test which is scored out of 30 marks containing 11 questions, each of varying marks.¹⁶ Assistance was provided when required in case of language barrier.
- The results were tabulated and analyzed statistically.

Inclusion criteria

- Patients between 55-65 years who are suffering from hypertension and taking beta blockers as antihypertensive medication.
- The patient must take the antihypertensive medication for at least 5 years.

Exclusion criteria

- Normotensive patients.
- Hypertensive patients who are not in the 55-65 years age group.
- Hypertensive patients who are taking antihypertensive drugs other than beta blockers.
- Patients already diagnosed with dementia or have a family history of dementia.
- Patients who have other mental illnesses like depression etc.
- Patients who are not willing to take part in the study.

It is a cross sectional study, not randomized, including 54 patients with the study duration of 2 months. There are no risks in the study. Benefits of the study are -

- Understanding the risk of dementia in the hypertensive population in the 55-65 years age group.
- People with the risk of dementia can be intimated in advance so that necessary lifestyle modifications can be made.

Expected outcome

To analyse use of beta blockers in preventing dementia and hence, a database would be provided which would help doctors to decide the best modality of treatment to delay/prevent the onset of dementia.

There were few limitations of this study only patients taking beta blockers are included in this study, patients taking other anti-hypertensive medications are not included. Patients in the age group 55-65 are included in this study. Small sample size was taken, and no control group was involved in the study.

RESULTS

In the study, 54 patients have been taking beta blockers, 8 out of 54 patients taking beta blockers have obtained a score of 30 which is 15% of the study population taking beta blockers, 15 out of 54 patients taking beta blockers have obtained a score of 29 which corresponds to 28% of the study population. The maximum number of beta blockers taking people have obtained a score of 28, 21 out of 54 individuals taking beta blockers have obtained a score of 28 which is 39% of the population taking it. 7 patients taking beta blockers have obtained a score of 27 pertaining to 13% of the population. One patient has obtained a score of 26 and two patients have scored 25 out of 30. The average score obtained was 28.2963 (Figure 1, Figure 2).

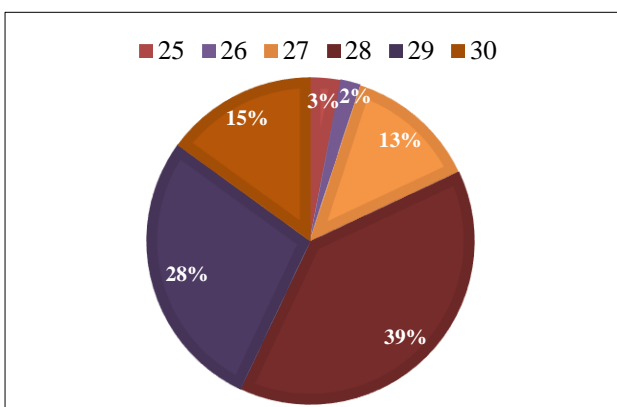


Figure 1: Score of beta blocker users.

In the study population, 27 of them were females. 6 patients out of 22 have got a score of 30 and 4 patients

have got a score of 29 pertaining to 27% and 18% respectively of the female population taking beta blockers. The maximum number of patients have obtained a score of 28. 9 patients have obtained a score of 28 which is 41% of the female population taking beta blockers. 2 patients have obtained a score of 27 whereas one patient has obtained a score of 26. The average score of this group is 28.5455 (Figure 3, Figure 4).

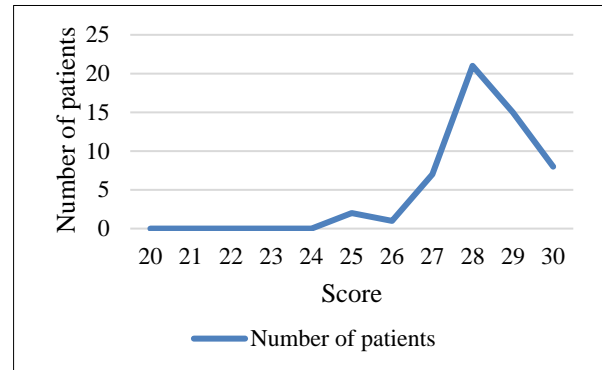


Figure 2: The score of patients taking beta blockers.

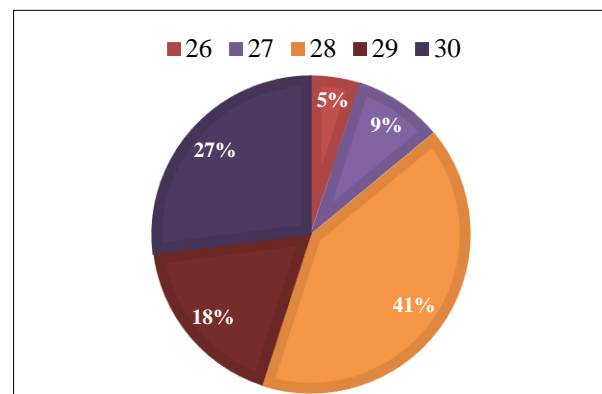


Figure 3: Score of women using beta blocker.

The standard deviation indicates show that the impact of the drug is the same in men and women.

The drugs which were studied among beta blockers were atenolol, bisoprolol and carvedilol. The average score of men taking atenolol is 28.16 whereas the standard deviation indicates for the same group is 0.75. The average score of men taking bisoprolol is 28.125 whereas the standard deviation indicates is 0.64. The average score of men taking carvedilol is 28.11 whereas the standard deviation indicates is 1.45. The average score of women taking atenolol is 28.75 and the standard deviation indicates is 1.164. The average score of women taking bisoprolol is 28 and the standard deviation indicates is 1.22. The average score of women taking carvedilol is 28.66 whereas the standard deviation indicates is 1.118. Among the men using beta blockers, atenolol users have the highest average score and carvedilol users have the highest standard deviation. Among women using beta blockers, atenolol users have

the highest average and bisoprolol users have the highest standard deviation indicates.

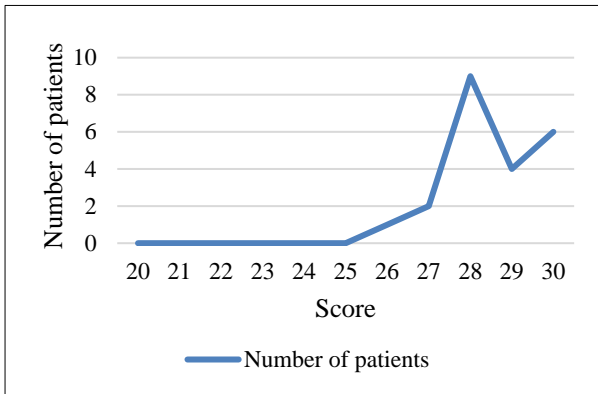


Figure 4: Number of female beta blocker users who have obtained each score.

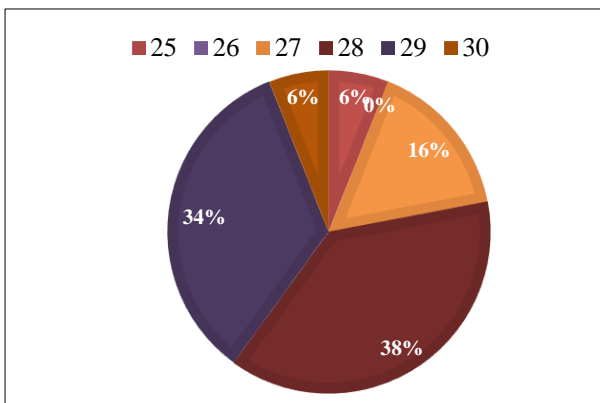


Figure 5: Score of men taking beta blockers.

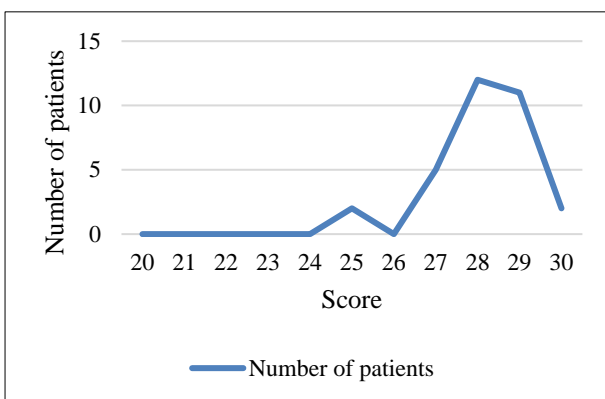


Figure 6: Number of male beta blocker users who have obtained each score.

The number of men who took part in the study were 32. 2 out of 32 men have obtained a score of 30, which is 6% of the population of men taking beta blockers, 11 men have obtained a score of 29 pertaining to 34% of the population of men taking beta blockers. The maximum number of men have obtained a score of 28, 12 men have obtained a score of 28 which is 38% of the men taking

beta blockers, 5 men have obtained a score of 27, which is 16% of the male patients taking beta blockers, 2 patients have obtained a score of 25. The average score obtained in this group is 28.125 (Figure 5, Figure 6).

DISCUSSION

According to ICD-10 classification of Mental and Behavioral Disorders, Dementia is a type of disorder, a progressive decline in memory, learning, orientation, language, comprehension, and judgment.¹⁷ This cause a health problem with substantial economic impact. Thus, a methodical questionnaire was prepared to acquire complete data to accrue important conclusions. Based on the scores, the degree of impairment is either questionably significant, mild, moderate or severe. The degree of impairment is considered questionably significant when the score is between 25 and 30. Such people may have clinically significant but mild deficits. There is a chance of disturbance only in the most demanding activities of day-to-day life. When the score is between 20 and 25, the person is said to have mild impairment. Such people might require some assistance in daily life along with supervision and support. If the score is between 10 and 20, the person is said to have moderate degree of impairment and may need 24 hour supervision. When the score is between 0 to 10, they are said to have severe impairment and would mostly not be testable.¹⁶

In the study conducted by the Medical Research Council (MRC) among 2584 elderly subjects over a time period of 54 months, no significant result was found in the neuropsychometric test done among the group treated with beta-blockers, and the placebo group. In the Systolic Hypertension in the Elderly Program (SHEP) study, there was no significant result among the group taking diuretics, the group taking beta blockers and the placebo group, although the risk was lower in the first group.¹⁰ The MRC study and the SHEP study was done in the European zone, where the genetic makeup of the population, habits and style of living is much different compared to the south Asian region. This study was done so as to understand the scenario in the South Indian region.

Also, the analysis of results based on comparing the effect of drugs on the dementia risk by considering only a single drug is difficult. In the given population, all patients have obtained scores between 25 and 30. 27% of female beta blocker users and 6% of male beta blocker users have obtained a score of 30. They do not show any significant deficits.

As the score of the person decreases, he/she has an increased possibility to end up with a cognition defect. The patients who have obtained scores in the lower side of the range have an increased risk of dementia than the rest of the study population. Among beta blocker users,

2% of patients have obtained a score of 26 and 3% of patients have obtained a score of 25.

This is the fraction of the study population which has obtained a score on the lower end. This fraction of people have an increased risk of getting dementia than the rest of the study population.

The standard deviation indicates in men is best for bisoprolol followed by atenolol and carvedilol. Among women taking beta blockers the standard deviation indicates is best for carvedilol followed by atenolol and bisoprolol. Thus, in beta blockers, bisoprolol plays a better role in reducing the risk of dementia in men and carvedilol plays a better role in reducing the risk of dementia in women.

CONCLUSION

About 18.5% of the study population had scores below the average value of 28 in this study. This population is at higher risk of developing dementia in the future and need follow up. Bisoprolol plays a better role in reducing the risk of dementia in men and carvedilol plays a better role in reducing the risk of dementia in women.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2224-60.
2. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005 Jan 15;365(9455):217-23.
3. Gupta R. Trends in hypertension epidemiology in India. *J Hum Hypertens*. 2004 Feb;18(2):73.
4. Anchala R, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, et al. Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. *J Hypertens*. 2014 Jun;32(6):1170-7.
5. Singh S, Shankar R, Singh GP. Prevalence and associated risk factors of hypertension: a cross-sectional study in urban Varanasi. *Inter J Hypertens*. 2017;2017.
6. Uludag A, Cevizci S, Uludag A. Epidemiology of Alzheimer's Disease with the Projection of Falls Among the Aged Population. *Alzheimer's Dis: Challenges Future*. 2015 Jul 1:1.
7. Podcasy JL, Epperson CN. Considering sex and gender in Alzheimer disease and other dementias. *Dialogues Clini Neurosci*. 2016 Dec;18(4):437.
8. Laurent S. Antihypertensive drugs. *Pharmacol Res*. 2017 Oct;124:116-125.
9. Forette F, Seux ML, Staessen JA, Thijs L, Birkenhäger WH, Babarskiene MR, et al. Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial. *Lancet*. 1998 Oct 24;352(9137):1347-51.
10. in't Veld BA, Ruitenberg A, Hofman A, Stricker BH, Breteler MM. *Neurobiol Aging*. 2001 May-Jun;22(3):407-12.
11. Hanon O, Forette F. Treatment of hypertension and prevention of dementia. *Alzheimer's Dementia*. 2005 Jul 1;1(1):30-7.
12. Tzourio C. Hypertension, cognitive decline, and dementia: an epidemiological perspective. *Dialogues Clini Neurosci*. 2007 Mar;9(1):61.
13. Ertekin A, Demir R, Özdemir G, Özel L, Özyıldırım E, Ulvi H. An investigation of the risk factors and prevalence of alzheimer's disease in the eastern region of Turkey: A population based door-to-door survey. *Europ J Gen Med*. 2015 Jul 6;12(2):144-51.
14. Rouch L, Cestac P, Hanon O, Cool C, Helmer C, Bouhanick B, et al. Antihypertensive drugs, prevention of cognitive decline and dementia: a systematic review of observational studies, randomized controlled trials and meta-analyses, with discussion of potential mechanisms. *CNS Drugs*. 2015 Feb 1;29(2):113-30.
15. Yi-Chun Kuana, Kuang-Wei Huang, Der-Jen Yen, Chaur-Jong Hu, Cheng-Li Ling, Chia-Hung Kao. Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers reduced dementia risk in patients with diabetes mellitus and hypertension. *International Journal of Cardiology* 220 (2016) 462–466.
16. Folstein MF, Folstein SE, McHugh PR. Mini-mental state: A practical method for grading the cognitivestate of patients for the clinician. *J Psychiatr Res*. 1975;12:189-98.
17. Dening T, Sandilyan MB. Dementia: definitions and types. *Nursing Standard* (2014+). 2015 May 13;29(37):37.

Cite this article as: Soman MK, Thiagarajan S, Priyanka S, Subashini V. Risk of dementia in patients taking beta blocker as antihypertensive treatment: a cross sectional study. *Int J Adv Med* 2020;7:6-10.