Original Research Article

Expert opinion on the clinical use of bisoprolol and telmisartan combination therapy in the management of hypertension in Indian settings

ABSTRACT

Background: Although there were clinical studies conducted on the efficacy and safety of bisoprolol and telmisartan combination, there were lack of studies among clinicians in actual practice. So, this study was conducted to gather expert opinions regarding the clinical use of bisoprolol and telmisartan combination therapy for hypertension management in Indian settings**.**

Methodology: The cross-sectional, multiple-response questionnaire-based study, consisting of 19-items, gathered expert opinions on current practices, clinical observations, and experiences related to the use of combination therapy of bisoprolol and telmisartan in routine settings for managing hypertension. The survey respondents were specialists with expertise in managing hypertension.

Results: Majority (98.9%) of the clinicians reported that telmisartan is the preferred angiotensin II receptor blocker (ARB) with bisoprolol. Around 84% of the respondents preferred telmisartan +bisoprolol as the ARB and beta-blocker combination therapy in patients with hypertension and cardiovascular conditions. More than half (50.82%) of the clinicians recommended combination of bisoprolol+ telmisartan as the second-line drug for hypertension management and about 47% of them advocated combination of telmisartan+ bisoprolol as the first-line drug. About 51% of clinicians believed that using the telmisartan + bisoprolol combination offers better cardiovascular protection than the telmisartan + metoprolol combination. Nearly 32% of clinicians stated that the fixed dose combination (FDC) of telmisartan + bisoprolol has the advantage of better blood pressure (BP) control.

Conclusion: The survey highlighted the clinician's preference for the telmisartan + bisoprolol combination in the management of hypertension and cardiovascular conditions. The respondents also underscored its clinical utilization as both first- second-line treatment, along with its capability to achieve improved blood pressure regulation.

Keywords: Hypertension, Bisoprolol, Telmisartan, Beta-blockers, Angiotensin II receptor blocker

1. INTRODUCTION

Hypertension significantly contributes to the emergence of non-communicable diseases and stands as a leading cause of premature death on a global scale. It accounts for 12.8% of worldwide fatalities, particularly impacting low- and middle-income countries. Among the 1.3

billion individuals with hypertension globally, 82% reside in these regions and fall within the 30 to 79 years age range. A crucial global target for non-communicable diseases is to reduce hypertension prevalence by 33% from 2010 to 2030 [1,2].

As per the 2016 estimates, hypertension was responsible for 53.8%, 55.7%, and 54.3% of deaths attributed to heart disease, stroke, and chronic kidney disease in India, respectively. With an estimated 220 million adults in India facing hypertension, the country has set a target for a 25% relative reduction in prevalence by 2025. Hypertension is a key risk factor for cardiovascular diseases (CVDs) globally, being the leading cause of death. CVDs account for one-third of total deaths in India, yet only 12% of the estimated 220 million people with hypertension in the country have their blood pressure (BP) under control [2-5]. It directly contributes to 57% of all stroke-related deaths and 24% of coronary heart disease (CHD) deaths in the country [6].

Most hypertension management guidelines suggest fixed-dose combinations for better patient compliance and BP control. Studies show that 75% of patients on single antihypertensive medication have poor BP management [7]. In India, the combination therapy of bisoprolol and telmisartan is recognized for hypertension management. Bisoprolol, a beta-blocker, and telmisartan, an angiotensin II receptor blocker (ARB), act synergistically to target multiple pathways in BP regulation, leading to improved control [8].

By reducing the pill burden, the combination therapy enhances treatment adherence, which is essential for long-term BP control and prevention of complications. Bisoprolol reduces heart rate and contractility, while telmisartan blocks the effects of angiotensin II, resulting in vasodilation and decreased fluid retention. By balancing the vasodilatory effect of telmisartan with the potential for increased peripheral vascular resistance caused by beta-blockers like bisoprolol, the combination therapy minimizes the incidence of adverse effects, improving patient tolerability [9,10].

The present cross-sectional survey aims to gather expert opinions on the prescription practice of antihypertensive medication, especially bisoprolol and telmisartan combination therapy for hypertension management in Indian settings.

2. MATERIALS AND METHODS

We carried out a cross sectional, multiple-response questionnaire-based study involved experts in the management of hypertensionin the major Indian cities from June 2023 to December 2023.

2.1 Questionnaire

The questionnaire booklet titled BEST (Bisoprolol and Telmisartan in management of Hypertension) study was sent to the physicians who were interested to participate. The BESTstudy questionnaire comprised of19-item survey primarily focused on current practices, clinical observations, and experiences related to the use of the bisoprolol and telmisartan combination in routine settings for the management of hypertension. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

2.2 Participants

An invitation was sent to leading physicians in treatinghypertensionin the month of March 2023 for participation in this Indian survey. About 913clinicians from major cities of all Indian

states representing the geographical distribution shared their willingness to participate and provide necessary data. Clinical Practitionerswere asked to complete the questionnaire without discussing with their peers. A written informed consent was obtained from each doctors before initiation of the study.

2.3 Statistical Methods

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to provide a clear insight into their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, graphs were created using Microsoft Excel 2013 (version 16.0.13901.20400).

3. RESULTS

The survey included 913 clinicians, with 52% of them reporting that 11 to 20% of patients with hypertension have a high risk of CVDs. Nearly 71% of the clinicians reported bisoprolol as the preferred choice of beta-blockers in their clinical practice and 44% of the respondents stated that they have been using bisoprolol for 2 to 5 years. Around 59% of the clinicians responded that 11 to 20% of patients with hypertension are on bisoprolol in their clinical practice. About 83% of the clinicians opined with definite improvement in BP in patients with the use of bisoprolol. Approximately 59% of respondents opined that 25 to 50% of patients require two drugs in the treatment of hypertension. The majority (98.9%) of the clinicians reported that telmisartan is the preferred ARB with bisoprolol (Figure 1).

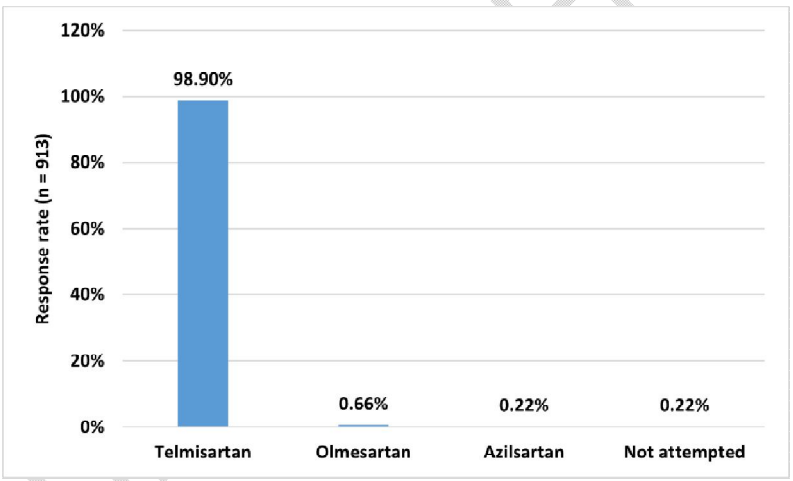

Figure 1. Distribution of response on the preferred ARB with bisoprolol

Around 48% of the respondents preferred the combination of ARB with beta-blocker in patients with uncontrolled hypertension, in young patients with newly diagnosed hypertension, and in hypertensive patients with increased risk of cardiovascular risk. As reported by 69% of the clinicians, the common reason for initiating combination therapy is to ease achieving BP goals. About 50% of the respondents reported preferring a fixed-dose combination of telmisartan and bisoprolol for patients with hypertension and comorbidities

such as diabetes, cardiovascular complications, renal complications, and respiratory conditions.

Around 45% of the clinicians reported that 21 to 30% of the patients with hypertension comorbid diabetes were on ARB and beta-blocker combination therapy. About 69% of the clinicians prefer telmisartan and bisoprolol fixed-dose combination (FDC) in hypertension management for the age group of 35 to 50 years. The majority (81.93%) of the clinicians preferred bisoprolol beta-blocker in patients with respiratory conditions.

About 84% of the respondents preferred using telmisartan +bisoprolol as the ARB +beta blocker combination in patients with hypertension and cardiovascular conditions (Table 1). More than half (50.82%) of the clinicians recommended combination of bisoprolol+ telmisartan as the second-line drug for hypertension management and about 47% of them preferred a combination of telmisartan+ bisoprolol as the first-line drug (Figure 2). As reported by 51% of the clinicians, the advantage of using the telmisartan + bisoprolol combination over the telmisartan + metoprolol combination is better cardiovascular protection.

Table 1: Distribution of response on the preference of ARB + beta-blocker in patients with hypertension and cardiovascular conditions

Preference of ARB + beta-blocker	Response rate (n = 913)
Telmisartan + bisoprolol	84.34%
Telmisartan + nebivolol	0.99%
Telmisartan + metoprolol	14.02%
Telmisartan + carvedilol	0.55%

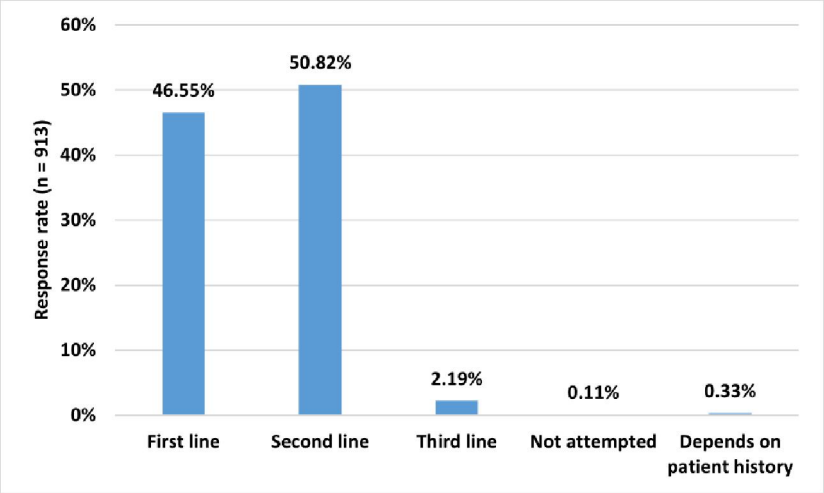

Figure 2: Distribution of response on the position of bisoprolol + telmisartan in hypertension management

For educating patients with hypertension, about 33% of the clinicians preferred forming small group interactive sessions. Nearly 46% of clinicians considered the lack of patient education as the cause of non-adherence to medication in patients with hypertension. About 32% of the clinicians opined that the advantages of the FDC of telmisartan + bisoprolol include better BP control (Table 2).

Table 2: Distribution of response on the advantage of FDC of telmisartan+ bisoprolol

Advantages	Response rate (n = 913)
Complement each other well	23.44%
Better BP control	32.31%
Acts on two different pathways	3.29%
Cardiovascular protection	8.43%
Useful in comorbid conditions like diabetes	2.52%
Useful in comorbid conditions like asthma	0.88%
Improves patient compliance	5.37%
All the above	23.66%

4. DISCUSSION

The survey findings underscored the preference for the telmisartan + bisoprolol combination in managing hypertension in Indian settings. The study highlighted medication adherence as a critical factor in achieving successful therapeutic outcomes for hypertensive patients and reported telmisartan as the preferred ARB combination with bisoprolol. This finding is consistent with previous research by Strauss et al., who emphasized that combining these well-established antihypertensive medications into a single pill remains effective in lowering blood pressure and enhancing cardiovascular outcomes [11]. Kadam et al. stated that telmisartan offers several benefits over alternative antihypertensive medications. Its superior

tolerability and reduced incidence of side effects make it a preferred option for numerous patients [12].

The survey also noted that combination therapy enables a larger percentage of patients to promptly attain their treatment goals **[**11]. In a cross-sectional study, it was found that nearly 95% of participants favored telmisartan as their preferred ARB among the commonly used options [1]. Wright et al. found that the addition of β-blockers to a regimen of ACE inhibitors or ARBs adequately controls BP in almost 40% of patients with diabetes and hypertension [13].

The current respondents stated that combining ARBs with beta blockers effectively manages uncontrolled hypertension in young patients with newly diagnosed hypertension and those at increased cardiovascular risk. Similarly, Tucker et al. found that respondents recommended bisoprolol dosages of 5 mg and 2.5 mg for hypertensive patients with cardiovascular risk. Bisoprolol's selectivity for beta-1 adrenergic receptors, primarily in the heart, is believed to contribute to its efficacy in reducing heart rate and BP, potentially leading to improved outcomes [14].

Literature evidence has corroborated the advantages of using beta-blockers and ACE inhibitors in patients with hypertension, elevated heart rate, coronary artery disease (CAD), atrial fibrillation (AF), and heart failure. Combining these agents into a single pill offers a valuable treatment option for various patient profiles, enabling faster attainment of target heart rate and BP levels, while concurrently lowering the risk of cardiac events [11]. The present survey has also reported similar findings regarding the FDC of telmisartan and bisoprolol for patients with hypertension and comorbidities.

The present survey also observed that telmisartan +bisoprolol combination is an effective ARB +beta blocker for the management of hypertension. In line with these findings, a survey on expert opinion of clinicians in Indian settings observed that although telmisartan was the preferred choice as an ARB, bisoprolol was favored as the beta-blocker for newly diagnosed hypertension patients. The combination of bisoprolol + telmisartan has been shown to be effective in managing hypertension, reducing cardiovascular risk, and improving organs.[1] Similarly, Sawhney et al. concluded that bisoprolol in combination with telmisartan is a useful tool to manage hypertension and comorbidities [15]. Several studies have concluded that in the management of hypertension, the combination of the beta blocker, bisoprolol, and the ARB, telmisartan has garnered attention. According to the majority of respondents in the current study, the bisoprolol + telmisartan combination demonstrated a reduction in cardiovascular risk [16,15]. Bodh I Jigdutt reported that the combination of telmisartan is a promising drug for controlling hypertension and reducing vascular risk in high-risk elderly patients [17].

In the present survey, it was observed that the combination of telmisartan + bisoprolol is used both as first- and second-line treatment for hypertension management. It was noted that the advantage of using the telmisartan + bisoprolol combination is better cardiovascular protection and improved BP control. Similarly, there was a significant decrease in cardiovascular risk among patients administered the combination of bisoprolol and telmisartan, highlighting the treatment's potential to safeguard target organs impacted by hypertension, such as the heart, kidneys, and blood vessels. There are limited studies on this specific drug combination, and the synergistic effects of both drugs are expected to provide optimal BP control. Channaraya et al. concluded that bisoprolol serves as a safe and effective means of BP control, suggesting its suitability as a primary antihypertensive option for Indian patients [18]. Similarly, Ramakrishnan et al. advocated the use of ARBs as first-

line treatment, either alone or in conjunction with other antihypertensive medications, in managing essential hypertension in Indian settings [19].

The present survey offers valuable insights into the use of a combination of bisoprolol and telmisartan in managing hypertension in Indian settings, based on clinician preferences and prescription practices. It may aid in decision-making and optimizing treatment strategies and patient care. The major strength of the present survey is the utilization of a meticulously designed and validated questionnaire for data collection. However, it is crucial to acknowledge certain limitations. Relying on expert opinion introduces potential bias, as diverse clinician perspectives may have influenced the reported findings. Additionally, the survey may not fully capture evolving trends or emerging evidence in hypertension management. To address these limitations, prospective trials or real-world observational studies are necessary to validate the survey results and provide a more comprehensive understanding of optimal treatment approaches.

4. CONCLUSION

The survey has emphasized the effectiveness and preference for the telmisartan + bisoprolol combination as the preferred FDC for patients with hypertension and its associated comorbidities. It has also underscored the benefits of the combination, such as reducing cardiovascular risk, decreasing blood pressure levels, and enhancing organ function.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

REFERENCES

1. Manjula S, Krishna Kumar M. Expert Opinion on the use of Bisoprolol-Telmisartan Combination in Indian Patients with Hypertension. Indian J Cardio Biol Clin Sci. 2024;7(1): 113.
2. Varghese JS, Venkateshmurthy NS, Sudharsanan N, Jeemon P, Patel SA, Thirumurthy H, et al. Hypertension Diagnosis, Treatment, and Control in India. JAMA Netw Open. 2023 Oct 23;6(10):e2339098.
3. Hypertension [Internet]. [cited 2024 Mar 22]. Available from: https://www.who.int/india/health-topics/hypertension
4. Chakraborty S, Ussatayeva G, Lee MS, Dalal K. Hypertension: A National Cross-Sectional Study in India. Turk Kardiyol Dern Ars. 2022 Jun;50(4):276-283.
5. Varghese JS, Venkateshmurthy NS, Sudharsanan N, Jeemon P, et al. Hypertension Diagnosis, Treatment, and Control in India. JAMA Netw Open. 2023 Oct 2;6(10):e2339098.

6. Anchala R, Kannuri NK, Pant H, Khan H, 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.
7. Gorostidi M, de la Sierra A. Combination therapy in hypertension. Adv Ther. 2013 Apr;30(4):320–36.
8. Gradman AH, Basile JN, Carter BL, Bakris GL, Group on behalf of the AS of HW. Combination Therapy in Hypertension. The Journal of Clinical Hypertension. 2011;13(3):146–54.
9. Bazroon AA, Alrashidi NF. Bisoprolol. [Updated 2023 Aug 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551623/
10. Baguet JP, Ormezzano O, Barone-Rochette G. Impact of telmisartan in modifying vascular risk. Integr Blood Press Control. 2010 Jun 15;3:81–9.
11. Strauss MH, Hall AS, Narkiewicz K. The Combination of Beta-Blockers and ACE Inhibitors Across the Spectrum of Cardiovascular Diseases. Cardiovasc Drugs Ther. 2023;37(4):757–70.
12. Kadam S, Boppana SS, Manna S, Datta S, Karande S. Management of hypertension: Comparison of Telmisartan with other antihypertensive drugs. Medico Research Chronicles. 2022 Apr 9;9(2):88–93.
13. Wright Jr JT, Bakris GL, Bell DSH, Fonseca V, Katholi RE, McGill JB, et al. Lowering Blood Pressure With β-Blockers in Combination With Other Renin-Angiotensin System Blockers in Patients With Hypertension and Type 2 Diabetes: Results From the GEMINI Trial. The Journal of Clinical Hypertension. 2007;9(11):842–9.
14. Tucker WD, Sankar P, TheethaKariyanna P. Selective Beta-1 Blockers. [Updated 2023 Jan 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499982/
15. Sawhney J, Garg R, Makkar J, Dani S, Guha S, Dalal J, et al. Consensus towards the utilisation of bisoprolol in combination with telmisartan in Indian patients with hypertension. Journal of Hypertension. 2023 Jun;41(Suppl 3):e122.
16. Bangalore S, Kamalakkannan G, Parkar S, Messerli FH. Fixed-dose combinations improve medication compliance: a meta-analysis. Am J Med. 2007 Aug;120(8):713–9.
17. Jugdutt BI. Clinical effectiveness of telmisartan alone or in combination therapy for controlling blood pressure and vascular risk in the elderly. Clin Interv Aging. 2010;5:403–16.
18. Channaraya V, Marya RK, Somasundaram M, Mitra D, Tibrewala KD, BRIGHT investigators. Efficacy and tolerability of a β-1 selective β blocker, bisoprolol, as a first-line antihypertensive in Indian patients diagnosed with essential hypertension

(BRIGHT): an open-label, multicentric observational study. BMJ Open. 2012;2(3):e000683.

19. Ramakrishnan S, Ingole S, Dey A, Jain R. Management of Hypertension: Insights Into Prescribing Behavior with Focus on Angiotensin Receptor Blockers. Journal of the Practice of Cardiovascular Sciences. 2017 Apr;3(1):22..