International Journal of Advances in Medicine
Ramesh D et al. Int J Adv Med. 2022 Mar;9(3):249-252
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20220426

Original Research Article

Nationwide surveillance for S-Metoprolol treatment effect on blood pressure control against sympathetic overdrive in Indian patients with hypertension (PROTECT)

D. Ramesh[1], Parminder Singh Kumar[2], Priya Palimkar[3], Krishna Dhoot[4], Dhammdeep C. Dabhade[5]*, Sanket Newale[6]

[1]Department of Cardiology, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India
[2]Consultant Cardiologist, Ayaan Cardiac Center, Nanded, Maharashtra, India
[3]Interventional Cardiologist, Jehangir Hospital, Pune, Maharashtra, India
[4]Cardiologist, Hrudaysparsh Heart Care Centre, Pune, Maharashtra, India
[5]Senior Medical Advisor, Medical Services, Emcure Pharmaceuticals Limited, Pune, Maharashtra, India
[6]Deputy General Manager, Medical Services, Emcure Pharmaceuticals Limited, Pune, Maharashtra, India

Received: 03 February 2022
Revised: 19 February 2022
Accepted: 21 February 2022

***Correspondence:**
Dr. Dhammdeep C. Dabhade,
E-mail: dhammadeep.dabhade@emcure.co.in

ABSTRACT

Background: Patients with hypertension in India been reported with high heart rate owing to sympathetic overdrive (SO). Beta-blockers provides several positive effects to reduce SO in patients with hypertension. The aim of present survey study was to understand current real-world prevalence of SO in Indian patients with hypertension and usage of beta-blocker therapy in them.
Methods: A cross sectional, observational, questionnaire-based survey conducted across India between June 2020 to October 2020. A specially designed validated questionnaire was shared with 157 registered health care practitioners (HCP), their anonymous inputs were captured and analysed in qualitative manner. Categorical data was summarized by number (n) and percentage (%).
Results: Total 157 HCP participated and completed the survey. Around 53% of HCP observed that patients with average heart rate above 75 beats/min were associated with negative prognosis. Around 43% of HCP reported that raised heart rate is associated with advanced age and increased body mass index (BMI). Two-third of HCP reported that tachycardia is associated with stage-2 hypertension and marked by restlessness and anxiety which is suggestive of SO. Over 70% HCP agreed that the HR below 75 beats/min is associated with good prognosis. Around 89% HCP reported beta-blockers as the drug of choice in patients with augmented SO. S-Metoprolol was reported to be the most preferred beta-blocker agent and was recommended by 76% HCP in patients with hypertension and coexisting SO.
Conclusions: SO been reported prevalent condition in Indian patients with hypertension which likely worsens the prognosis in these patients. Beta-blockers reported to be the preferred choice of anti-hypertensive and S-Metoprolol seem to be the most preferred agent amongst the available beta-blockers against SO in patients with hypertension in India.

Keywords: Hypertension, Sympathetic overdrive, Beta-blocker, S-Metoprolol, PROTECT

INTRODUCTION

Persistent elevated heart rate is an independent risk factor for adverse clinical outcomes in cardiovascular diseases (CVD). Hypertension is one of the most important independent predictors of CVD and cerebrovascular events. It accounts for an estimated 54% of all strokes and 47% of all ischemic heart disease events globally.[1] A large

body of evidence has shown that resting heart rate (RHR) holds important prognostic factor in several clinical conditions and specifically, an over activation of sympathetic nervous system (SNS) is strongly associated with essential hypertension.

In majority of studies involving general population, a graded association between RHR and mortality from all causes, CVD, ischemic heart disease, stroke etc. has been observed. These associations appeared even stronger and more consistent in hypertensive patients. Studies performed with 24-hour ambulatory recording have shown that an elevated night-time heart rate may confer an additional risk to RHR. Fast RHR is a strong predictor of future hypertension, metabolic disturbances, obesity, and diabetes.[2] Reported evidence point to high RHR as a main risk factor for the development of atherosclerosis, large artery stiffness, and CVD.[2,3]

Patient with hypertension would benefit from a treatment which decreases RHR in addition to anti-hypertensive action. Modulation of sympathetic activation is considered an important goal of antihypertensive therapy, particularly in young or middle-aged patients.[4] Beta blockers are recommended as an initial therapy by various hypertension guidelines such as European (ESH/ESC 2013), Canadian (CHEP 2015) etc.[5-7] UK guidelines (NICE 2019) specifically recommend beta blockers for hypertension in younger patients with SO.[8]

Available evidence showing the relationship between resting HR and clinical outcomes in patients with hypertension been predominantly confined to the caucasian population. In this situation, beta-blockers conceivably have an important role. This knowledge, attitude and practice survey aimed to understand the real-world prevalence of sympathetic overdrive (SO) in patients with hypertension and usage of beta-blocker therapy in such patients in India.

METHODS

This was a cross sectional, observational, questionnaire-based survey conducted across India between June 2020 to October 2020. The survey was facilitated by the authors. Registered medical practitioners with recognized qualifications in cardiology, internal medicine or diabetology and working in outpatient departments of public and privately run clinics/hospitals participated in this survey. The survey consisted of total 157 HCPs across India.

Survey questionnaire design

The survey questionnaire was specially designed with reference to a format cited at hands-on guide to questionnaire research.[9] Around 10 multiple choice questions were designed. The salient features of the questionnaire included information regarding proportion of patients with hypertension also noted with high resting heart rate (HR), association of resting HR with prognosis, observed stage of hypertension linked with increased HR, observed common symptom of increased HR, subset of patients of hypertension linked with increased HR, preferred therapy in hypertensive patients with evidence of increased sympathetic overdrive and the most efficacious beta-blocker in reducing HR.

All participating HCPs attempted survey questionnaire; based on their knowledge, attitude and practice regarding prevalence of SO in patients of hypertension in India and usage of beta-blocker therapy in Indian patients with hypertension. HCPs were approached for seeking their perception, opinions, and prescribing behaviour. The HCPs were explained about the purpose of the study; if interested and willing, they were requested to complete the validated questionnaire which was collected back and analysed.

This was a voluntary knowledge, attitude and practice (KAP) survey and therefore it was not necessary to answer all the questions and participants were free to choose more than one response to a question if desired and suitable. As this was a cross-sectional survey and no patient data was obtained, ethics committee approval was not taken.

Statistical analysis

Data was entered with the help of Microsoft excel. Descriptive statistics were used to summarize the qualitative data by number and percentage for each category in each question. The denominator for calculating proportion for a particular question was total number of participants replied to a particular question.

RESULTS

Total 157 HCP completed with the survey questionnaire. Demographic characteristic of participants is depicted in Table 1. Around 50% of HCPs reported that almost 25% of patients with hypertension been associated with high resting heart rate (Figure 1).

Around 53% of HCP observed that patients with average heart rate above 75 beats/min were associated with bad prognosis. Forty-three percentage of HCP reported that raised heart rate is accompanied by advance age and increased BMI. Around 70% HCPs reported that tachycardia is associated with stage-2 hypertension and marked by restlessness and anxiety suggestive of SO as the major reason behind the increased heart rate. Majority of HCP (70%) agreed that the HR below 75 beats/min is associated with good prognosis in patients with hypertension. While choosing the anti-hypertensive drug, 89% HCP reported that beta-blockers should be the drug of choice in patients with augmented SO.

Amongst beta-blockers, S-Metoprolol was reported to be most efficacious drug and recommended by 76.6% HCP in patients with hypertension and sympathetic overdrive (Figure 2).

Table 1: Demographic characteristic of participants.

Category of participant	No. of participants (N)
Cardiologists	013
Consulting physicians	135
Diabetologists	009
Total	157

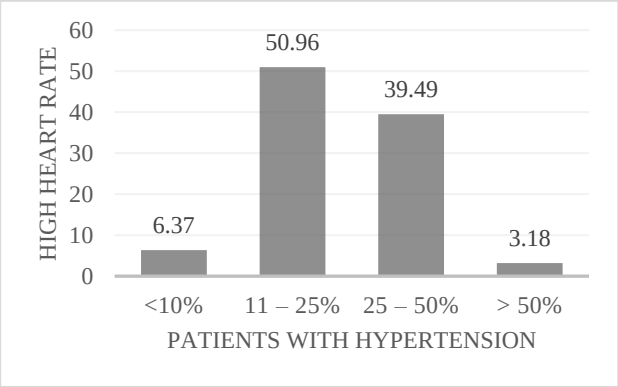

Figure 1: Percentage of high resting heart rate in patients with hypertension.

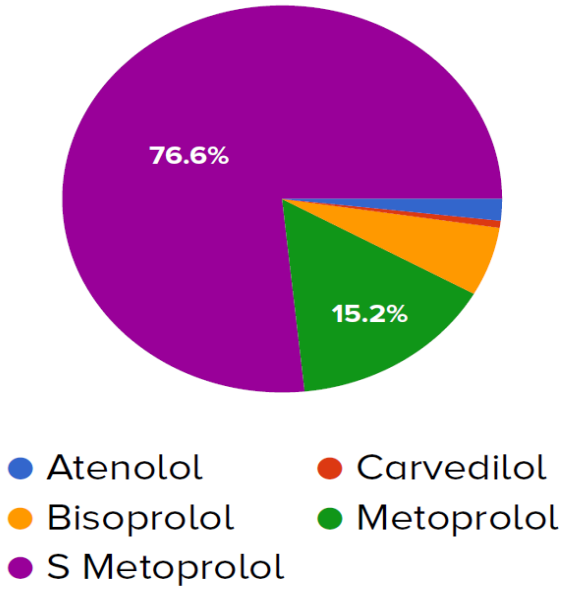

Figure 2: Preferred beta-blocker therapy (based upon the observed efficacy).

DISCUSSION

Sympathetic neural factors played an important role in blood pressure (BP) regulation. Dysregulation in sympathetic function may favour the development and progression of the hypertensive state. The hyperadrenergic state may aggravate hypertension-related CV risk. Adrenergic overdrive may favour the occurrence of end-organ damage.[10] Reported prevalence of higher resting heart rate is in line with the recently published India Heart study which has reported higher than average resting heart rate of 80 beats per minute in Indian patients with hypertension.[11]

Available Indian epidemiological data suggests the ongoing epidemic of uncontrolled hypertension, strongly leading to various CV complications. Almost 71% higher risk of death attributable to cerebrovascular disease and around 31% higher risk of death attributable to CVD in uncontrolled hypertensives in India.[12]

Therapeutic interventions should favourably interfere with sympathetic function. Modulation of SO represent an important goal of antihypertensive treatment additive to BP control, allowing to achieve greater CV protection. Beta-blockers seem to have a promising role in counteracting the SO via reducing the sympathetic nerve activity in patients with hypertension.[13]

Beta-blockers are recommended as a first-line antihypertensive therapy in young patients, particularly those with tachycardia.[7] NICE guidelines recommend beta-blockers as initial therapy for hypertension in younger people. The guidelines recommend that beta-blockers should be considered for initial therapy of hypertension in younger people, particularly when there is evidence of increased sympathetic drive, in those with an intolerance or contraindication to ACE inhibitors and angiotensin II receptor antagonists, in women of childbearing potential.[8]

The use of beta-blocker like Metoprolol succinate in the treatment of hypertension is supported by a large amount of published evidence and clinical experience. In a reported evidence Metoprolol been observed to be the most commonly prescribed antihypertensive drug with the average reduction in systolic and diastolic BP from the first to the third visit was 24.61 and 13.99 mmHg respectively in an Indian scenario and in the same study the average reduction in heart rate for this particular subpopulation was found to be 14.53 bpm.[13] S-Metoprolol is the chirally pure beta-blocker with certain clinical advantages and seem to have a beneficial role in hypertension associated with sympathetic overdrive.[15] S-Metoprolol seem to be the most efficacious among beta-blockers to reduce SO in patients with hypertension in the current study.

Clinical studies have demonstrated that S-Metoprolol verses racemate form exhibit different pharmacokinetic and metabolic profiles, reduced adverse events, improved safety profiles and similar therapeutic activity at lowered drug dosage. S-Metoprolol being chirally pure enantiomer, exhibit greater affinity and higher beta-1 receptor blocking activity than the R isomer with S: R activity ratio being 33:1.[16] The Pan-India coverage and participation of a large number of consulting physicians and cardiologists are some of the strengths of this study. The present KAP survey was cost-effective and the results were based on real-life experiences of HCPs.

Limitation

This survey study had certain limitation such as inclusion of fixed number of questions with predefined options and recall bias. Survey questionnaire were designed to match observations in clinical practice and was based on a subjective opinion. Nevertheless, this was an attempt to understand the knowledge, attitude and practice of Indian HCP towards current real-world prevalence of SO in Indian patients of hypertension and usage of beta-blocker therapy, which revealed some known facts. However, these findings must be considered cautiously and can be further confirmed by relevant clinical studies.

CONCLUSION

Sympathetic overdrive is usually prevalent in Indian patients with hypertension which likely worsen the prognosis. Beta-blocker provides several positive effects to hinder overactivity of sympathetic nerve in patients with hypertension. S-Metoprolol seem to be the effective therapeutic option in management of sympathetic overdrive in hypertension.

ACKNOWLEDGEMENTS

Authors gratefully acknowledge and thank the 157 HCPs across India who participated in this survey, Dr. Onkar Swami (Emcure Pharmaceuticals Ltd, Pune) for his guidance during development of this manuscript and Mr. Laxman Patil (Emcure Pharmaceuticals Ltd, Pune) for providing the administrative support during the conduct of this survey.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Palatini P. Resting Heart Rate as a Cardiovascular Risk Factor in Hypertensive Patients: An Update. Am J Hypertens. 2021;34(4):307-17.
2. Cooney MT, Vartiainen E, Laatikainen T, Juolevi A, Dudina A, Graham IM. Elevated resting heart rate is an independent risk factor for cardiovascular disease in healthy men and women. Am Heart J. 2010;159(4):612-9.
3. Palatini P. Elevated heart rate: a "new" cardiovascular risk factor? Prog Cardiovasc Dis. 2009;52(1):1-5.
4. Grassi G. Sympathomodulatory Effects of Antihypertensive Drug Treatment. Am J Hypertens. 2016;29(6):665-75.
5. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2013;31(7):1281-357.
6. Houle SK, Padwal R, Poirier L, Tsuyuki RT. The 2015 Canadian Hypertension Education Program (CHEP) guidelines for pharmacists: An update. Can Pharm J (Ott). 2015;148(4):180-6.
7. Ibrahim MM. The Egyptian hypertension society: Egyptian hypertension guidelines. Egypt Heart J. 2014; 66(2):79-132
8. NICE. Hypertension in adults: diagnosis and management. London: National Institute for Health and Care Excellence; 2019.
9. Boynton PM, Greenhalgh T. Selecting, designing, and developing your questionnaire. BMJ. 2004;328(7451):1312-5.
10. Mancia G, Grassi G, Giannattasio C, Seravalle G. Sympathetic activation in the pathogenesis of hypertension and progression of organ damage. Hypertension. 1999;34(4):724-8.
11. Kaul U, Wander GS, Sinha N, Mohan JC, Kumar S, Dani S, et al. Self-blood pressure measurement as compared to office blood pressure measurement in a large Indian population; the India Heart Study. J Hypertens. 2020;38(7):1262-70.
12. SPRINT Research Group, Wright JT, Williamson JD, Whelton PK, Snyder JK, Sink KM, et al. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med. 2015;373(22):2103-16.
13. Mann SJ. Redefining beta-blocker use in hypertension: selecting the right beta-blocker and the right patient. J Am Soc Hypertens. 2017;11(1):54-65.
14. Padmanabhan TN, Dani S, Chopra VK, Guha S, Vasnawala H, Ammar R. Prevalence of sympathetic overactivity in hypertensive patients - a pan India, non-interventional, cross sectional study. Indian Heart J. 2014;66(6):686-90.
15. Dasbiswas A, Shinde S, Dasbiswas D. S-Metoprolol: the 2008 clinical review. J Indian Med Assoc. 2008;106(4):259-62.
16. Mohan JC, Shah SN, Chinchansurkar S, Dey A, Jain R. Rediscovering Chirality - Role of S-Metoprolol in Cardiovascular Disease Management. J Assoc Physicians India. 2017;65(6):74-9.

Cite this article as: Ramesh D, Kumar PS, Palimkar P, Dhoot K, Dabhade DC, Newale S. Nationwide surveillance for S-Metoprolol treatment effect on blood pressure control against sympathetic overdrive in Indian patients with hypertension (PROTECT). Int J Adv Med 2022;9:249-52.