International Journal of Advances in Medicine
Kathiresan M et al. Int J Adv Med. 2023 May;10(5):367-376
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20231071

Original Research Article

Management of hypertensive patients with ischemic heart disease and the role of a fixed-dose combination of telmisartan and metoprolol: a physician-based research survey

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Received: 18 October 2022
Revised: 02 February 2023
Accepted: 09 February 2023

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ABSTRACT

Background: We aimed to understand the current practices of Indian practitioners in the management of hypertensive patients with ischemic heart disease.
Methods: A quantitative, cross-sectional, questionnaire-based survey involving 145 cardiologists and consulting physicians who each saw 10 patients with hypertension and IHD in their clinical practice was conducted. The questionnaire consisted of 35 questions divided into three sections on prevalence and treatment of hypertension and IHD and role of fixed-dose combinations in therapy.
Results: In all, 49.0% of physicians treated 25%-50% patients with hypertension and IHD in their routine practice, majority of whom were in the age group of 40-60 years regardless of gender. Telmisartan (97.0%) and metoprolol (86.0%) were the most preferred angiotensin receptor blocker (ARB) and beta-blocker, respectively, and 91.0% of physicians preferred a combination of metoprolol with telmisartan when monotherapy fails. In the opinion of the physicians, prevention of new cardiovascular events (63.0%) and improvement in quality of life (61.0%) were the leading benefits of telmisartan and metoprolol FDC, and all agreed that this FDC improves patient compliance and adherence to therapy. Furthermore, 97.0%, 90.0%, and 40.0% of physicians agreed/strongly agreed that the FDC could be prescribed to hypertensive patients with IHD, heart failure, and IHD and diabetes, respectively.
Conclusions: In this pan-India survey, it was observed that FDCs of telmisartan and metoprolol could help in improving blood pressure, heart rate, patient compliance, and adherence to therapy. Nevertheless, large-scale, prospectively designed studies are warranted to validate these findings.

Keywords: Hypertension, Ischemic heart disease, Telmisartan, Metoprolol, Cardiovascular events, Angiotensin receptor blocker, Beta-blocker

INTRODUCTION

Hypertension is a significant risk factor for cardiovascular disease (CVD) and chronic renal disease, accounting for about 7 million deaths and 57 million disability adjusted life-years worldwide each year. The burden of hypertension is most acute in the Asian Pacific region, which accounts for 60% of the global population and has seen a significant increase in the incidence of hypertension in recent decades.[1] Hypertension increases the risk of heart

attack, stroke, kidney disease and heart failure (HF) and is the leading preventable risk factor for global cardiovascular (CV) disease burden worldwide. Each 20 mmHg increase in systolic blood pressure (SBP) between the ages of 40 and 69 years is related with a more than doubling of the baseline fatality rate from CVD.[2] Hypertension is a ubiquitous risk factor for ischemic heart disease (IHD). Among other Framingham risk factors of tobacco use, diabetes mellitus (DM), dyslipidemia, and left ventricular hypertrophy (LVH), hypertension plays an independent role in augmenting IHD risk, as well as acts as a multiplier for adverse outcomes when present concurrently with other key risk factors for IHD. In addition to the typical IHD risk factors, hypertension adds to increased myocardial oxygen demand as a result of increased myocardial workload, which is commonly characterized as after load or the aortic resistance to left ventricular ejection. When combined with increased work done by the heart due to hypertension, the already reduced coronary blood flow (as a result of the coronary artery stenosis-mediated drop in myocardial oxygen supply) may result in an oxygen supply-demand mismatch, resulting in symptoms of angina or myocardial infarction.[3] There is a strong epidemiological relationship between IHD and hypertension.[4] A registry-based analysis of over 1.25 million patients revealed that IHD (angina and myocardial infarction-MI) accounted for a significant number of cardiovascular disease-free years of life lost due to hypertension from the age of 30 years.[5] Most of the agents that reduce blood pressure correspondingly lower myocardial workload. As a result, in the context of IHD, a pharmacotherapeutic strategy targeted to reduce myocardial oxygen consumption (by reducing blood pressure) is quite advantageous. beta-blockers exhibit a special advantage in patients with IHD because beta-blockers lower both heart rate and cardiac inotropy.[3] Angiotensin receptor blockers (ARBs) have shown to reduce the incidence or severity of IHD events and cerebrovascular events.[6] They are also considered appropriate therapy for patients with coronary artery disease (CAD) and hypertension who are intolerant or allergic to angiotensin-converting-enzyme (ACE) inhibitors.[6,7] Angiotensin-receptor blockers (ARB) have been found to have similar efficacy as ACE inhibitors in reducing cardiovascular event end points.[6] The 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend that adults with stable ischemic heart disease (SIHD) and hypertension (BP ≥130/80 mmHg) should be treated with beta-blockers, ACE inhibitors, or ARBs for compelling indications, e.g., previous MI or stable angina) as first-line therapy, with the addition of other drugs (e.g., dihydropyridine calcium channel blockers (CCBs), thiazide diuretics, and/or mineralocorticoid receptor antagonists as needed to further control hypertension.[8] The 2018 European Society of Cardiology (ESC)/European Society of Hypertension (ESH) guidelines for the management of arterial hypertension recommend a single pill, dual combination of ACEI/ARB with beta-blockers as initial therapy for hypertension with IHD.[4] The 2020 International Society of Hypertension (ISH) practice guidelines recommend adding a beta-blockers at any treatment step where there is a specific indication for use, i.e. HF, angina, post-MI, atrial fibrillation, or younger pregnant women or those planning to get pregnant.[9] Despite several global guidelines with recommendations on initial monotherapy or combination therapy and known role of beta-blockers in the management of hypertension in patients with IHD, there is a paucity of real-world evidence in India. The objective of conducting this questionnaire-based survey was to collect real-world data regarding the association of hypertension and IHD in Indian patients and to understand need for use and compliance with combination therapies, with special focus on the fixed-dose combination (FDC) of telmisartan and metoprolol in the management of hypertension with IHD in Indian clinical practice.

METHODS

Survey design

This was a quantitative, cross-sectional, questionnaire-based survey designed to understand Indian practitioners' current practices in the management of hypertensive patients with IHD and to assess compliance with an FDC of telmisartan and metoprolol in the management of hypertension. A total of 145 cardiologists and consulting physicians were included. Each clinician was asked to respond to the survey questions based on their clinical experience with a minimum 10 patients with hypertension and concomitant IHD.

Survey participants

Survey participation was entirely voluntary. Cardiologists and consulting physicians who saw patients who had already been identified with IHD with hypertension and were on medication therapy. To take part in the survey, all cardiologists and physicians had to give their e-consent, after which all participants received a link to the survey website along with their login details. The survey was carried out in accordance with the principles of the Helsinki Declaration, the International Conference on Harmonization-Good Clinical Practice (GCP) recommendations, and the Indian Council of Medical Research and Indian GCP standards. Because this survey did not entail any intervention on the subject, ethical clearance by an external ethics review board was not necessary in compliance with local legislation and national requirements. The confidentiality and identity of cardiologists and physicians were preserved throughout the survey and data processing.

Survey questionnaire

The questionnaire was divided into three sections: sections 1 and 2 consisted of 12 and 8 questions on prevalence and management of hypertension and IHD, respectively, and section 3 consisted of 15 questions on profiling of patients for treatment with telmisartan and metoprolol in the

management of hypertension and IHD. The survey questionnaire is presented in (Table 1).

Statistical analysis

Because the current survey was designed to learn about clinical practice and treatment recommendations of cardiologists and consulting physicians, a formal sample size estimate was not done. In line with previous studies recommending a respondent-to-item ratio of >2, with 35 questions and 145 clinicians, we maintained a respondent-to-item ratio of >4.[10] Responses to survey questions were calculated using Microsoft Excel, and data were represented as N (%).

RESULTS

Presence of hypertension and IHD among Indian patients

The survey revealed that proportion of patients 15.0%, 49.0%, 32.0%, and 4.0% of the cardiologists and consulting physicians in their respective clinical practice saw <25%, 25%-50%, 50%-75%, and >75% patients with hypertension and IHD, respectively (Table 2). Most of the male and female patients who present with hypertension and IHD lie in the age group of 40-60 years (77.0% males and 72.0% females; Table 2). In all, 34.0% clinicians each opined that patients with resistant hypertension and IHD or secondary hypertension and IHD require referral to a specialist cardiologist, whereas 21.0% opined that all patients with hypertension and IHD needed referral. The remaining 11.0% thought that no referral to cardiologist was required.

Factors guiding choice of treatment for hypertension

Majority of the survey participants (62.0%) reported that presence of comorbidities was the leading factor influencing choice of antihypertensive treatment, followed by severity of hypertension (54.0%), treatment guidelines (41.0%), known treatment-related adverse events (41.0%), and treatment costs (Table 3). As initial choice of pharmacotherapy, 73.0% of cardiologists and consulting physicians preferred angiotensin-converting enzyme inhibitors (ACEis) or angiotensin receptor blockers (ARBs), 61.0% preferred beta blockers (61.0%), 35.0% preferred calcium channel blockers (CCBs) and 29.0% preferred diuretics (Table 3). A majority of the clinicians (74.0%) preferred an FDC of ARB with beta blocker (Table 3). The desired target blood pressure was <120/80 mmHg by 55.0% of the clinicians, <130/80 mmHg or <140/90 mmHg by 22% of clinicians each, and only 1.0% thought that the desired blood pressure to be <150/90 mmHg (Table 3). In addition, 46.0% of cardiologists and consulting physicians strongly agreed while 52.0% agreed that by following the treatment guidelines recommended by ACC, ESC, or Joint National Committee (JNC), the desired outcome can be achieved in Indian hypertensive patients with IHD. The survey results also revealed that 51.0% of clinicians had <25% patients on antihypertensive monotherapy, whereas 47.0% had 25%-50% patients on antihypertensive FDCs (Table 3). When asked about the reasons for inadequate blood pressure control in patients with hypertension and IHD, nonadherence to treatment was reported by 59% clinicians, use of monotherapy by 26.0%, drug cost by 9.0%, and drug-induced side effects by 6.0%.

Management of patients with hypertension and IHD in Indian practice

With regard to choice of therapy, metoprolol was the preferred beta blocker by 86.0% of clinicians, whereas telmisartan was the preferred ARB by 97.0% of clinicians. Other beta blockers such as bisoprolol, carvedilol, and nebivolol and other ARBs such as valsartan and Olmesartan were less preferred (Table 4). Similarly, metoprolol was preferred by 91.0% of clinicians as combination therapy with telmisartan (Table 4). As high as 70.0% of clinicians thought that a combination of factors such as beta-1 receptor selectivity, guideline recommendations, mechanism of action comprising nitric oxide mediated vasodilation and antioxidant property, and safety profile guided the choice of a beta blocker in patients with hypertension and IHD (Table 4). The time of initiation of combination therapy was thought to be uncontrolled blood pressure with monotherapy by 44.0% of the participating cardiologists and consulting physicians, initial blood pressure in the range of 140-159/90-99 mmHg by 25.0% respondents, presence of comorbidities by 23.0% respondents, and initial blood pressure in the range 130-139/85-89 mmHg by 8.0% respondents.

Treatment with FDC of telmisartan and metoprolol in the management of hypertension with IHD

According to 50% of the respondents, 25%-50% of patients in their clinical practice were on FDC of telmisartan and metoprolol (Table 5). Use of this FDC was able to achieve adequate blood pressure control in 50%-75% of patients according to 47.0% of respondents, in 25%-50% of patients according to 36.0% of respondents, in >75% of patients according to 13.0% of respondents, and in <25% of patients according to 4.0% of patients (Table 5). Causes of inadequate blood pressure control were nonadherence to treatment, associated comorbidities/complications, suboptimal FDC dose, or drug-induced side effects as reported by 54.0%, 46.0%, 34.0%, and 16.0% of participating clinicians, respectively (Table 5). With regard to choice of patients targeted to receive the FDC of telmisartan and metoprolol, 72.0% of the respondents opined that hypertensive patients who have had a recent cardiovascular event, hypertensive patients with cardiovascular comorbidities (such as heart failure, atrial fibrillation, post myocardial infarction, or angina), and patients who are non-responsive to monotherapy with telmisartan or metoprolol should be initiated on the FDC (Table 5).

Table 1: Survey questionnaire.

Questions					
Section 1: Hypertension with IHD in Indian patients					
Q1	What percent of adults in your clinical practice have hypertension with IHD?				
	<25%	25%-50%		50%-75%	>75%
Q2	What is the age group of male patients presenting with hypertension with IHD?				
	<40 years	40-60 years		60-80 years	>80 years
Q3	What is the age group of female patients presenting with hypertension with IHD?				
	<40 years	40-60 years		60-80 years	>80 years
Q4	Does treatment of hypertensive patients with IHD require referral to a cardiologist?				
	All cases	Resistant hypertension with IHD		Secondary hypertension with IHD	Never
Q5	What are the factors that influence your choice of antihypertensive treatment? (one/more options can be selected)				
	Patient comorbidities	Known treatment-related AEs	Severity of patient's hypertension	Treatment guidelines	Cost
Q6	What is your initial choice of pharmacotherapy for hypertensive patients with IHD? (one/more options can be selected)				
	ACEi/ARBs	Diuretics		Beta blockers	CCBs
Q7	Which FDC of ARB do you prefer in the management of hypertension with IHD?				
	ARB + beta blocker	ARB + CCBs		ARB + diuretic	Triple combination involving ARB
Q8	What is the target BP you would like to achieve in hypertensive patients with IHD?				
	<120/80 mmHg	<130/80 mmHg		<140/90 mmHg	<150/90 mmHg
Q9	Do you think that adhering with guidelines recommended by ACC/ESC/JNC would produce the desired outcome in Indian hypertensive patients with IHD?				
	Strongly agree	Agree		Disagree	Strongly disagree
Q10	What percent of adults in your clinical practice with hypertension and IHD are on antihypertensive monotherapy?				
	<25%	25%-50%		50%-75%	>75%
Q11	What percent of adults in your clinical practice with hypertension and IHD are on antihypertensive FDCs?				
	<25%	25%-50%		50%-75%	>75%
Q12	What is the most common cause of inadequate control of blood pressure?				
	Use of monotherapy	Drug cost		Drug-induced side effects	Nonadherence to treatment
Section 2: Management of hypertension with IHD in Indian clinical practice					
Q1	Which beta blocker you usually prefer for the management of hypertensive patients with IHD?				
	Metoprolol	Bisoprolol	Carvedilol	Nebivolol	Atenolol
Q2	Which beta blocker would you prefer with telmisartan in the FDC for the management of hypertensive patients with IHD?				
	Metoprolol	Bisoprolol	Nebivolol	Atenolol	Carvedilol
Q3	Which of the following factors you take into consideration while selecting a beta blocker in the management of hypertensive patients with IHD?				
	Guideline recommendations	β1 receptor selectivity	Safety profile	Additional MOA nitric oxide mediated vasodilation, antioxidant property	All of the above
Q4	Which ARB you usually prefer for the management of hypertensive patients with IHD?				
	Telmisartan	Olmesartan	Valsartan	Losartan	Candesartan	Irbesartan
Q5	When would you start combination antihypertensive therapy in your patients?				
	When BP is not controlled by monotherapy	When initial BP is 130-139/85-89 mmHg	When initial BP is 140-159/90-99 mmHg		Hypertensive patient with comorbidities

Continued.

Questions				
Q6	What percent of adults in your clinical practice with hypertension and IHD are on telmisartan + metoprolol FDC?			
	<25%	25%-50%	50%-75%	>75%
Q7	What percent of adults in your clinical practice with hypertension and IHD on telmisartan + metoprolol FDC have adequate BP control?			
	<25%	25%-50%	50%-75%	>75%
Q8	Which of the following could be the cause of inadequate control of blood pressure with FDC of telmisartan + metoprolol? (one/more options can be selected)			
	Suboptimal dose of FDC	Drug-induced side effects	Nonadherence to treatment	Associated comorbidities/ complications in the patient
Section 3: Telmisartan and metoprolol in the management of hypertension with IHD in Indian clinical practice				
Q1	In which patient group your choice of therapy is FDC of Telmisartan + Metoprolol in the management of hypertension with IHD?			
	Hypertensive patient with a recent CV event	Non-responsive to monotherapy of telmisartan or metoprolol	Hypertensive patient with CV comorbidities (HF, AF, post MI, angina)	All of the above
Q2	Which of the following factors you take into consideration while prescribing FDC of telmisartan + metoprolol in the management of hypertension with IHD? (one/more options can be selected)			
	Patient comorbidities	Known treatment-related AEs	Severity of hypertension	Treatment guidelines	Age of the patient
Q3	What are benefits seen with FDC of telmisartan + metoprolol in the management of hypertension with IHD? (one/more options can be selected)			
	Angina symptom control	Preventing new CV events	Improvement in quality of life	Improvement in exercise quality
Q4	FDC of telmisartan + metoprolol is commonly prescribed in hypertensive patients with IHD.			
	Strongly agree	Agree	Disagree	Strongly disagree
Q5	FDC of telmisartan + metoprolol is commonly prescribed in hypertensive patients with heart failure.			
	Strongly agree	Agree	Disagree	Strongly disagree
Q6	FDC of telmisartan + metoprolol is commonly prescribed in hypertensive patients with IHD and diabetes.			
	Strongly agree	Agree	Disagree	Strongly disagree
Q7	What are the parameters that you look out for while deciding the dosage of the telmisartan + metoprolol FDC? (one/more options can be selected)			
	Clinical presentation (HR, BP, associated HF)	Known treatment-related AEs	Severity of hypertension	Treatment guidelines	Age of the patient
Q8	FDC of telmisartan + metoprolol helps in improving patient compliance and adherence to therapy.			
	Strongly agree	Agree	Disagree	Strongly disagree
Q9	At what heart rate range would you start with FDC of telmisartan 40 mg + metoprolol 25 mg?			
	61-70	71-80	81-90	≥91
Q10	At what heart rate range would you start with FDC of telmisartan 40 mg + metoprolol 50 mg?			
	71-80	81-90	91-100	≥101
Q11	At what BP (mmHg) threshold would you start with FDC of telmisartan 40 mg + metoprolol 25 mg?			
	130-139/80-89	140-159/90-99	160-179/100-109	>180/110
Q12	At what BP (mmHg) threshold would you start with FDC of telmisartan 40 mg+metoprolol 50 mg?			
	130-139/80-89	140-159/90-99	160-179/100-109	>180/110
Q13	At what BP (mmHg) threshold would you start with FDC of telmisartan 80 mg+metoprolol 25 mg?			
	130-139/80-89	140-159/90-99	160-179/100-109	>180/110
Q14	At what BP (mmHg) threshold would you start with FDC of telmisartan 80 mg+metoprolol 50 mg?			
	130-139/80-89	140-159/90-99	160-179/100-109	>180/110
Q15	Will you prefer availability of FDC of telmisartan 80 mg + metoprolol 100 mg?			
	Strongly agree	Agree	Disagree	Strongly disagree

Table 2: Prevalence of hypertension with IHD in Indian clinical practice (n=145).

Parameters	Proportion of physicians (%)	
Proportion of patients with hypertension and IHD (%)		
<25	15.0	
25-50	49.0	
50-75	32.0	
>75	4.0	
Age groups of patients with hypertension and IHD (years)		
	Male patients	**Female patients**
<40	7.0	6.0
40-60	77.0	72.0
60-80	16.0	22.0

IHD, ischemic heart disease

Table 3: Factors associated with the treatment of patients with hypertension and IHD (n=145).

Parameter	Proportion of physicians (%)
Factors influencing choice of antihypertensive treatment	
Comorbidities	62.0
Severity of hypertension	54.0
Treatment guidelines	41.0
Known treatment-related AEs	41.0
Cost	35.0
Initial choice of pharmacotherapy	
ACEis/ARBs	73.0
Beta blockers	61.0
CCBs	35.0
Diuretics	29.0
Combination therapy with ARBs	
Beta blockers	74.0
CCBs	17.0
Diuretics	4.0
Triple combination involving ARB	5.0
Desired target blood pressure in mmHg	
<120/80	55.0
<130/80	22.0
<140/90	22.0
<150/90	1.0
Patients on antihypertensive monotherapy (%)	
<25	51.0
25-50	34.0
50-75	12.0
>75	3.0
Patients on antihypertensive FDCs (%)	
<25	12.0
25-50	47.0
50-75	35.0
>75	6.0

Table 4: Management of patients with hypertension and IHD by type of therapy (n=145).

Parameter	Proportion of physicians (%)
Preferred beta blocker	
Metoprolol	86.0
Bisoprolol	11.0
Carvedilol	2.0
Nebivolol	1.0
Preferred ARB	
Telmisartan	97.0
Valsartan	2.0
Olmesartan	1.0
Preferred beta blocker with telmisartan	
Metoprolol	91.0
Bisoprolol	4.0
Carvedilol	2.0
Atenolol	2.0
Nebivolol	1.0
Factors affecting choice of beta blocker	
Guideline recommendation	14.0
β1 receptor selectivity	10.0
Safety profile	5.0
Additional MOA	1.0
All of the above	70.0

ACEi, angiotensin converting enzyme inhibitor; AEs, adverse events; ARB, angiotensin receptor blocker CCB, calcium channel blocker; FDC, fixed-dose combination; IHD, ischemic heart disease

Factors guiding prescription of this FDC in decreasing order of frequency were treatment guidelines (57.0%), severity of hypertension (56.0%), presence of comorbidities (5.0%), known treatment-related adverse events (37.0%), and patient age (35.0%; Table 5).

Prevention of new cardiovascular events (63.0%), improvement in quality of life (61.0%), control of angina symptoms (57.0%), and improvement in exercise quality (43.0%) were the benefits of telmisartan and metoprolol FDC in decreasing order of response frequencies (Table 5), whereas clinical presentation such as elevated heart rate or blood pressure and associated heart failure (70.0%), treatment guidelines (56.0%), severity of hypertension (48.0%), patient age (41.0%), and known treatment-related adverse events (34.0) were the parameters guiding dose of the telmisartan and metoprolol FDC in decreasing order of response frequencies. In this survey, it was observed that 53.0% of physicians strongly agreed and 46.0% of physicians agreed that the FDC of telmisartan and metoprolol could be prescribed to hypertensive patients with IHD, 54.0% agreed and 36.0% strongly agreed that this FDC could be prescribed to hypertensive patients with heart failure, and 25.0% agreed, 15.0% strongly agreed, and 58.0% strongly disagreed that this FDC could be prescribed to hypertensive patients with IHD and diabetes. All the cardiologists and consulting physicians strongly agreed or agreed that the FDC of telmisartan and

metoprolol helped in improving patient compliance and adherence to therapy.

Table 5: Treatment patterns with FDC of telmisartan and metoprolol (n=145).

Parameter	Proportion of physicians (%)
Proportion of patients on telmisartan and metoprolol FDC (%)	
<25	22.0
25%-50	50.0
50%-75	27.0
>75	1.0
Proportion of patients with adequate BP control with telmisartan and metoprolol FDC	
<25	4.0
25-50	36.0
50-75	47.0
>75	13.0
Causes of inadequate BP control	
Nonadherence to treatment	54.0
Associated comorbidities/complications	46.0
Suboptimal dose of FDC	34.0
Drug-induced side effects	16.0
Patient profile for recommendation of telmisartan + metoprolol FDC	
Hypertensive patient with CV comorbidities	14.0
Hypertensive patient with a recent CV event	10.0
Non-responsiveness to telmisartan or metoprolol monotherapy	4.0
All of the above	72.0
Factors guiding prescription of telmisartan + metoprolol FDC	
Treatment guidelines	57.0
Severity of hypertension	56.0
Patient comorbidities	55.0
Known treatment-related AEs	37.0
Patient age	35.0
Parameters guiding dose of telmisartan + metoprolol FDC	
Clinical presentation	70.0
Treatment guidelines	56.0
Severity of hypertension	48.0
Patient age	41.0
Known treatment-related AEs	34.0
Benefits of telmisartan + metoprolol FDC	
Preventing new CV events	63.0
Improvement in QoL	61.0
Angina symptom control	57.0
Improvement in exercise quality	43.0

CV comorbidities include such as heart failure, atrial fibrillation, post myocardial infarction, and angina.

The heart rate range and blood pressure threshold for the initiation of FDC of telmisartan and metoprolol in the opinion of cardiologists and consulting physicians. In all, 66.0% of respondents stated that an FDC of telmisartan 40 mg and metoprolol 25 mg should be initiated at a heart rate range of 71-90, whereas 50.0% of respondents stated that at heart rate ≥91, an FDC of telmisartan 40 mg and metoprolol 50 mg should be initiated. A blood pressure threshold of 140-159/90-99 mmHg was considered by 72.0% of respondents to be an indication to initiate FDC of telmisartan 40 mg and metoprolol 25 mg, while 45.0% and 48.0% of respondents thought that FDCs of telmisartan 40 mg + metoprolol 50 mg and telmisartan 80 mg + metoprolol 25 mg should be initiated at a threshold of 160-179/100-109 mmHg, respectively. An FDC dose of telmisartan 80 mg+metoprolol 50 mg was recommended by 30.0% of respondents when blood pressure threshold exceeds 180/110 mmHg. When the respondents were asked if the availability of an FDC of telmisartan 80 mg + metoprolol 100 mg would be preferred, 41.0% disagreed, 25.0% agreed, 34.0% strongly agreed.

DISCUSSION

The most important strategy for lowering the burden of CVD (IHD or CAD) is rapid blood pressure control.[5] Over the past two decades, several studies and guidelines have been published with the aim to investigate the pathogenesis of IHD, to identify an acceptable blood pressure range for initiating pharmacotherapy, and to determine optimal therapeutic options. While there is continuing disagreement about the existence and importance of the J-curve (inverse relation between low blood pressure and cardiovascular complications in IHD patients with hypertension and the numerical blood pressure threshold justifying drug therapy in the general population, there is a general consensus that the target blood pressure in patients with IHD should be lower than 140/90mmHg.[3] Treatment of hypertension in patients with IHD is generally started either with ACEis and/or ARBs alone or in combination with beta-blockers.[11] A meta-analysis of randomized controlled trials on antihypertensive therapy revealed that a 10 mmHg reduction in SBP was associated with a 20% reduction in the risk of major cardiovascular events and a 17% reduction in CAD.[12] Blood pressure lowering significantly reduces vascular risk across various baseline blood pressure levels and comorbidities. Results of this meta-analysis provided strong support for lowering SBP to <130 mmHg and providing blood pressure-lowering treatment to individuals with a history of CVD, coronary heart disease (CHD), stroke, diabetes, heart failure, and chronic kidney disease.[12]

An overview of randomized controlled trials and prospective observational studies provided the most reliable data on the association between blood pressure and CHD.[13] Evidence indicates a continuous log linear association between blood pressure and CHD down to levels of about 115 mm Hg SBP and 70 mm Hg DBP.[13] Overall, in patients aged 60 to 69 years, a 10 mmHg

decrease in SBP is associated with about one-fifth lower risk of a CHD event. The size and shape of this association is consistent across regions, for men and women, and for fatal events as well as nonfatal myocardial infarction.[13]

Table 6: Heart rate range and blood pressure threshold guiding initiation of telmisartan+metoprolol FDC.

Parameters	Proportion of physicians (%)			
Heart rate range (beats per min)	**Telmisartan 40 mg +metoprolol 25 mg**	**Telmisartan 40 mg+metoprolol 50 mg**		
61-70	15.0	-		
71-80	38.0	20.0		
81-90	28.0	30.0		
≥91	19.0	-		
91-100	-	29.0		
≥101	-	21.0		
Blood pressure (mmHg)	**Telmisartan 40 mg+metoprolol 25 mg**	**Telmisartan 40 mg+metoprolol 50 mg**	**Telmisartan 80 mg+ metoprolol 25 mg**	**Telmisartan 80 mg+ metoprolol 50 mg**
130-139/80-89	12.0	5.0	5.0	4.0
140-159/90-99	72.0	43.0	32.0	19.0
160-179/100-109	15.0	45.0	48.0	16.0
>180/110	1.0	7.0	15.0	30.0

FDC, fixed-dose combination

The present survey reveals the association of hypertension with IHD in Indian patients. In the present survey, it was found that most of the male and female patients who present with hypertension and IHD lie in the age group of 40-60 years. When prescribing antihypertensive treatment, cardiologists and consulting physicians take into consideration several factors such as presence of comorbidities, severity of hypertension, treatment guidelines, clinical presentation (with elevated heart rate or blood pressure, and associated heart failure), treatment-related adverse events, and costs of treatment. When treatment was started with monotherapy, ACEis or ARBs are recommended by the physicians as the initial choice of pharmacotherapy for hypertensive patients with IHD. Physicians also agreed that by adhering to guidelines recommended by ACC, ESC, or JNC, the desired outcome can be achieved in hypertensive patients with IHD. Most cardiologists and consulting physicians choose ACEis or ARBs as their initial choice of pharmacotherapy for hypertensive patients with IHD. An FDC of ARB and beta-blocker was preferred for patients with hypertension and IHD when the symptoms are not controlled by antihypertensive monotherapy, when initial blood pressure is 140-159/90-99 mmHg, or when patients have comorbidities.

A cross-sectional, observational survey conducted by Jadhav et al revealed that amongst the ARBs, telmisartan was the preferred ARB by >80% respondents, and metoprolol was the preferred beta-blocker by almost 64% respondents.[14] Based on the rationale of sympathetic overactivity, most clinicians choose a β-blocker as part of antihypertensive prescription in hypertensive adults. Telmisartan and metoprolol single-pill combination achieved the blood pressure target in 40%-60% of patients as reported by 41.3% of the physicians.[14] The combination therapy was well tolerated in young hypertensive patients. Initiation of an early and appropriate antihypertensive treatment in young population may lower the burden of CVD in this population. ARBs and beta-blockers were the preferred classes of antihypertensive drugs for young hypertensive patients.[14] Metoprolol is a cardioselective beta1-adrenergic receptor inhibitor that competitively blocks beta1-receptors with minimal or no effects on beta-2 receptors. Metoprolol significantly lowers the heart rate. The metoprolol atherosclerosis prevention in hypertensives (MAPHY) trial specifically showed benefit of metoprolol over diuretics regarding sudden cardiac death and myocardial infarction. Combination therapy has been proven to achieve blood pressure control in that more patients can reach target blood pressure faster.[14] A dose-escalation approach using monotherapy reduces coronary events by 29% and cerebrovascular events by 40%, while combining two antihypertensive agents with a different mechanism of action reduces coronary events by 40% and cerebrovascular events by 54%. Hence, the use of combination therapy offers greater target organ protection than increasing the dose of monotherapy.[14] Cardiologists tend to prefer beta-blockers as initial antihypertensive therapy in the real-world setting, with metoprolol being the most commonly prescribed drug.[14] Similarly in our survey, approximately >90% of the participating cardiologists and consulting physicians prefer an FDC of a beta-blocker (metoprolol) and ARB (telmisartan) for the management of hypertension with IHD. Beta-blockers reduce myocardial oxygen consumption and heart rate and enhance coronary flow by increasing diastolic filling period,[15] whereas ARBs act by blocking the vasoconstrictor and aldosterone-secreting effects of

angiotensin II via selective blocking of the binding of angiotensin II to the angiotensin II type 1 receptor in many tissues, such as vascular smooth muscles and the adrenal glands. Blockade of the angiotensin II receptor inhibits the negative regulatory feedback of angiotensin II on renin secretion.[16]

The majority of physicians in our survey strongly believe that an FDC of telmisartan and metoprolol can be administered in hypertensive patients with IHD because it can manage angina symptoms, avoid new cardiovascular events, improve quality of life, and improve exercise quality. In addition, the survey findings revealed that majority of the cardiologists and consulting physicians agree that a combination of telmisartan and metoprolol would be useful in hypertensive patients with heart failure and in hypertensive patients with IHD and diabetes. Furthermore, it was observed from the survey that the majority of the physicians preferred telmisartan and metoprolol combination because it helps in improving patient compliance and adherence to therapy. The lack of questions on occupational exposure history, socioeconomic position, or past hospitalization that may have influenced treatment patterns, as well as the relatively short follow-up period, are some of the survey limitations. To validate the current findings, multicenter studies with larger sample sizes and longer follow-up periods are required.

CONCLUSION

In this pan-India survey conducted among cardiologists and consulting physicians, it was observed that hypertension and IHD are most commonly seen in patients of both sexes who are above 40 years and a combination of metoprolol and telmisartan is the most commonly recommended therapy by Indian clinicians for these patients. The survey findings further revealed that the telmisartan and metoprolol combination could be beneficial in hypertensive patients with heart failure, but also in hypertensive patients with IHD and diabetes. The combination helps improving blood pressure, heart rate, patient compliance, and adherence to therapy. Nevertheless, large-scale, prospectively designed, randomized controlled studies with long-term clinical goals are warranted to validate these findings.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. R. Gulshan from Spirant Communications Private Limited for her medical writing and editorial assistance.

Funding: Funding for writing support was provided by Abbott Healthcare Pvt. Ltd.
Conflict of interest: M Kathiresan has received research grants from Abbott, Sun Pharma, USA, and MicroLabs. Atul Saxena, Priyadarsi Tripathy, and Sushil Tripathi have received research grants from Abbott for participation in the survey. Greeshma Upendra is an employee of Abbott.
Ethical approval: Not required

REFERENCES

1. Lu Y, Li J, Wang X, Cho J, Dorajoo SR, Feng M, et al. Characterizing dual combination therapy use in treatment escalation of hypertension: real-world evidence from multinational cohorts. MedRxiv. 2021;2:1-31.
2. MacDonald T, George J. Home blood pressure monitoring. Eur Cardiol. 2015;10:95-101.
3. Agbor-Etang BB, Setaro JF. Management of hypertension in patients with ischemic heart disease. Current Cardiol Rep. 2015;17:1-7.
4. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39:3021-3104.
5. Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. Lancet. 2014;383:1899-911.
6. Rosendorff C, Black HR, Cannon CP, Gersh BJ, Gore J, Izzo JL. Treatment of hypertension in the prevention and management of ischemic heart disease: a scientific statement from the American heart association council for high blood pressure research and the councils on clinical cardiology and epidemiology and prevention. Circulation. 2007;115:2761-88.
7. Shiga T, Kasanuki H, Hagiwara N, Sumiyoshi T, Honda T, Haze K, et al. Angiotensin receptor blocker-based therapy and cardiovascular events in hypertensive patients with coronary artery disease and impaired renal function. Blood Press. 2010;19:359-65.
8. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018;71:e127-248.
9. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. Hypertension. 2020;38:982-1004.
10. Anthoine E, Moret L, Regnault A, Sébille V, Hardouin JB. Sample size used to validate a scale: a review of publications on newly-developed patient reported outcomes measures. Health Qual Life Outcomes. 2014;12:176.
11. Špinar J. Hypertension and ischemic heart disease. Cor et Vasa. 2012;54:e433-8.
12. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, et al. Blood pressure lowering for prevention of cardiovascular disease and

death: a systematic review and meta-analysis. Lancet. 2016;387:957-67.
13. Lawes CM, Bennett DA, Lewington S, Rodgers A. Blood pressure and coronary heart disease: a review of the evidence. Semin Vasc Med. 2002;2: 355-68.
14. Jadhav U, Tiwaskar M, Khan A, Kalmath BC, Ponde CK, Sawhney J, et al. Hypertension in young adults in India: Perspectives and therapeutic options amongst clinician's in a cross-sectional observational study. J Assoc Physicians India. 2021;69:11-2.
15. Olafiranye O, Zizi F, Brimah P, Jean-Louis G, Makaryus AN, McFarlane S, et al. Management of hypertension among patients with coronary heart disease. Int J Hypertens. 2011;2011: 653903.
16. Telmisartan. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/Telmisartan. Accessed on 24 April 2022.

Cite this article as: Kathiresan M, Saxena A, Tripathy P, Tripathi S, Upendra G. Management of hypertensive patients with ischemic heart disease and the role of a fixed-dose combination of telmisartan and metoprolol: a physician-based research survey. Int J Adv Med 2023;10:367-76.