



**Assessment on Rational use of Beta Blockers in Cardiology
Department at Tertiary Care Hospital**

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ABSTRACT:

Beta blockers are the class of drugs that blocks the action of adrenaline, decreases the heart rate, lowers the blood pressure, widens veins and facilitates easier blood flow. Being one of the essential class of drugs in treating cardiovascular diseases, assessment of rational use of beta blockers will help to identify irrational use and promote better clinical care. So this study aims to assess the Prescribing pattern of beta blockers in cardiology department. The main objectives of the study is to assess the rational use of beta blockers in cardiology department by analyzing the compliance of the prescription with ACC and ESC guidelines and to identify potential drug interactions, adverse drug reactions and also to identify frequently prescribed beta blockers in cardiology department.

METHOD: A prospective observational study was conducted in cardiology department of Aster CMI hospital, Bengaluru for the period of 6 months. All in-patients of both Gender and aged above 18 Years administered with at least one beta blocker for cardiovascular diseases with or without comorbidities were included in this study. Demographic, clinical and medication data was collected from patient case files and prescribing pattern of beta blockers was analyzed by using ACC and ESC guidelines.

RESULTS: 171 patients were included according to inclusion criteria among them 72 % were males and 28 % were females. The most common prescribe Beta blockers for the indication

were Myocardial infarction (46.8%), Angina pectoris (18.7%), Coronary artery disease (13.5%), Congestive cardiac failure (13.5%). less comonly prescribed for the indication for Atrial fibrillation (1.2%), Myocardities (1.2%), LV dysfunction (2.3%), Severe mitral regurgitation (0.6%), Severe aortic regurgitation (1.2%), and Hypertension (0.6%). more frequently prescribed beta blockers in cardiology department was Metoprolol tartrate (52.7%), followed by Metoprolol succinate(18.47%), carvedilol(9.23%), bisoprolol(7.6%), nebivolol(5.97%), labetalol(1.63%), sotalol(0.53%) and 3.8% beta blockers are combined with ACE inhibitors and calcium channel blockers. 71.3% beta blocker therapy adhered to both ESC and ACC guidelines 15.2% adhered to ACC guidelines ,10.5% adhered to ESC guidelines and 2.9% therapy did not comply with any of these guidelines due to adverse drug reactions. major drug interactions were found between carvedilol with levosalbutamol (4.1%). the sign of bradycardia(0.58%) and hypotension(2.33%) were found and ADR reported .

CONCLUSION: 97% of beta blocker therapy prescribed in cardiology department of Aster CMI was rational in compliance with ACC/ESC guideliness while 3% of the therapy as not in compliance causing adverse drug reactions. Most commonly prescribed beta blocker was Metoprolol tartrate (52.7%). Drug related issues like drug interactions should considred while treating the patients with beta blocker therapy.Signs of hypotension and bradycardia should be carefully monitered during the course of the treatment. Major drug interaction identified with beta blocker was carvedilol administered with levosalbutamol.

Key words: Hypertension(HTN), Myocardial Infraction(MI), Arterial febrilation(AR), ACC/AHA(American College of Cardiology and American Heart Association), European Society of Cardiology (ESC)

INTRODUCTION:

Beta blockers are also called as beta adrenergic blockers that blocks the receptor sites for catecholamine's adrenaline and nor adrenaline. They help the heart to beat more slowly that can lower the blood pressure and enhance the blood flow through veins and arteries. These drugs should not be prescribed to asthmatic patients as it may increase the Chance of asthmatic attacks [1].

There are three types of β receptors present in the body, they are

β_1 – receptors located in the heart & kidney which can rise the heart rate, and stimulate release of renin.

β_2 - receptors found in smooth muscles and tissues in respiratory system.

β_3 –receptors in fat cells and in bladder^[2].

Beta blockers are divided as beta-1 blockers or selective beta blockers which blocks on beta-1 receptors in the heart. These drugs are Atenolol, Bisoprolol, Metoprolol and Esmolol. Beta-1, Beta-2, and Beta-3 blockers or non-selective beta blockers and the drugs include Propranolol, Nebivolol, Carvedilol, Sotalol, and Labetalol.^[2] Non selective beta blockers are blocks beta 1 and beta 2 receptors where cardio selective beta blockers blocks only beta 1 receptors of the heart.^[4]

Beta blockers helps in the treatment of HTN, Angina, MI, Arrhythmia and Heart failure. The mechanism involves reduce the atrial BP by decreasing cardiac output. It is effective when used with diuretics and makes treatment effective by reducing cardiac output. Beta blockers decrease the oxygen requirement of the heart by decreasing the heart rate, atrial pressure by relieving pain in heart diseases. This mechanism is helpful in treating MI as they are proven to reduce mortality.

Beta blockers are class 2 antiarrhythmic drugs and inhibits sympathetic influence on cardiac electrical activity. They increase the sinus rate by increasing pacemaker currents thus it is known to increase SA node automaticity. This action leads to increase in conduction velocity. This mechanism helps beta blockers in treatment of Arrhythmia^[3].

It is used to treat HF where the contractile function of heart is reduced. FDA approved beta blockers for HF are Carvedilol, Metoprolol and Bisoprolol. Beta blockers has intrinsic sympathomimetic activity (ISA) while some stabilizes the membrane.^[5]

Beta blockers are combined with antihypertensive drugs to control blood pressure. and also combined with dihydropyridine calcium channel blockers to reduce the chance of bradycardia. beta blockers with diuretics and angiotensin converting enzyme inhibitors is not recommended. Alpha blockers with beta blockers is proven to show better effectiveness in patients aged 70 years and younger^[7].

WHO estimates either the drugs are prescribed/sold/dispensed which are not appropriate to the patient or patients not consume the medication correctly promotes overuse, underuse, misuse of

drugs which leads to health problems. This can be overcome by using clinical guidelines and use of national essential medicines list.^[8] The Rational usage of drugs to the patients is justified when medicines are appropriate to the patients according to the medical needs, in adequate doses for this requirement for suitable duration in less cost.

when medicines are used for correct indication considering the efficacy, safety, suitability in correct doses, Route of administration and also considering the contraindications to the patients and adhere of the patient to medicines are called as Rational use of medicine.

Irrational use of drugs refers to usage of drugs which is not complaint to the patient. clinical guidelines include systematically developed criteria based on evidence that will help the prescribers to choose appropriate treatments for specific diseases/disorders. Evidence based clinical guidelines will be helpful for promoting the appropriate use of medicines.^[9] Examples of irrational use are poly-pharmacy, ineffective medicines, incorrect use and adverse effects.^[9]

Cardiovascular diseases is one of the important public concern which causes morbidity and mortality. Beta blockers are one of the essential class of drugs which is used in treating cardiovascular diseases. Earlier studies indicate that beta blockers are over utilized or underutilized and used inappropriately in terms of drug, dose, and route of administration in treating cardiovascular conditions. Therefore, there is a need to ensure the rational use of beta blockers to promote better clinical cares.

METHODOLOGY:

- ❖ **Study site:** The study was carried out in Aster CMI hospital, Hebbal, Bengaluru, Karnataka-92.
- ❖ **Study design:** Prospective observational study.
- ❖ **Study duration:** The study was carried out for the period of 6 months.
- ❖ **Sample size:** The sample number was found to be 171.
- ❖ **Study criteria:**

Inclusion criteria:

- All in-patients of both Gender and who are aged above 18 Years
- All in-patients with administration of at least one beta blocker for cardiovascular diseases in cardiology department with or without comorbidities.

Exclusion criteria:

- Pregnant and Lactating women.
- Pediatric patients.
- All outpatients and Patients who were prescribed with beta blockers in other departments.

Documents:

- Data collection form.
- Lexicomp database.
- CDSCO ADR Reporting Form.
- ACC/AHA guidelines and ESC guidelines.

HUMAN ETHICAL CLEARANCE STATUS:

The proposal was initiated after ethical approval from Institutional Human Ethical Committee, ASTER CMI Hospital, Bengaluru-92.

❖ **Study procedure:**

Step-1: Patients who meets the study criteria were enrolled into the study, informed consent was taken before patient is recruited.

Step-2: Demographics, Clinical and Medication details of the patient were collected and documented in data collection form.

Step-3: The rational use of beta blockers was assessed with respect to ACC and ESC guidelines.

Step-4: Potential drug interactions was evaluated by using lexicomp drug database.

Step- 5: Results was be subjected to statistical analysis.

❖ **Statistical analysis:**

The data was analyzed statistically using MS Excel software. Excel sheet was used for managing all the data, descriptive statistics were presented in the form of percentage and graph.

RESULTS:

This was a prospective observational study carried out for 6 months. During the study we have collected 171 cases as per the inclusion criteria. The data collected was analyzed & presented.

Demographic details:

Age distribution:

Out of 171 patients 17(10%) patients are age group between 21-40 years, 78 (45.6%) were age group between 41-60 years, 69 (40.3%) of patients were aged between 61-80 years & 7 (4.1%) of patients were aged between 81-100 years.

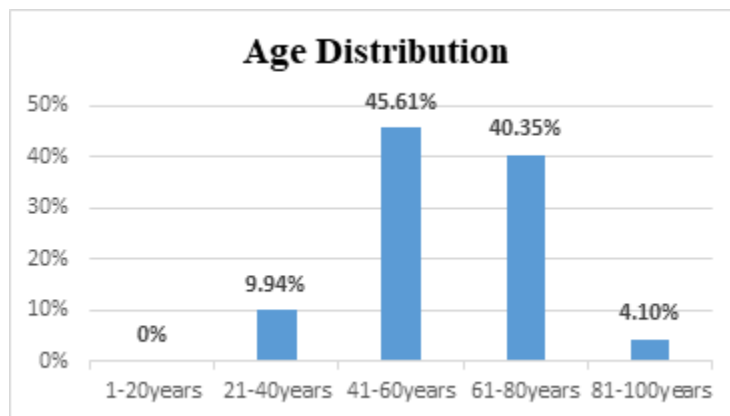


Figure 1: Age distribution

Gender distribution:

In this study 128 (71.9%) patients were male & 43 (28%) were female the data shows the number of male patients were more.

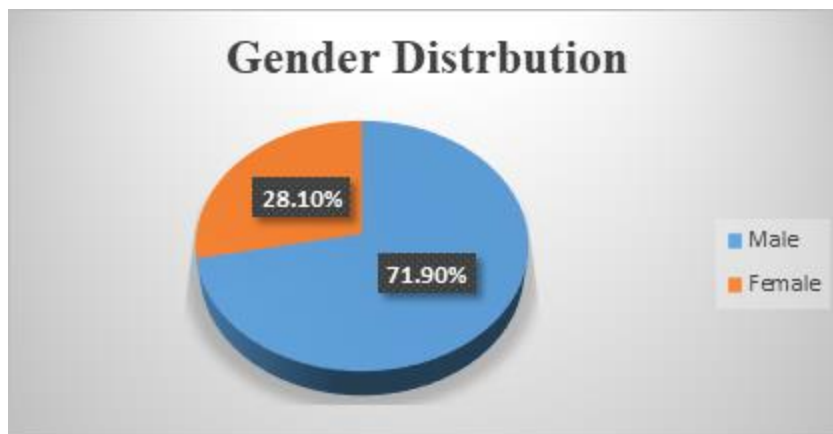


Figure 2: Gender distribution

CLINICAL STATUS OF STUDY POPULATION

Indication of beta blockers among various cardiovascular disease:

Out of 171 patients, 80 (46.8%) patients received beta blockers for the indication Myocardial infarction, 23 (13.5%) patients received for the indication Coronary artery disease, 24 (14%)

patients received for Congestive cardiac failure, 2 (1.2%) patients received for Atrial fibrillation, 2(1.2%) patients received for Myocarditis, 4(2.3%) patients received for LV dysfunction, 1(0.6%) patients for Severe mitral regurgitation, 2 (1.2%) patients for Severe aortic regurgitation, 1(0.6%) patient for Hypertension and 32 (18.7%) patients for Angina pectoris.

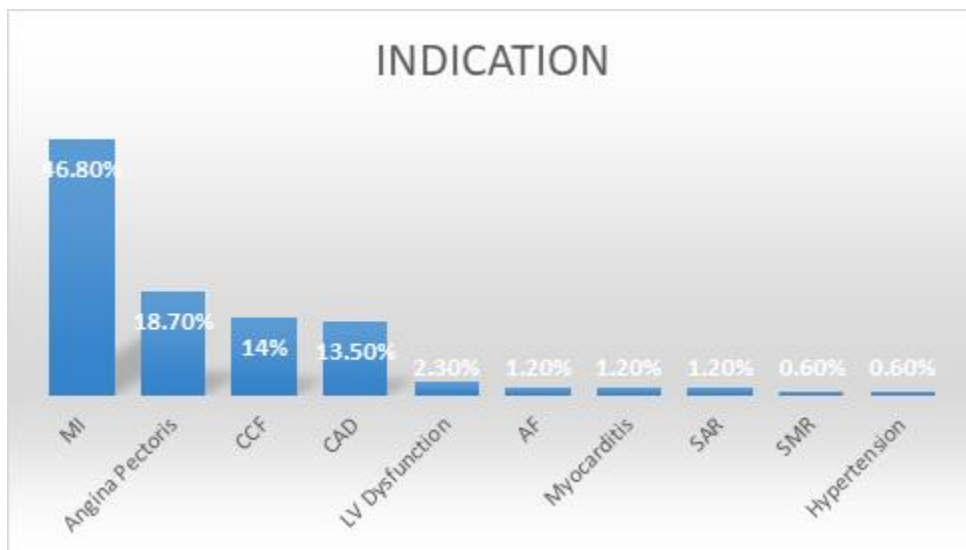


Figure 3: Indication of beta blockers among various cardiovascular disease

Beta blockers drugs administered for treating cardiovascular diseases:

Mono-therapy:

Out of 171 study population Metoprolol tartrate has prescribed in 97 patients (54.40%). Metoprolol succinate prescribed in 28 patients (15.70%), Nebivolol in 11 patients (5.9%), Carvedilol in 17 patients (9.2%), Bisoprolol in 14 patients (7.6%), Sotalol in 1 patient (0.5%) and labetalol in 3 patients (1.6%). The most frequently prescribed Beta blocker was Metoprolol tartrate 97 (52.7%) followed by Metoprolol succinate 14 patients (7.6%). out of 171 patients in the study 152 patients (88.8%) were prescribed with cardio selective beta blockers and 19 (11.1%) patients were prescribed with non selective beta blockers.

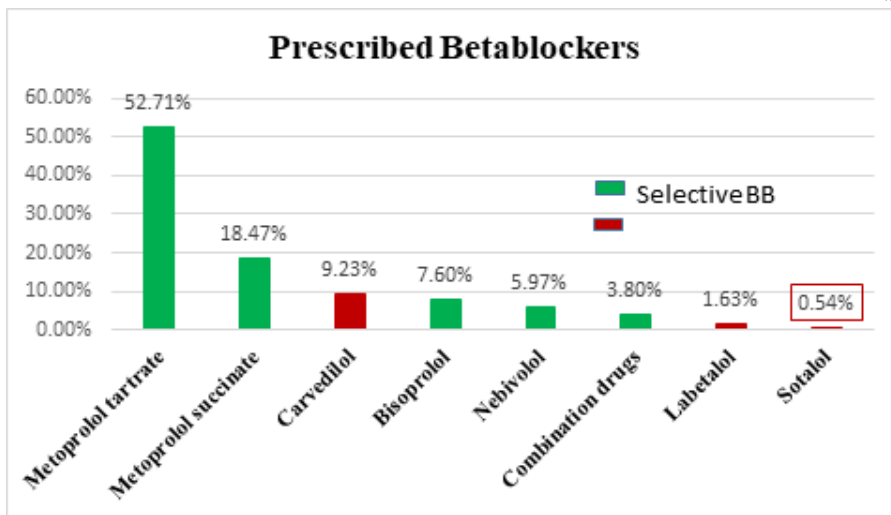


Figure 4: distribution of beta blockers mono therapy

Combination therapies:

Among the study population 7 patients (3.90%) were prescribed with combination treatment of beta blockers with other anti hypertensive drugs. 1 patient was prescribed with Nebivolol and Clinidipine for the indication Angina pectoris, 3 patients were prescribed Metoprolol with Ramipril for the indication of MI, 1 patient was prescribed Metoprolol with Amlodipine for the CCF, one patient prescribed with Metoprolol, Telmisartan and Clinidipine for the treatment of angina pectoris, and one patient was prescribed Metoprolol with telmisartan for CAD.

Table 1: distribution of beta blockers combination therapy

Drug Name	Dose	Indication
Nebivolol +clinidipine	10mg+5mg	Angina
Metoprolol +ramipril	25mg+2.5mg	MI
Metoprolol +ramipril	25mg+2.5mg	MI
Metoprolol +ramipril	25mg+2.5mg	MI
Metoprolol + amlodipine	50mg+5mg	CCF
Metoprolol+Telmisartan+clinidipine	25mg+10mg+10mg	Angina
Metoprolol +Telmisartan	25mg+40mg	CAD

Beta blocker distribution along with Indications:

Beta blocker drugs used in treatment of myocardial infarction are Metoprolol Tartrate 57(32.02%), Metoprolol succinate 12(6.74%), Carvedilol 4(2.24%), Bisoprolol 8(4.49%), Nebivolol 1(0.56%), Labetalol 1(0.56%). for the treatment of Angina pectoris Metoprolol Tartrate14(7.86%), Metoprolol succinate9(5.05%), Carvedilol1(0.56%), Bisoprolol1(0.56%),

2(1.12%) Nebivolol are used. In congestive cardiac failure 10(5.61%) Metoprolol Tartrate, Metoprolol succinate1(0.56%), Carvedilol3(1.68%), Bisoprolol 3(1.68%), Nebivolol7(3.9%), Labetalol1(0.56%) are used. For LV dysfunction Metoprolol Tartrate 4(2.24%), Carvedilol 4(2.24%) are used. For Atrial fibrillation Metoprolol Tartrate1(0.56%) and Sotalol1(0.56%) are used. For Myocarditis Metoprolol Tartrate2(1.12%) and Nebivolol 1(0.56%) are used. In severe Aortic Regurgitation Metoprolol Tartrate1(0.56%), Metoprolol succinate1(0.56%), Carvedilol 1(0.56%) are used. In Severe mitral regurgitation Carvedilol1(0.56%) are used. for Hypertension Bisoprolol1(0.56%) are used.

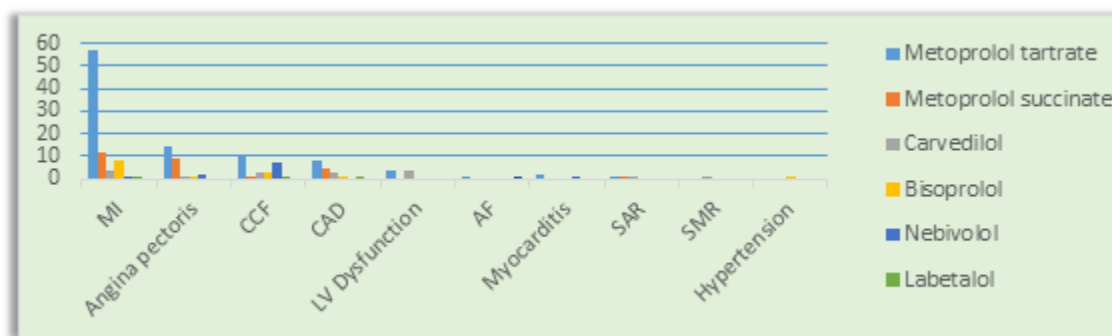


Figure 5 : Beta blocker distribution with Indications

Route of Administration:

In this study we observed that total 171 patients has administered with 178 Beta blockers, 175 (98.3%) beta blockers were administered through oral route in tablet dosage form, 3 (1.6%) beta blockers was administered through intravenous route as injection form. The ROA of all the prescribed beta blockers are correct as per ACC & ESC guidelines.

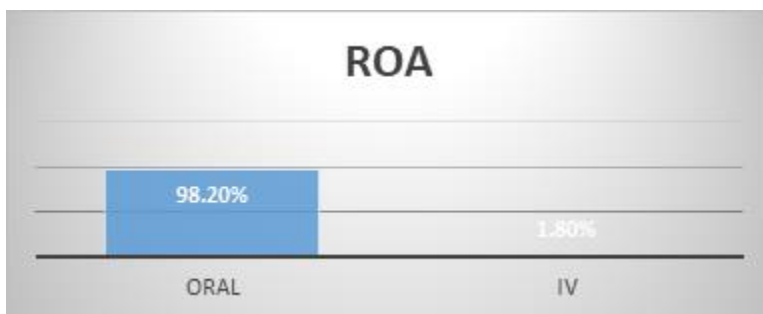


Figure 6: distribution of route of Administration of beta blockers

COMPLAINECE:

Appropriateness of Beta blockers used in cardiology department

The prescribed dosage regimen, frequency and duration of Beta blockers was appropriate as per the ACC & ESC guidelines. 97.07% beta blockers were prescribed indication was correct which is compliance with ACC/ESC guidelines and 5 patients were treated with beta blocker therapy indication was incorrect according to ACC/ESC guidelines

Table 2: complince of beta blockers used in cardiology department

Dosage regimen	Variable	Frequency	Percentage
Dose	Correct dose	171	100
	Under dose	0	0
	Over dose	0	0
Frequency	Correct frequency	171	100
	Incorrect frequency	0	0
Duration	Correct duration	171	100
Indication	Correct indication	166	97.07
	Incorrect indication	5	2.9

ACC and ESC Guidelines:

Out of 171 patients treated with beta blockers therapy 15.2% (26 patients) treatment was according to ACC/AHA guidelines, 10.5%(18 patients) treatment was compliance with ESC guidelines. 71.3% (122 patients) complied with both ACC and ESC guidelines, and 2.9% (5 patients) did not comply with any guidelines due to incorrect indication like chronic stable angina, myocarditis, atrial fibrillation, Severe Aortic regurgitation, Hypertension as per ACC & ESC guidelines.

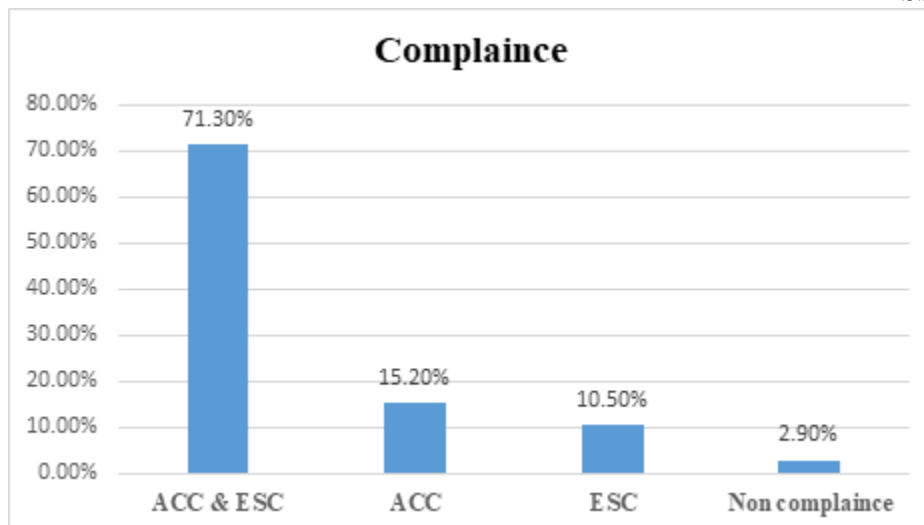


Figure 7: compliance of treatment with ACC and ESC Guidelines

CONCOMITENT DRUGS:

Concomitant drugs administered with beta blockers are: Antibiotics 7.5%, Anti thyroids 1.4%, Diuretics 8.1%, Anticoagulants 7.8%, corticosteroids 0.6%, Antiplatelet 23.2%, PPI 12.8%, Analgesic 2.7%, Statin 12.1%, vasodilator 2.7%, Anti Anginal 2.9%, CCB 1.1%, Laxatives 0.5%, Anti arrhythmic 1.2%, Anti hypertension 0.5%, Anticancer 0.08%, Nutrition supplement 2.7%, Antacid 2.0%, Erythropoietin stimulating agents 0.16%, ARB'S 0.9%, Anti-diabetes 2.5%, Alpha blocker 0.4%, Benzodiazepines 0.4%, Antihistamines 0.2%, Anticonvulsant 0.4%, ACE inhibitors 1.3%, Bronchodilator 2.5%

SAFFETY PROFILE:

Drug Interaction:

147 drug interactions were observed totally due to drugs prescribed for comorbidity condition, out of which 5(3.4%) were minor, 136(92.4%) were moderate and 6 prescription (4.1%) were having major drug interaction

Major:

Major drug interaction was found when non selective beta blocker carvedilol is administered with levosalbutamol. this combination should be avoided as beta blockers may diminish the bronchodilatory effects of beta 2 agonists.

Moderate:

Moderate drug interactions occur commonly when beta blockers are administered with diuretics, anti-diabetics, antianginals and other anti hypertensives. That can be controlled by monitoring the blood pressure and blood glucose levels.

Adverse drug reaction:

Among the study population 4 patients experienced adverse drug reaction hypotension and 1 patient observed with bradycardia. The therapy was modified after observing the adverse drug effect.

DISCUSSION

Beta blockers are the cornerstone for various cardiovascular disease conditions. Several studies revealed that there are inappropriate prescription of Beta blockers in the cardiovascular disease patients. Evaluating the rationality of Beta blockers is important to achieve the optimum patient outcome.

A prospective observational study was conducted on Assessment of rational use of Beta blockers in cardiology department at aster CMI hospital. The study sample includes 171 patients who were prescribed with Beta blockers for the cardiovascular disease.

Among the 171 cases, 128 (71.9%) patients diagnosed with cardiovascular disease were male and 43 (28%) patients were female study observed that male patients were more compare to female. More number of patients were found between 40-60 years of age and followed by 61-80 years. A study conducted by Ginenus Fekadu et.al^[10] showed that maximum patients were male and aged between the 41-50 years.

In the current study we observed that maximum patients prescribed with Beta blockers for the indication of cardiovascular disease were non-smokers (86.54%) and non-alcoholic (84.21%).

The result of the current study showed that maximum number of patients were having the past medical history of diabetes mellitus (46.1%) and hypertension (40.9%).

In our study we observed that Beta blockers were prescribed more frequently for the indication of Myocardial infraction (46.80%) followed by angina pectoris (18.70%) , CCF (14%), CAD(13.5%),and less frequently prescribed for LV dysfunction(2.30%), arterial febrilation(1.20%), Myocarditis(1.20%), SAR(1.20%), SMR(0.6%), and for hypertension (0.6%).

in a study conducted by Ginenus Fekadu et al^[10] found that most frequently prescribed Beta blockers for the indication of hypertension.

Current study revealed that Beta blocker therapy for the indication hypertension were less frequent, similarly Beta therapy was downgraded by the European Society of commission for hypertension^[11].

Our study result showed that most frequently prescribed Beta blockers was Metoprolol tartarate (54.40%) , followed by Metoprolol succinate (15.70%), Carvidelol(9.50%), bisoprolol(7.80%) and less frequently prescribed drug was Nebivolol(6.10%). In a study conducted by Ginenus Fekadu et al^[10] concluded that most frequently prescribed beta blocker was propranolol and atenolol

In the current study we observed that most frequently prescribed Beta blockers was cardio selective (88.2%) this result was more when compared with previous study conducted by Ginenus Fekadu et al^[10] study revealed that most frequently prescribed Beta blockers was cardio selective (88.2%) this result was more when compared with previous study conducted by Ginenus Fekadu et al^[10] study revealed that most frequently prescribed Beta blockers were non selective Beta blockers for the treatment of cardiovascular disease.

From our study we analyzed that most frequently prescribed Beta blockers were administered through oral route(98.2%) in the form of tablet where as 1.8% beta blockers were administered through intravenous route. The study also revealed that out 171 cases, 18.7% patients were prescribed for short duration 139 patients were prescribed for long period of duration, this result is more when compared with research conducted by Ginenus Fekadu et al,^[10] The study showed 14.01% prescription contain short duration therapy of beta blockers were as 39.60% of prescription contain long duration therapy of beta blockers.x

From the study, 97.07% Beta blockers prescribed for correct indication as per the ACC/ESC guidelines and 2.9% of Beta blockers prescribed incorrectly with regard to the chronic stable angina, myocarditis, arterial fibrillation, sever aortic regurgitation and hypertension. Ginenus Fekadu et al^[10], study revealed that 4.1% of beta-blockers were prescribed incorrectly for stage 1 hypertension, stage2 hypertension with respiratory problems and diabetes mellitus.

Additionally the therapeutc dose of Metoprolol tartrate (12.5mg, 25mg and 50mg) , Metoprolol succinate(12.5mg, 25mg and 50mg) , Carvidelol (3.125mg, 6.25mg) , Nabevolol (1.25mg,

2.5mg, 5mg and 10mg), Bisoprolol(1.25mg, 2.5mg, 5mg), Labetolol (10mg) and Sotalol (40mg) prescribed among 171 patients were also compliance with ACC/ESC guideline.

the current study showed that the prescribing pattern of Beta blockers including drug, dose, duration, frequency among the patients with cardiovascular disease are as per the ACC or ESC guidelines. this result is more compared with the study done by Ginenus Fekadu et al^[10] . .

The study result revealed that out of 171 study population 15.2% of prescription were in accordance with ACC/AHA guideline, 10.5% prescription were compliance with ECS guideline and 71.3% complied with both ACC and ESC guideline. 2.9% of prescription were noncompliance with any ACC and ESC guideline due to the incorrect indication.

A study result shown that 147 drug interaction were detected during the study period in which 4% were minor interaction, 91.8% were moderate, and 4% were having major drug interaction. minor drug interaction required no intervention, moderate interaction was monitored for the bradycardia, no patients has experienced bradycardia during the study period, major interaction was monitored for the bronchodilator effect we observed no patient has experienced the same effect .

The majority of the drug interaction was detected during study period was between the Metoprolol and Furosemide (22%) followed by Metoprolol and Nicordil (10.2%) and it was moderate type of interaction. major drug interaction was found with Carvedilol and Salbutamol, also with Carvedilol and Levosalbutamol. Ginenus Fekadu et al^[10], study shown that maximum drug interaction were between Propranolol and Cimitidine 68.42% followed by Propranolol with aluminium containing Antacid 23.68% and Atenolol with Digoxin (7.89%).

During the study period beta blockers therapy associated with hypotension seen in 4 patients and one patient experienced bradycardia. The result was low compared with the study conducted by Dennis T ko, MD et al,^[12] this study shown high incidence of adverse drug effect of Hypotension, Dizziness and Bradycardia. From this study we observed that 97% of Beta blockers prescribed in Cardiology department were Rational and 2.9 % of the treatment with Beta blockers were Irrational.

CONCLUSION:

Assessment on rational use of beta blockers in cardiology department is a prospective study in Aster CMI hospital.171 patients were recruited in the study which showed that cardiovascular

disease is more prevalent in male and most common in patients aged between 41-60 years..Majority of beta blockers were prescribed for the indication myocardial infarction followed by Angina pectoris and least prescribed for the indication hypertension.

Most commonly prescribed beta blocker was Metoprolol tartrate and Metoprolol succinate.

The study showed that most frequently prescribed beta blocker for cardiovascular disease with comorbidity was cardioselective beta blockers. The majority of beta blockers were indicated according to ACC/ESC guidelines. The study found that prescribing pattern of beta blockers including drug, dose, duration, frequency among cardiovascular disease. Patients was appropriate and in compliance with ACC/ESC guidelines. Prescribers of Aster CMI hospital in cardiology department has adhered strictly to the guidelines when prescribing medications for treatment of cardiovascular disease.

Some of the prescriptions in our study were irrational and did not follow standard guidelines resulting in hypotension and bradycardia.

This highlights the importance of improving awareness among health care professionals particularly pharmacists regarding rational prescribing practices for beta blockers.

Authors Contributions

All the authors contributed equally in design of the work, acquisition and interpretation of data, and manuscript preparation, all authors have read and approved the manuscript.

Conflict of Interest

There is no conflict of interest from all the authors.

Funding:

It is self-financed; no funding was obtained from any organization and research funding bodies.

Data Availability Statement:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgement:

The Authors are thankful to the Dr.Rajamma AJ, Principal, KLE College of Pharmacy, Bengaluru, Dr. Mahesh NM, Head of department head, KLE College of Pharmacy, Bengaluru, Dr. Praveen Kumar, Head Clinical pharamcologist, Aster CMI hospital, Bangalore for their valuable inputs to our research for providing necessary facilities to carry out this work.

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