

RESEARCH ARTICLE**THE PRESCRIBING TRENDS OF ACE-INHIBITORS AFTER MYOCARDIAL INFARCTION IN TERTIARY CARE HOSPITALS OF HAZARA REGION**

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ABSTRACT

Background: There is good evidence that angiotensin-converting enzyme (ACE) inhibitors are beneficial after myocardial infarction (MI). However, it is not known how widely this evidence is used in practice or whether all eligible patients receive this therapy. **Objective:** In three sizable tertiary care hospitals in the Hazara region, the study's objective was to evaluate the usage of ACE-inhibitors in patients who had experienced MI. **Methods:** Data collection from patients was used to collect the cases and examine the prescription pattern of use of ACE inhibitors, combination-based therapy, reasons for prescribing ACE inhibitors in STEMI, or reasons for prescribing ACE inhibitors in NSTEMI. To determine if proof-based prescribing of ACE-inhibitors following MI is taking place, data about ACE-inhibitor prescriptions is compared with recommended criteria. Descriptive statistics were used to estimate percentage frequencies. **Results:** There were 460 patients. 63.3% are male and 36.7% are female. 30% of patients who suffered an ST elevation MI received ACE inhibitors; in contrast, a greater part of patients (70%) who suffered a non-ST elevation MI received ACE inhibitors. 43.3% of the patients were prescribed ramipril, and 42% of the patients received lisinopril. Captopril, enalapril, quinapril, and fosinopril were prescribed to 7.4%, 5.4%, 1.5%, and 0.4% of patients, respectively. Ramipril was most commonly prescribed. It was also assessed that 44% of the patients received B-blockers as combination therapy. The most prescribed B-blocker was bisoprolol and then metoprolol. **Conclusion:** Most patients admitted to three tertiary care hospitals with myocardial infarction (MI) were prescribed an ACE inhibitor in an appropriate manner.

Keywords: Myocardial infarction, ACE inhibitors, STEMI, NSTEMI, Prescription, Hospital

INTRODUCTION

Drugs called angiotensin-converting enzyme inhibitors (ACE inhibitors) prevent the enzyme from turning inert angiotensin I into active angiotensin II. (1). The principal function of the hormone angiotensin II, which circulates in the blood and has several impacts on the cardiovascular system, is to narrow blood vessels. The heart must work harder to pump blood into the body's major arteries because of this constriction, which can raise blood pressure. If the heart muscle has been weakened by a heart attack or heart failure, this poses a challenge for it. (2). By preventing the formation of angiotensin II, ACE inhibitors can reduce blood pressure, prevent blood vessel constriction, and reduce the amount of energy the heart must exert to beat (3). ACE inhibitors reduce angiotensin II production and, due to this, exert their therapeutic effect. The inhibitor also does not have a direct interaction with other renin-angiotensin system components. Medical research supports the use of ACE-inhibitors in high blood pressure, congestive cardiac failure, nephropathic conditions of diabetes, and myocardial infarction (4). The pleiotropic effect of ACEI is primarily based on their antioxidant qualities, and there are increasing numbers of papers demonstrating evidence that ACEI can be helpful in the treatment of numerous different disorders (5). In a heart attack, often referred to as a myocardial infarction, your heart muscle starts to deteriorate and eventually die from a lack of blood flow. Typically, there is a blockage in the arteries supplying blood to your heart (6). Acute myocardial infarction can be divided into two categories: non-ST-segment elevation MI (NSTEMI) and ST-segment elevation MI (STEMI) (7). STEMI is defined as an acute coronary thrombosis or persistent ST-segment elevation of ≥ 1 mm in ≥ 2 contiguous electrocardiographic leads or results from complete and prolonged occlusion of an epicardial coronary blood vessel and is defined based on ECG criteria (8).

NSTEMI is characterized as ischemic symptoms at rest caused by an abrupt coronary plaque rupture or erosion that last less than 10 minutes, occur within 24 hours of admission to the hospital, and are followed by either an increased

cardiac biomarker (either creatinine kinase or cTn) within 24 hours of the initial presentation (7). Following a MI, the renin-angiotensin system is more activated, which raises the heart rate and systemic vascular resistance. Due to the increased myocardial wall stress caused by this, ventricular remodeling and dilatation develop. An increased risk of heart failure, cardiac rupture, arrhythmia, and death can result from this. In addition, endogenous fibrinolytic activity may be negatively impacted by renin-angiotensin system activation. A increasing body of research shows that ACE-inhibitors have good benefits in lowering morbidity and death in people who have had a MI because they halt these processes. (9). By avoiding the hyperactivation of RAS caused by ACE2 downregulation and so averting acute lung injury, the administration of ACEI may also be advantageous. Lately, ACEI have been utilized to treat COVID-19 patients' hypertension, and the results have been positive. However, further evidence was needed to confirm this benefit (10). Angiotensin converting enzyme (ACE) inhibitors have been used extensively in treating a wide range of cardiovascular (CV) illnesses ever since the first one, captopril, became available in 1981. More than a dozen years after the ACE inhibitor captopril was initially introduced, in 1995, losartan became the first angiotensin receptor blocker (ARB). Patients with diabetes, heart failure, ACE inhibitors, ARBs, hypertension, and chronic kidney disease (CKD) are frequently treated with these medications. ARBs were only thought of as an alternate treatment for people who were intolerant to ACE inhibitors, even though numerous American and European guidelines for the management of patients with CV disease suggested ACE inhibitors as a first-choice therapy. ACE inhibitors have been compared to placebo in numerous clinical trials, but they are not as effective against hypertension in heart failure. When enalapril treatment was given to patients with severe heart failure, the Cooperative North Scandinavian Enalapril Survival Study demonstrated an astounding 31% reduction in mortality at one year when compared to placebo (11).

The objective of this study was to evaluate the usage of ACE inhibitors in patients with myocardial infarction in tertiary care facilities at the Hospital of Hazara. This is the first type of study, and no data is available in the literature reporting the use of inhibitors after MI. The overuse of these drugs can significantly increase mortality (4). The study was conducted to evaluate the use of ACE-inhibitors according to different demographic factors, dosing parameters, associated co-morbidities, route of administration, cost of drug therapy, and its use according to guidelines. The study also evaluates the use of different ACE inhibitors for STEMI and NSTEMI and prescribing patterns for ventricular ejection fraction. The study also indicates the most commonly prescribed drug in this group, and β blockers are used mostly for additive effects (12).

METHODOLOGY

A representative cross-sectional study was conducted by including 900 prescription files in three hospital's health information system. Data collections were conducted between August 2021 till May 2022. Only 460 Cases/ Prescription were selected and analysed keeping in view the inclusion criteria. Out of total 460, 37.5% were collected from AMC (Ayub Medical Complex), 33.9% from DHQ Abbottabad, 28.5% from DHQ Haripur. The data was collected from inpatient and outpatient departments of the above-mentioned hospitals. The data was collected from three tertiary care hospitals of Hazara region. The details about the hospitals are as follows.

The main hospital in Northern Pakistan is the Ayub Medical Complex, a tertiary care teaching hospital. It began operations in 1995, and in 1998 it attained the 1460-bed status. The ATH is a cutting-edge medical centre with excellent sophisticated treatment and diagnostic equipment.

District Headquarter Hospital is the oldest set up in the city covering area of about fifteen acres. It is a tertiary care facility of 350 beds and equipped with all of necessities.

Districts headquarter hospital Haripur was established in 1993 covering 25.5 acres of land. It is a tertiary care hospital of 352 beds equipped with all essential medical facility.

Between August 2021 and May 2022, 900 patients with MI were recognized who were in CCU. The diagnostic tests records were also used to identify the patients in CCU with MI because a patient might have suffered a MI while in the unit. The prescription records and medical histories of every patient identified throughout this time period who participated in the trial were examined.

All prescriptions for patients of all ages having confirmed diagnosis of MI, irrespective of gender and duration of ailment were included in the study. The prescriptions with unproven diagnosis, illegible written prescriptions, and prescriptions without demographics were excluded from the study.

The approval of the study was taken from the Ethical Committee on Research at the department of Pharmacy, COMSATS University, Islamabad, Abbottabad Campus. In order to determine if ACE-inhibitor prescriptions following MI are being made on the basis of evidence, data on ACE-inhibitor prescribing were compared with recommended criteria. The rationale for using ACE-inhibitors following MI were examined.

The kind of MI that was diagnosed for the patient as ST -elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (non-STEMI) were also recorded. Reasons for any non-use of ACE-inhibitors following MI were examined. The length of medication uses and the discharge prescribing of ACE-inhibitors are also evaluated.

Study parameters:

1. Total patients and male %/female %
2. Age of patient, duration of treatment
3. Most frequently approved ACE-Inhibitors & cost of therapy
4. Route of administration & dosage form
5. Related co-morbidities.
6. Ejection fraction % & smokers
7. ACEIs in combination with B-blockers
8. Most frequently prescribed B-blocker.

STATISTICAL ANALYSIS

Modified data collection from patients was used to collect the cases and analysed for prescription pattern of use of ACE-inhibitors after MI, combination-based therapy, reasons for prescribing ACE inhibitors in STEMI or reasons

for prescribing ACE inhibitors in NSTEMI, to assess the dose at discharge, using statistical software i.e., Microsoft excel.

RESULTS

There were 460 patients (291 males) (63.3%) and 169 females (36.7%) who had been diagnosed with an MI and passed the inclusion criteria. The average age was 63.5 years (range 25–102 years), with an average stay of 5 days (range 1–15 days). The duration of medication use for ACE inhibitors was a minimum of three months and continued. Diabetes is indicated as a risk factor for coronary artery disease and is a major leading factor for MI, hypertension, and other cardiac diseases (13). Smoking is also a risk factor for myocardial infarction because continuous smoking causes irritation in the arteries, causing vasospasm and ultimately increasing blood pressure (14). The risk factors for myocardial infarction are shown in Table 1.

Table 1. The table shows the risk factor of number of patients with Myocardial infarction (MI).

Risk factor	Number of patients
Male	291
Female	169
Diabetes mellitus	118
Current smoker	325
Ex-smoker > 10 years	22
Hypertension	302
Post-menopausal female	92
Weight in kg (45-55)	69
Weight in kg (55-65)	253
Weight in kg (> 65)	138
Age in years (25-40)	33
Age in years (40-55)	165
Age in years (>55)	262

Total of 460 patients were prescribed an ACE-inhibitor, 290 of whom were in-patients. 63 patients had ventricular ejection fraction less than 35% and all patients on ACEIs who have ejection fraction less than 35%. But patients who have ejection segment more than 35% but less than 55% are also on ACEIs.

In relation to the categorization of the ischemia event, the prescribing of an ACE-inhibitor was also investigated. ACE-inhibitor use was assessed to that of ST elevation Myocardial

infarction vs non-ST elevation Myocardial infarction, data about MI types were separated. Patients (30%) who suffered an ST elevation MI were receiving ACE-inhibitors, while in comparison, a greater proportion of patients (70%) who suffered non-ST elevation MI received ACE-inhibitors.

The kind of ACE-inhibitors prescribed are shown in Table 2. Prescribing the Ramipril to (199 patients)(43.3%) and giving the medication after admission in hospital to (124 patients), Prescribing the Lisinopril to (193 patients)(42%) and giving the medication after admission in hospital to (107 patients), Prescribing the Captopril to (34 patients)(7.4%) and giving the medication after admission in hospital to (28 patients), Prescribing the Enalapril to (25 patients)(5.4%) and giving the medication after admission in hospital to (22 patients), Prescribing the Quinapril to (7 patients)(1.5%) and giving the medication after admission in hospital to (7 patients), Prescribing the Fosinopril to (2 patients)(0.4%) and giving the medication after admission in hospital.

Table 2. Type of ACEIs prescribed.

ACEIs	Number of Patients	Initiated after admission in hospital
Ramipril	199	124
Lisinopril	193	107
Captopril	34	28
Enalapril	25	22
Quinapril	7	7
Fosinopril	2	2

The ramipril was most commonly prescribed because its present in lowest strength i.e. 1.25mg, if patient have impaired renal function or hypotensive so they are able to use ACEIs(ramipril) due to its lowest strength it little effect on renal function and blood pressure(15) and, easily available in a Hazara region. All ACE-inhibitors initiated in patients after MI at three different tertiary care units (460 patients, all in CCU) were recommended by cardiologists. 290 patients were initiated on

ACE-inhibitors after admission in hospital. 170 patients were discharged from three different tertiary care units with advice to start them on an ACE-inhibitor from their cardiologist.

The data were collected from ward and OPD, there are 290 cases (63%) of admitted patient and 170 prescription (37%) of out-patient department.

The most commonly used route of administration for ACE inhibitors was the oral route (460 patients). Because most of the ACEIs are present in solid dosage form (tablets), and ACEIs are commonly prescribed for life unless any contraindication is present, it is easier and more convenient for patients to take tablets rather than injections or other dosage forms. The tablet is the most convenient management tool with an accurate dose (16).

The most commonly prescribed ACEI was ramipril because it has the lowest price, i.e., 77 PKR, and is present in the lowest strength, i.e., 1.25mg. The data were collected from government hospitals, i.e., DHQ Haripur, DHQ Abbottabad, and Ayub Medical Complex, and the patients were mostly poor and could not afford expensive treatment. That's why prescribing cheap and effective ACEIs and ramipril is effective (17).

Table 3. Cost of ACEIs

Drug with lowest strength	Cost
Ramipril 1.25mg	77 PKR/28 tablets
Lisinopril 5mg	55 PKR/14 tablets
Captopril 25mg	134 PKR/24 tablets
Enalapril 5mg	102 PKR/20
Quinapril 5mg	214 PKR/28 tablets
Fosinopril 10mg	333 PKR/28 tablets

The patient use B-blocker in combination with ACEIs were 201(43.7%), and without B-blocker were 259(56.3%). B-blocker were probably helpful when used in combination with ACE inhibitors to reduce morbidity and mortality rate(18). Those patients who did not use B-blocker due to presence of any contraindication e.g. asthmatic patients because it cause bronchoconstriction, and brady cardiac patients

its slow the heart rate(19). Acute myocardial infarction patients with left ventricular dysfunction and atherosclerotic sequelae have a lower death rate when using β -blockers and ACE inhibitors together, according to clinical trials (20).

Most commonly prescribed B-blocker was bisoprolol and then metoprolol, because of cost, it has lowest cost and easily available in a Hazara region.

Table 4. Type of B-blocker prescribed in combination with ACEIs:

Drug	Number of patients
Bisoprolol	73
Carvedilol	42
Nebivolol	10
Metoprolol	58
Propranolol	18

DISCUSSION

The data assortment only from those patients who to prescribe ACEIs or patients who use ACEIs. So, all 460 patients (male: 291, female: 169) uses ACEIs. 445 cases out of 460 (97%) cases of ACEIs prescribing were appropriately. The later 15 cases (3%) some have use high dose of ACEIs, some have present contraindication to ACEIs but prescribed ACEIs.

302 individuals have hypertension, 118 patients have diabetes, and some patients have several risk factors. These patients are using ACEIs. Due to the fact that ACE-inhibitors are recommended for use in these patients in order to protect renal function, these risk factors may have influenced the choice to use them. (21). Nine (9) individuals were using high doses of ACE inhibitors and had compromised renal function. The patients suffering from renal artery stenosis are contraindicated to use ACE inhibitors. Therefore, it is always advised to not prescribe ACE inhibitors for patients with impair renal function (22). Ramipril was the most frequently use ACEIs at hospitals because of they have low cost, easily available in a Hazara region and available in the lowest strength (1.25mg), also due to its once-daily dosage schedule. Moreover, the reason for the

use of ramipril and lisinopril in every other patient is the low dose and cost of these drugs of this class and its easy availability in this region. 201 cases out of 460 cases (44%) uses β blocker in combination with ACEIs, and B-blocker probably helpful to reducing morbidity and mortality rate in MI patients when use with ACEIs. 259 cases out of 460 cases (66%) not using B-blocker because of presence of contraindication to B-blocker.

After myocardial infarction, the use of ACE inhibitors is generally beneficial and important because of their effect on an enlarged reduction in the morbidity and mortality rates of the patients (23). On questioning prescribers about the use of ACE inhibitors after myocardial infarction, we get that this class of medication has an effect on remodeling of the heart anatomy, which gets changed or damaged after the continuous acute attacks of the heart attack or after infarct expansion (24). The key answer generated after evaluating its overprescribing is the remodeling of heart anatomy, which also has a positive effect on ejection fraction (24). It was observed that ACE inhibitors were initiated by the cardiologist for the patients admitted to the CCU and not by the general practitioners.

CONCLUSION

Most patients admitted to three tertiary care hospitals with myocardial infarction were appropriately prescribed an ACE inhibitor. Most of the patients received medication and its dose according to the prescribed guidelines. B blockers used in combination with ACE inhibitors were probably helpful in reducing morbidity and mortality rates. The study concludes that ramipril and lisinopril were probably the drugs of choice.

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DECLARATIONS

Authors' Contributions

FA contributed to the study concept; GB, SN, and MSK contributed to the study design and data collection. M contributed to the data analysis and interpretation. JR and IZ did the literature review and critically reviewed the manuscript. All the authors read and approved the final manuscript.

Ethical Approval

Ethical approval was obtained from Research Ethics committee of Bolan Medical Complex Hospital, Quetta.

Conflict of Interest

The authors declared no conflict of interest among them.

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