



Clinical evaluation of prescription pattern of drugs administered for myocardial infarction in Magadh region Bihar

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Abstract

Different strategies were recommended for patients with AMI based on certain guidelines to reduce mortality and applied in practice routinely. But strict application of the same would bring better outcome in clinical practice. But it was observed adhering to these guidelines are in suboptimal in clinical setting due to variation in temporal and geographical variations. Many of the drugs (E.g. statins, antiplatelet drugs, ACE inhibitors etc.) that could save the life are still being deficit in the prescriptions. Underutilization of drugs is seen more seen females showing gender difference for drug usage and exact cause for this difference is not still known. Hence based on above findings the present study was planned for Clinical Evaluation of Prescription Pattern of Drugs Administered for Myocardial Infarction in Magadh Region Bihar.

The present study was planned in Anugrah Narayan Magadh Medical College, Gaya, Bihar, India. In this study 50 cases diagnosed with the Myocardial infarction were enrolled and evaluated. After recording the obtained information in the case record form the data were analyzed further according to demographic profile, social habits, coexisting illness and the drug utilization pattern including routes of administration, category of the drug used in the treatment and fixed-dose combination prescribed.

The data generated from the present study it is observed that Anti-platelets, Anti-anginals and Hypo-lipidemic are the mainly drugs prescribed for the Myocardial infarction. The trends in prescribing medication in case of myocardial infarction and the strategies towards its approach has been changes over past few years and it will show further changes in next decade as indicated by the results of this study.

Keywords: myocardial infarction, prescription pattern, retrospective study, tertiary care hospital, etc.

1. Introduction

A myocardial infarction (MI), also known as a heart attack, occurs when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle. The most common symptom is chest pain or discomfort which may travel into the shoulder, arm, back, neck or jaw. Often it occurs in the centre or left side of the chest and lasts for more than a few minutes. The discomfort may occasionally feel like heartburn. Other symptoms may include shortness of breath, nausea, feeling faint, a cold sweat or feeling tired. About 30% of people have atypical symptoms. Women more often present without chest pain and instead have neck pain, arm pain or feel tired. Among those over 75 years old, about 5% have had an MI with little or no history of symptoms. An MI may cause heart failure, an irregular heartbeat, cardiogenic shock or cardiac arrest.

Initial stabilization of patients with suspected MI and ongoing acute chest pain should include administration of sublingual nitroglycerin if patients have no contraindications to it. The American Heart Association (AHA) recommends the initiation of beta blockers to all patients with STEMI (unless beta blockers are contraindicated) ^[1, 2]. If STEMI is present and the patient is within 90 minutes of a PCI-capable facility, the patient should undergo emergent coronary angiography and primary PCI. If the patient is longer than 120 minutes from a PCI-capable facility, fibrinolysis should be considered ^[2].

Although patients presenting without ST-segment elevation (non-STE-ACS) are not candidates for immediate administration of thrombolytic agents, they should receive anti-ischemic therapy and may be candidates for PCI urgently or during admission. Myocardial infarction (MI) usually results from an imbalance in oxygen supply and demand, which is most often caused by plaque rupture with thrombus formation in an epicardial coronary artery, resulting in an acute reduction of blood supply to a portion of the myocardium. Although the clinical presentation of a patient is a key component in the overall evaluation of the patient with MI, many events are either "silent" or are not clinically recognized by patients, families, and health care providers. The appearance of cardiac biomarkers in the circulation generally indicates myocardial necrosis and is a useful adjunct to diagnosis.

MI is considered part of a spectrum referred to as acute coronary syndrome (ACS). The ACS continuum representing ongoing myocardial ischemia or injury consists of unstable angina, non-ST-segment elevation MI (NSTEMI)-collectively referred to as non-ST-segment acute coronary syndrome (NSTE ACS)-and ST-segment elevation MI (STEMI). Patients with ischemic discomfort may or may not have ST-segment or T-wave changes denoted on the electrocardiogram (ECG). ST elevations seen on the ECG reflect active and ongoing transmural myocardial injury. Without immediate reperfusion therapy,

most patients with STEMI develop Q waves, reflecting a dead zone of myocardium that has undergone irreversible damage and death.

Those without ST elevations are diagnosed either with unstable angina or NSTEMI—differentiated by the presence of cardiac enzymes. Both these conditions may or may not have changes on the surface ECG, including ST-segment depressions or T-wave morphological changes. MI may lead to impairment of systolic or diastolic function and to increased predisposition to arrhythmias and other long-term complications. Coronary thrombolysis and mechanical revascularization have revolutionized the primary treatment of acute MI, largely because they allow salvage of the myocardium when implemented early after the onset of ischemia.

The modest prognostic benefit of an opened infarct-related artery may be realized even when recanalization is induced only 6 hours or more after the onset of symptoms; that is, when the salvage of substantial amounts of jeopardized ischemic myocardium is no longer likely. The opening of an infarct-related artery may improve ventricular function and collateral blood flow; prevent ventricular remodeling, as well as decrease infarct expansion, ventricular aneurysm formation, and left ventricular dilatation; and reduce late arrhythmia associated with ventricular aneurysms, and mortality [3].

Evidence suggests a benefit from the use of beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, and statins. The American College of Cardiology (ACC)/American Heart Association (AHA)/European Society of Cardiology/World Heart Federation released the Observations From the TRITON-TIMI 38 Trial (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel—Thrombolysis in Myocardial Infarction), which better outlines a universal definition of MI, along with a classification system and risk factors for cardiovascular death [4].

Myocardial infarction (MI), commonly known as a heart attack, is defined pathologically as the irreversible death of myocardial cells caused by ischemia. Clinically, MI is a syndrome that can be recognized by a set of symptoms, chest pain being the hallmark of these symptoms in most cases, supported by biochemical laboratory changes, electrocardiographic (ECG) changes, or findings on imaging modalities able to detect myocardial injury and necrosis. According to the third universal definition of MI, implemented by a joint task force from the European Society of Cardiology (ESC), American College of Cardiology (ACC) Foundation, American Heart Association (AHA), and the World Heart Federation (WHF), MI is diagnosed when either of the following two criteria are met. [5].

Atherosclerosis is the disease primarily responsible for most acute coronary syndrome (ACS) cases. Approximately 90% of myocardial infarctions (MIs) result from an acute thrombus that obstructs an atherosclerotic coronary artery. Plaque rupture and erosion are considered to be the major triggers for coronary thrombosis. Following plaque erosion or rupture, platelet activation and aggregation, coagulation pathway activation, and endothelial vasoconstriction occur, leading to coronary thrombosis and occlusion.

Within the coronary vasculature, flow dynamics and endothelial shear stress are implicated in the pathogenesis of

vulnerable plaque formation. A large body of evidence indicates that in numerous cases, culprit lesions are stenoses of less than 70% and are located proximally within the coronary tree. Coronary atherosclerosis is especially prominent near branching points of vessels. Culprit lesions that are particularly prone to rupture are atheromas containing abundant macrophages, a large lipid-rich core surrounded by a thinned fibrous cap [6].

A myocardial infarction requires immediate medical attention. Treatment aims to preserve as much heart muscle as possible, and to prevent further complications. Treatment depends on whether the myocardial infarction is a STEMI or NSTEMI. Treatment in general aims to unblock blood vessels, reduce blot clot enlargement, reduce ischemia, and modify risk factors with the aim of preventing future MIs. In addition, the main treatment for myocardial infarctions with ECG evidence of ST elevation (STEMI) include thrombolysis or percutaneous coronary intervention, although PCI is also ideally conducted within 1–3 days for NSTEMI. In addition to clinical judgement, risk stratification may be used to guide treatment, such as with the TIMI and GRACE scoring systems [7].

The pain associated with myocardial infarction may be treated with nitroglycerin or morphine. Nitroglycerin (given under the tongue or intravenously) may improve the blood supply to the heart, and decrease the work the heart must do. It is an important part of therapy for its pain relief, despite there being no benefit to overall mortality. Morphine may also be used, and is effective for the pain associated with STEMI. The evidence for benefit from morphine on overall outcomes, however, is poor and there is some evidence of potential harm [8].

Aspirin, an antiplatelet anticoagulant, is given as a loading dose with the goal of reducing the clot size and reduce further clotting in the affected artery. It is known to decrease mortality associated with acute myocardial infarction by at least 50%. P2Y12 inhibitors such as clopidogrel, prasugrel and ticagrelor are given concurrently, also as a loading dose, with the dose depending on whether further surgical management or fibrinolysis is planned. Prasugrel and ticagrelor are recommended in European and American guidelines, as they are active more quickly and consistently than clopidogrel. P2Y12 inhibitors are recommended in both NSTEMI and STEMI, including in PCI, with evidence also to suggest improved mortality. Heparins, particularly in the unfractionated form, act at several points in the clotting cascade, help to prevent the enlargement of a clot, and are also given in myocardial infarction, owing to evidence suggesting improved mortality rates. In very high-risk scenarios, inhibitors of the platelet glycoprotein α IIb β 3a receptor such as eptifibatid or tirofiban may be used [9].

There is varying evidence on the mortality benefits in NSTEMI. A 2014 review of P2Y12 inhibitors such as clopidogrel found they do not change the risk of death when given to people with a suspected NSTEMI prior to PCI, nor do heparins change the risk of death. They do decrease the risk of having a further myocardial infarction [10].

Primary percutaneous coronary intervention (PCI) is the treatment of choice for STEMI if it can be performed in a timely manner, ideally within 90–120 minutes of contact with a medical provider. Some recommend it is also done in NSTEMI within 1–3 days, particularly when considered high-risk. A 2017 review, however, did not find a difference between early versus later PCI in NSTEMI [11].

PCI involves small probes, inserted through peripheral blood vessels such as the femoral artery or radial artery into the blood vessels of the heart. The probes are then used to identify and clear blockages using small balloons, which are dragged through the blocked segment, dragging away the clot, or the insertion of stents. Coronary artery bypass grafting is only considered when the affected area of heart muscle large, and PCI is unsuitable, for example with difficult cardiac anatomy. After PCI, people are generally placed on aspirin indefinitely and on dual antiplatelet therapy (generally aspirin and clopidogrel) for at least a year [12].

If PCI cannot be performed within 90 to 120 minutes in STEMI then fibrinolysis, preferably within 30 minutes of arrival to hospital, is recommended. If a person has had symptoms for 12 to 24 hours evidence for effectiveness of thrombolysis is less and if they have had symptoms for more than 24 hours it is not recommended. Thrombolysis involves the administration of medication that activates the enzymes that normally dissolve blood clots. These medications include tissue plasminogen activator, reteplase, streptokinase, and tenecteplase. Thrombolysis is not recommended in a number of situations, particularly when associated with a high risk of bleeding or the potential for problematic bleeding, such as active bleeding, past strokes or bleeds into the brain, or severe hypertension. Situations in which thrombolysis may be considered, but with caution, include recent surgery, use of anticoagulants, pregnancy, and proclivity to bleeding. Major risks of thrombolysis are major bleeding and intracranial bleeding. Pre-hospital thrombolysis reduces time to thrombolytic treatment, based on studies conducted in higher income countries, however it is unclear whether this has an impact on mortality rates [13].

In the past, high flow oxygen was recommended for everyone with a possible myocardial infarction. More recently, no evidence was found for routine use in those with normal oxygen levels and there is potential harm from the intervention. Therefore, oxygen is currently only recommended if oxygen levels are found to be low or if someone is in respiratory distress. If despite thrombolysis there is significant cardiogenic shock, continued severe chest pain, or less than a 50% improvement in ST elevation on the ECG recording after 90 minutes, then rescue PCI is indicated emergently [14].

Those who have had cardiac arrest may benefit from targeted temperature management with evaluation for implementation of hypothermia protocols. Furthermore, those with cardiac arrest, and ST elevation at any time, should usually have angiography. Aldosterone antagonists appear to be useful in people who have had an STEMI and do not have heart failure [15].

Different strategies were recommended for patients with AMI based on certain guidelines to reduce mortality and applied in practice routinely. But strict application of the same would bring better outcome in clinical practice. But it was observed adhering to these guidelines are in suboptimal in clinical setting due to variation in temporal and geographical variations. Many of the drugs (E.g. statins, antiplatelet drugs, ACE inhibitors etc.) that could save the life are still being deficit in the prescriptions [16]. Underutilization of drugs is seen more seen females showing gender difference for drug usage and exact cause for this difference is not still known [17]. Hence based on above findings the present study was planned for Clinical

Evaluation of Prescription Pattern of Drugs Administered for Myocardial Infarction in Magadh Region Bihar.

Methodology

The present study was planned in Anugrah Narayan Magadh Medical College, Gaya, Bihar, India. In this study 50 cases diagnosed with the Myocardial infarction were enrolled and evaluated. After recording the obtained information in the case record form the data were analyzed further according to demographic profile, social habits, coexisting illness and the drug utilization pattern including routes of administration, category of the drug used in the treatment and fixed-dose combination prescribed.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria

Patients diagnosed with the myocardial infarction.

Exclusion Criteria

When diagnosis was not certain. Patients with multiple diseases like stroke, structural heart diseases, liver failure and renal failure. Pregnant/lactating females and children less than 18 years. Patients who refuse to give informed consent.

Results and Discussion

Acute myocardial infarction (MI) remains a leading cause of morbidity and mortality worldwide. Critical myocardial ischemia can occur as a result of increased myocardial metabolic demand, decreased delivery of oxygen and nutrients to the myocardium via the coronary circulation, or both. An interruption in the supply of myocardial oxygen and nutrients occurs when a thrombus is superimposed on an ulcerated or unstable atherosclerotic plaque and results in coronary occlusion.1

MI can be symptomatic or asymptomatic. Symptoms of MI ranges from none at all to sudden cardiac death. Despite the diversity of manifesting symptoms of MI, there are some characteristic symptoms like chest pain described as a pressure sensation, fullness, or squeezing in the midportion of the thorax, radiation of chest pain into the jaw or teeth, shoulder, arm, and/or back, it can associated with dyspnea or shortness of breath, epigastric discomfort with or without nausea and vomiting, diaphoresis or sweating, syncope or near syncope without other cause impairment of cognitive function without other cause.

Drug utilization research is an important branch of pharmacoepidemiology as it elucidate the scope, character and determinants of drug exposure [18]. The world health organization (WHO)in 1997 defined drug utilization as the prescribing, allotment, marketing and use of drugs in a civilization, among a particular focus on the medical, social, and economic consequence resulted [19]. Drug use is a complex process. In any country a large number of socio-cultural factors assign to the manner in which drugs are used. In India, these includes national drug policy, illiteracy, poverty, use of multiple health care systems, drug marketing and promotion, sale of prescription drugs without prescription, competition in the medical and pharmaceutical

market place and limited availability of independent, unbiased drug information. The complexity of use of drug means the optimal profits of drug therapy in patient care may not be attained because of underuse, overuse or abuse of drugs. Unfortunate drug use might also cause to elevate rate of medical concerns, antimicrobial resistance, adverse effects and patient mortality [20]. Hence contemporary studies on drug utilization have developed into a probable mean to be used in the assessment of health systems [21]. The awareness of drug utilization studies starts in the early 1960s [22-23], and its importance has elevated since then because of augmentation in marketing of new drugs, deep distinction in the pattern of drug prescribing and utilization, rising concern about delayed adverse events and the mounting concern regarding the charge of drugs [24-27].

Table 1: Demographic Details

Parameters	No. of Cases
Sex	
Males	33
Females	17
Age	
21 – 30 years	1
31 – 40 years	12
41 – 50 years	23
51 – 60 years	10
61 & above years	4
Locality	
Urban	30
Rural	20
Total	50

Table 2: Drug Used

Drug Class	Administered in No. of Cases
Anti-platelets	46
Anti-anginals	33
Hypo-lipidaemics	32
H2-Blockers	22
Antianxiety	17
Laxatives	17
Beta blockers	17
ACE Inhibitors	16
Antidiabetic drugs	12
Diuretics	12
Opioids	9
Anticoagulants	7
Antibiotics	7
Antiemetics	7
CCB's	7
ART's	7
Thrombolytics	6
Inotropic drugs	5
NSAID's	4
Antipsychotic	3
PPI's	2
Anti-epileptics	2
Bronchodilators	1
Alpha blockers	1
Others	1

In Chandana N *et al* study (2013) [28], anticoagulant was also prescribed in (100%) patients, 10 which is similar to present study but other classes of drugs like (Antianginal, Antihypertensive, Hypolipidemic, and Thrombolytics) were not according to present study. While Jesso George *et al* [29],

in their study in 2013 found that the five commonly prescribed drug classes were platelet inhibitors (88.7%), statins (76.3%), ACE Inhibitors/Angiotensin receptor blockers (72%), beta-blockers (58%), and heparin (57%). Polypharmacy (>5 drugs) was noticed in (71%) patients. Beta blockers and/or ACE inhibitors are recommended as first line therapy along with addition of other drugs as required, for treatment of patients with blood pressure more than or equal to 140/90 mm Hg. similarly statin therapy is recommended to achieve LDL cholesterol of less than 100 mg/dl and total cholesterol less than 200mg/dl. Dual Antiplatelet Therapy and anticoagulant agents like aspirin 75 to 162 mg/day in patients with no contraindications or clopidogrel 75 mg daily for patients who are intolerant or allergic to aspirin. AP2Y12 receptor antagonist in combination with aspirin is indicated in patients after acute coronary syndrome or per cutaneous intervention with stent placement. ACE inhibitors should be started and continued indefinitely in all patients with left ventricular ejection fraction (LVEF) less than or equal to 40% and in those with hypertension, diabetes or chronic kidney disease. ARBs are recommended in patients who have heart failure or MI with LVEF less than or equal to 40% and who are intolerant to ACE inhibitors. Beta blockers should be used in all patients with left ventricular systolic dysfunction, unless contraindicated and is continued for at least three years or beyond.

Beta blockers are a class of drugs, which are used primarily in hypertension. Antihypertensive and cardioprotective effects β -blockers support more frequently use as found in our study. In a previous study by Heaton *et al* [30], reported that beta blockers decrease the mortality rate in myocardial infarction patient. Cardio-selective β blockers, metoprolol and carvedilol, were the most prescribed drugs in the present study which was a rational approach to the therapy. With an objective to control various complications of CVDs patients were prescribed the combination of drugs. Physicians mostly prescribed dual and triple drug regimen. Patients were advised to do physical exercise with daily blood pressure monitoring. Our study showed that most of the hyperlipidemic patients were prescribed atorvastatin which decreases blood LDL cholesterol level while increasing the HDL level. In addition, it also reduces the risk of CHD, MI and stroke, etc [31]. The patients with ischemic heart disease were treated with antiplatelet drugs which prevent blood clotting or atheroma. Atheroma in coronary blood vessels may lead to a sudden heart attack or myocardial infarction. Drugs like antiplatelet agents are used individually or in the combination for prevention as well as terminating the heart attack. In the present study antiplatelet drugs such as clopidogrel, aspirin and nitrates such as nitroglycerine, isosorbide mononitrate was used most frequently in IHD patients.

Different studies on drug utilisation have revealed wide geographical differences in use of same group of drugs. Drug utilisation study addresses the relationship between the recommended therapeutic practice and actual clinical practice. Despite the advances in detection, treatment and management of acute coronary syndrome, it continues to be a significant contributor to the mortality and morbidity attributed to cardiovascular diseases, even in developing countries. Prompt and early detection of cardiovascular emergencies and immediate initiation of therapy are therefore necessary for reduction in mortality and morbidity

due to cardiovascular emergencies [32-33].

Myocardial infarction is a major cause of death and disability worldwide. Currently, India leads the World with the largest number of patients with myocardial infarction. It is the dream of the new millennium that the care of the patients should be evidence based and validated. The study of prescribing pattern is a component of a medical audit that does monitoring and evaluation of the prescribing practice of the prescribers as well as recommends necessary modifications to achieve rational and cost-effective medical care.

Conclusion

The data generated from the present study it is observed that Anti-platelets, Anti-anginals and Hypo-lipidemic are the mainly drugs prescribed for the Myocardial infarction. The trends in prescribing medication in case of myocardial infarction and the strategies towards its approach has been changes over past few years and it will show further changes in next decade as indicated by the results of this study.

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