IMPACT OF MEDICATION ERRORS ON OUTCOMES IN ADMITTED CORONARY ARTERY DISEASE PATIENTS: A REVIEW

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Abstract

Background: Medication errors are unintended and can be reduced by considering the related factors. Tactics to this are expected to be diverse in research and routine care. Elderly patients, pregnant women, and patients suffering from chronic disease are at higher risk of getting medication-related errors**.**

Methods: A thorough literature search was performed using PubMed and Google scholar. The author selected the articles bases on their relevance. Medication error, drug-related error, cardiovascular disease, and cardiovascular drugs were the major searched keyword. Secondary sources included from the published medical news articles.

Results: Through the literature, it has been observed that patients with coronary artery disease admitted to the in-patient department are more prone to medication-related errors, especially the elderly population, and pregnant women are more vulnerable to medication-related errors. This review enlightened the medication errors, the patient at higher risk of a medication error, and various methods to overcome medication errors.

Conclusion: In the pregnant and elder populations, treating physicians should consider age and physiological-related change in pharmacodynamic and pharmacokinetic parameters during prescribing to avoid medication related errors. To reduce medication error, clinical pharmacists should be considered as a part of a healthcare team.

Keywords: Medication error; Cardiovascular disease; Chronic disease; Vulnerable population

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Introduction

Medication errors are the utmost communal type of medical error and in-patient medication for cardiovascular disease holds a large proportion of these errors. An average of one medication error occurs per hospitalised patient per day [1]. Medication errors rank as the eighth leading cause of death in the United States (US) and are estimated to account for approx. 1,00,000 deaths per year [2]. Each year in the United States, the estimated avoidable medication-relatederrorcost around 3.5 billion US dollars [3]. In 2001, congress capitalized 50 million US dollars to initiate patient safety and directed the Healthcare Research and Quality agency to establish the Centre for Quality Improvement and Patient Safety. American Heart Association (AHA) in 2002, delivered its first scientific report on medication error in acute cardiac care [4]. In 2003, congress approved the Medicine Modernization Act to charge the Institute of Medicine to formulate a national agenda to reduce medication-related errors. Despite research and public awareness toward the medical error, the impression of medication error on patient safety remains a substantial problem [3]. The American College of Cardiology (ACC)/AHA developed guidelines with respect to classifications of recommendation and level of evidence which are as follow.

Classification of Recommendation

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.
Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa: Weight of evidence/opinion is in favour of usefulness/efficacy.
Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
Class III: Conditions for which there is evidence and/or general agreement that a procedure/ treatment is not useful/effective and in some cases may be harmful.

Level of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.
Level of Evidence C: Only consensus opinion of experts, cases studies, or standard of care.

Medication Error Definition and Categories

The US Food and Drug Administration define medication error as an event(s) related to professional practice, procedure, healthcare products and healthcare system including prescribing, communication, compounding, labelling, administration, education, monitoring and use [5]. Variation in definition and ability to uncover errors have contributed to a wide range of medication error rates estimates. In the present review, medication errors will include improper dosing and timing, delivery of unnecessary and incorrect medication, error of commission and error of omission.

Similar Medication Name

The US Pharmacopeia MEDMARX is an anonymous online-based program used by several hospitals and institutions to track, report and analyse the medication-related error. In 2006, MEDMARX reported several medication-related errors which were all directed to a drug that was sound alike, look alike (Table 01) [6]. Many errors were reported, related to the selection of incorrect drugs. For example, several anti-hypertensives and anti-anginal medications often come in several formulations for immediate versus sustained-release, including nifedipine, diltiazem, verapamil, metoprolol, carvedilol, and nitrates. In addition, it has become progressively known that acute administration of specific medications may cause QT-interval prolongation, which leads to an increased risk of torsade de points [7]. Failure to appropriately monitor the QT interval and adjust therapy in patients receiving QT-prolonging medications constitutes a medication error

Table 01: Drug names commonly used in acute cardiovascular practice

Medication Name	Sound-alike Medication Name
Isosorbide mononitrate	Isosorbide dinitrate
Plavix (anti-platelet)	Paxil (anti-depressant)
Pravachol (HMG-CoA reductase inhibitor)	Propranolol (beta-blocker)
Zebeta (beta-adrenergic blocker)	Diabeta (hypoglycaemic)
Tiazac (calcium channel blocker)	Ziac (beta-adrenergic blocker and diuretic)
Tricor (hypo-lipidemic)	Tracleer (endothelin antagonist)
Protamine (heparin reverser)	Protonix (proton pump inhibitor)

Medication Dosing, Dispensing and Timing

Institute for Healthcare Improvement and Institute for Safe Medication Practices stated anti-coagulants, narcotics and insulin as high alert medication [8]. The joint commission defines high alert drugs as those that have the highest jeopardy of causing damage when misused. Many investigators have stated that anti-coagulants and anti-platelets, frequently used in cardiovascular disease accounts for a majority of the medication-related error [9,10]. In 2009, the joint commission approved Patient Safety Goals to advance the safety of medication use by directing on reducing the possibility of injury from anticoagulation.

Omission Error

Omission errors are one of the major underrecognized medication-related errors in patients with acute cardiovascular diseases. The proportion of reperfusion-qualified patients presenting with ST-segment elevation myocardial infarction (STEMI) who received instant reperfusion therapy endured only 71% in 2006. Failure to prescribe adjunctive therapies, including antiplatelet agents, [11] β-blockers, [12] angiotensin-converting enzyme inhibitors,[13] and cholesterol-lowing agents,[14] for patients with the acute coronary syndrome (ACS) is an additional example of an error of medication omission.

Patient Groups at High Risk of Medication Errors

Elder Patients

Elder patients are at higher jeopardy of medication error and are more prone to undergoing lethal and harmful medication errors [15]. Omission and improper dose are the major medication-related error in the elder population. Most cardiovascular drug errors in an elder population are omission errors [16].The use of heparin, aspirin and fibrinolytic agents remains suboptimal even among ideal older adults with acute myocardial infarction with indications for these medications and no contraindications to their use [17,18]. In 1992, a population study from 15,000 hospitals discharge, showed that patients with age more and equal to 65 had a twofold rate of avertible adverse medication events [19].

In an elder population, pharmacokinetic and pharmacodynamic factors are altered hence one size fits approach to anticoagulants might result in major bleeding disorders [20].

Chronic Kidney Disease

Estimation of kidney functions is one of the significant factors that physicians should ponder while prescribing both in out-patient and in in-patients. In 2007, unstable angina/non-STEMI guidelines suggested regulating doses of renal cleared cardiovascular drugs on the foundation of eCrCl[21]. As per the CRUSADE study, medication dose alternation should be done based ontheCockcroft gault formula [22]. The use of the Cockcroft gault formula is highly controversial as the National Kidney Foundation and National Kidney Disease Education Program have suggested using either eCrCl or eGFR for drug doing [23,24]. FDA has recently delivered a public health advisory asserting that exposure to gadolinium-based contrast agents increases the jeopardy for nephrogenic systemic fibrosis in patients with acute or stage IV chronic kidney disease or acute renal insufficiency of any severity [25]. It has been recommended that policies to avert contrast-induced nephrotoxicity or an alternative imaging method be measured in patients with stage forth or fifth chronic kidney disease who undertake angiography with an iodine-based contrast agent or magnetic resonance imaging with a gadolinium-based contrast agent.

Disease Based Contraindication

Acute Coronary Syndrome

The most common type of medication-related error in this group of patients include dose error, omission and miscalculation of patient weight. In STEMI patients, the most commonly found error is omission error, which includes a low rate of reperfusion therapy, aspirin, clopidogrel, beta-blockers, ACE inhibitors, and statins [26,24,21,28]. Guideline recommendations have been reformed recently for the administration of IV beta-blockers in STEMI patients [29]. Because of an increased risk of cardiogenic shock in patients treated with intravenous β-blockers, present recommendations now counsel the evasion of therapy in patients with any signs of heart failure and in those at increased risk of developing heart failure. What former may have been measured as an error of omission may now be measured as a medication error. Data analysis from CRUSADE National Quality Improvement initiative assessing unnecessary dosing in NSTEMI patients, 42% of the patients with antithrombotic agents received at least one initial dose outside the suggested range [18]. Similarly, excess dosing was found in unfractionated heparin, low molecular weight heparin and glycoprotein IIb/IIIa inhibitors. The overall author

concluded that 15% of the major bleeding was credited to unnecessary dosing (Table 02).

Table 02: Medication-related error in acute coronary syndrome patients.

Drug Name	Error Type	Use	Preventable AE	Recommendation [21, 29]
Aspirin	Underuse, misuse	Infarct prevention	Increased risk of thrombotic and haemorrhagic complications	Consider dose reduction in patients taking clopidogrel
Beta-blocker	Overuse, misuse	Prevention of reinfarction and arrhythmia	Bradyarrhythmia and cardiogenic shock	Patients with hypotension, lung congestion and patient with increased cardiogenic shock
Heparin	Misuse	Prevention of reinfarction	Haemorrhagic complications	Weight-based dosing
Low molecular weight heparin	Misuse	Prevention of infarction	Increased risk of thrombotic and haemorrhagic complications	Weight-based dosing, patient with renal impairment
Small molecule GP IIb/IIIa inhibitors	Misuse	Prevention of infarction	Increased risk of thrombotic and haemorrhage	Weight-based dosing, patients with renal disorder
Fibrinolytics	Underuse	Prevention of infarct progression	Failure to attain reperfusion, risk of haemorrhage	Confirm dosing corresponds to proper fibrinolytic

Anti-platelet Agents

The Second International Study of Infarct Survival (ISIS-2) used 162.5 mg of aspirin while in the US commonly prescribed dose is 325mg [30]. Cross-sectional data showed that the use of a lower aspirin dose (81mg) after discharge may be safer, particularly when combined with clopidogrel [31]. However, a higher dose of aspirin may be useful in the immediate percutaneous coronary intervention [32]. The CURRENT-OASIS 7 trial found no significant difference between a lower and higher dose of aspirin in ACS patients regarding ischemic or bleeding outcomes at 30 days [33].One of the complexities with aspirin is drug allergy, 3-4% of patients have been identified as aspirin intolerant [34]. Recently, omission error with clopidogrel has been reported in patients with NSTEMI. The number of patients with NSTEMI, treated with clopidogrel within 24 hours of admission who did not undertake primary percutaneous coronary intervention has amplified from 30% in 2002% to 50% in 2005 [35].The majority of the randomised control trial reported that women and elder adults are at higher risk of having a bleeding disorder.

Women getting glycoprotein IIb/IIIa inhibitors were more likely to have excessive doses than men [36].

Fibrinolytic Agents

In 5-12% of STEMI patients, inappropriate dosing of fibrinolytic drugs has been reported [37]. Regimens for every fibrinolytic i.e., tissue plasminogen activator, reteplase and streptokinase vary significantly. Global Use of Strategies To Open occluded arteries (GUSTO-I) trial reported dosing error with the use of streptokinase (13.5%) and with alteplase (11.5) [38]. However, dosing errors with the combination drug (reteplase and tenecteplase) were suggestively lower [36,39]. ASsessment of the Safety and Efficacy of a New Thrombolytic (ASSENT-2) study reported that in 4.9% and 3.6% of patients, an incorrect dose of alteplase and tenecteplase were administered respectively. Among patients with tenecteplase, 3.1% received underdose and 1.5% received overdose. A trial reported that female, elder patients, weight and patients with higher Killip class were more linked to medication-related errors.

Anticoagulant Agents

Nearly 4% of the preventable medication error occurs with anticoagulant therapy. About 49% of the patients with STEMI receive an unnecessary dose of unfractionated heparin in current medical practice [40, 41]. High dose error of anticoagulants was found to be more in females and individuals with lower body weight [20]. Recently ACC/AHA guided physicians to prescribe unfractionated heparin based on individual body weight (60 U/kg and maximum up to 4000 U). One of the causes for dosing error with unfractionated heparin is in ACS patients with pulmonary embolism (80 U/kg and maximum up to 5000 U) [42].CRUSADE, reported that 35% of the time excess weight-adjusted unfractionated heparin was administrated and female sex and older age was the significant factor found to be associated with dosing error. [20]. CRUSADE Quality Improvement Initiative also reported that 19% of the patients on enoxaparin received overdose while 29% of the

patients on enoxaparin received an underdose of the recommended dose [43]. In 2008, The Joint Commission National Patient Safety Goal designed strategies to improve the safety of anticoagulants in hospitalized patients [44].

Statins

For a patient with an acute coronary syndrome, omission error with statins is common [14]. Statin's concentration was found to be high in the presence of cytochrome inhibitors like diltiazem, amiodarone, verapamil, clarithromycin and ketoconazole. Recently, FDA reported the dose-dependent drug interaction between simvastatin and amiodarone [45]. Simvastatin dose greater than recommended dose with amiodarone can lead to rhabdomyolysis. In a patient with myocardial infarction, amiodarone is one of the prescribed drugs to manage supraventricular or ventricular tachyarrhythmias hence dose of simvastatin should be prescribed and monitor with proper consideration.

Acute Heart Failure

Patients with acute heart failure usually have polypharmacy and are highly associated with medication errors. For example, amiodarone and dronedarone can alter digoxin serum concentration.As patients shift from stable heart failure to acute heart failure, administration of vasopressor or inotrope therapy may be obligatory. In this setting, care should be taken to decrease or stop dosages of β-blockers or ACE inhibitors in the aspect of low blood pressure. Vigilant monitoring of potassium and magnesium concentrations and renal function is significant for patients receiving diuretics, ACE inhibitors, angiotensin-receptor blockers, and aldosterone inhibitors [46].Renal and hepatic functions in heart failure patients should be considered even in the absence of cardiogenic shock. The serum concentration of drugs like digoxin, lidocaine, milrinone, anticoagulants and antiplatelet can be altered in the presence of impaired renal functions.Medication errors occur while heart failure patients are being transitioned back to the outpatient setting. Because heart failure medicines are titrated hastily during hospitalization, precise prescriptions that wage courtesy to dosing, electrolyte management, and monitoring of renal function are important soon after discharge [47].

Methods to limit Medication Errors

The chief methods for detecting medication errors and related adverse drug-related events are chart review, computerized monitoring, administrative databases, and claims data, and direct observation. All of these methods have both advantages and confines.

Chart Review

It is retrospective and based on practice sources like medication charts, lab reports. It can be improved by using computerised data like computer integrated triggers and computerised physician order entry. The most precise way to detect adverse events is chart review but at the same time chart review is not useful for detecting medication error [48,49].

Computerized monitoring

Advanced software applications can be used as a support in the health care system with the integration of laboratory and clinical data, which can prevent and detect medication-related errors. Computerised physician order entry or CPOE can be used with a clinical decision support system (CDSS). The application of information technology is expensive and essential for safety, but it can also give rise to new, unknown risks. [50,51].

Administrative Database

Administrative databases screen International Classification of Diseases, 9th revision codes, for arithmetical purposes. Patient safety indexes and adverse event-adjusted rates are explained from a grouping of discharge data. Though, due to the dearth of clinical data, adverse events are poorly observed.

Claims Data

The value of screening of claims data is partial by the fundamental reasons for lawsuits, which are sometimes frolicsome. Events often still need to be established, and about one-third of entitlements lack evidence of errors. Claims data have a positive analytical value for adverse events of about 50%, of which only about 18% point to a medication source [52].

Direct Observation

Direct observation is one the of methods to detect errors in drug administration. A registered nurse is a person who observes drug administration, registration of observingtheaction and compare physician order. The observer must be qualified and should visit diverse units.

Conclusion

Despite being in the spotlight for most researchers, medication errors that affect the outcome in cardiovascular diseases continue to be theutmostcommon and expensive problem. When

prescribing to older patients, a physician should consider age-related changes in pharmacodynamic parameters, pharmacokinetics, hepatic function, and renal function. The majority of the cardiovascular drugs are prescribed based on patient weight and renal functions hence it is critical to analyzeeCrCl with the Cockcroft Gault method. To eradicate medication errors, clinical pharmacists should be considered as a part of the health care team.

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