University of Al Qadisiyah

Collage of Pharmacy

Medication errors in intensive care unit of Al-diwaniyia teaching hospital

Graduation research submitted to college of Pharmacy, University of Al-Qadisiyah

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Supervisor Certificate

I Certify that this Project

(Scope on medication errors in intensive care unit in AL-Diwania Teaching Hospital)

was prepared under our supervision at the College Of Pharmacy, University of Al-Qadisiyah as Graduation research

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Summary

Introduction

Medication errors are the single most preventable cause of patient injury.They are responsible for about 25% of litigation/medicolegal cases against general practitioners The problems, sources and methods of avoiding medication errors are multifactorial and multidisciplinary. Illegibility, drug name confusion and use of decimal points are common contributory factors.

Aim of study

The present study was designed to evaluate the frequency and impact of medication errors in AL-diwaniyia Teaching hospital .

Method

to achieve this aim we discuss and analyse 100 priscription files to patient suffred from acute coronary syndrome with age ranged between (45 - 85) year.

The data we discuss in this study were the age of patient ,weight,date of admission and discharge,medical condition and diagnosis,and all details related to medication like name of drugs,dose ,route of adminstrition,duration and way of administration in all days of admission.

Result indicated that :

- Among of 100 case study in Al-Diwaniyia teaching hospital the over all frequency of medication errors was 100%.
- The majority of medication errors was due monitoring and follow up errors which was 92%, while 91% of medication errors was due to dose errors, 62% due to drug-drug and drug-disease interactions and 30% of medication errors was due to way of administration.

In conclusion

Critical care settings provide lifesaving care for the sickest patients but are also associated with significant risks for adverse events and serious errors. It will be especially important to “engineer out” slips and lapses, to improve the likelihood that treatment in the ICUs is implemented as intended.

Chapter one

Introduction and Literature Review

1.1 Medication errors

defined as any error in the prescribing, dispensing or administration of a drug whether there are adverse consequences or not, are the single most preventable cause of patient injury.[1,2] These errors can occur at any stage in the drug use process from prescribing to administration to the patient. A recent report by the Institute of Medicine (IOM) estimated that errors in medical management cause between 44,000 and 98,000 deaths each year

in USA hospitals.[3] In the USA it has been suggested that the rate of serious medication error is approximately 7%.2 Medication errors are not confined to the hospital setting. Reports from the Medical Defence Union and the Medical Protection Society revealed that 25% and 19%, respectively, of legal claims against general practitioners related to medication errors.[4,5]

The occurrence of medication errors can compromise patient confidence in the healthcare system and in addition, increase healthcare costs.[6] Economic consequences may include the award of damages to the patient, extension of a patient's stay in hospital and the potential financial support required for long term care of a patient who suffers permanent injury[.7]In the USA, it has been estimated that the cost of adverse drug events, a proportion of which are due to medication errors, was $5.6m per year for a 700 bed teaching hospital.

1.1.2 Types of Medication Errors

Medication errors can be broadly classified as prescribing, dispensing or drug administration.

1.1.2.2 Prescribing errors

Prescribing errors may be defined as an incorrect drug selection for a patient, be it the dose, the strength, the route, the quantity, the indication, the contraindications.[9] This definition can be further expanded to include failure to comply with legal

requirements for prescription writing. The .prescriber must specify the information which the pharmacist needs to dispense the drug in the correct dosage and form and the directions the patient needs to take it safely[.10,11] A study undertaken in the hospital setting by Lesar *et al* found an error rate of 4 errors per 1000 medication orders. Of the errors with potential for adverse patient effects, drug allergies accounted for 12.1%, wrong drug name, dosage form or abbreviation

1.1.2.3 Dispensing Errors

Dispensing errors are errors that occur at any stage during the dispensing process from the receipt of a prescription in the pharmacy through to the supply of a dispensed product to the patient.[13] Studies in the USA have estimated that dispensing errors occur at a rate of 1-24%.14 Dispensing errors may undermine the patient's confidence in the pharmacist and increase the likelihood of litigation procedures[.15] These errors include the selection of the wrong strength/product. This occurs primarily when two or more drugs have a similar appearance or similar name . The use of computerised labelling has led to the emergence of transposition and typing errors which are among the most common causes of dispensing error.[13] Other potential dispensing errors include wrong dose, wrong drug, wrong patient.

1.1.2.4 Administration errors

A drug administration error may be defined as a discrepancy

between the drug therapy received by the patient and the drug therapy intended by the prescriber.[16] Drug administration is associated with one of the highest risk areas in nursing practice. The “five rights” have long been the basis for nurse education on drug administration i.e. giving the right dose of the right drug to the right patient at the right time by the right routeroute[16,17] Drug administration errors largely involve errors of omission where administration is omitted due to a variety of factors e.g wrong patient, lack of stock. Other types of drug administration errors include wrong administration technique, administration of expired drugs and wrong preparation administered.

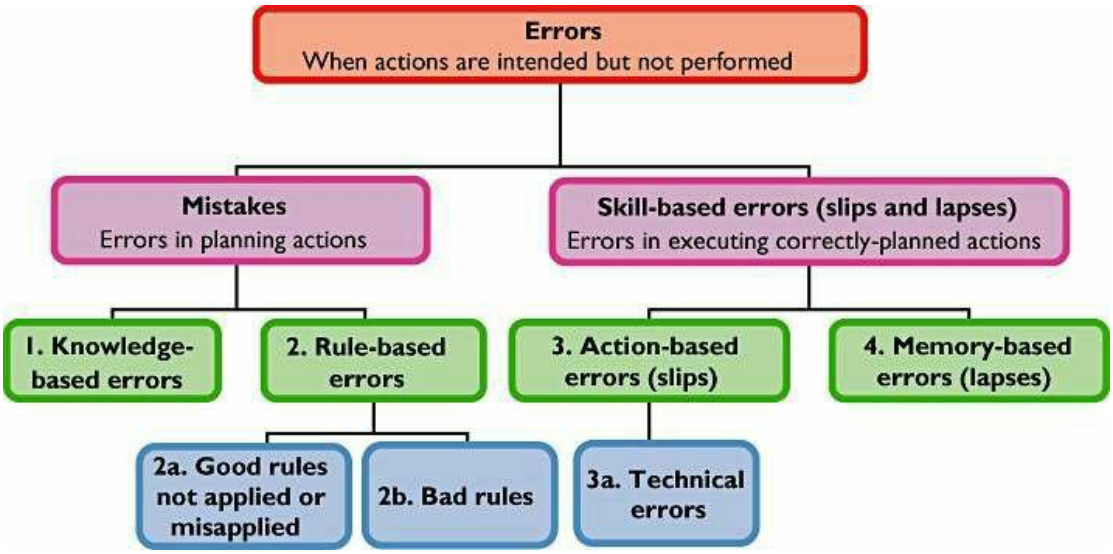

Figure 1: Classification of medication errors depending on their cause.

1.2 Prevelance and incidence

Globally, it is estimated that 142,000 people died in 2013 from adverse effects of medical treatment; in 1990, the number was 94,000.[18] A 2000 Institute of Medicine report estimated that medical errors result in between 44,000 and 98,000 preventable deaths and 1,000,000 excess injuries each year in U.S. hospitals.[19][20][21] In the UK, a 2000 study found that an estimated 850,000 medical errors occur each year, costing over £2 billion.[22] Some researchers questioned the accuracy of the IOM study, criticizing the statistical handling of measurement errors in the report,[23] significant subjectivity in determining which deaths were "avoidable" or due to medical error, and an erroneous assumption that 100% of patients would have survived if optimal care had been provided.[24] A 2001 study in the Journal of the American Medical Association of seven Department of Veterans Affairs medical centers estimated that for roughly every 10,000 patients admitted to the subject hospitals, one patient died who would have lived for three months or more in good cognitive health had "optimal" care been provided.[24] A 2006 follow-up to the IOM study found that medication errors are among the most common medical mistakes, harming at least 1.5 million people every year. According to the study, 400,000 preventable drug-related injuries occur each year in hospitals, 800,000 in long-term care settings, and roughly 530,000 among Medicare recipients in outpatient clinics. The report stated that these are likely to be conservative estimates. In 2000 alone, the extra medical costs

incurred by preventable drug-related injuries approximated $887 million—and the study looked only at injuries sustained by Medicare recipients, a subset of clinic visitors. None of these figures take into account lost wages and productivity or other

costs.According to a 2002 Agency for Healthcare Research and Quality report, about 7,000 people were estimated to die each year from medication errors - about 16 percent more deaths than the number attributable to work-related injuries (6,000 deaths). Medical errors affect one in 10 patients worldwide. One extrapolation suggests that 180,000 people die each year partly as a result of iatrogenic injury. One in five Americans (22%) report that they or a family member have experienced a medical error of some kind. A study released in 2016 found medical error is the third leading cause of death in the United States, after heart disease and cancer.

1.3 Etiology and cause

Medical errors are associated with inexperienced physicians and nurses, new procedures, extremes of age, and complex or urgent care.[25] Poor communication (whether in one's own language or, as may be the case for medical tourists, another language), improper documentation, illegible handwriting, inadequate nurse-to-patient ratios, and similarly named medications are also known to contribute to the problem. Patient actions may also contribute significantly to medical errors. Falls, for example, may result from patients' own misjudgements. Human error has been implicated in nearly 80 percent of adverse events that occur in complex

healthcare systems. The vast majority of medical errors result from faulty systems and poorly designed processes versus poor practices or incompetent practition Complicated technologies, powerful drugs, intensive care, and prolonged hospital stay can contribute to medical errors.

In 2000, The Institute of Medicine released "To Errer is Human," which asserted that the problem in medical errors is not bad people in health care—it is that good people are working in bad systems that need to be made safer.[26]

Poor communication and unclear lines of authority of physicians, nurses, and other care providers are also contributing factors.[27] Disconnected reporting systems within a hospital can result in fragmented systems in which numerous hand-offs of patients results in lack of coordination and errors.[28]

Other factors include the impression that action is being taken by other groups within the institution, reliance on automated systems to prevent error.,[29] and inadequate systems to share information about errors, which hampers analysis of contributory causes and improvement strategies.[30] Cost-cutting measures by hospitals in response to reimbursement cutbacks can compromise patient safety.[31] In emergencies, patient care may be rendered in areas poorly suited for safe monitoring. The American Institute of Architects has identified concerns for the safe design and construction of health care facilities.[32] Infrastructure failure is

also a concern. According to the WHO, 50% of medical equipment in developing countries is only partly usable due to lack of skilled operators or parts. As a result, diagnostic procedures or treatments cannot be performed, leading to substandard treatment.

The Joint Commission's Annual Report on Quality and Safety 2007 found that inadequate communication between healthcare providers, or between providers and the patient and family members, was the root cause of over half the serious adverse events in accredited hospitals.[33] Other leading

causes included inadequate assessment of the patient's condition, and poor leadership or training .Human factors; Cognitive errors commonly encountered in medicine were initially identified by psychologists Amos Tversky and Daniel Kahneman in the early 1970s. Jerome Groopman, author of How Doctors Think, says these are "cognitive pitfalls", biases which cloud our logic. For example, a practitioner may overvalue the first data encountered, skewing his thinking (or recent or dramatic cases which come quickly to mind and may color judgement). Another pitfall is where stereotypes may prejudice thinking.[34] Sleep deprivation has also been cited as a contributing factor in medical errors.[35] One study found that being awake for over 24 hours caused medical interns to double or triple the number of preventable medical errors, including those that resulted in injury or death.[36]

1.4 Medication errors in Intensive care unit (ICU)

Medication errors in intensive care are frequent, serious, and predictable. Critically ill patients are prescribed twice as many medications as patients outside of the intensive care unit (ICU) and nearly all will suffer a potentially life-threatening errer at some point during their stay. The aim of this article is to provide a basic review of medication errors in the ICU, identify risk factors for medication errors, and suggest strategies to prevent errors and manage their consequences. Health care delivery is not infallible. Errors are common in most health care systems and are reported to be the seventh most common cause of death overall [37]. James Reason developed a well-recognized system for human error classification based on observations from industries that have become highly reliable such as aviation and nuclear power [38]. He states that

errors arise for two reasons: active failures and latent conditions. Active failuresare unsafe acts committed by people who are in direct contact

with the patient. They take a variety of forms: slips, lapses, and mistakes . Slips and lapses are skill-based behavior errors, when a routine behavior is misdirected or omitted. The person has the right idea but performs the wrong execution. For example, forgetting to restart an infusion of heparin postoperatively is a lapse. Restarting the heparin infusion but entering an incorrect infusion rate despite knowing the correct rate is a slip. Mistakes are knowledge-based errors (perception, judgment, inference, and

interpretation) and occur due to incorrect thought processes or analyses. For example, prescribing heparin in a patient diagnosed with heparin induced thrombocytopenia is a mistake. Situational factors (fatigue, drugs, alcohol, stress, and multiple activities) can divert attention and increase the risk of active failures.

1.4.2 Unique about the ICU and medication errors

The ICU brings together high-risk patients and interventions in a complex environment [38]. The single strongest predictor of an ADE is patient illness severity [39]. Critically ill patients are prescribed twice as many medications as patients outside of the ICU [40]. Most medications in the ICU are administered as weight-based infusions. These infusions require mathematical calculations and frequently are based on estimated weights increasing the risk of error [41,42]. Multicentered studies by Ridley and colleagues [43] and Calabrese and colleagues [44] identified potassium chloride, heparin, magnesium sulphate, vasoactive drugs, sedatives, and analgesics as the medications with the greatest risk of

error. Antibiotics frequently are empirically prescribed in the ICU and errors have potential implications both for individual patients and populations [45],[46]. Patients are prescribed these medications in an environment that is stressful, complex, changing, under the stewardship
of multiple providers, and frequently managing patients in crisis [47]. It is important to remember that critically ill patients have fewer defenses against adverse events than other patients do.

They have limited ability to participate in their medical care and they lack the physiological reserve to tolerate additional injury. Moreover, they are reliant on sophisticated technologies and equipment to deliver essential care and yet relatively little is known about medical equipment failures and the associated safety risks. Finally, lack of continuity of care at discharge from the ICU is a well-known feature putting the patient at risk for errors .

1.4.3 The consequences of medication errors

Medication errors are an important cause of patient morbidity and mortality [48]. Although only 10% of medication errors result in an ADE, these errors have profound implications for patients, families, and health care providers [49,50,51]. The IOM report high lights that 44,000 to 98,000 patients die each year as a result of medical errors, a large portion of these being medication-related [52]. Approximately one fifth (19%) of medication errors in the ICU are life-threatening and almost half (42%) are of sufficient clinical importance to warrant additional life-sustaining treatments [53]. However, deaths are only the tip of the iceberg. The human and societal burden is even greater with many patients experiencing costly and prolonged hospital stays and some patients never fully recovering to their premorbid status [54,55]. Bates and colleagues [55] estimated that in American hospitals the annual cost of serious medication errors in 1995 was $2.9 million per hospital and that a 17% decrease in incidence would result in $480,000 savings per hospital. Finally, the psychological impact of errors should not be ignored [55]. Errors erode patient, family, and public confidence in healthcare organizations [56]. Memories of error can haunt providers for many years [57].

1.5 Research Question

1- What is the frequency of medication errors in ICU in Al-Diwaniyah Teaching hospital?

2- What is the impact of these medication errors ?

1.6 The aim of research

1- Investigate the frequency of medication errors in Al-Diwaniyah teaching Hospital in ICU .

2- Assess the impact of these medication errors .

Chapter two

Materials and Methods

2.1 Subjects

A study was approved by scientific comity, pharmacy collage university of Al-Qadisiyah, Iraq, verbal informed consent of the pharmacist was taken.

A total 100 prescription files included in this study were collected from September 2016 till march 2017 .

2.2 Patient Group

The study performed on 100 patient (62 male and 38 female) the patient ages ranged between 45-85 year

patients were diagnosed by specialist physicians in Al DiwaniaTeaching Hospital in ICU .

All patient were suffered from acute coronary syndrome include :

1- Unstable angina

2-STEMI

3-Non-STEMI

2.3 Method

A formal was used to collect data include The name of patient,age, doctor's diagnosis , drug dispensed , and ther dose , route , duration , frequency and strength .

BNF 70 and drug.com drug interactions checker used to identify the drug intraction.

We recorded and discuss all details related to medication give to

patient in each single day of admission, and that include

- drug name
- dosage form
  (tablet ,capsule, vial ,ampule..)
- route of administration
  - oral
  - sublingual
  - paraenteral like intravenous, intramuscular, subcutaneous..
- way of administration
  for example if paraenteral route give as direct intravenous injection or by intravenous fluid
- duration of administration
- frequency
- the type of fluid use
  (normal saline, glucose water, ringer solution..) and the type of intravenous bag use(glass, polylfin ,plastic ....)
- Dose

Chapter Three

Result and Discussion

3.1 Result

Among of 100 case study in Al-Diwaniyia teaching hospital the over all frequency of medication errors was 100%.

The majorityof medication was due to monitoring and follow up errors which was 92%, while 91% of medication errors was due to dose related, 62% of medication errors was due to drugs-drugs interaction and drugs-diseases interactions and 30% of medication errors was due to way of administration.

The most frequent medication errors we found in Al-Diwaniyia teaching hospital was related to incorrect dose and absence of of monitoring of heparin which account for 98% of cases, follow by medication errors due to monitoring of atorvaststin, incorrect dosing of enoxaparin,medication errors of furosemide due to way of administration followed by medication errors of amiodaron due to monitoring and way of administration errors.

The most serious dugs-drugs interaction we found from the 100 cases are ceftriaxone and calcium in which there is potential risk of fatal particulated preceptited in kidney, omperazol and clopidogrel and furosemide and amikacin.

The most common drugs-drugs interaction we found in 100 cases is ceftriaxone with heparin in which the ceftriaxone will increase the effectiveness of heparine.

3.2.Discussion

3.2.2. Acute coronary syndrome

The most common types of medication errors in this group include medication dose errors (including failure to account for renal dysfunction), omission (failure to either give the medication or to resume treatment), and miscalculation of a patient's weight. In STEMI patients, omission errors are represented dramatically by the relatively low rates of use of immediate reperfusion therapy,[58]. Aspirin [59] clopidogrel, angiotensin-converting enzym inhibitorsrs,[60] and statins during hospitalization.[61] For the acute administration of intravenous -blockers in STEMI patients, guideline recommendations have changed recently[.62]Because of an increased risk of cardiogenic shock in patients treated with intravenous beta-blockers, current recommendations now advise the avoidance of therapy in patients with any signs of heart failure and in those at increased risk of developing heart failure. What previously may have been considered an error of omission may now be considered a medication error if intravenous beta-blocker therapy is given to a patient with evidence of heart failure, because of the increased risk of cardiogenic shock.The non-STEMI population tends to be an older population with greater comorbid illnesses, worse renal function, and a higher proportion of women. These characteristics

predispose to untoward medication reactions if appropriate dosing adjustments are not made. In a comprehensive analysis from the CRUSADE National Quality Improvement Initiative evaluating excessive dosing in patients with non–ST-elevation ACS, 42% of patients who were administered an

antithrombotic agent received at least 1 initial dose outside the recommended range.[63] The excess dosing was seen with unfractionated heparin (33%), low-molecular-weight heparin (14%), and glycoprotein
IIb/IIIa inhibitors (27%). The factors associated with excessive dosing included older age, female sex, renal insufficiency, low body weight, diabetes mellitus, and congestive heart failure. It was estimated that 15% of all major bleeding in this population was attributable to excessive dosing. The latest quality metrics for patients with acute myocardial infarction include the frequency of excessively dosed heparin, low-molecular-weight heparin, and glycoprotein IIb/IIIa inhibitors; omission of clopidogrel in medically managed patients; the presence of a weight based heparin-dosing protocol; and the ability to track bleeding events related to anticoagulants.[64] Systems approaches, such as the AHA's evidence-based Get With The Guidelines, have been shown to improve adherence to guidelines, with an emphasis on reducing medication errors of omission and commission.[65] The following section highlights errors in prescribing that are related to specific agents in ACS .

3.2.3 Antiplatelet Agents

We found that 25 % of patient in intensive care unite discharged with GIT up set because of use of NSAIDs like aspirin.

The gastric mucosa protects itself from gastric acid with a layer of mucus, the secretion of which is stimulated by certain prostaglandins. NSAIDs block the function of cyclooxygenase 1 (COX-1), which is essential for the production of these prostaglandins.

Another cause is stress patient serious health problems such as those requiring treatment in an intensive care unit is well described as a cause of peptic ulcers, which are termed stress ulcers.[66]

prophylaxis and treatment to such condition shoud be occur in ICU

3.2.4 Amiodaron

The most common error in ICU was related to way of adomistration , in all cases it which amiodaron involved in therapy it was give in plastic intravenous bag and set.

loss of amiodarone from i.v. admixtures to flexible polyvinyl chloride (PVC) infusion bags and i.v. administration sets was studied. Admixtures containing amiodarone hydrochloride 600 micrograms/mL and either 5% dextrose injection or 0.9% sodium chloride injection were stored at room temperature in glass bottles (both with and without contact of the drug solution with

the rubber bottle closure), in flexible PVC bags, or in rigid PVC bottles. After 120 hours, the contents of each flexible PVC bag were emptied and replaced by methanol, which was allowed to remain in the bag for an additional 120 hours and was then analyzed for amiodarone content. To determine availability of amiodarone after infusion through a 1.8-m PVC i.v. administration set, solutions stored in glass containers were run through the set at 0.5 mL/min for 90 minutes. Samples of drug solutions were collected at appropriate intervals and analyzed by a stability-indicating high-performance liquid chromatography (HPLC) assay. Admixtures containing 0.9% sodium chloride injection were not stable; visual incompatibility was evident after 24 hours of storage in glass bottles, and no further testing was performed. In admixtures containing 5% dextrose injection that were stored in 50-mL flexible PVC

bags, 60% of the initial amiodarone concentration remained after 120 hours; approximately half of the lost drug was recovered with the methanol. In effluent collected from the PVC administration set, 82% of the initial amiodarone concentration remained. Amiodarone concentrations did not decrease appreciably, after storage in glass or rigid PVC bottles.[67]

3.2.5 Medicaion errors related to investigation

The estimation of creatinine clearance is one of the most important factors that should be readily available to any healthcare provider who prescribes medicines, both in the

emergency and the in-hospital setting. Medications such as enoxaparin, eptifibatide, tirofiban, bivalirudin, dofetilide, and sotalol are dosed on the basis of estimated creatinine clearance (eCrCl) with the Cockcroft-Gault formula,[69] not based on the estimated glomerular filtration rate calculated by the Modification of Diet in Renal Disease formula.[70] The 2007 unstable angina/non-STEMI practice guidelines recommend adjusting doses of renally cleared cardiovascular medication on the basis of the eCrCl.[71] The clinical studies and labeling that define adjustments for cardiovascular medication have been based on the Cockcroft-Gault formula, which is not identical to the Modification of Diet in Renal Disease equation. According to the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress Adverse outcomes with Early implementation of the ACC/AHA guidelines) study, clinically important disagreements between eCrCl and estimated glomerular filtration rate occurred in one fifth of ACS patients; the authors concluded that medication dosing should be based on the Cockcroft-Gault formula.[72] Although use of the Cockcroft-Gault formula

is recommended by the present writing group, this topic remains controversial, because the National Kidney Foundation, 73] and the National Kidney Disease Education Program [74] have recommended using either eCrCl or estimated glomerular filtration rate for drug dosing.

Ideally, the eCrCl should be calculated automatically for all patient

admitted to ICU befor begining in treatment .

3.2.6 Weight-Based Medication Dosing

Accurate weight assessment is a challenge for ICU patients who are incapacitated. Because many acute cardiovascular medications are dosed according to actual (and not ideal) body weight, overestimation and underestimation of body weight constitute an important source of medication errors that result in adverse medication events and ineffectiveness,[75] respectively. Examples of acute cardiovascular medications that require accurate weight assessment include unfractionated heparin, low-molecular-weight heparin, glycoprotein IIb/IIIa receptor antagonists, fibrinolytic agents (eg, alteplase and tenecteplase), inotropes (eg, dobutamine), vasopressors (eg, dopamine and norepinephrine), vasodilators (eg, nesiritide and nitroprusside), and the inodilator milrinone.

although patients had a mean absolute error of only 3 kg in their estimation of body weight, paramedics, nurses, residents, and attending physicians had a mean absolute error of 9 to 10 kg.38 Although only 1.5% of patient weight estimations were more than 20% off, 13% to 17%

of healthcare providers' estimations were inaccurate by more than 20%. Other studies agree that weight estimation by medical staff is a potential contributor to medication errors.[76,77] These errors are more pronounced in patients at extremes of body weight.

3.2.7 Medication error related to age

Older adults are at a higher risk of medication errors and have a greater propensity for experiencing harmful and fatal errors. [78].The most common types of medication errors among the elderly are those of omission (26%) and improper dose (26%). The use of aspirin, fibrinolytic agents, and heparin acutely and of statins at discharge remains suboptimal even among ideal older adults with acute myocardial infarction with indications for these medications and no contraindications to their
use[79,80] Medication errors of omission are also more likely to occur in elderly patients with ACSs considered to be secondary to another diagnosis. These secondary ACS events are independent predictors of the lack of recommended medication therapy[.90] Omission of evidence-based medications that results from reasonable clinical judgment are of little concern compared with those due to misdiagnosis or misclassification of risk and benefit among those eligible for treatment. In a population study from 15 000 hospital discharges in 1992, those 65 years of age had twice the rate of preventable adverse medication events as those 16 to 64 years old (5.3% versus 2.8%, P0.001); however, in multivariable analysis adjusted for comorbidity and case mix, age was not independently associated with preventable adverse events[81] Rather, older adults are at risk for medication errors for other age-associated reasons. There are very few cardiovascular medications for which doses are adjusted by age alone. In fact, most cardiovascular medication errors

in older adults are omission errors[.82] High rates of

polypharmacy also increase the likelihood of drug-drug interactions. Older adults are less likely to receive appropriate follow-up laboratory monitoring for 1 or more of their medications, including angiotensin converting enzyme inhibitors, amiodarone, and statins. There are age-related changes in pharmacokinetics (eg, medication absorption, metabolism, and hepatic or renal elimination) and pharmacodynamics , both of which necessitate dose adjustments or heighten susceptibility to medication adverse events. Age tends to be a surrogate for worse renal function, which is important for medications that are cleared renally. [83]

3.2.8 Medication errors related to monitering

3.2.8.2 Heparin

3.2.8.2.2 Heparin-induced thrombocytopenia

Clinically important heparin-induced thrombocytopenia is immune-mediated and does not usually develop until after 5–10 days; it can be complicated by thrombosis. Platelet counts should be measured just before treatment with unfractionated or low molecular weight heparin, and regular monitoring of platelet counts may be required if given for longer than 4 days*. Signs of heparin-induced thrombocytopenia include a 30% reduction of platelet count, thrombosis, or skin allergy. If heparin-induced thrombocytopenia is strongly suspected or confirmed, the heparin should be stopped and an alternative anticoagulant, such as argatroban or danaparoid, should be given. [85]

3.2.8.2.3 Hyperkalaemia

Inhibition of aldosterone secretion by unfractionated or low molecular weight heparin can result in hyperkalaemia; patients with diabetes mellitus, chronic renal failure, acidosis, raised plasma potassium or those taking potassium-sparing drugs seem to be more susceptible. The risk appears to increase with duration of therapy, and plasma-potassium concentration should be measured in patients at risk of hyperkalaemia before starting the heparin and monitored regularly thereafter, particularly if treatment is to be continued for longer than 7 days- Heparin [85]
in ICU unfractionated and low molecular weight heparin in most cases used with another drugs like ACEIs drugs ,Beta blockers , Aspirin and ARBs that have additional effect by increase the level of potassium by additional intraction.

Normal potassium levels are between 3.5 and 5.0 mmol/L (3.5 and 5.0 mEq/L) with levels above 5.5 mmol/L defined as hyperkalemia.[86][87]] Typically this results in no symptoms.[88] Occasionally when severe it results in palpitations, muscle pain, muscle weakness, or
numbness.[88][89] An abnormal heart rate can occur which can result in cardiac arrest and death.[88][86]
Common causes include kidney failure, hypoaldosteronism, and rhabdomyolysis.[96] A number of medications can also cause high blood potassium including spironolactone, NSAIDs, and angiotensin converting enzyme inhibitors.[88]

3.2.8.2.4 Activated partial thromboplastin time

The activated partial thromboplastin time is used to monitor therapeutic doses of UFH in venous thromboembolism. A target ratio versus mid-point of normal range of 1.5 to 2.5 is typically employed. This is principally based on evidence that delay in the achievement of

adequate anticoagulation is associated with an increased rate of thrombosis recurrence or progression. It is, however, clear that the sensitivity of the test to heparin is highly reagent and instrument dependent and ideally local calibration of the APTT should be employed Sample collection systems, sample anticoagulants and storage conditions also have clinically important effects on the results .

The inconvenience and limited precision of monitoring of UFH therapy has contributed to the increasing use of LMWH preparations, as several randomised studies have demonstrated their efficacy and safety when administered in fixed dosage and without laboratory monitoring (Lensing et al, 1995). Despite this positive development there is still debate over the need to monitor treatment with LMWH in certain subgroups. [90]

3.2.8.3 Statin

Muscle effects The risk of myopathy, myositis, and rhabdomyolysis associated with statin use is rare. Although myalgia has been reported commonly in patients receiving statins, muscle toxicity truly attributable to statin use is rare. Muscle toxicity can occur with all statins, however the likelihood

increases with higher doses and in certain patients .Statins should be used with caution in patients at increased risk of muscle toxicity, including those with a personal or family history of muscular disorders, previous history of muscular toxicity, a high alcohol intake, renal impairment, hypothyroidism, and in the elderly. There is an increased incidence of myopathy if a statin is given at a high dose, or if it is given with a fibrate. close monitoring of liver function and, if muscular symptoms occur, of creatine kinase is necessary. In patients at increased

risk of muscle effects, a statin should not usually be started if the baseline creatine kinase concentration is more than 5 times the upper limit of normal. Hypothyroidism should be managed adequately before starting treatment with a statin .

Statins should be used with caution in those with a history of liver disease or with a high alcohol intake—, a NICE guideline* suggests that liver enzymes should be measured before treatment, and repeated within 3 months and at 12 months of starting treatment, unless indicated at other

times by signs or symptoms suggestive of hepatotoxicity. Those with serum transaminases that are raised, but less than 3 times the upper limit of the reference range, should not be routinely excluded from statin therapy. Those with serum transaminases of more than 3 times the upper limit of the reference range should discontinue statin therapy. [85]

3.2.9 Medication errors related to drug - drug Interaction

Patients admitted to intensive care unit (ICU) present with severe and life-threatening illnesses. Most of them suffer from various comorbidities. They usually receive complex pharmacotherapy with large number of medicines which increase the risk of drug-drug interactions (DDIs).

we found many intraction in ICU the most important and frequent interaction were

3.2.9.2 Ceftriaxon + calcium

Ceftriaxone (CRO), an expanded-spectrum cephalosporin approved for use by the United States Food and Drug Administration (FDA) in 1984[91] has a wide range of antimicrobial activity and is currently recommended in the national guide- lines for the treatment of many community-acquired infec- tions, including pneumonia and meningitis

[92, 93]. In Sep- tember 2007, the FDA issued an Alert to Healthcare Professionals to revise the U.S. package labeling due to con- cerns of adverse events [94]. Specifically, the warning sug - gested that CRO and calcium-containing products should not be coadministered to any patient receiving either agent within the previous 48 h in order to prevent possible end-organ dam- age secondary to CRO-calcium precipitation. The FDA warn- ings were provoked by a report of fatal outcomes in neonates, in whose lungs and kidneys CRO-calcium precipitates were discovered [95].However, the majority of these outcomes were due to a Y-site incompatibility between CRO and calcium administered simultaneously through the same intravenous line.

3.2.9.3 Amikacin+ Furosemide

Either increases toxicity of the other by Mechanism: additive drug effects. Increased risk ototoxicity and nephrotoxicity [96]

3.2.9.4 Ceftriaxon + heparin

Ceftriaxone has been associated with an increase in prothrombin time and episodes of bleeding. These effects may potentiate the effects of heparin. Usually, no special management is necessary, but the patient should be monitored for bleeding if ceftriaxone and heparin must be given together. Vitamin K has been successfully used to treat cephalosporin-induced coagulopathies[97]

3.2.9.5 Omperazole +Clopidogrel

The co-administration of clopidogrel with omeprazole results in significantly reduced exposure to the active metabolites of clopidogrel.

A 30% reduction in the mean inhibition of platelet aggregation was observed when omeprazole was given at the same time as clopidogrel compared to clopidogrel alone.4 Decreases in bleeding times and

increases in platelet reactivity index were also observed, consistent with a reduction in anti-clotting ability.

3.2.10 Medication errer related to organ toxicity

Patients cared for in the intensive care unit (ICU) undergo multiple interventions to treat serious medical conditions. In addition to the acute illness being treated, underlying chronic conditions require ongoing drug therapy. As a result, these patients are exposed to

numerous pharmaceutical agents, many of which have narrow therapeutic windows and toxic potential. Comorbid conditions, altered drug pharmacokinetics, and drug– drug interactions further enhance the risk for both drug overdosing and underdosing and adverse medication effects. Underdosing is complicated by reduced efficacy, whereas overdosing results in various end-organ toxicities. One such complication is acute kidney injury (AKI), a relatively common problem in the ICU, which results from multiple insults. Importantly, potentially nephrotoxic medications contribute significantly to the development of AKI. In view of these issues, it is crucial that clinicians caring for these patients use appropriate drug dosing based on the knowledge of altered pharmacokinetics, vigilant monitoring of drug efficacy and toxicity, recognition of drugs with nephrotoxic potential, and early identification of drug-induced AKI when it develops.

Numerous medications are prescribed to seriously ill patients in the intensive care unit (ICU). Although they provide significant benefits, adverse events may develop from these agents, including acute kidney injury (AKI), hepatotoxicity, neurological dysfunction, cardiopulmonary

toxicity, and other end-organ disturbances. Several studies have documented that AKI occurs frequently in the ICU, affecting as many as two-thirds of patientsIt is often the result of multiple insults and may be severe enough to require renal replacement therapy (RRT) in ~6% of patients. As with other acute organ injury syndromes, AKI has significant consequences, which include

prolonged hospital length of stay, increased hospital-related morbid events, development of chronic kidney disease (CKD), and requirement for acute and/or chronic RRT.Increased hospital and overall mortality also complicate this untoward event.

The major culprits that cause AKI include processes, such as infections complicated by sepsis, systemic inflammatory response syndrome, and septic shock, cardiac, hepatic, and multiorgan dysfunction/failure, as well as volume depletion. Many of these events prime the kidney for injury by causing renal hypoperfusion and promoting oxidative stress. Importantly, nephrotoxic drugs contribute to AKI in 19–25% of cases in the ICU [98.]

3.2.11 Conclusion

Patient safety is an important health care issue because

of the consequences of iatrogenic injuries. Medication errors in critical ca. re are frequent, serious, and predictable. Human factor research in nonmedical settings suggests that dema nding greater vigilance from providers of medical care may not result in meaningful safety improvement. Instead, the approach of identifying failures and redesigning faulty systems appears to be a more promising way to reduce human error.

3.2.12 Recommendation

1- Adherance to the treatment guidelines.

2- Encouraging a proper doctor – pharmacist and pharmacist– patient communication.

3- Further studies to assess the impact of medications errors in patient with Acute Coronary syndrome in ICU .

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Group.

Appendix 1 :Formal design

Ministry of Higher Education and Scientific Research

College Of Pharmacy

University of Al-Qadisiyah

Patient Name	Age	Gender

Diagnosis

Mediaction	Scintific name	Trade name	Dose	Dosage form	Strenght	Route	Frequency

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