NEAR EAST UNIVERSITY

INSTITUTE OF GRADUATE STUDIES

DEPARTMENT OF CLINICAL PHARMACY

EVALUATION OF DRUG-RELATED PROBLEMS OF HYPERTENSIVE PATIENTS AT THE INTENSIVE CARE UNIT

M.Sc. THESIS

Batoul KHODER

Nicosia

June, 2023

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Approval

We certify that we have read the thesis submitted by Batoul Khoder titled **"Evaluation of Drug Related Problems of Hypertensive Patients at the Intensive Care Unit"** and that in our combined opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Educational Sciences.

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Declaration

I hereby declare that all information, documents, analysis and results in this thesis have been collected and presented according to the academic rules and ethical guidelines of Institute of Graduate Studies, Near East University. I also declare that as required by these rules and conduct, I have fully cited and referenced information and data that are not original to this study.

Batoul KHODER

15/06/2023

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Batoul KHODER

Abstract

Evaluation Of Drug Related Problems of Hypertensive Patients At The Intensive Care Unit

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DRPs are a major source of morbidity and death, particularly in ICU patients. Critically ill ICU patients are particularly susceptible to DRPs due to the diversity in administered medications which may raise DRPs. CP plays a prominent role in helping patients by recognizing and treating DRPs and adverse events. This research examines DRP frequency and distribution in hospitalized patients at the ICU of Near East University Hospital. For that, a retrospective observational study on patients of ≥23 years older admitted to the ICU between December 2020 and December 2021. 264 patients participated. Pharmaceutical Care Network Europe (PCNE) DRP categorization method V9.1 was used to record and classify DRPs. The study recorded clinical pharmacist and specialized physician reviews of DRPs. The outcomes showed 71.3% of the patients had DRPs. Identifying and eliminating DRPs improves health and patient safety. Prospective research is recommended with CP intervention to minimize DRP incidents.

Key words: *ICU, Inpatient, drug related problem, inpatient, medication errors, DRPs, Interactions, clinical pharmacy, Antihypertensives*

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List of Abbreviations

ICU: Intensive Care Unit

DRPs: Drug Related Problems

HT\HTN: Hypertension

BP: Blood Pressure

SBP: Systolic Blood Pressure

DBP: Diastolic Blood Pressure

JNC: Joint National Committee

PCNE: Pharmaceutical Care Network Europe

PO: Oral

OTC: Over-The-Counter

CYP: Cytochrome P450

COPD: Chronic Obstructive Pulmonary Disease

CP: Clinical Pharmacist

ACCP: American College of Clinical Pharmacy

ACE: Angiotensin-Converting Enzyme

ARA: Angiotensin Receptor Blocker

APH: Acute Postoperative Hypertension

CT: Computed Tomography

HELLP: Hemolysis Elevated Liver Enzymes and Low Platelets

GI: Gastro Intestinal

NEU: Near East University

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

PPI: Proton-Pump Inhibitor

MAP: Mean Arterial Pressure

NMD: N-methyl-d-Aspartae

i.e.: that is

e.g.: example

CHAPTER I

Introduction

This chapter provides a general overview of hypertension and hypertensive crises. It also states the problem to be studied, the purpose behind this research, the hypothesis and the limitations that restricted the inducted project.

Statement of the Problem

Hypertension is a common chronic condition with high morbidity; early treatment is recommended to decrease end-organ damage, morbidity, and mortality. Antihypertensive medications are frequently administered to ICU patients. These medications have diverse modes of action and are frequently taken in combination. All have side effects, primarily cardiovascular, and significant drug interactions that must be evaluated throughout the perioperative period. However, there is a near complete absence of understanding about how clinical is organized when prescribing antihypertensive medicine and/or following up treatment from patients already taking such medications. Because direct contact and collaboration between patient and physician in the clinical context are critical for patient adherence to treatment regimens, focusing on difficulties associated with antihypertensive medications is essential.

Purpose of the Study

The aim of this research is to evaluate the drug-related problems of hypertensive patients in the intensive care unit. This aim will be achieved by evaluating the clinical pharmacist outcomes related to the targeted patients. The conducted research is based on an evaluation for the medications administered by the intensive care unit patients during their hospitalization days.

Significance of the Study. This proposed study aims to investigate the drug-related problems associated with hypertensive patients in the intensive care unit. Drug-related problems have always been an issue to consider in dealing with indoor or outdoor patients. In order to decrease the mortality rate and improve the quality of life for hospitalized patients, for all the on-therapy patients, this study has emerged. That,

this study is important because it can provide valuable insights into the potential effects of drug dosing, interactions, adverse effects, therapeutic thresholds and drug-related problems when administering antihypertensive agents, especially in the intensive care unit. This can also benefit education and informs the development of effective teaching strategies to enhance patients' living and improve students' learning outcomes.

Limitations. This research, however, has potential limitations. (1) Formulation of research aims and objectives. The study set too many broad parameters that might narrow the focus level. (2) Sample size. Inadequate sample size prevents statistical tests from detecting significant relationships within the same data set. (3) There hasn't been enough prior study in this area. It is an essential component of every study because it helps identify the scope of work done in the research area.

Definition of Terms.

The intensive care unit (ICU) is a special department in the hospital that provides the maximum possible types of health care for patients who suffer from critical injuries or wounds or chronic diseases that need hourly monitoring. It is a medical staff equipped to take care of the cases in the department. There are several sections:

- The prematurity is an intensive care unit for newborns, as it receives all newborns suffering from breathing and heart problems and newborns not fully developed in the wombs.
- There is also what is known as intensive care for children, which receives children under 16 years old.
- The intensive care unit, in which all serious patients suffering from heart problems are received.
- The surgical intensive care unit: where all difficult surgical cases are received, such as severe accident injuries and difficult surgical cases, such as open heart and brain and nerve operations.
- The internal intensive care unit receives all cases that suffer from chronic diseases such as lung and nerve diseases (cerebral agitation, severe lung infections, asthma and some cancerous cases).

Hypertension (HT); the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure regularly reviews the classification

and approach to hypertension; the most recent report (JNC 8) was published in 2014. This most recent report is extremely contentious and, in contrast to earlier ones, did not classify hypertension. In contrast to the preceding four stages in JNC 6, the 2003 study (JNC 7) identified two stages of hypertension, namely Stage 1 with a systolic blood pressure (SBP) of 140-159 and diastolic blood pressure (DBP) of 90-99, and Stage II hypertension with an SBP of 160 or a DBP of 100 mmHg. Although not particularly mentioned in the JNC 7 report, patients are typically considered to be in a "hypertensive crisis" if their systolic or diastolic blood pressure is greater than 179 mmHg or 109 mmHg, respectively. According to the JNC's 1993 study, hypertensive crises should be operationally classified as "hypertensive emergencies" or "hypertensive urgencies". This division is still relevant today. Severe BP increases were categorized as:

- Hypertensive crises where there is acute end-organ damage or
- Hypertensive urgencies that do not involve an acute target organ.

Making a therapeutic plan requires carefully separating hypertensive emergencies from urgent cases. Those with a hypertensive emergency should have their blood pressure decreased quickly (in the ICU), though not to "normal" levels. In contrast, those with hypertension urgency should have it reduced within 24-48 hours (with PO medication). The phrase "malignant hypertension" has been used to describe a state that includes increased blood pressure together with encephalopathy or acute nephropathy. However, this phrase has been replaced with "hypertensive emergency" in National and International Blood Pressure Control guidelines. (Whelton PK et al, 2017)

- A rapidly acting, titratable intravenous antihypertensive is used in the intensive care unit (ICU) to treat hypertensive emergencies.
- Hypertensive emergencies are typically treated with oral antihypertensive medications on an outpatient basis.

Drug-related problems (DRPs); table (2) summarizes the causes (including possible causes for potential issues); older adults frequently experience problems related to drugs, such as drug inefficacy, unpleasant drug effects, over dosage, under dosage, inappropriate treatment, inadequate monitoring, no adherence, and pharmaceutical interactions. (Hasil, 2018)

Drugs may not work as well in elderly patients due to under-dosing by doctors (for instance, increased concern about side effects) or poor adherence (for example, due to financial or cognitive limitations).

Unwanted adverse drug effects are those effects that are unwanted, uncomfortable, or dangerous. Frequent examples such as over sedation, confusion, hallucinations, falls, and bleeding. Under the age of 65, ambulatory individuals have adverse drug effects at a rate of approximately 50 events per 1000 person-years. Hospitalization rates for adverse drug side effects are four times higher in older patients (17%) than in younger people (4%). (WSC, 2018)

Reasons behind DRPs; Although adverse drug reactions can happen to any patient, elders are more likely to have them due to specific factors Table, (2). For instance, older persons frequently take many medications, and their pharmacodynamics and pharmacokinetics are altered by their age. That's why the last two raise the chance of witnessing undesirable side effects. (Viktil KK et al, 2007)

Even when prescribed and used correctly, medications may have unintended consequences for anybody at any age, such as developing a new allergy. However, at least 25% of the time, negative consequences for older people are considered avoidable. Antipsychotics, anticoagulants, antiplatelet medicines, hypoglycemic, insulin, mood stabilizers, and sleep aids are all in the crosshairs. (Haili BY et al,2020)

Many of the most prevalent reasons medications have unintended consequences are ineffective, or both, in the elderly, are also easily avoidable. Inadequate communication with patients or healthcare providers (especially during healthcare transitions) is a primary contributor. Medication reconciliation should be prioritized when patients are admitted or discharged from the hospital or undergo other care transitions (such as moving from a nursing home to an acute care hospital or a skilled nursing facility to their own house). Table (1) illustrates PCNE Classification for Drug-Related Problems V9.1 The Basic Classification.

Table 1: PCNE Classification for Drug-Related Problems V9.1 The Basic Classification

The Causes (including possible causes for potential problems)

[N.B. One problem can have more causes]

	Primary Domain	Code V9.1	Cause
Prescribing & drug selection	**1. Drug selection** The cause of the (potential) DRP is related to the selection of the drug (by patient or health professional)	C1.1	Inappropriate drug according to guidelines/formulary
		C1.2	No indication for drug
		C1.3	Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements
		C1.4	Inappropriate duplication of therapeutic group or active ingredient
		C1.5	No or incomplete drug treatment in spite of existing indication
		C1.6	Too many different drugs/active ingredients prescribed for indication
	2. Drug form The cause of the DRP is related to the selection of the drug form	C2.1	Inappropriate drug form/formulation (for this patient)
	3. Dose selection The cause of the DRP is related to the selection of the dose or dosage	C3.1	Drug dose too low
		C3.2	Drug dose of a single active ingredient too high
		C3.3	Dosage regimen not frequent enough
		C3.4	Dosage regimen too frequent
		C3.5	Dose timing instructions wrong, unclear or missing
	4. Treatment duration The cause of the DRP is related to the duration of treatment	C4.1	Duration of treatment too short
		C4.2	Duration of treatment too long
Disp	**5. Dispensing** The cause of the DRP is related to the logistics of the prescribing and dispensing process	C5.1	Prescribed drug not available
		C5.2	Necessary information not provided or incorrect advice provided
		C5.3	Wrong drug, strength or dosage advised (OTC)
		C5.4	Wrong drug or strength dispensed
Use	**6. Drug use process** The cause of the DRP is related to the way the patient gets the drug administered *by a health professional or other carer*, despite proper dosage instructions (on label/list)	C6.1	Inappropriate timing of administration or dosing intervals by a health professional
		C6.2	Drug under-administered by a health professional
		C6.3	Drug over-administered by a health professional
		C6.4	Drug not administered at all by a health professional
		C6.5	Wrong drug administered by a health professional
		C6.6	Drug administered via wrong route by a health professional
	7. Patient related The cause of the DRP is related to the patient and his behaviour (intentional or non-intentional)	C7.1	Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason
		C7.2	Patient uses/takes more drug than prescribed
		C7.3	Patient abuses drug (unregulated overuse)
		C7.4	Patient decides to use unnecessary drug
		C7.5	Patient takes food that interacts
		C7.6	Patient stores drug inappropriately
		C7.7	Inappropriate timing or dosing intervals
		C7.8	Patient unintentionally administers/uses the drug in a wrong way

Drug-disease interactions; Drugs prescribed for one illness might worsen the symptoms of another, which worries patients of all ages, especially the elderly. As shown in the table medicine-condition Interactions of Concern in Older Adults, it may be difficult to tell the difference between the effects of a medicine and those of a condition, which can lead to an unnecessary cascade of prescriptions. (PCNE, 2010)

When a drug's unwanted side effect is misunderstood as a symptom or indicator of a different condition, a "prescribing cascade" ensues. Potential side effects of the new, needless medicine might be mistaken as symptoms of another condition, leading to more unwarranted medical intervention. (Griese-Mammen N et al, 2018)

The side effects of many medications are like those of conditions more frequent in the elderly or normal aging processes. Here are a few illustrations:

- Antipsychotics might result in Parkinsonism-like symptoms. Anti-Parkinson medications may cause unwanted side effects in the elderly, such as orthostatic hypotension, delirium, hallucinations, and nausea if misdiagnosed as Parkinson's disease.
- Patients with dementia may be administered cholinesterase inhibitors (such as donepezil, rivastigmine, or galantamine). Infrequent or urgent urination, or diarrhea, are possible side effects of these medications. Anticholinergic medication (such as oxybutynin) might then be provided to the patient to alleviate the emerging symptoms. This results in adding a medicine when unnecessary, which might have harmful consequences or interfere with other medications. If you're on a cholinesterase inhibitor for dementia, lowering your dosage or switching to a medication like meantime that works differently may be a better option.
- Patients with hypertension may benefit from calcium channel blockers like amlodipine, nifedipine, or felodipine. While these medications might effectively treat hypertension, they could also lead to peripheral edema. If the patient's condition worsens, diuretic medication (such as furosemide) may be administered, leading to hypokalemia and the need for potassium supplements. The likelihood that a new symptom or sign in an elderly patient is related to their current medication regimen should always be considered by prescribers.

Drug-drug interactions; The elderly are especially at risk for drug-drug interactions since they often take many medications. Older adults often utilize dietary supplements like therapeutic herbs but don't always notify their doctors. Herbal supplements and conventional medicine don't always get along. Serotonin syndrome is dangerous if you take St. John's wort and an SSRI simultaneously and there is an increased risk of bleeding if you take ginkgo biloba extract and warfarin simultaneously. As a result, doctors need to probe patients more regarding their use of nutritional aids like vitamins and herbs. (Hussein M et al, 2014)

There is minimal variation between medication interactions in the general population and those in the elderly. However, the degree to which certain medications (such as

phenytoin, carbamazepine, and rifampin) induce cytochrome P-450 (CYP450) drug metabolism may be attenuated in older adults. The risk of toxicity from medications that rely on the CYP450 metabolic pathway increases using several other drugs. Drug interactions involving CYP450 enzymes are more likely to occur in the elderly since they tend to take more medications. Concomitant use of more than one medicine with potentially additive or synergistic effects is also a concern. (Nasution A et al, 2016)

Inadequate monitoring;

- The process of recording a new drug's indication
- Documenting the patient's current medication regimen
- Evaluation of treatment efficacy and other pharmacological effects
- Keeping an eye on any laboratory tests that need to be done to determine success or failure.
- Checking prescriptions regularly

The elderly population is particularly in need of these precautions. A lack of careful monitoring raises the likelihood of polypharmacy, unpleasant effects, and ineffectiveness, particularly following the prescription of new medications. The Health Care Financing Administration's expert consensus group on medication use review criteria has produced criteria for monitoring. The criteria emphasize such issues as excessive or prolonged treatment, unnecessary treatment, and medication interactions. (Chobanian AV, et al)

Inappropriate drug selection; When a drug's risks outweigh its benefits, it is not a good choice. When drugs are used incorrectly, they may cause:

- Treatment failure due to inappropriate medication, dosage, frequency, or duration
- Therapeutic repetition
- Refrain from thinking about how medicine would react with others and in what situations it should be used.
- When a patient moves from one healthcare environment to another without having their indication reevaluated, there is a risk that they will continue taking an appropriate medication after the acute ailment has resolved.

Several pharmacological categories pose unique risks to the elderly. Some medications should never be used in elderly patients, some should only be used under exceptional circumstances, and others might be taken with care. Other lists are available that categorize possibly unsuitable pharmaceuticals for the elderly, such as the Beers Criteria®, developed by the American Geriatrics Society. Some non-pharmaceutical treatment options are included with references. Each patient's potential advantages and hazards must be weighed individually. Patients towards the end of life have very distinct needs regarding pharmacological therapy, thus, these criteria are not applicable. (Hapsari PP et al, 2014)

Inappropriate medicines are still being given to older persons, despite the diffusion and understanding of the American Geriatrics Society Beers Criteria® and other criteria; generally, roughly 20% of community-dwelling older adults get at least one inappropriate prescription. Such patients are more likely to have unwanted side effects. The risk of hospitalization and mortality is also increased among nursing home residents due to improper usage. Two-and-a-half percent of hospitalized patients in one study were given the wrong medication. (Redszuan AM et al, 2017)

Clinicians should ask patients directly about their use of over-the-counter (OTC) medications since certain of these medications (such as diphenhydramine and oral nonsteroidal anti-inflammatory medicines [NSAIDs]) may be harmful if misused.

Drugs (typically analgesics, proton pump inhibitors, or hypnotics) are frequently prescribed to older adults for minor symptoms (including adverse effects of other drugs) that may be better treated with nonpharmacologic therapies (e.g., exercise, physiotherapy, massage, dietary changes, cognitive-behavioral therapy). Further medication therapy is generally unwarranted due to limited benefits, increasing expenditures, and potential toxicity. (Lee SP et al, 2011)

Noting drug categories of concern and avoiding a small list of medications is not enough to address the issue of improper drug usage among the elderly. In addition to evaluating individual medications, patients' overall treatment plans should be reviewed frequently. (Amran Y et al, 2018)

Lack of patient adherence; When taking their medications as prescribed, older persons who are still mobile frequently fall short. Many variables, such as language

challenges, influence adherence, although age itself does not. One study found that as many as half of all seniors did not take their medications as recommended (under adherence). Similar to the causes seen in young adults. The following also play a role:

- Constraints on one's financial and physical resources may make it harder to get medications.
- Mental impairments that might make it hard to follow treatment regimens.
- Polypharmacy, i.e., the practice of using numerous medications.
- Drugs that need to be taken at specified times or in a certain way many times a day
- Insufficient knowledge of a drug's intended effects (benefits) or potential risks (harms) might lead to unintended consequences.

Patients may need help to adhere to a treatment plan involving a dosage that is either too regular or infrequent, contains many medicines, or does both. Clinicians should evaluate patients' health literacy and abilities to adhere to a drug regimen (e.g., dexterity, hand strength, cognition, vision) and try to accommodate their limitations (e.g., by arranging for or recommending easy-access containers, drug labels and instructions in large type, containers equipped with reminder alarms, containers filled based on daily drug needs, reminder telephone calls, or medication assistance). Helpful interventions include educating and revisiting medication instructions with older persons at each interaction with pharmacists and nurses. If a patient is not getting refills when they should be or if a prescription makes no sense, the pharmacist may know what's going on. If a patient's prescription isn't renewed at the recommended intervals, the pharmacy may often see this information and contact them. (Hidayat AR et al, 2015)

Overdosage; If the physician does not consider age-related changes that impact pharmacokinetics and pharmacodynamics, the patient may be given an excessive dosage of a suitable medicine. Patients with renal impairment may need dosage adjustments for medications cleared by the kidneys, such as gabapentin, some antibiotics, and digoxin.

Drugs should be begun at the lowest dosage in older persons, but individual needs vary greatly. In cases where the medicine's therapeutic index is narrow, the drug may worsen another disease, or if the patient is very fragile, initial dosages of around one-

third to one-half the average adult dose is advised. The starting dosage is gradually increased over time to achieve the intended outcome. When increasing a patient's dosage, it's essential to watch for any unwanted side effects and check their medication levels closely. (Bailey RR & Neale TJ, 1976)

Therapeutic duplication occurs when two or more healthcare providers prescribe the same or a comparable medication to the same patient without realizing they have already done so.

Poor communication; Up to half of all medication mistakes and up to 20% of adverse drug effects in the hospital result from poor transmission of medical information at transition points (between healthcare settings). Discharging prescribers may needlessly maintain prescription regimens (e.g., sedative-hypnotics, laxatives, proton pump inhibitors) that were begun and required only in the hospital. This may happen for various reasons, including laziness, busy schedules, or failure to consult the patient's primary care physician. On the other hand, a lack of communication upon hospital admission might lead to the accidental absence of maintenance medication. Drug reconciliation formally examines all medications on a patient's prescription list before, during, and after a change in care providers. (Levy P et al, 2011)

Under prescribing; beneficial medications may be under-prescribed. Under prescribing may worsen people's health and shorten their lives. Correct dosing and, where appropriate, combination therapy are clinician duties.

Depressive, Alzheimer's, heart failure, post-MI (beta-blockers), atrial fibrillation (anticoagulants), and hypertension medications are often under-prescribed in the elderly. Furthermore, vaccinations are not always administered. (Pollack C et al, 2015)

- **Beta-blockers** decrease mortality and hospitalizations in patients with a history of myocardial infarction and/or heart failure, including the elderly at high risk of complications (e.g., those with pulmonary problems or diabetes).
- Even among elderly people who are already fragile, treating hypertension with **antihypertensive** seems helpful (lowering the risk of stroke and severe cardiovascular events). Researchers have shown that hypertension is not always well managed in the elderly.

- **Alzheimer's disease medication:** Patients with Alzheimer's disease have benefited from acetyl cholinesterase inhibitors and NMDA (N-methyl-d-aspartate) antagonists. Although the benefits are small and may be inconsistent, patients and their loved ones should be allowed to make an educated choice regarding their usage.
- Patients with atrial fibrillation who take **anticoagulants** (such as warfarin or the newer direct oral anticoagulant medications) have a lower chance of stroke. Even though anticoagulation generally increases the risk of bleeding, some elderly people who may benefit from it are not getting it.
- **Immunizations:** Influenza, pneumococcal infection, and herpes zoster all provide a higher threat of severe illness or even death in the elderly. Increases in vaccination rates among the elderly are still possible.

Acute or unrelated illnesses may be untreated in elderly individuals with a chronic ailment (for instance, hypercholesterolemia may go untreated in patients with COPD [chronic obstructive pulmonary disease]). When a patient has a short life expectancy, doctors may hesitate to provide them with life-extending medicines out of fear for their well-being. Sometimes doctors assume that their patients can't afford the supplementary medications or that they'd rather focus on getting well from the underlying condition. Clinicians may better grasp their patients' interests and concerns if they actively include patients and careers in decision-making regarding medication therapy. (Amin A et al, 2010)

Table 2: PCNE Classification for Drug-Related Problems V9.1 - Page 5
The Causes (including possible causes for potential problems)

	Primary Domain	Code V9.1	Cause
Prescribing & drug selection	**1. Drug selection** The cause of the (potential) DRP is related to the selection of the drug (by patient or health professional)	C1.1	Inappropriate drug according to guidelines/formulary
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	2. Drug form The cause of the DRP is related to the selection of the drug form	C2.1	Inappropriate drug form/formulation (for this patient)
	3. Dose selection The cause of the DRP is related to the selection of the dose or dosage	C3.1	Drug dose too low
		C3.2	Drug dose of a single active ingredient too high
		C3.3	Dosage regimen not frequent enough
		C3.4	Dosage regimen too frequent
		C3.5	Dose timing instructions wrong, unclear or missing
	4. Treatment duration The cause of the DRP is related to the duration of treatment	C4.1	Duration of treatment too short
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Disp	**5. Dispensing** The cause of the DRP is related to the logistics of the prescribing and dispensing process	C5.1	Prescribed drug not available
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		C5.4	Wrong drug or strength dispensed
Use	**6. Drug use process** The cause of the DRP is related to the way the patient gets the drug administered *by a health professional or other carer*, despite proper dosage instructions (on label/list)	C6.1	Inappropriate timing of administration or dosing intervals by a health professional
		C6.2	Drug under-administered by a health professional
		C6.3	Drug over-administered by a health professional
		C6.4	Drug not administered at all by a health professional
		C6.5	Wrong drug administered by a health professional
		C6.6	Drug administered via wrong route by a health professional
	7. Patient related The cause of the DRP is related to the patient and his behaviour (intentional or non-intentional)	C7.1	Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason
		C7.2	Patient uses/takes more drug than prescribed
		C7.3	Patient abuses drug (unregulated overuse)
		C7.4	Patient decides to use unnecessary drug
		C7.5	Patient takes food that interacts
		C7.6	Patient stores drug inappropriately
		C7.7	Inappropriate timing or dosing intervals
		C7.8	Patient unintentionally administers/uses the drug in a wrong way
		C7.9	Patient physically unable to use drug/form as directed
		C7.10	Patient unable to understand instructions properly
Seamless	**8. Patient transfer related** The cause of the DRP can be related to the transfer of patients between primary, secondary and tertiary care, or transfer within one care institution.	C8.1	Medication reconciliation problem
	9. Other	C9.1	No or inappropriate outcome monitoring (incl. TDM)
		C9.2	Other cause; specify
		C9.3	No obvious cause

This chapter summarizes and analyses previous research and theories on drug-related problems in the intensive care unit. Besides, It reveals areas of contention and contested assertions, as well as any gaps in prior research..

The intensive care unit is a potential hotspot for issues connected to drugs. Because a significant number of the patients being treated are complicated patients, clinical pharmacy intervention may uncover issues with medication treatment.

Traditional dispensing duties in the intensive care unit (ICU) have given way to a more prominent role in critical care pharmacy services. These are now acknowledged as integral to the multidisciplinary care provided to critically ill patients. This shift in roles has allowed pharmacists to provide valuable services, such as assisting physicians and clinicians with the decision-making process regarding pharmacotherapy, reducing the number of medication errors, and improving medication safety systems to maximize patient outcomes. These services have been made possible by the utilization of technology and resources. (Mayer SA et al,2011)

When a clinical pharmacist (CP) was a full part of a multidisciplinary team in the intensive care unit (ICU), many studies revealed a substantial reduction in prescription mistakes, adverse medication events, treatment costs, and better patient outcomes. This was especially true when the ICU was a level 4 or 5 trauma center.

Critical care pharmacists, who play a significant role in the care teams made up of various healthcare specialists, have a big impact on the way patients are treated in the ICU. They are able to get treatment from several ICU teams thanks to their unique talents and expertise, which increases the number of proposals made and results in better, more cutting-edge medical care for patients in urgent circumstances. (Levy P et al, 2011)

Theoretical Framework

If the patient's systolic or diastolic blood pressure is greater than 180 mmHg or 120 mmHg, respectively, it is possible to detect a hypertensive emergency. The target organ has also been shown to have recently sustained damage. If a patient has a systolic blood pressure of more than 180 mmHg or a diastolic blood pressure of more than 120 mmHg and is otherwise healthy and exhibits no symptoms of acute target organ

damage in the clinical or laboratory setting, hypertensive urgency may be diagnosed. Antihypertensive drug therapy for these patients has to be enhanced. (Varon J, 2009)

Patients with a dissecting aortic aneurysm, intense pneumonic edema, intense myocardial localized necrosis, unstable angina pectoris, intense renal disappointment, intense intracranial hemorrhage, intense ischemic stroke, hypertensive encephalopathy, eclampsia or pre-eclampsia, peri-operative hypertension, and a pheochromocyto are among those who experience hyper These patients require medications with an efficient and quick-acting mechanism that are administered intravenously in order to safely regulate the elevated blood pressure, maintain the function of the target organs, soothe symptoms, avoid unwanted effects, and advance clinical outcomes. The median survival period for these patients without antihypertensive medication is 10.4 months, and the 1-year mortality frequency for hypertensive episodes is more than 79%. (Fixen PR, 2009)

Presentation in the Clinic

The specific end-organ malfunction that has developed determines the clinical signs of a hypertensive emergency, which may include:

- Hypertensive encephalopathy (and persistent hypertension in the brain)
- Acute dissection of the aorta
- Sudden cardiac arrest
- Sudden Cardiac Arrest
- Edema of the lungs leading to respiratory failure
- Eclampsia, HELLP syndrome, and severe pre-eclampsia
- Anemia with microangiopathic thrombocytopenia
- Short-term hypertension after surgery

Individuals may have different hypertensive crisis symptoms. Shortness of breath (29 percent), chest discomfort (26 percent), headache (23 percent), changed mental state (20 percent), and localized neurologic impairment (11 percent) were the most prevalent first symptoms reported in the STAT registry. There have been reports of microangiopathic hemolysis.

Initial Evaluation

Hypertensive emergency patients often seek medical attention because they have developed a new symptom complex associated with their heightened blood pressure. Timely triage and medical assessment are essential for stopping organ failure. (Varon J & Marik PE, 2003)

A targeted medical history should include the following:

- Hypertension diagnosis and treatment history; current anti-hypertensive drugs and their dosage, compliance, and time since last dose; and time since last dose.
- Medications, whether they are prescribed or purchased over-the-counter
- A decision should be made to use recreational drugs or monoamine oxidase inhibitors (such as amphetamines, cocaine, or phencyclidine).

An actual checkup needs to:

- Verify the high blood pressure by taking readings from both arms using a cuff of a suitable size.
  - Using a too-small cuff for the arm has been proven to artificially inflate BP readings in obese people, making using the correct size cuff especially critical.
- Evaluate for signs of end-organ damage by
  - all limbs with detectable pulses
  - listening for murmurs or gallops in the heart, bruits in the renal arteries, and lung rales.
  - Focus your neurologic and funduscopic testing on the patient.

The most common symptoms of hypertensive encephalopathy are a change in awareness and a severe headache. Hypertensive encephalopathy is less likely to be accompanied by focal neurological abnormalities, such as lateralizing symptoms. In individuals with a severe headache that comes on suddenly, subarachnoid hemorrhage should be suspected. Ocular examinations may aid in diagnosing hypertensive encephalopathy by revealing signs of advanced retinopathy such as arteriolar abnormalities, exudates, hemorrhages, or papilledema. Evaluation of the heart should concentrate on identifying angina or myocardial infarction and explaining any abnormal symptoms, such as dyspnea, cough, or weariness, that might be missed,

according to 28 Hypertensive Crises 433. Hematuria and oliguria are possible side effects of severe renal damage. After making this assessment, the doctor will be better equipped to decide whether the patient is experiencing a hypertensive emergency and what steps should be taken next. (Marik PE & Varon J, 1962)

A first, impartial look should consist of the following:

- Electrolytes, creatinine, and blood urea nitrogen levels are analyzed as part of a metabolic panel.
- A urinalysis is recommended to check for proteinuria or microscopic hematuria, a complete blood count (and smear if microangiopathic hemolytic anemia is suspected), and a physical examination.
- An EKG for detecting cardiac ischemia.
- Radiographic exams are appropriate in the appropriate clinical environment, such as a chest x-ray for a persistent patient with cardiopulmonary reasons or a head CT scan for a persistent patient with neurological indications.
- If significant chest discomfort, uneven pulses, or a dilated mediastinum are present, a contrast computed tomography scan of the chest should be conducted without delay to rule out aortic dissection. Trans-esophageal echocardiography offers high sensitivity and specificity for detecting aortic dissection, but it shouldn't be used to diagnose the condition until after the patient's blood pressure has been stabilized.
- Echocardiography is necessary to differentiate between diastolic failure, transitory systolic dysfunction, and mitral regurgitation in individuals presenting with pulmonary edema. Many people, especially the elderly, get heart failure because of isolated diastolic dysfunction while having an average ejection fraction. These individuals are treated differently than those with transitory mitral regurgitation or significant systolic dysfunction.

Initial Treatment of High Blood Pressure

Hypertensive urgency exists in most patients with severe hypertension (SBP > 160, DBP > 110 mmHg) diagnosed on first examination, but there is no indication of acute end-organ damage. This may be an immediate awareness of chronic hypertension

since there is no evidence of acute end-organ injury, and the patients may come for examination of another complaint. The optimal method of treatment for these individuals is the use of oral medicines to reduce blood pressure gradually over a period of 24-48 h. Due to a rightward change in the pressure/flow auto-regulatory curve in important artery beds (cerebral, coronary, renal), rapid BP reduction may be linked with considerable morbidity in hypertensive urgency. Ischemia and infarction may occur if perfusion to these vascular beds is drastically decreased when hypertension is rapidly reduced below the autoregulatory range of these vessels. (Chang R et al, 2012)

Because of the risk of organ hypoperfusion, lowering the BP in these individuals must be done gradually and carefully.

Patients in need of urgent treatment for hypertension should NOT be given intravenous antihypertensive medications.

What Should Be Done If a Resident or Hospitalist Is Called to the Floor for Hypertension?

- Conduct a self-blood pressure check using a cuff of the appropriate size on both arms.
- Review chart
  - Alcoholism, drug abuse, and hypertension
  - Current HTN medications
- Check the patient out.
- The EMERGENCY of hypertension
  - Alert the Intensive Care Unit
- Urgent hypertension
  - Pain, anxiety, a swollen bladder, low body temperature, low oxygen levels, dehydration, and a lack of volume are all treatable reasons for high blood pressure.
  - Maintain the nurse's composure.
  - Metoprolol, lisinopril, and other oral anti-HTN medications

Since hypertensive situations are characterized by altered autoregulation and preexisting end-organ damage, excessive and hasty correction of the BP might further

decrease perfusion and propagate additional harm. Consequently, a short-acting, titratable antihypertensive drug given by continuous infusion is the preferred method of treating hypertension emergencies in patients. The sublingual and intramuscular routes should be avoided because of their uncertain pharmacodynamic effects. A hypertensive crisis requires the specialized care of an intensive care unit. Patients with the most severe clinical signs or labile BP may benefit from intra-arterial BP monitoring. Patients in need of emergency treatment for hypertension may choose from several different fast-acting intravenous medicines, each with its benefits and drawbacks. (Barker NW, 1974)

Hypertensive Emergency Management

- ICU Admission
- Gradual lowering of blood pressure (BP) using a titratable, short-acting injectable antihypertensive drug to prevent additional organ damage.
- Aortic dissection in 10 minutes Type A—Surgery Type B—SBP 140 mmHg
- 15% decrease in DBP or to 110 mmHg over 1 hour
- After the first hour, continue slowing down to drop blood pressure by 25% over 24 hours.
- Intravenous crystalloids for volume depletion (excluding pulmonary edema)

Preventing sudden drops in blood pressure that may lead to severe complications shouldn't be attempted using rapid-acting intravenous medicines outside of a well-supervised intensive care unit. The initial objective is to lower diastolic blood pressure by 10–15%, or to about 110 mmHg, within 30–60 minutes. This should be accomplished in aortic dissection patients within 5-10 minutes. Once end-organ damage has stopped and blood pressure has been stabilized with intravenous medicines, the intravenous agents may be tapered down, and oral treatment can begin. Considering the patient's volume status before starting intravenous therapy is crucial. Restoring intravascular volume with intravenous saline would help restore organ perfusion and avoid a sudden drop in blood pressure (BP) when anti-hypertensive regimens are commenced in patients with hypertensive crises who have had volume depletion due to pressure natriuresis. (Rhoney D & Peacock WE, 2009)

Drugs to AVOID

- Although ACE inhibitors have a lengthy half-life and are difficult to titrate, they may be beneficial in the emergency treatment of hypertension.
- Clonidine
- Vasodilators like hydralazine work quickly and directly. After 5-15 minutes of lag time after intramuscular or intravenous injection, blood pressure (BP) drops gradually and, in some cases, suddenly for up to 12 hours. Although hydralazine only has a 3-hour half-life in the bloodstream, its effects on blood pressure only last around 10 hours. Hydralazine SHOULD BE AVOIDED in treating hypertensive crises due to its lengthy and unexpected anti-hypertensive effects and the difficulty of appropriately titrating the medications' hypotensive impact.
- Nifedipine used sublingually or intranasally, has been linked to hypotension, stroke, heart attack, kidney failure, and even death. This method of BP control is heavily "discouraged" because of its potential dangers.
- Furosemide is strictly forbidden. Patients experiencing hypertensive crises often have volume depletion; therefore, combining a diuretic with a hypertensive medication might cause a rapid decrease in blood pressure. Except in cases of volume overload caused by conditions like renal parenchymal disease or concomitant pulmonary edema, diuretics are strongly discouraged. (Barker NW, 1974)
- Only at very high dosages can nitroglycerin impact arterial tone; otherwise, it acts as a potent vasodilator. The volume loss typical of hypertensive situations exacerbates the resulting hypotension and reflex tachycardia. Patients with impaired cerebral and renal perfusion may not benefit from the blood pressure-lowering benefits of nitroglycerin because it affects preload and cardiac output. However, in patients with hypertensive crises accompanied by acute coronary syndromes or acute pulmonary edema, low-dose (60 mg/ min) nitroglycerin may be given as an adjuvant to intravenous antihypertensive treatment.
- Sodium nitroprusside is a vasodilator that reduces both afterload and preload in the cardiovascular system. Patients with hypertensive encephalopathy or those recovering from a cerebrovascular accident are especially vulnerable to the adverse effects of nitroprusside, which include a reduction in cerebral blood

flow and an increase in intracranial pressure. Nitroprusside is a highly effective drug with a short time to action (seconds), a short duration of action (minutes), and a short plasma half-life (minutes). Toxic medication nitroprusside. Infusion rates of more than 4 g/kg/min of nitroprusside for as little as 2 to 3 hours have been shown to produce cyanide concentrations in the lethal range. The cyanide production rate at the "recommended" dosage of nitroprusside (up to 10 g/kg/min) is much higher than in humans. Nitroprusside has the potential for severe toxicity; hence it should only be used in restricted clinical conditions and in individuals with normal renal and hepatic function when no other intravenous anti-hypertensive medications are available. Treatments should last as little time as feasible, with an infusion rate of no more than 2 micrograms per kilogram per minute. (Allison M et al, 2015)

Acute Hypertension After Surgery

The term "acute postoperative hypertension" (APH) refers to a significant rise in blood pressure (BP) in the first few days after surgery that may cause life-threatening neurologic, cardiovascular, or surgical-site problems if not treated immediately. While APH is well-known, a precise definition of the illness is lacking. In our opinion, APH is present when either the SBP or the DBP rises by more than 20% or rises to more than 110 mm/Hg. In most cases, APH appears within 2 hours after surgery and subsides a few hours later. Myocardial ischemia, infarction, cardiac arrhythmias, congestive heart failure, pulmonary edema, hemorrhagic stroke, cerebral ischemia, and encephalopathy are all possible outcomes of APH. The surgical site will bleed more, and vascular anastomoses will be at risk when APH is present. There is still much mystery around the pathophysiologic process that causes APH, and it might change depending on the kind of surgery performed. In individuals with APH, however, higher plasma catecholamine concentrations point to sympathetic nervous system activation as the ultimate common mechanism leading to hypertension. The most prominent hemodynamic change seen in APH is an increase in afterload, characterized by elevated SBP and/or DBP and/or tachycardia. While each major operation risks APH, those involving the heart, lungs, blood vessels, head, neck, and nervous system are the most at risk. Blood pressure (BP) > 140/90 mmHg or mean arterial pressure (MAP) > 105 mmHg are often therapy targets for cardiac surgery patients. Careful blood pressure regulation is advised for these individuals. There is disagreement on what

constitutes a "treatment threshold" for patients who do not need heart surgery. The degree of hypertension, the kind of surgery, the patient's comorbidities, and the therapy risk all factor into how to treat these individuals. Antihypertensive medication should not be given until the patient's pain and anxiety have been addressed. It is essential to evaluate the patient's volume status. Reduced intravascular volume increases sympathetic activity and vasoconstriction; a volume challenge may be beneficial in this situation. Treatable conditions, such as hypothermia with shivering, hypoxia, hypercarbia, and a distended bladder may also bring on APH. When there is no apparent medical basis for the patient's hypertension, it is advised that a short-acting intravenous drug be administered. Since elevated sympathetic activity is central to the pathogenesis of APH, a -blocker or alpha-beta blocker alone makes sense as a treatment. Calcium channel blockers with a short half-life given intravenously are also helpful. Agents like labetalol, esmolol, nicardipine, and clevidipine are often recommended for treating APH. Clevidipine has been demonstrated to be particularly successful in treating postoperative hypertension in several clinical studies. The ECLIPSE study, which just wrapped up, showed that this medication is effective and safe for treating APH. The ECLIPSE study assigned clevidipine or a comparator medication (nitroprusside or nicardipine) to 1,964 cardiac patients who needed therapy for perioperative hypertension. When comparing levidipine with nitroprusside for blood pressure regulation, levidipine was more effective and safer than nitroprusside (1.7 vs. 4.7%; $p = 0.045$). (Varon J et al, 2014)

Recommended Antihypertensive Agents

The pharmacokinetics and dosages of the recommended intravenous antihypertensive agents are listed below:

- Esmolol administered intravenously, is the medication of choice for treating acute aortic dissection. The loading dosage consists of 500–1,000 mcg/kg/min given over one minute, followed by an infusion rate of 50 mcg/kg/min. The highest possible rate of infusion is 200 mcg. Patients diagnosed with acute aortic dissection need a drastic and prompt drop in blood pressure during the first five to ten minutes of treatment. In these individuals, achieving a systolic blood pressure that is lower than 120 mmHg is the target blood pressure objective. After a beta blocker has been delivered, if the hypertensive crises

continues, a vasodilator such as intravenous nitroglycerin or nitroprusside may be given. (Dyke CM et al, 2008)

- Nitroglycerin, clevidipine, or nitroprusside are the intravenous medications recommended for use in the treatment of a hypertensive emergency accompanied by acute pulmonary edema. In managing acute pulmonary edema, beta blockers are not an appropriate choice of medication. Patients who are experiencing hypertensive crises should have their blood pressure dropped within minutes to one hour by about 20% to 25%, and then progressively to 160/100 mmHg during the following 2 to 6 hours, and then carefully to normal over the course of the next 24 to 48 hours. This is except acute aortic dissection. Nitroglycerin administered intravenously will have a starting infusion rate of 5 mcg per minute. The highest amount which will be infused each minute is 20 mcg. The introductory infusion rate of sodium nitroprusside by means of the intravenous course is between 0.3 and 0.5 mcg/kg/min. The most elevated permitted rate of infusion is 10 mcg/kg/minute. The initial dose of clevidipine intravenously is between 1 and 2 mg per hour. The maximum rate of infusion of mixture is 32 mg/h.

Esmolol should be administered intravenously to patients who have severe hypertension, an acute myocardial infarction, or unstable angina pectoris. Nitroglycerin intravenously may also be administered as a kind of therapy, if necessary. Patients with acute myocardial infarction or unstable angina pectoris who are hemodynamically stable should aim for a blood pressure level of less than 140/90 mmHg. A blood pressure result of less than 130/80 mmHg should be taken into consideration while leaving the hospital. When decreasing these people's blood pressure, care should be taken to prevent dropping the diastolic blood pressure below 60 mmHg, as this might cause myocardial ischemia and decrease coronary perfusion. Bringing the diastolic pressure down to under 60 mmHg may also cause myocardial ischemia to become more severe. (Espinosa A et al, 2016)

The drugs of choice for treating patients with acute renal failure and acute hypertensive crisis include clevidipine, fenoldopam, and nicardipine. Fenoldopam is first infused at a rate of 0.1 to 0.3 mcg/kg/min by intravenous administration. The maximum permitted infusion rate is 1.6 micrograms per kilogram per minute. The initial infusion rate is 5 mg/hour of intravenously given nicordinpine. 30 mg is the most that may be

administered in an hour. Within 30 minutes of treatment, 92% of patients treated with intravenous nicardipine reached the target systolic blood pressure compared to 78% of patients treated with intravenous labetalol in 104 patients with a hypertensive emergency and renal dysfunction. (Sharkey CM et al, 2016)

Hydralazine, labetalol, and nicardipine are the medications of choice for treating people experiencing a hypertensive crisis in conjunction to eclampsia or pre-eclampsia. It is not recommended to treat these individuals with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, direct renin inhibitors, or sodium nitroprusside. 20 milligrams is the maximum first intravenous dosage for hydralazine, and a slow intravenous infusion is required to deliver it. If more is required, repeat this dose every 4-6 hours. The first intravenous dosage range for labetalol ranges from 0.3 to 1.0 mg/kg, with a maximum beginning dose of 20 mg. The second stage is an intravenous infusion that never goes beyond 3 mg/kg/h and ranges from 0.4 to 1.0 mg/kg/h. 300 mg is the total dosage during the course of the treatment. If necessary, dose must be repeated every 4 to 6 hours.

The best drugs to treat high blood pressure after surgery are clevidipine, esmolol, nitroglycerin, and nicardipine when given through an IV. Clevadipine is the preferred drug for treating high blood pressure that happens suddenly after surgery, according to investigation and meta-analysis.

Intravenous clevidipine, nicardipine, or phentolamine are the drugs of choice for treating a hypertensive crisis brought on by a pheochromocytoma, a hyperadrenergic state brought on by cocaine, amphetamines, phencyclidine, or monoamine oxidase inhibitors, or by abruptly stopping the use of clonidine or other sympatholytic medications. A 5 mg intravenous bolus of phentolamine may be the recommended beginning dosage for this medication. Encourage intravenous bolus measures of 5 mg should be handled every 10 minutes to drop the patient's blood weight to the appropriate range. (Char D et al, 2014)

Patients who are experiencing a hypertensive crisis that is also accompanied by a high plasma renin state may be given enalaprilat intravenously. When given intravenously, the starting dosage of enaliprilat is 1.25 milligrams over five minutes. To achieve the desired blood pressure level, it may be necessary to provide further doses of enaliprilat intravenously at a rate of up to 5 mg every 6 hours.

For this study, 104 patients with acute heart failure and hypertension were randomized to either intravenous clevidipine or intravenous antihypertensive drugs (87% IV nitroglycerin or nicardipine). The results of this study showed that 71% of patients receiving clevidipine attained the target blood pressure level, compared to just 37% of patients receiving intravenous antihypertensive drugs as per standard of care. After 45 minutes, dyspnea was demonstrated to be improved by clevidipine more effectively than drugs regarded as the gold standard of treatment.

226 hypertensive crisis patients were randomly selected as part of a study to receive intravenous nicardipine or intravenous labetalol therapy in a crisis unit. In 91.7% of patients treated with intravenous nicardipine and 82.5% of patients treated with intravenous labetalol, the target blood weight level was reached in less than 30 minutes. In this trial, there was a subset of 141 people who had symptoms and/or indicators of target organ damage. In contrast, 76.1% of the patients arbitrarily assigned to receive intravenous labetalol were able to reach their goal blood weight level within 30 minutes, as opposed to 91.4% of the patients arbitrarily assigned to receive intravenous nicardipine.

High Blood Pressure Prior to Surgery

Although preoperative hypertension is a strong predictor of postoperative morbidity, it has not been shown that treating hypertension before surgery lessens the risk of problems. Regarding cardiovascular risk factors, aggressive preoperative optimization is recommended for all patients undergoing elective surgery. This includes blood pressure control, electrolyte correction, glucose control, smoking cessation, and nutritional optimization (in high-risk patients). Except for ACE inhibitors and angiotensin II receptor antagonists (ARA), all antihypertensive drugs should be maintained in preoperative hypertensive patients. Prior to surgery, stop taking ACEIs and ARAs at least 10 hours in advance. (Peacock WF et al, 2011)

Related Research

A Cochrane effective audit of the pharmaceutical treatments for hypertensive crisis included 15 randomized controlled trials, 869 individuals, and seven specific sedative classes. There was insufficient evidence to determine whether one antihypertensive medication is superior to another in terms of its ability to reduce the

risk of death and illness. Randomized clinical studies must be done to evaluate the short- and long-term mortality outcomes of patients with hypertensive crisis who were treated with various antihypertensive medicines. Information from randomized clinical studies is too important to be ignored when determining how soon or how much the patient's blood pressure has to be lowered in a hypertensive crisis. (Cannon CM et al, 2013)

In a study, 2,794 patients with severe intracerebral hemorrhage and hypertensive crisis were randomly assigned to receive intravenous antihypertensive medications selected by various specialists to lower their blood pressure to a target level of less than 140 mmHg within an hour or less than 180 mmHg within an hour. Both of these locations were completed with intravenous antihypertensive medications. Systolic blood pressure dropping to less than 140 mmHg was associated with better practical outcomes than a drop to less than 180 mmHg within an hour, though it was also possibly associated with a 13% reduction in the critical result of passing or notable impedance. Superior outcomes were nonetheless associated with this systolic blood pressure. Superior beneficial outcomes were in any case associated with this reduction in systolic blood pressure. A meta-analysis of four randomized clinical trials including 3,315 patients with a hypertensive crisis and severe intracerebral hemorrhage revealed a 13% borderline decrease in 3-month passing or reliance when the blood pressure of these patients was brought down to less than 140 mmHg. This was discovered in patients whose blood pressure had to be lowered to less than 140 mmHg in order to achieve this outcome. Serious blood weight loss appears to be associated with a decreased rate of hematoma development in individuals with severe cerebral hemorrhage.

Randomized clinical studies must be carried out to determine whether antihypertensive medication effectively treats severe brain death. It makes sense to regard clevidipine, nicardipine, labetalol, and urapidil as first-line medications for these patients given their quick onset of action, simplicity of titration, and intravenous administration. (Huang Y et al, 2013)

The blood pressure goal level for people who have had an acute ischemic stroke is unknown, and it is also unknown which antihypertensive medication should be advised, according to the acute ischemic stroke recommendations published in 2013

by the American Heart Association and the American Stroke Association. According to the new recommendations, blood pressure shouldn't be decreased for the first 24 hours after an acute ischemic stroke unless the patient's blood pressure is beyond 220/120 mmHg or there is a specific medical condition that might benefit from it. These guidelines recommend lowering the blood pressure to below 180/110 mmHg using either intravenous labetalol or intravenous nicardipine before administering fibrinolytic therapy to patients with acute ischemic stroke who are qualified for acute reperfusion therapy. It is also advised to take into account additional intravenous antihypertensive medications as necessary. (Jauch EC et al, 2013)

CHAPTER III

Methodology

This chapter provides information about the research design, participants/sample, data collection and analysis procedures, and how the findings are analyzed.

Research Design

This research was a cross-sectional study permitted to conduct by the ethical committee of Near East University. This research was carried out between December 2020 and December 2021 utilizing secondary data collected from the medical records, medications, and nursing records of critically ill patients treated at the intensive care unit of Near East University Hospital.

Participants

The inclusion criteria were set at random, with participants having hypertension as a chronic condition and most participants being older than 23 years old. Those who were their medical and nursing records were either missing or illegible (no data on gender, age, illness, or medication), as well as those who had not hypertensive patients or had not been given any antihypertensive medicine by a physician were disqualified from participation in the study. All outpatients who fulfilled the requirements were included in this research to exclude any possibility of selection bias. For that, out of 510 patients, 264 were selected to participate in this study, as they matched the estimated criteria.

Data Collection. The prescriptions, patient medical records, and nursing records were combed through to acquire information on the patient's demographics and medications. The following information was gathered for each patient: medical record number, gender, age, diagnosis, sepsis, number of days spent in the hospital, DRPs, treatment status, and medications used (including the drug's name, dose form, the drug's strength, dosing interval, and volume of medication).

Data Analysis. Using the PCNE V6.02, the researchers established the presence of a DRP by concentrating on two domains: treatment efficacy (P1) and adverse medication responses (P2). In addition, DRPs were categorized under the reasons category, which was further broken down into the subcategories of medication

selection, drug form, dosage selection, treatment length, dispensing, drug use/administration process, patient-related, and other categories.

The literature, national and international recommendations served as the basis for the medication review that was carried out.

In order to identify the frequency distribution of patient characteristics according to demographic parameters and clinical features of patients, such as drugs given, DRPs, and also the causes of DRPs, a univariate descriptive analysis was carried out using Microsoft Excel and SPSS. This analysis was used to determine the results of the conducted study.

CHAPTER IV

Findings

This chapter presents the findings based on the collected data.

A total of 510 patients, mostly with hypertension, who were treated at Near East University Hospital between December 2020 and December 2021 were initially considered for inclusion in the study. After applying the inclusion and exclusion criteria, 264 patients were included in the research, and 246 patients were excluded because they were not hypertensive and due to incomplete medical and nursing records. Most of the participants in the study were between more than 65 years old (70.5%) and males (54.5%), tables 3 and 4. Besides, as shown in Table 4, it was revealed that 42.8% of the patients were hospitalized for a maximum of four days (42.8%).

Table 3: Demographic characteristics of studied patients

Age

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 65	78	29.5	29.5	29.5
	≥ 65	186	70.5	70.5	100.0
	Total	264	100.0	100.0	

Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	male	144	54.5	54.5	54.5
	female	119	45.1	45.1	99.6
	no data	1	.4	.4	100.0
	Total	264	100.0	100.0	

Table 4: Hospitalization days

Hospitalization Days

	Frequency	Percent	Valid Percent	Cumulative Percent

Valid	(0-4)	113	42.8	43.1	43.1
	(5-17)	101	38.3	38.5	81.7
	(18-49)	42	15.9	16.0	97.7
	(50-64)	6	2.3	2.3	100.0
	Total	262	99.2	100.0	
Total		264	100.0		

The highest number of medications used among patients was between 7- 10 different types of drugs (54.2%) for each patient, table 5. This combination in therapy created 41.3% of DRPs (two DRPs) among the tested criteria, table 6.

Table 5: Total number of medications used among patients.

Total Number of Medications

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	≤ 6	12	4.5	4.5	4.5
	7-10	143	54.2	54.2	58.7
	11-14	98	37.1	37.1	95.8
	>15	11	4.2	4.2	100.0
	Total	264	100.0	100.0	

Table 6: Total number of detected drug-related problems

Number of DRPs

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	null	13	4.9	5.0	5.0
	one DRP	78	29.5	29.8	34.7
	two DRPs	109	41.3	41.6	76.3
	three DRPs	50	18.9	19.1	95.4
	four DRPs	12	4.5	4.6	100.0
	Total	262	99.2	100.0	
Missing	System	2	.8		
Total		264	100.0		

Table 7: Classes of Drugs given to the tested criteria.

Drug Type

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Gastric acid reducing agents (ARAs)	16	6.2	6.2	6.2
	Diuretics	2	.9	.9	27
	Anticoagulants	2	.9	.9	13.05
	Antibiotics	16	6.30	6.30	12.43
	Methylxanthines	4	1.8	1.8	26.71
	NSAIDs	19	7.21	7.21	25.02
	Analgesics	9	3.53	3.53	17.80
	Electrolytes	2	.9	.9	10.11
	>one drug	194	72.26	72.26	100.0
	Total	264	100.0	100.0	

Table 7 shows that the most common type of drug-caused problem was using Non-Steroidal Anti-Inflammatory drugs (NSAIDs) which registered the highest percentage % of 7.21 among 19 patients. On the other hand, it was obvious that the combination of the type of medications has widened the possibility of having more drug-caused problems. That's why 72.26% of 194 patients have witnessed an optimum level of drug-caused problems.

Table 8: Hypertensive patients' diagnosis upon their admission to the intensive care unit

Diagnosis

		Frequency	Percent
Valid	Oncology disorders	11	4.45
	Endocrinology disorders	2	0.9
	Neurology disorders	2	0.9
	Cardiovascular disorders	70	26.7
	Respiratory disorders	68	25.9
	Post-operation	37	14.2
	Renal disorders	2	0.9
	Bone and joint disorders	9	3.5
	Infectious diseases	32	12.4
	Car Accident	28	10.7
	> one disorders	51	19.6
	Others	79	30.3
	Gastrointestinal disorders	6	2.6
	Total	264	100.0

Table 8 shows that most patients were diagnosed with cardiovascular disorders 70%, respiratory disorders 68%. However, the highest percentage was among the patients who were admitted with more than one critical illness 79%.

Table 9: Sepsis among the studied patients

Sepsis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	+	72	27.3	27.3	27.3
	-	190	72.0	72.0	99.2
	null	2	.8	.8	100.0
	Total	264	100.0	100.0	

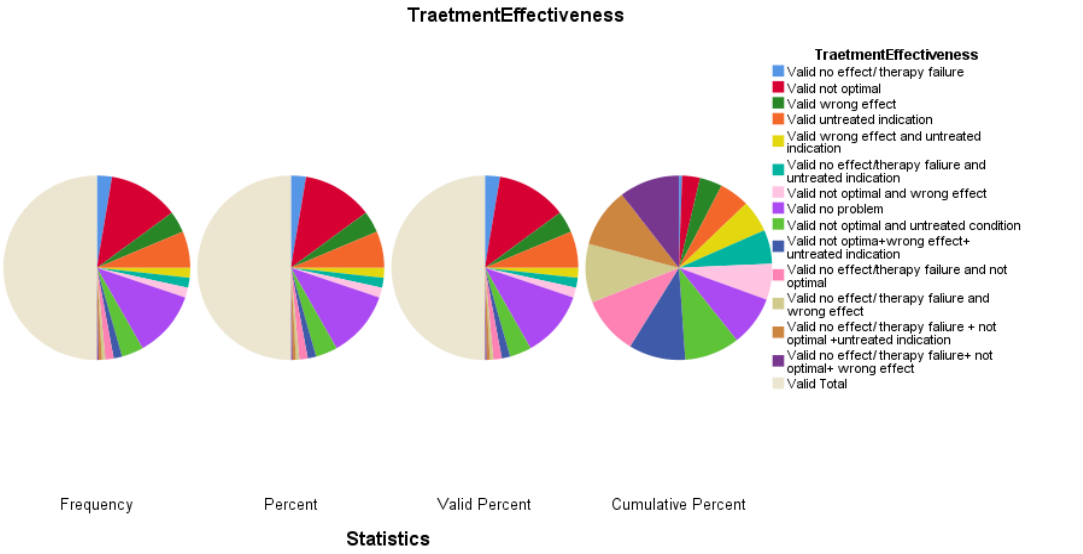
Table 10: Mortality rate

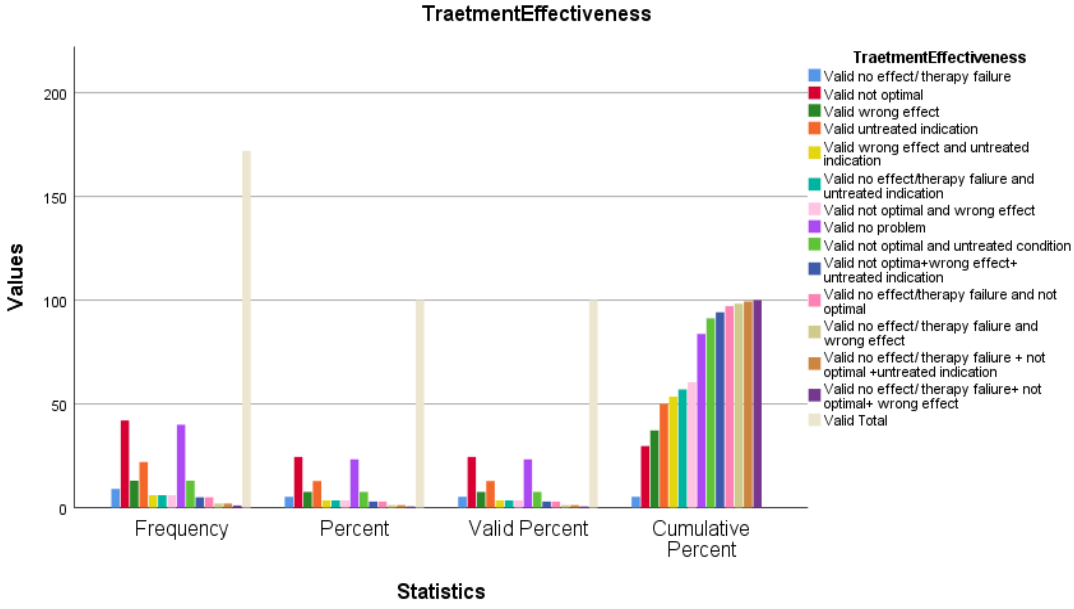
Mortality

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	113	42.8	42.8	42.8
	no	151	57.2	57.2	57.2
	Total	264	100.0	100.0	

Upon analyzing the collected data, it was shown that only 27.3% of the patients developed sepsis as shown in Table 9. Sepsis is important to consider in ICU patients, especially those with hypertension. When bacteria release toxins, the tiny blood arteries may be damaged to the point that they leak fluid into the surrounding tissues if not treated. Because of this, blood pressure drops, and oxygen-rich blood isn't delivered to the brain and liver, among other essential organs. Moreover, 151 (57.2%) patients survived whereas 113 (42.8%) died which is considered a high rated compared to the sample size.

Figure 1: Treatment effectiveness





Based on the reported outcomes to check the treatment effectiveness for the conducted agents used in the research

Figure 2: Adverse Reactions

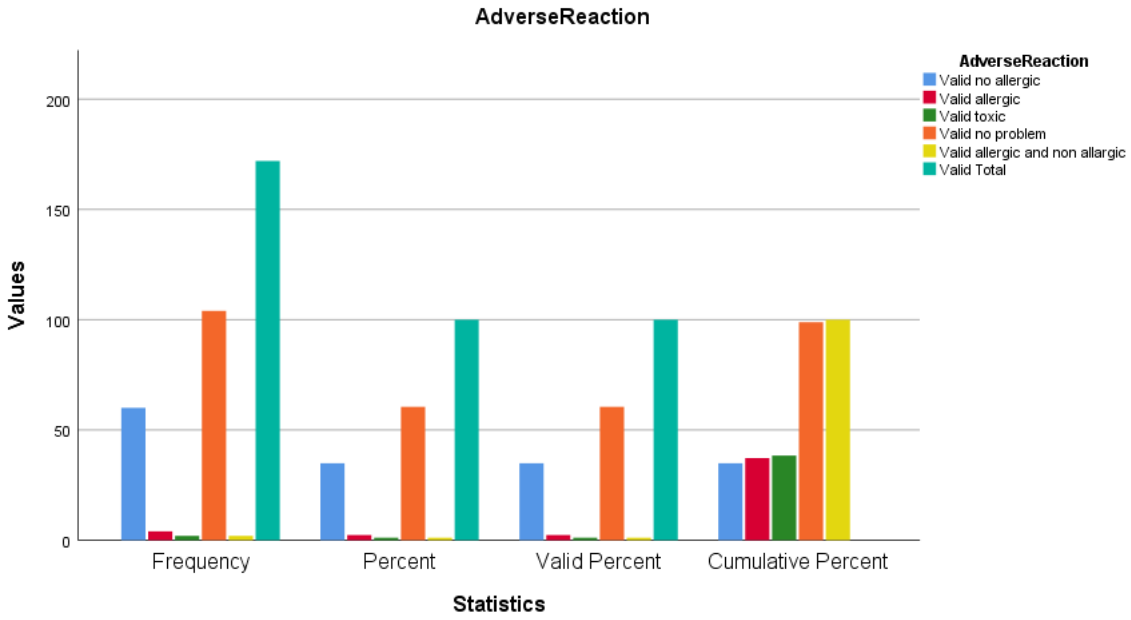


Table 8: Adverse reactions reported due to the administration of the prescribed agents.

Adverse Reaction

		Frequency	Percent
Valid	No allergic response	141	53.6
	Allergic response	10	3.9
	Toxicity	4	1.8
	Allergic and non-allergic reaction	4	1.8
	No adverse effect	105	38.9
	Total	264	100.0

Table 9: Coincidence of the drug given with its form.

Drug Form

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	inappropriate form	87	33	33	33
	no problem	177	67	67	100.0
	Total	264	100.0	100.0	

The study showed that 53.6% of the patients treated at Near East University hospital hadn't developed any allergic response and 38.9% didn't register any case of adverse effect, table 8. On the other hand, 67% of the drug forms administered were suitable to the patients without any problem and 33% were not appropriate to the patient, leading to the reported adverse effects and drug-related problems, table 9.

Table 10: Selected drug doses for the criteria under study

Dose Selection

	Frequency	Percent
dose too low	72	27.6
dose too high	39	16.1
dose not enough	10	4.4
dose too frequent	2	0.9
no monitoring	32	13.4
pharmacokinetic problem	17	7.2
improvement of dose	6	2.6
no problem	72	64.3
dose too low+ too high	4	3.5
dose too frequent+ no monitoring	6	2.6
dose too high+ too frequent	4	1.8
dose too low + not enough	2	0.9
dose too low + no monitoring	6	2.6
dose too high+ pharmacokinetic problem	2	0.9
dos too high + no monitoring	2	0.9
dose too high + not enough+ pharmacokinetic problem	2	0.9
dose too low + not enough+ no monitoring	2	0.9
dose too low+ improvement of dose	2	0.9
dose too low+ pharmacokinetic problem	2	0.9
Total	264	100.0

Figure 3: Dose Selection Bar Chart

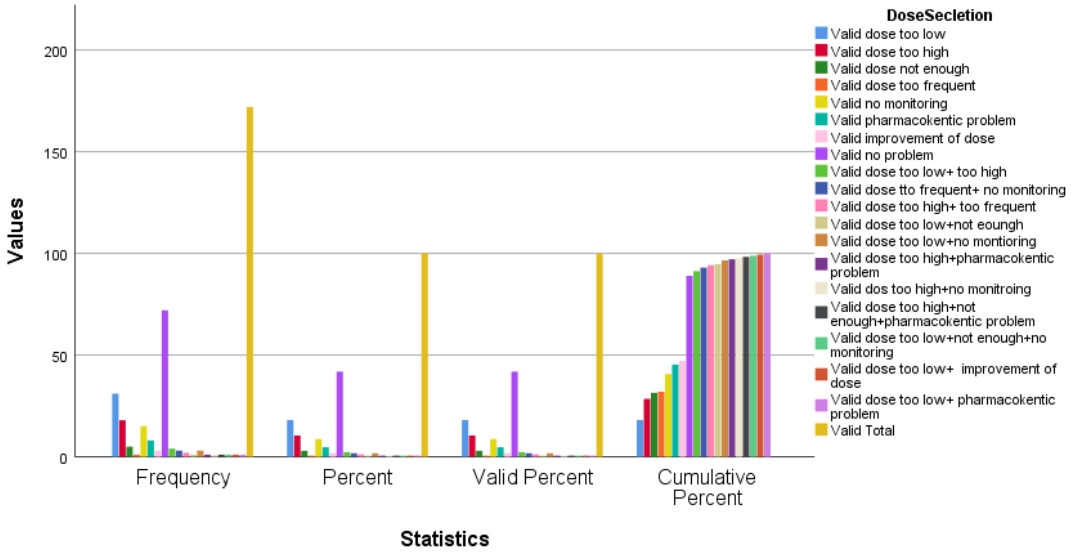


Table 10 shows that 64.3% of the selected drugs had no problem, 27.6% of the dose was too low, and 16.1% was too high. It was obvious the absence of monitoring in 13.4% of the patients. On the other hand, 7.2% varied between too frequent doses, low and not enough dose, high with pharmacokinetic problems, increased with the absence of monitoring and others. According to PCNE Classification for Drug-Related Problems, the last outcomes must be considered to maintain the desired health outcomes. Moreover, 26.1% of patients had unnoticed indications.

CHAPTER V
Discussion

This chapter presents a discussion of these findings in comparison to the studies in the literature.

This study's DRPs were associated with treatment efficacy and adverse medication reactions. Many variables, including dosing, medication interactions, and drug selection, might affect the efficacy of a treatment. According to this research, combining antihypertensive medication with other cardiovascular or symptomatic drugs may reduce treatment efficacy and increase the risk of unwanted effects. Drug interactions between an antihypertensive and antiplatelet medication were shown to be the most common DRPs (33.7% of all DRPs) in a study of hypertensive patients with comorbidities conducted in Malaysia. (Butcher KS et al, 2014)

Diastolic blood pressure more than 120 mmHg or systolic blood pressure greater than 180 mmHg in the context of immediate target organ damage constitutes a hypertensive emergency. A hypertensive emergency is defined as systolic blood pressure of 180 mmHg or more and diastolic blood pressure of 120 mmHg or more in a patient who is otherwise stable and has no additional symptoms or signs of immediate target organ damage. These patients need a higher dosage of their antihypertensive medication.

Hypertensive emergencies can occur in patients with a variety of conditions, such as a dissecting aortic aneurysm, acute pulmonary edema, acute myocardial infarction, unstable angina pectoris, acute renal failure, acute intracranial hemorrhage, acute ischemic stroke, hypertensive encephalopathy, eclampsia or pre-eclampsia, peri-operative hypertension. To control the raised blood pressure safely, maintain the function of target organs, alleviate symptoms, decrease complications, and enhance clinical outcomes, these patients need drugs that work quickly and effectively intravenously. Without antihypertensive medication treatment, the death rate for those experiencing hypertensive crises is over 79% after 1 year, with a median survival of 10.4 months. (Wand JG et al, 2008)

Intravenous esmolol is the drug of choice in situations with severe aortic dismemberment. The mixing rate is then reduced to 50 mcg/kg/min after a stacking measurement of 500–1,000 mcg/kg/min is applied over 1 minute. Per miniature, a

maximum of 200 mcg may be infused. Patients with severe aortic dissection require rapid blood weight lowering, ideally within 5–10 minutes. The goal in these patients is to lower their systolic blood pressure to less than 120 mmHg. If the blood pressure is still too high after beta-blocking, a vasodilator like intravenous nitroglycerin or nitroprusside may be administered.

In a hypertensive emergency accompanied by acute pulmonary edema, intravenous nitroglycerin, clevidipine, or nitroprusside are the medications of choice. When treating acute pulmonary edema, beta-blockers should not be used. Patients experiencing hypertensive crises, except those experiencing an acute aortic dissection, should have their blood pressure decreased by around 20% to 25% within minutes to 1 hour, then progressively to 160/100 mmHg over the following 2 to 6 hours, and then gently to normal over the next 24 to 48 hours. Intravenous nitroglycerin infusion rates typically begin at 5 mcg/min. The highest possible rate of infusion is 20 mcg/min. Intravenous sodium nitroprusside infusion rates typically start between 0.3 and 0.5 mcg/kg/min. 10 mcg/kg/min is the maximum recommended infusion rate. Clevidipine is administered intravenously at a 1-2 mg/h dose initially. The highest safe rate of infusion is 32 mg/h. (Varon J et al, 2014)

Esmolol is advised to be administered intravenously to patients with significant hypertension who are suffering from abrupt myocardial localized necrosis or unstable angina pectoris. Nitroglycerin can also be administered intravenously. For individuals with severe myocardial dead tissue or unstable angina pectoris who are hemodynamically stable, the goal blood weight is less than 140/90 mmHg. A patient's blood pressure should be less than 130/80 mmHg when they leave the hospital. Diastolic blood pressure in these patients shouldn't be reduced to less than 60 mmHg since doing so might worsen myocardial ischemia and impair coronary perfusion. (Allison M et al, 2015)

In cases of severe renal failure and hypertensive crises, clevidipine, fenoldopam, and nicardipine are the medications of preference. Intravenous fenoldopam mixture rates typically begin between 0.1 and 0.3 mcg/kg/min. Mixture rates greater than 1.6 mcg/kg/min are not advised. Intravenously, nicardipine implantation rates typically start at 5 mg/h. The pace of implantation is limited to 30 mg/h. Within 30 minutes of being transported, 92% of patients treated with intravenous nicardipine and 78% of

patients treated with intravenous labetalol achieved the desired systolic blood weight in 104 patients with hypertensive crises and renal impedance in the crisis room.

Patients with hypertensive crises, eclampsia, or pre-eclampsia can be treated with hydralazine, labetalol, and nicardipine. These patients should not be treated with ACE inhibitors, sodium nitroprusside, angiotensin receptor blockers, or direct renin inhibitors. The greatest beginning dose of hydralazine that is advised is 20 mg when administered by gradual intravenous infusion. If more dose is required, you may take one every 4 to 6 hours. 0.4 to 1.0 mg/kg/h to 3 mg/kg/h of an intravenous infusion are administered following an initial dosage of 0.3 to 1.0 mg/kg, with a maximum initial dose of 20 mg. A total dose of 300 mg will be administered. Repeat the dose if required every 4 to 6 hours. (Allison M et al, 2015)

Intravenous clevidipine, esmolol, nitroglycerin, and nicardipine are frequently used to manage surgical hypertension. Clevidipine is frequently used to treat acute postoperative hypertension, according to a systematic review and meta-analysis.

The preferred drugs for emergency hypertension caused by a pheochromocytoma, a hyperadrenergic state caused by cocaine, amphetamines, phencyclidine, or monoamine oxidase inhibitors, or by abruptly stopping taking clonidine or other sympatholytic drugs are intravenous clevidipine, nicardipine, or phentolamine. Phentolamine is frequently injected as a 5-mg bolus at the initial dosing. If the blood pressure is still too high after 10 minutes, an additional 5 mg bolus should be injected intravenously.

When hypertensive emergencies are accompanied by a high plasma renin state, intravenous enalaprilat might be given to patients. The standard starting dosage is the intravenous administration of 1.25 milligrams of enalaprilat over 5 minutes. If necessary, up to 5 mg of intravenous enaliprilat may be administered every 6 hours to achieve the desired blood pressure effect.

Intravenous clevidipine was compared to intravenous antihypertensive medications used routinely (87% intravenous nitroglycerin or nicardipine) in a trial of 104 patients with acute heart failure and hypertension. Seventy-one percent of patients given clevidipine in this trial achieved their blood pressure goal, compared to just 37 percent of patients given the gold standard of intravenous antihypertensive medications. At 45

minutes, clevidipine was similarly more efficacious than gold-standard medications in reducing dyspnea. (Sharkey CM et al, 2016)

Treatment with intravenous nicardipine or labetalol for hypertensive emergencies was randomized to 226 patients in an emergency room. 91.7% of patients treated with intravenous nicardipine attained the target blood pressure level within 30 minutes compared to intravenous labetalol. This investigation comprised 141 individuals with symptoms suggesting injury to their target organs. Ninety-one percent of patients given intravenous nicardipine attained their blood pressure goal within 30 minutes, but only seventy-six percent of those given intravenous labetalol did so.

A Cochrane systematic audit of pharmacological therapies for hypertensive crisis comprised fifteen randomized controlled trials, 869 individuals, and seven pharmaceutical classes. To determine which hypertension medication is effective for reducing mortality and horribleness, insufficient data were available. Randomized clinical studies were to be conducted to examine the short- and long-term mortality outcomes of patients with hypertensive crisis treated with various antihypertensive medications. To determine the appropriate pace and degree of blood weight decline in a hypertensive emergency, data from randomized clinical studies are also necessary. (Espinosa A et al, 2016)

The authors of the study randomly assigned 2,794 patients who had a serious intracerebral hemorrhage and a hypertensive emergency to receive intravenous antihypertensive drugs that would drop blood pressure to less than 140 mmHg or less than 180 mmHg within an hour. In comparison to systolic blood pressure reduction to less than 180 mmHg in 1 hour, systolic blood pressure reduction to less than 140 mmHg was linked with a slightly lower risk of death or substantial impairment and improved functional results. A meta-analysis of four randomized clinical trials including 3,315 patients found that patients with hypertensive crisis and acute intracerebral hemorrhage who had intensive blood pressure reduction to less than 140 mmHg had a modestly decreased probability of mortality or dependence at 3 months. In situations of acute cerebral bleeding, vigorous blood pressure lowering may help prevent the formation of hematomas.

To determine which medication works best for treating unexpected brain hemorrhage, research must be conducted. In the beginning, it is best to treat these

individuals with fast-acting, simple-to-adjust medications such as clevidipine, nicardipine, labetalol, and urapidil.

The normal BP range for individuals with acute ischemic stroke is not established, according to the 2013 American Heart Association/American Stroke Association guidelines. In the first 24 hours following an acute ischemic stroke, blood pressure shouldn't be decreased unless the patient has a blood pressure reading of at least 220/120 mmHg or has a condition that would benefit from it. According to these recommendations, patients with acute ischemic stroke who qualify for acute reperfusion treatment should decrease their blood pressure using intravenous labetalol or nicardipine, with other intravenous antihypertensive medications being considered as needed. (Jauch EC et al, 2013)

Treatment efficacy may be altered due to amlodipine and clopidogrel drug interactions. Combining clopidogrel with amlodipine may decrease clopidogrel's efficacy because amlodipine inhibits the enzyme CYP3A4, which is responsible for converting inactive clopidogrel to its active form. The effectiveness of amlodipine in treating coronary heart disease after coronary percutaneous intervention was shown in a randomized clinical trial including 900 patients from Korea. Clopidogrel and acetylsalicylic acid were combined with a calcium antagonist and administered to the patients. This regimen increases cardiovascular mortality, nonfatal myocardial infarction, and ischemic stroke risk, while clopidogrel's antiplatelet effect decreases. However, the study's hypertensive outpatients at Near East University Hospital showed no signs of this impact. The patient is instructed to take amlodipine in the morning and clopidogrel throughout the day, as the pharmacist recommends. This training lessens the potential for such encounters. (Pollack C et al, 2015)

Aspirin and clopidogrel have been shown to interact in a nonallergic way, leading to an increased risk of bleeding and gastrointestinal (GI) harm. Through inhibition of cyclooxygenase-1, low-dose aspirin produces GI mucosal and systemic consequences of prostaglandin depletion. Prostaglandins are crucial in maintaining the health of the stomach mucosa by stimulating the production of mucus and bicarbonate and enhancing local blood flow. Accumulation of aspirin in stomach mucosal cells, altered cell permeability, and ulceration result from the acidic environment preventing aspirin from being ionized. Some individuals with cardiovascular disease need dual

antiplatelet medication, despite these two medicines having a considerable drug interaction. Pharmacists at NEU Hospital had warned patients about the need for a delay between administering aspirin in the morning and clopidogrel in the afternoon to mitigate the harmful consequences of this medication interaction. However, patients must still undergo GI bleeding and blood monitoring to avoid adverse effects. (Jauch EC et al, 2013)

Amlodipine is a CYP3A4 inhibitor. Thus when taken at the same time as domperidone, it may raise the domperidone levels in the blood and induce QT prolongation. Cohort studies have linked the use of domperidone at doses >30 mg/day in patients >60 years old to serious ventricular arrhythmias and sudden cardiac death, demonstrating the potentially fatal nature of this interaction. Domperidone should be used for the shortest possible period and at the lowest effective dose to prevent this interaction. Seizures, fainting, and heart palpitations are serious side effects of domperidone that need immediate treatment discontinuation.

There is a potential for sinus bradycardia due to the combination of clonidine and bisoprolol. Therefore, it is vital to constantly check the heart rate while using both medicines. Rebound hypertension, caused by uninhibited alpha-stimulation, may occur if clonidine is stopped while taking bisoprolol. Patients taking both clonidine and bisoprolol and desire to discontinue clonidine must first stop taking bisoprolol within a few days. Individuals should be monitored and educated, particularly when deciding to discontinue one of the drugs, since the clinical effect of this interaction did not manifest in the evaluated individuals. (Allison M et al, 2015)

Researchers in the Netherlands found that a combination of amitriptyline and meloxicam raised patients' bleeding risk, adding another factor to DRPs. Study results showed that compared to patients who got tricyclic antidepressants alone, those who also took nonsteroidal anti-inflammatory medicines (NSAIDs) had a higher risk of gastrointestinal (GI) adverse effects. Tricyclic antidepressants explain this discovery since they significantly inhibit CYP2C9, but not more so than selective serotonin reuptake inhibitors.

List of drugs that mostly caused drug-related problem in outpatients with hypertension:

Drugs having potential interactions

Amlodipine-clopidogrel
Acetosal-clopidogrel
Amlodipine-domperidone
Clonidine-bisoprolol
Amitriptyline-meloxicam
Overprescribed drugs without cleared indications
Analgesic-anti-inflammation (potassium diclofenac and paracetamol)
Laxative (paraffin)
Antiseptic mouthwash (povidone-iodine)
Antiemetic (domperidone)
Antiulcer (lansoprazole, omeprazole, and sucralfate)

CHAPTER VI

Conclusion and Recommendations

This chapter presents conclusions based on the research findings according to the research's objective and sub-objective (s) and gives recommendations accordingly.

In an effort to help hypertensive patients cope with discomfort, doctors at NEU Hospital occasionally should prescribe a combination of amitriptyline and meloxicam once daily. Because giving patients the lowest possible dosages of amitriptyline (5 mg) and meloxicam (3 mg) prevents any negative interactions from occurring. Bleeding consequences from this combination must be monitored with routine complete blood count and laboratory testing.

Patients were provided non-indicated medicines, including acetaminophen, diclofenac potassium, mucolytic syrup, laxative agent, mouthwash, domperidone, and antiulcer pharmaceuticals. Hypertension patients often experience discomfort or headache, which may be treated with an analgesic-anti-inflammatory medication. In cardiovascular patients, a peptic ulcer caused by an antiplatelet drug is often treated with an anti-ulcer medication, such as a proton-pump inhibitor (PPI). These pharmaceuticals should only be taken when necessary; excessive usage for no reason is not recommended. This medicine can potentially cause several unwanted side effects, including but not limited to gastrointestinal distress (in the case of the NSAID), Clostridium difficult-associated diarrhea, nutritional deficiency, and bone fracture (in the case of the PPI).

This research also revealed difficulty with the dosage of the drugs. The doctor or clinical pharmacist should have paid attention to monitoring outcome therapy even if these medications were recommended merely for symptomatic treatment. The patient's quality of life may suffer if the treatment goal is unmet.

According to the research results, some patients were not prescribed the medicine they may have required. Diarrhea, heartburn, cough, headache, and myalgia were

unrecognized and untreated symptoms. The patients may already have symptomatic meds at home, or the doctor may have incorrectly reported their prescriptions.

One weakness of the study was that it relied only on written medical record entries from providers about patient concerns about integrated care rather than engaging clinicians to validate these reports. Researchers also lacked access to patients to confirm whether the prescribed medications were suitable and whether patients were already taking medication at home that successfully treated the condition documented in the medical record. In addition to that, the sample size was not enough to base our findings on. Furthermore, no control group was available for comparisons, and the assessments of pharmacist treatments were conducted retrospectively. More prospective and controlled studies must be conducted and written up for publication for the same reasons.

It may be inferred from this research that a significant proportion of hypertension patients suffer DRPs. To better assist in preventing and resolving DRPs in patients with hypertension, the involvement of clinical pharmacists and doctors in medication monitoring must be enhanced.

Using valid measures to evaluate what's added by pharmacists' services is an additional field of focus. Effectiveness objectives should measure things like hospitalization, death, or outpatient visits; however, long follow-up periods are required to show a possible input for these endpoints. Therefore, treatments' short-term impacts may be assessed using intermediate or surrogate measures. This review further elaborated on how the included studies conducted their interim analyses.

According to the American College of Clinical Pharmacy (ACCP), clinical pharmacists are a "primary source of scientifically valid information and advice" for the safe, appropriate, cost-effective administration of pharmaceuticals and for optimizing medication treatment against the backdrop of pharmaceutical care. They consistently disseminate new information to enhance patients' and doctors' health and quality of life.

Clinical pharmacists have quickly gained a position in front-line patient care. Over the past ten years, a clinical pharmacist's responsibilities have greatly expanded from managing pharmacodynamics and pharmacokinetics to being a vital member of the

multidisciplinary critical care team. Their engagement in clinical research, teaching, medication reconciliation, and drug management has increased. Additionally, clinical pharmacists have established themselves as crucial members of the healthcare team to improve outcomes in the ICU and post-recovery stage because to the COVID-19 pandemic. In essence, they have evolved from being only involved in the delivery of medication thirty years ago to becoming a crucial member of the healthcare team, and their duties are growing. Hospitals that don't already offer these services ought to make plans to include them in their toolbox. To fulfill the need and forthcoming difficulties, pharmacy schools, organizations, and hospitals must focus their efforts and resources on training clinical pharmacists and specialized clinical pharmacists.

Overall, clinical pharmacy is on the rise, but the field still needs a common understanding of what it entails, how it fits into the more extensive healthcare system, and how it can be evaluated for its effect on patients' health. It is shown that clinical pharmacy services may make a significant contribution to the healthcare system even with institutional effort; nevertheless, government and educational support should be provided to provide a trustworthy and sustainable service.

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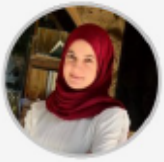
Curriculum Vitae



BATOUL KHODOR

Date of birth: 27/01/1994 | **Nationality:** Lebanese | **Gender:** Female |

(+90) 5428557040 | batoul.khodor.27@gmail.com | http://www.battakh.com.lb/ |

Whatsapp Messenger: Ready to answer any questions as soon as possible. |

Kucuk Kaymakli, Sht. Mehmet Kemal sokak, Akasya Apt 10, Daire 4, Lefkosa, Turkey

About me: I am outgoing, dedicated, and open-minded. I get across to people and adjust to changes with ease. I believe that a person should work on developing their professional skills and learning new things all the time. Currently, I am looking for new career opportunities my current job position cannot provide.

WORK EXPERIENCE

01/05/2022-01/09/2022 LEFKOSA — 01/10/2022- Current

COMMUNITY PHARMACIST – PHARMACIST — Pinar Keklik Eczane, Alsancak-Kibris

* Selling prescribed drugs by physicians
* Diagnosing and prescribing OTC medications
* Uploading drugs' orders on the computer system
* Dealing with the sales representatives
* Providing the patients with all the inquired information about the drugs or their healthcare

03/01/2020 – 28/12/2020 – Tyre, Lebanon

COMMUNITY PHARMACIST LEADER – PHARMACIST

Responsible about ordering the drugs, selling, prescribing, dealing with patients, stock as well as the financial sections .

01/09/2020 – CURRENT – Tyre, Lebanon

LECTURER IN PHARMACOLOGY – PHARMACY LECTURER

Pharmacology instructor for nursing students at Al-Afak Institutions as well as medical terminology and pre- operation courses.

EDUCATION AND TRAINING

09/2021 – CURRENT – Lefkosa, Turkey

CLINICAL PHARMACY MASTERS – Near East University

09/2016 – 28/01/2020 – North Cyprus, Lefkoşa , Turkey

MASTERS OF SCIENCES IN PHARMACY DEGREE – Near East University

During my studying clinical pharmacy practice took a big part in which we used to provide direct patient care, at Near East University Hospital, optimizes the use of medication and promotes health, wellness, and disease prevention. In addition to that, we studied everything about the pharmacology of all the medications for almost all the human systems and disorders. Moreover, we used to prepare some medications at the pharmaceutical technology laboratories.

Field(s) of study

- Pharmacy Department

Thesis: The Tender Cream from Krameria triandra (creating new pharmaceutical products for skin diseases)

2.86 | www.neu.edu.tr

02/01/2021 – 01/04/2021 – Cairo, Egypt, Cairo, Egypt
OTC ONLINE COURSE – Al Sharkawi Academy

10/2013 – 03/2016 – Beirut , Beirut, Lebanon
BACHELOR DEGREE IN PHARMACY – Lebanese International University

Lefkoşa , Lefkoşa , Turkey
CLINICAL PHARMACY TRAINING – Near East University Hospital

Borj Al Chemali, Tyre, Lebanon
COMMUNITY PHARMACY TRAINING – Al Sadek Pharmacy

Beirut, Lebanon
ENGLISH LANGUAGE CERTIFICATE LEVEL C2 – American Lebanese Language Center

LANGUAGE SKILLS

Mother tongue(s): **ARABIC**

Other language(s):

	UNDERSTANDING		SPEAKING		WRITING
	Listening	Reading	Spoken production	Spoken interaction	
ENGLISH	C2	C2	C2	C2	C2
FRENCH	A1	A1	A1	A1	A1
TURKISH	A1	A1	A1	A1	A1

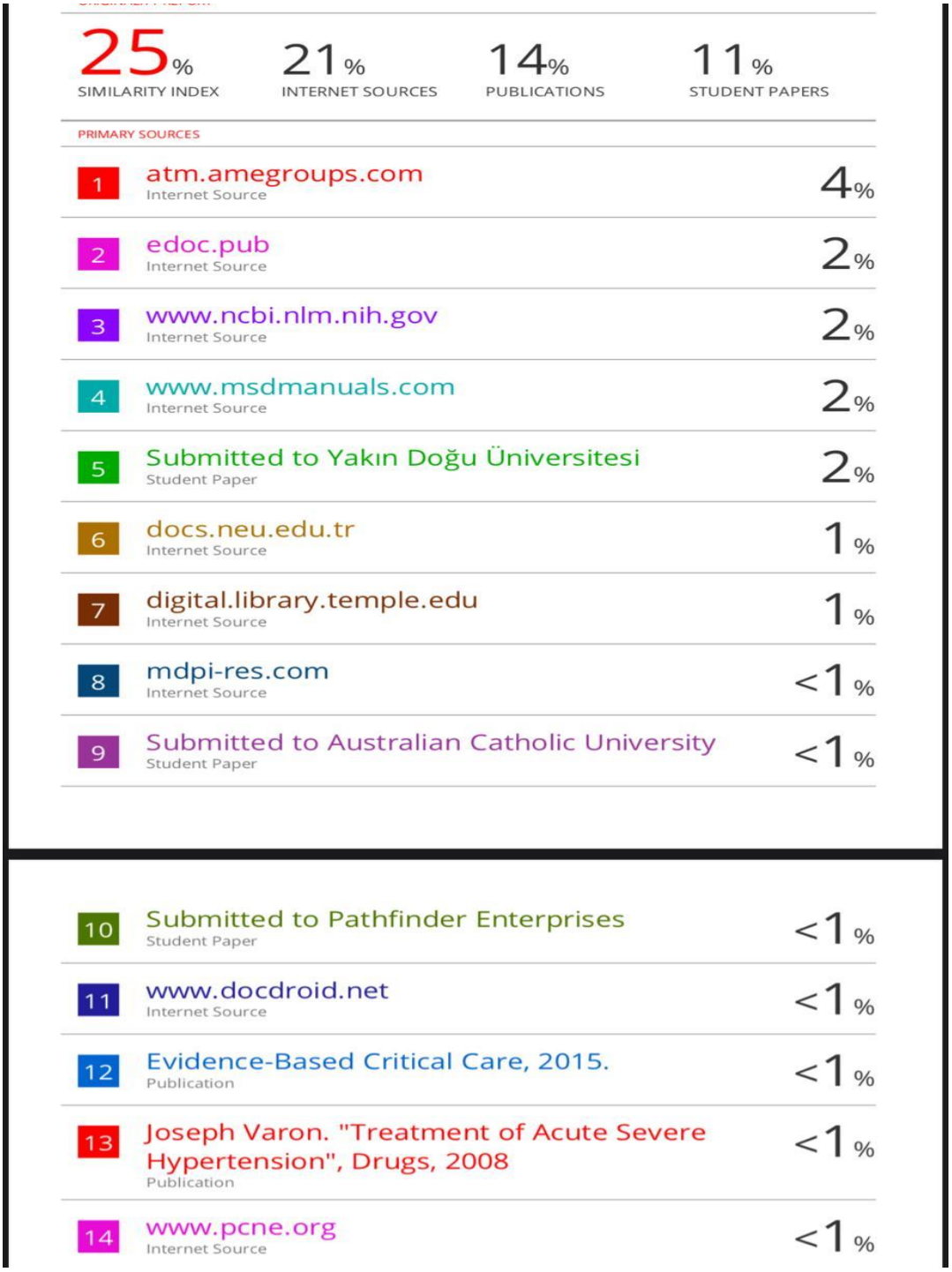
Levels: A1 and A2: Basic user; B1 and B2: Independent user; C1 and C2: Proficient user

DIGITAL SKILLS

Microsoft Office | Microsoft Word | Microsoft Excel | Microsoft Powerpoint | Social Media | Outlook | Google Drive | Google Docs | Zoom | Instagram | Facebook | Skype | Power Point | Written and Verbal skills | Good listener and communicator | Motivated | Decision-making | Internet user | Organizational and planning skills | Conflict resolution | Presenting | Creativity | Team-work oriented | Responsibility | Gmail | WhatsApp | Critical thinking | Detail-Oriented | Good time management | LinkedIn | Teamwork | Excellent writing and verbal communication skills | Good Communication | positive thinking | leadership | flexible | Ability to Work Under Pressure | Excellent organizational planning and solving problems in short time | Good at being proactive and efficient in high stress situations | Problem-solving | Presentation and negotiation skills | Communications | Active listening | Friendly | Research | Word | Efficient multi-tasking | Microsoft PowerPoint | E-mail use | hardworking | Open and respectfull towards others | Self-Discipline | Self control | Respect and good atmosphere in teamwork | Respect the importance of confidentiality as will be dealing with employee and personal details | Quick Learner and adaptable to new exposures and experiences | Creativity and problem solving | Quick learner

Appendix X

Similarity Index



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