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Original Research Article

Evaluation and clinical management of drug-drug interactions in hypertensive patients associated co-morbidities: A study in general medicine and ICU ward

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ABSTRACT

This comparative study aims to evaluate and compare the clinical management of drug-drug interactions (DDIs) in hypertensive patients with associated co-morbidities, specifically focusing on the practices in general medicine and ICU ward settings. Hypertensive patients commonly experience co-morbidities that require multiple medications, increasing the risk of DDIs and subsequent adverse events. Understanding the current evaluation and management strategies for DDIs in these patient populations is essential for optimizing patient outcomes. This research investigates the approaches employed in general medicine and ICU wards, including DDI identification, assessment, and intervention methods. By comparing these practices, the study aims to identify potential variations, challenges, and areas for improvement in DDI management across these clinical settings. The findings of this study will contribute to the development of evidence-based guidelines and recommendations for enhancing the clinical management of DDIs in hypertensive patients with co-morbidities, ultimately improving patient safety and therapeutic outcomes.

1. Introduction

A drug interaction is a reaction between two (or more) drugs or between a drug and a food, beverage, or supplement. Taking a drug while having certain medical conditions can also cause a drug interaction. For example, taking a nasal decongestant if you have high blood pressure may cause an unwanted reaction.[1] A drug interaction can affect how a drug works or cause unwanted side effects.[2]

Hypertension, characterized by elevated blood pressure, effects a significant proportion of the global population and is a major risk factor for cardiovascular diseases.[3] Managing hypertension becomes particularly challenging when patients present with associated co-morbidities, such as diabetes, chronic kidney disease, or mental health disorders, as these conditions often require multiple medications.[4] The administration of multiple drugs increases the likelihood of drug-drug interactions (DDIs), which can potentially result in compromised therapeutic efficacy and adverse events.[5]

DDIs occur when the pharmacokinetics or pharmacodynamics of one drug are affected by the presence of another drug. In hypertensive patients with co-morbidities, DDIs can lead to poor blood pressure control, suboptimal treatment outcomes, and increased risks of drug-related adverse effects.[6] Consequently, the evaluation and clinical management of DDIs are of paramount importance in optimizing patient safety and therapeutic efficacy.[7] Drug-drug interactions (DDI) potentially occurring between medications used in the course treatment

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in these studies and those for the management of observed comorbidities were evaluated for possible worsening of the clinical outcome.[3] DDI contributes to 3%–4% of adverse drug reactions and fourth leading cause of mortality.

Polypharmacy is common in drug prescriptions of chronic kidney disease patients. A study of the prescription patterns of drugs with potential interactions would be of interest to prevent drug-related adverse events.[4] PDDI may cause treatment failure or adverse drug events (ADEs), which are major causes of increased morbidity, mortality, and healthcare costs.[8] ADEs rank as the 4th to 6th leading causes of death in inpatients.[6] In the United States, for every dollar spent on medication in 2000, more than a dollar was estimated to have been spent on direct medical costs related to drug misadventures.

While both general medicine and ICU wards play critical roles in the care of hypertensive patients with co-morbidities, differences in patient acuity, monitoring capabilities, and medication administration practices may influence the management of DDIs in these two settings.[9] Therefore, a comparative study is warranted to assess the evaluation and clinical management of DDIs in hypertensive patients with co-morbidities, specifically examining the practices in general medicine and ICU ward settings.[10] A study done by Patel et al. showed a higher percentage of drug interactions (83.42%) in patients with age above 40 years, comorbidities, and polypharmacy than compared to our study (48%).[11]

The objectives of this study are to evaluate and compare the current approaches to DDI management in general medicine and ICU wards, identify potential variations in practices, explore challenges encountered, and identify opportunities for improvement.[12] By conducting a comprehensive assessment of the existing strategies employed in these clinical settings, valuable insights can be gained to enhance the clinical management of DDIs in hypertensive patients with co-morbidities.[13]

The findings of this study will contribute to the development of evidence-based guidelines and recommendations for healthcare professionals involved in the management of hypertensive patients with co-morbidities, assisting them in identifying and mitigating potential DDIs more effectively. Ultimately, this research aims to improve patient safety, optimize therapeutic outcomes, and provide a basis for further advancements in the field of DDI management in hypertensive populations with associated co-morbidities.

2. Objective

To find out drug-drug interaction between antihypertensive drug and treatment for associated disease

1. To find out DRP due to Drug drug Interactions
2. Prevalence of D-D interaction among ICU and Wards
3. To know the D-D interaction and to prevent it

3. Materials and Methods

Detailed demographic and clinical information of the patient will be entered in the Performa. The data collected will be transferred to MICROSOFT EXCEL software. The variable will be analyzed by percentage and proportion.

3.1. Study design

A prospective study conducted among the HTN patient in general medicine in-patient in tertiary care hospital

Total Time Period: - 2 months (Jan-2023 to Feb 2023)

Sample Size: - 50 patients

3.2. Inclusion criteria

Hypertensive patient with associated co-morbidities-

1. Diabetes
2. CAD
3. ASCVD
4. CVA
5. CKD

Age- 40-90 years

3.3. Exclusion criteria

1. Pregnant women
2. Surgical patient
3. Psychiatric patients

4. Result and Discussion

The study was carried out to assess the antibiotic use and prescribing pattern by medical practitioner in Hypertensive patient with co-morbidities. The study was conducted at CAPITOL HOSPITAL, Jalandhar, Punjab. In our prospective study analysis, a total of 50 Hypertensive patients were selected on the basis of W.H.O. guidelines. Hence the result was based on the data of 50 patients.

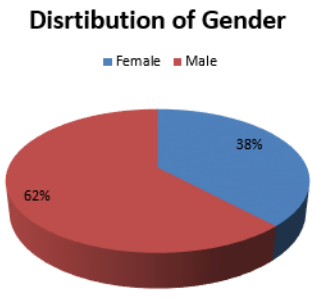

Fig. 1: Distribution of gender

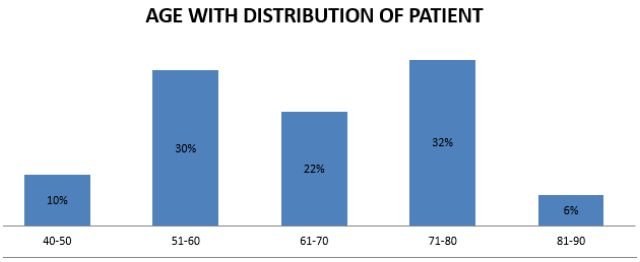

Fig. 2: Distributionof patients on basis of their age

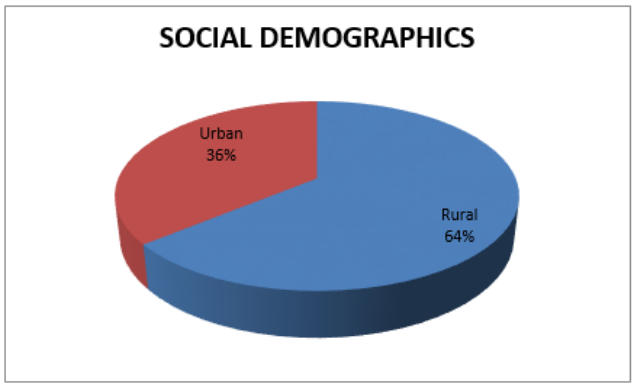

Fig. 3: Descriptionof patient according to residence of the patient

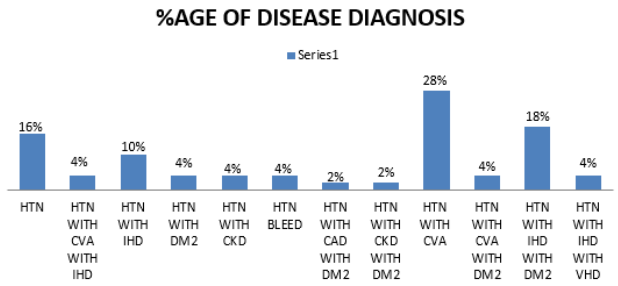

Fig. 4: Causativepatient with the diagnosis

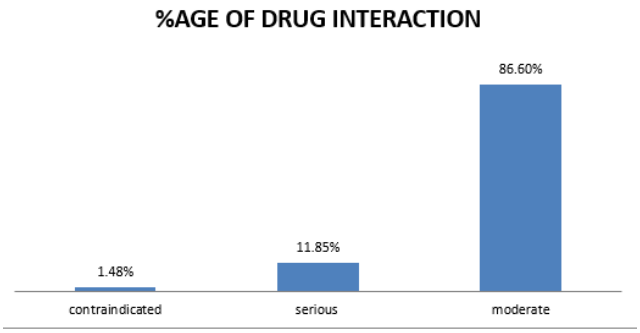

Fig. 5: Descriptionof patient according to residence of the patient

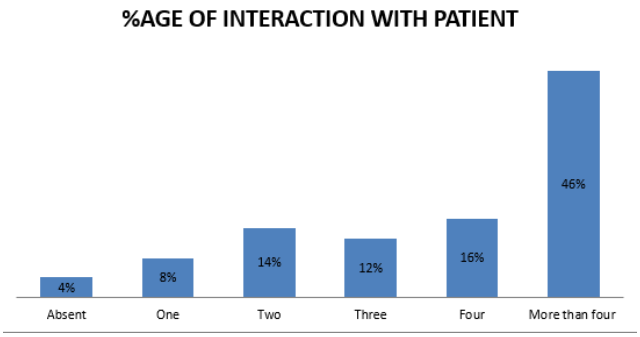

Fig. 6: Distributionof patients on basis of interaction

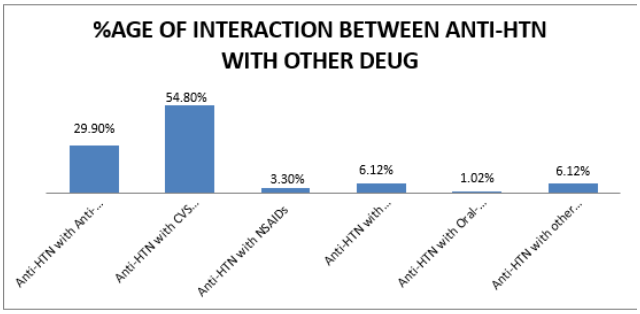

Fig. 7: Distributiondrug- drug interaction between anti-HTN drug with other class of drug

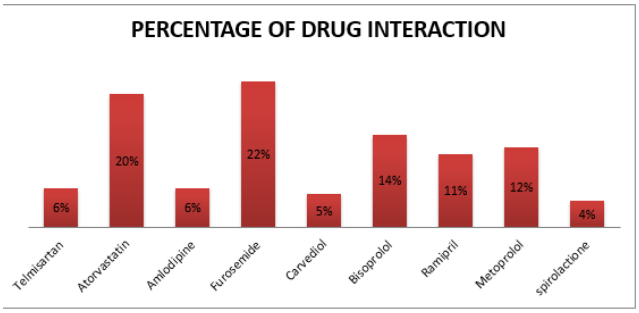

Fig. 8: Distributondrug- drug interaction between anti-HTN drug

Table 1: Distributionof potantial drug interacting pair among anti- HTN drug group

Pair of drug	**Frequency**	**Possible adverse outcome**	**Management**	Reference
Telmisartan + Furosemide	4	Effect on Sr. Potassium	Regularly monitor potassium levels while taking Telmisartan and Furosemide; adjust dosages based on patient's condition.	Medscape
Telmisartan + Atorvastatin	7	Increase risk of Myopathy	Instead of Telmisartan, we can advise Amlodipine to the patients.	Medscape
Ramipril + Furosemide	1	Risk of acute hypotension	Monitor patient's condition, adjust medications(Its dose and frequency of administration) if necessary	Medscape
Spironolactone + furosemide	1	Effect on sr. Potassium	Monitor potassium levels ; Modify therapy based on patient's condition.	Medscape
Ramipril + torsemide	1	Risk of acute hypotension	Monitor patient's condition, adjust medication dose and frequency if necessary.	Medscape
Ramipril + Eplerenone	3	Increase risk of hyperkalemia	Monitor serum potassium levels while taking ramipril and eplerenone, promote balanced diet, and avoid excessive potassium-rich foods.	Medscape
Clonidine + Metoprolol	4	Pharmacodynamic synergism	Metoprolol can be used instead of clonidine. in order to avoid pharmacodynamic synergism	Medscape
Clonidine + Prazosin	1	Dysfunction of the sinus node and AV block	Clonidine and prazosin are sympathetic blockers; methyldopa can prevent sinus node dysfunction and AV block.in place of clonidine	Medscape
Metoprolol + prazosin	1	Pharmacodynamic antagonism	Although metoprolol and prazosin have opposing actions on adrenergic receptors, an alternate kind of antihypertensive medicine may be recommended in accordance with the patient's situation.	Medscape
Telmisartan + Carvediol	1	Increase sr. potassium	Instead of Telmisartan(ARB) we advise ACE inhibitor i.e Captopril.	Medscape
Telmisartan + Aspirin	10	Increase sr. potassium	Regularly serum potassium level should be checked, Stop potassium intake and offending drug, in consult with health care professional.	Medscape

Continued on next page

Table 1 continued

Furosemide + Carvedilol	1	Decrease sr. potassium	While using furosemide with carvedilol, serum potassium levels should be checked on a frequent basis. Encourage the patient to take potassium-rich meals to help maintain healthy levels.	Medscape
Furosemide + Aspirin	6	Monitor/significance unknown. NSAIDS decrease prostaglandin synthesis.		Medscape
Furosemide + Dobutamine	1	Increase sr. potassium	Regularly serum potassium leveled should be checked, according to patient condition modified therapy based on patients conditions, Avoid potassium rich diet	Medscape
Metoprolol + Tolvaptan	1	Increase sr. potassium	Regularly serum potassium leveled should be checked, according to patient condition modified therapy based on patients' conditions, Avoid potassium rich diet.	Medscape
Amlodipine + Carvedilol	1	Increase sr. potassium	Regularly serum potassium leveled should be checked, according to patient condition modified therapy based on patients' conditions, Avoid potassium rich diet	Medscape
Furosemide + digoxin	2	Increase pharmacodynamic synergism	Change the furosemide and digoxin dose frequency based on the patient's condition.	Medscape
Atorvastatin + Digoxin	2	P-glycoprotein efflux transporter	Change the Atorvastatin and Digoxin dose frequency based on the patient's condition.	Medscape
Furosemide + Tolvaptan	1	Effect on Sr. potassium	serum potassium levels should be checked on a frequent basis, Medicine may be recommended in accordance with the patient's situation.	Medscape
Furosemide + Epinephrine	1	Decrease sr. potassium	serum potassium levels should be checked on a frequent basis. Encourage the patient to take potassium-rich meals to help maintain healthy levels.	Medscape

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Table 1 continued

Atorvastatin + Diltiazem	1	Effecting hepatic CYP3A4 enzyme	serum potassium levels should be checked on a frequent basis. Encourage the patient to take potassium-rich meals to help maintain healthy levels.	Medscape
Ramipril + Aspirin	5	Risk of acute hypotension	These both drugs are pharmacodynamic antagonism, Avoid or use alternative drug in consult with a healthcare professional.	Medscape
Bisoprolol + Epinephrine	1	Pharmacodynamic antagonism	Pharmacodynamic antagonism, Avoid or use alternative drug in consult with a healthcare professional.	Medscape
Bisoprolol + Aspirin	8	Increase sr. potassium	Regularly serum potassium leveled should be checked, according to patient condition modified therapy based on patients' conditions, Avoid potassium rich diet	Medscape
Bisoprolol + Dobutamine	1	Effect on Sr. potassium	Monitor potassium levels ; Modify therapy based on patient's condition,	Medscape
Bisoprolol + Tolvaptan	1	Both increase sr. potassium	Monitor potassium levels ; Modify therapy based on patient's condition,	Medscape
Telmisartan + Tolvaptan	1	Both increase sr. potassium	Monitor potassium levels ; Modify therapy based on patient's condition,	Medscape
Telmisartan + Enoxaparin	1	Increase sr. potassium	Monitor potassium levels ; Modify therapy based on patient's condition,	Medscape
Atorvastatin + Tolvaptan	3	P-glycoprotein efflux transporter	Healthcare practitioner may change the dose of atorvastatin or tolvaptan based on patient health condition.	Medscape
Metoprolol + Aspirin	3	Increase sr. potassium	Regularly serum potassium level should be checked, Stop potassium intake and offending drug if its levels (5.5-6mEq/L).	Medscape

Table 2:

Pair of drug	Frequency	Possible adverse outcome
Telmisartan + Furosemide	4	Effect on sr. Potassium
Telmisartan + Atorvastatin	7	Increase risk of Myopathy
Ramipril + Furosemide	1	Risk of acute hypotension
Metoprolol + Torsemide	1	Effect on sr. potassium
Metoprolol + Amlodipine	1	Increases anti-HTN channel blocking
Spironolactone + Atorvastatin	1	P-glycoprotein efflux transporter
Spironolactone + furosemide	1	Effect on sr. Potassium
Ramipril + torsemide	1	Risk of acute hypotension
Bisoprolol + Amlodipine	3	Increases anti-HTN channel blocking
Ramipril + Eplerenone	3	Increase risk of hyperkalemia
Clonidine + Metoprolol	4	Pharmacodynamic synergism
Clonidine + Prazosin	1	Disfunction of sinus node and AV block
Metoprolol + prazosin	1	Pharmacodynamic antagonism

Table 3: Drug interaction between anti-HTN with other CVS drugs

DDI Pairs	Frequency	Possible ADR Outcome
Telmisartan + Carvediol	1	Increase sr. potassium
Telmisartan + Aspirin	10	Increase sr. potassium
Furosemide + Carvedilol	1	Decrease sr. potassium
Furosemide + Aspirin	6	Increase sr. serotonin level
Furosemide + Dobutamine	1	Increase sr. potassium
Metoprolol + Tolvaptan	1	Increase sr. potassium
Amlodipine + Carvedilol	1	Increase sr. potassium
Furosemide + digoxin	2	Increase pharmacodynamic synergism
Atorvastatin + Digoxin	2	P-glycoprotein efflux transporter
Furosemide + Tolvaptan	1	Effect on sr. potassium
Furosemide + Epinephrine	1	Decrease sr. potassium
Atorvastatin + Diltiazem	1	Effecting hepatic CYP3A4 enzyme
Ramipril + Aspirin	5	Risk of acute hypotension
Bisoprolol + Epinephrine	1	Pharmacodynamic antagonism
Bisoprolol + Aspirin	8	Increase sr. potassium
Bisoprolol + Dobutamine	1	Effect on sr. potassium
Bisoprolol + Tolvaptan	1	Both increases sr. potassium
Telmisartan + Tolvaptan	1	Both increases sr. potassium
Telmisartan + Enoxaparin	1	Increase sr. potassium
Atorvastatin + Tolvaptan	3	P-glycoprotein efflux transporter
Metoprolol + Aspirin	3	Increase sr. potassium

5. Discussion

The findings of this study revealed several important aspects related to DDI management in hypertensive patients with co-morbidities. Firstly, the prevalence of DDIs was found to be substantial in both general medicine and ICU ward settings. This highlights the importance of recognizing the potential for interactions when prescribing medications for hypertensive patients with co-morbidities, as overlooking these interactions can lead to suboptimal treatment outcomes and increased risks for adverse events.

In terms of DDI management practices, the study identified variations between general medicine and ICU ward settings. In the general medicine setting, the management of DDIs relied heavily on the expertise of physicians and pharmacists, with a focus on comprehensive medication review, identification of potential interactions, and adjustment of medication regimens. However, in the ICU ward, the urgency of critical care situations often necessitated prompt decision-making, which could lead to a higher likelihood of overlooking potential DDIs.

Based on the study results, several recommendations can be made to enhance the evaluation and clinical management of DDIs in hypertensive patients with associated co-morbidities. Firstly, the implementation of standardized protocols and guidelines for DDI evaluation and management is essential to promote consistency and reduce variability across different clinical settings. These protocols should include systematic screening for potential DDIs, utilizing electronic decision support systems, and ensuring effective communication between healthcare professionals.

Table 4: Druginteractions among between hypertensive drugs and nsaids-

DDI Pairs	Frequency	Possible ADR Outcome	Management	Reference
Metoprolol + Diclofenac	2	Decrease prostaglandin synthesis	Take antacid every day in empty stomach, to avoid ulcer.	Medscape
Ramipril + Diclofenac	1	Decrease anti-hypertensive effect	Avoid or use Alternative drug	Medscape

Table 5: Druginteractions among between hypertensive drugs and antimicrobial.

DDI Pairs	Frequency	Possible ADR outcome	Management	References
Atorvastatin + Clarithromycin	1	Effecting hepatic enzyme CYP3A4	Avoid or use Alternative drug, do not exceed atorvastatin dose of 20 mg/ day when coadminstered with clarithromycin	Medscape
Furosemide + Amikacin	1	Increase risk of ototoxicity and nephrotoxicity	Avoid or use alternative drug in consult with health care professional.	Medscape
Atorvastatin + Metronidazole	1	Effecting hepatic enzyme CYP3A4	change the dosage time interval between Atorvastatin and metronidazole, in consult with health care professional	Medscape
Atorvastatin + Azithromycin	2	P-glycoprotein efflux transporter	in consult with health care professional	Medscape

Table 6: Drug interactions among between hypertensive drugs and oral hypoglycemic agent

DDI Pairs	Frequency	Possible ADR outcome	Management	Reference
Amlodipine + Metformin	1	Pharmacodynamic synergism	To Avoid synergism, use alternative drug, or adjust medications its dose and frequency of administration.	Medscape

Table 7: Drug interactions among between hypertensive drugs and others.

DDI Pairs	Frequency	Possible adr outcome	Management	Reference
Bisoprolol + chlorthalidone	1	Effect on sr. Potassium	Regularly monitor potassium levels ; modify therapy based on patient's condition,	Medscape
Bisoprplol + sod.bicarbonate	1	Sodium bicarbonate decrease levels of bisoprolol by inhibition of gi absorption.	Applies only to oral form of both agents. Separate by 2hrs.	Medscape
Atorvastatin + methylprednisolone	1	Effect on hepatic enzyme cyp3a4	Avoid or use alternative drug, in consult with health care professional.	Medscape
Atorvastatin + hydrocortisone	1	Effect on hepatic enzyme cyp3a4	Regular monitoring of liver function is essential during hydrocortisone therapy, or use alternative drug, in consult with health care professional	Medscape
Spironolactone + kcl	1	Increase sr. Potassium	Regularly serum potassium level should be checked, stop potassium intake and offending drug, in consult with health care professional.	Medscape

6. Conclusion

In conclusion, this comparative study highlights the importance of evaluating and managing drug-drug interactions in hypertensive patients with co-morbidities. The findings emphasize the need for standardized protocols, interprofessional collaboration, and continuous education to enhance DDI management practices. By implementing these recommendations, healthcare professionals can optimize therapeutic outcomes, minimize adverse events, and improve the overall quality of care for this high-risk patient population.

The findings shed light on the prevalence of DDIs and the variations in management practices between the two clinical environments. The study highlighted the substantial prevalence of DDIs in hypertensive patients with co-morbidities, emphasizing the need for vigilant evaluation and management. Both general medicine and ICU ward settings experienced challenges in DDI management, including time constraints and limited resources. However, the study revealed the importance of comprehensive medication review, identification of potential interactions, and adjustment of medication regimens in the general medicine setting, while acknowledging the urgent decision-making required in the ICU ward.

7. Source of Funding

None.

8. Conflict of Interest

None.

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