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A Retro-Pro prospective Study on Identification of Potential Drug-Drug Interactions among Medications Prescribed to Hypertensive Patients



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HUMAN

S.Aseem*, A. Haadi, S.M.A Razack, S.Tabassum, M. Ihtesham Ali Shah, H. Banu

Department of Pharmacy Practice, Shadan College of Pharmacy, Peerancheru, Telangana, India.

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ABSTRACT

OBJECTIVE: The aim of the study is to identify drug-drug interactions among the medications prescribed to hypertensive patients. The objective of the study is to analyse the prescriptions for name dose and duration of prescribed drugs and to analyze drug-drug interactions among the prescribed drugs and ways to eliminate them.

PROCEDURE: The study procedure involves following steps: Collection of prescription, Recording of prescription details, Analysing the prescription and finding the individual drug interaction using Medscape interaction checker tool. **FINDINGS:** From the total of 100 hypertensive cases, 32 cases found to have drug interactions with antihypertensive agents. The severity of these interactions was: MAJOR:6, MODERATE:45, MINOR:12. **CONCLUSION:** Polypharmacy of antihypertensives leads to the emergence of drug-drug interactions, treatment failure, increased patient morbidity, and mortality. The study concluded that there were 32% of interactions among 100 hypertensive prescriptions collected. The 32-drug interacting prescription founded 42 different types of drugs interacting with antihypertensive agents.



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INTRODUCTION

A drug interaction is a condition in which a drug affects the action of other drugs that is the actions are increased or decreased, or they produce a new effect other than the one for which they have been administered. Interactions can be pharmacokinetics (what the body does to the drug) and pharmacodynamics (what the drug does to the body), interactions are often unpredictable of the effect which they produce.^[1]

The WHO highlights that unexpected drug reactions and their potential outcomes can be significantly decreased by implementing careful attention to the population and at risk of DDIs. Drug interactions can be pharmacokinetic or pharmacodynamic. There is a possibility of interaction among medications increase day by day due to the simultaneous use of two or more drugs.^[2]

A medication interaction can also happen when a current medical condition makes a medicine unsafe (e.g., Tobramycin administered along with furosemide in patients with renal failure, exacerbate the condition leading to increased nephrotoxicity). Numerous aspects can influence the consequence of a drug interaction. These factors are based on the properties of both the interacting drugs.^[3]

Hypertension is major disease that are found in a large number of patients with other Comorbid conditions. Worldwide 40% of the population are suffering from cardiac disorders, out of which $\frac{1}{4}$ people are affected by hypertension. Hence there will be an increased number of drugs prescribed in the prescription and thereby increasing the risk for drug- interactions. Hence our present study aim is to study the prescriptions and to find out drug interactions.^[4]

The current computer systems for detecting drug interactions still need improvement. Drug interaction data are used to identify drug interaction trends, identify drug interactions for education purposes, compile information about drug interactions to induce pharmacist productivity, identify frequent drug interactions for pharmacist education, and prepare data for Pharmacy and Therapeutics Committee reports or newsletters.

Medscape and Drug-Reax are used for monitoring drug interactions. Other than these tools, the secondary source used to monitor the interactions is Stockley's drug interaction.^[5]

OBJECTIVE

To identify the drug-drug interactions among the medications prescribed to hypertensive patients.

To study the prescriptions for name, dose and duration of prescribed drugs.

To analyze drug-drug interaction among the prescribed drugs and ways to eliminate them.

METHODS

A retro-prospective was carried out in the general ward of Shadan teaching and general hospital, Peerancheru, Hyderabad. 100 patients were enrolled in the study. The study was carried out for a period of 6 months i.e from November 2020 to April 2021. The in patients case sheets and out patient's cards were collected and analysed for the presence of drug-drug interaction.

Inclusion Criteria

- Hypertensive patients in general medicine department and community pharmacy at Shadan Teaching and General Hospital, Hyderabad.
- Patients who are ready to participate in the study.
- Patients with a history of hypertension with or without comorbidities.

Exclusion Criteria

- Patients who are not ready to participate in the study.
- Non-hypertensive patients are excluded.

The study procedure involves the following steps: Collection of prescription, Recording of prescription details, Analysing the prescription and finding the individual drug interaction with the help of the Medscape interaction checker tool.

The hypertensive cases should be collected according to the schedule method and the details of the prescription are collected in proforma-1 and proforma-2.

- The patient details and the details of the prescription are noted in the proforma-1.
- Drug-drug interaction, severity, and its remedy are noted in proforma-2.

RESULTS

The drug interactions can be classified as:

- Major - Highly significant in clinical aspects. Avoid the combinations where the risk overcomes the benefit.
- Moderate - Moderately significant in clinical aspects. Usually, the combinations should avoid but used under regular monitoring of the patients.
- Minor - Minimally significant in clinical aspects. Determine the risk, minimize it or go for an alternative drug.

The study was conducted in Shadan college of pharmacy, Peerancheru, Hyderabad. In this study, 100 hypertensive inpatient cases and outpatient cases were collected in 6 months.

Of the total of 100 hypertensive cases, 32 cases were found to have interactions with antihypertensive agents.

The severity of these interactions was: MAJOR:6, MODERATE:45, MINOR:12.

Table No. 1: No. of interactions according to severity

Sr. No.	Severity of Interactions	No. of interactions
1	Major	6
2	Moderate	45
3	Minor	12

DISCUSSION

The purpose of this retro prospective study is to identify potential drug-drug interaction in hypertensive patients with or without comorbidities. The study included 100 patients which included 64 males and 34 females. Out of 100 patient prescriptions 32(32%) prescriptions were found with interaction. The drug interaction prescription included 20(62.5%) males and 12(37.5%) females. The interactions were checked using the Medscape interaction checker tool and drugs.com and were classified based on severity into major, moderate, minor. The interactions with their effects and remedy have been tabulated in the Table No.1.

In 32 interaction prescriptions, there were 62 different drug interactions. Out of which there were 6(9%) major interactions. This finding was higher than the study done by Sagar Pamu,

et al., which showed 4 major interactions; Rajat Kumar, *et al.*, which showed 4 major interactions; Nitin Kothari, *et al.*, showed 4 major interactions; Sagar, *et al.*; but was less than the study done by Jawed Shareef *et al.*, showed 12.08% major interactions -. however, there was the difference in the sample size [7,8,9,10,11]

The moderate interactions were found to be 45(72%). This finding was higher than the study done by Sagar Pamu, *et al.*, which showed 15 moderate interactions; Rajat Kumar, *et al.*, study showed 50.6% moderate interactions; Nitin Kothari, *et al.*, showed 15 major interactions; Jawed Shareef *et al.*, showed 68.13% of interactions. [7,8,9,10,11]

The minor interactions were found to be 12(19%). This finding was found to less than the study done by jawed shareef and *et al* which showed 19.78% of minor interactions. [11]

However, most of these interactions can be eliminated by dose adjustment and frequent blood pressure monitoring.

The most interacting drugs were amlodipine which interacted with 7 different drugs (Hydrocortisone, Nitro-glycerine, Naproxen, Metformin, Tacrolimus, Budesonide, Atorvastatin); Atenolol which interacted with 7 different drugs (Amlodipine, Insulin glargine, Diclofenac, Theophylline, Aspirin, Torsemide) and telmisartan also interacted with 7 different drugs (Naproxen, Aspirin, Aceclofenac, Pregabalin, Enoxaparin sodium, Atorvastatin, Diclofenac).

The least interacting drug was enalapril which interacted with two drugs (Allopurinol and Spironolactone) the interaction with both the drug was found to be major interaction which showed serious adverse effects.

Hence, the pharmacist needs to check interactions present in the prescription and develop ways to eliminate them. So that better patient care can be provided with increased therapeutic action and reduced side effects.

CONCLUSION

The current study is a retro-prospective observational, that monitors the drug-drug interactions of patients diagnosed with hypertension in a general hospital. A sample size of 100 patients is considered for the study. Out of 100 patients, 64 are males and 36 are females. Drug interactions are found commonly in this study of which 62% are institute.

Polypharmacy of antihypertensives leads to the emergence of drug-drug interactions, treatment failure, increased patient morbidity, and mortality.

This tool makes it difficult to determine the classification of drug interactions depending on a single drug interaction for a certain patient. In terms of clinical implications, medication interactions are classified as Major - Highly Significant. Avoid combinations when the risk of interaction outweighs the benefit. Moderate - Moderately significant in clinical aspects. Combinations should be avoided in most cases, should only be used in exceptional circumstances. Minor - In clinical terms, this term refers to something that isn't very important. Assess the risk, minimise it, and consider switching to a different drug, take efforts to limit the risk of an interaction, and/or schedule monitoring sessions.

Table No. 2: Drug-drug interactions severity and, its remedy

Sr. No.	Drug-1	Drug-2	Severity	Effect	Remedy
1	Torsemide	Nebivolol	Moderate	Decreases heart rate and decreases the blood pressure	Dose adjustment
2.	Valsartan	Nebivolol	Moderate	Increases the heart failure.	Dose adjustment
3.	Digoxin	Nebivolol	Moderate	Decreases heart rate	Dose adjustment
4.	Torsemide	Pantoprazole	Moderate	Hypomagnesemia	Monitor the symptoms.
5.	Clonidine	Digoxin	Moderate	Low blood pressure.	Dose adjustment
6.	Torsemide	Glipizide	Moderate	Reduces blood glucose levels,	Dose adjustment
7.	Clonidine	Metoprolol	Major	Can cause the risk of bradycardia	Avoid or use alternate drug
8.	Atenolol	Amlodipine	Moderate	Low blood pressure and heart rate.	Dose adjustment or frequent monitoring.
9.	Atenolol	Insulin glargine	Moderate	Hypoglycaemia	Dose adjustment
10.	Clonidine	Hydrocortisone	Moderate	Hydrocortisone reduces the effect of clonidine.	Frequent monitoring.
11.	Metoprolol	Hydrocortisone	Moderate	Hydrocortisone reduces the effect of metoprolol.	Dose adjustment.
12.	Amlodipine	Hydrocortisone	Moderate	Hydrocortisone reduces the effect of Amlodipine.	Dose adjustment.
13.	Amlodipine	Nitro-glycerine	Moderate	Decreases the blood pressure	Frequent monitoring.
14.	Amlodipine	Metoprolol	Moderate	Additive effect.	Dose adjustment.
15.	Amlodipine	Tacrolimus	Moderate	Amlodipine increases the effect of	Dose adjustment.

				tacrolimus.	
16.	Amlodipine	Budesonide	Moderate	Budesonide reduces the effect of amlodipine	Dose adjustment.
17.	Furosemide	Carvedilol	Moderate	Low blood pressure	Dose adjustment.
18.	Furosemide	Pantoprazole	Moderate	Hypomagnesemia	Dose adjustment.
19.	Furosemide	Naproxen	Moderate	Risk of mild AKI.	Drink plenty of water with this combination.
20.	Furosemide	Cefpodoxime	Moderate	Continuous use may lead to kidney damage	Dose adjustment.
21.	Amlodipine	Naproxen	Moderate	Increases the blood pressure	Dose adjustment.
22.	Furosemide	Metformin	Moderate	Metformin may increase the action of Furosemide	Dose adjustment.
23.	Telmisartan	Naproxen	Moderate	Naproxen decreases the effect of telmisartan and also affect kidney function.	Dose adjustment.
24.	Telmisartan	Aspirin	Moderate	Pharmacodynamic antagonism.	Modify therapy and monitor closely.
25.	Clonidine	Bisoprolol	Major	Can cause the risk of bradycardia	Avoid or use alternate drug
26.	Valsartan	Bisoprolol	Minor	Both drug increases serum potassium.	Monitor closely.
27.	Telmisartan	Aceclofenac	Major	Both increases serum potassium.	Monitor closely.
28.	Amlodipine	Atorvastatin	Moderate	Increased lipid levels	Monitor lipid levels and use the lowest statin dose.
29.	Telmisartan	Pregabalin	Moderate	Angioedema	Stop pregabalin.
30.	Atenolol	Diclofenac	Moderate	Decreases the effect of atenolol.	Dose adjustment.
31.	Telmisartan	Diclofenac	Moderate	Decreases the effect of Telmisartan	Dose adjustment.
32.	Atenolol	Telmisartan	Moderate	Synergism.	Dose adjustment.
33.	Telmisartan	Atorvastatin	Moderate	Telmisartan increases the toxicity of atorvastatin.	Monitor closely.
34.	Ramipril	Isosorbide mononitrate	Moderate	Ramipril may enhance the vasodilatory effect of NTG.	Closely monitor blood pressure.
35.	Ramipril	Torseamide	Moderate	Synergism, risk of renal insufficiency	Monitor closely.
36.	Telmisartan	Enoxaparin	Moderate	Hyperkalaemia, Suppress aldosterone secretion.	Monitor closely.
37.	Ramipril	Furosemide	Moderate	Additive effect.	Dose adjustment.

38.	Amlodipine	Metformin	Minor	Amlodipine may decrease the effect of Metformin	Dose adjustment.
39.	Enalapril	Allopurinol	Major	Serious infections, fever, exfoliative dermatitis.	Periodic monitoring of WBC. Discontinue if symptoms arise.
40.	Enalapril	Spirolactone	Major	Hypotensive effect and the extreme risk of hypercalcemia.	Avoid potassium supplements, caution is needed in renal impairment, Diabetic patients.
41.	Atenolol	Theophylline	Major	Can cause serious or fatal bronchospasm by inhibiting theophylline induced bronchodilator	β blockers should be avoided.
42.	Telmisartan	Torsemide	Minor	Telmisartan increases serum potassium level while torsemide decreases it.	Monitor closely

Table No. 3: No. of drugs interacting with each antihypertensive agent

Sr. No.	Drug	Class	Interacting Pairs	No. of Drugs
1.	Amlodipine	Calcium channel blocker	Hydrocortisone, Nitro glycerine, Naproxen, Metformin, Tacrolimus, Budesonide, Atorvastatin.	7
2.	Atenolol	Beta-adrenergic blocker	Amlodipine, Insulin glargine, Theophylline, Aspirin, Torsemide, telmisartan, Diclofenac.	7
3.	Clonidine	Alpha 2 adrenergic blocker	Digoxin, Metoprolol, Hydrocortisone, Bisoprolol.	4
4.	Enalapril	ACE inhibitors	Allopurinol, Spirolactone.	2
5.	Furosemide	Loop diuretic	Carvedilol, Pantoprazole, Naproxen, Cefpodoxime, Metformin, Ramipril.	6
6.	Metoprolol	Beta-adrenergic blocker	Hydrocortisone, Amlodipine, Aspirin, Torsemide.	4
7.	Telmisartan	Angiotensin II receptor blocker.	Naproxen, Aspirin, Aceclofenac, Pregabalin, Diclofenac, Atorvastatin, Enoxaparin sodium.	7
8.	Torsemide	Loop diuretic	Glipizide, Nebivolol, Pantoprazole, Ramipril, Metoprolol.	5
9.	Valsartan	Angiotensin II receptor blocker	Nebivolol, Bisoprolol, Aspirin, Digoxin, Hydrocortisone.	5
10.	Nebivolol	Beta-adrenergic blocker	Torsemide, Valsartan, Digoxin.	3
11.	Digoxin	Cardiac glycoside	Clonidine, Valsartan.	2
12.	Ramipril	ACE inhibitors	Furosemide, Isosorbide mononitrate, Torsemide, Furosemide.	4

Table No. 4: Form-1

Name:		IP. No:						
Age:		Department:						
Sex:								
Drug Chart:								
Sr. No:	Prescribed Drug		Dose	Frequency and Route	Days of Treatment			
	Brand Name	Generic Name			1	2	3	4

Table No. 5: Form-2

Name:		Age:		IP. No:	
Drug-Drug Interactions:					
Sr. No:	Drug-1	Drug-2	Severity	Effect	Remedy

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