

Effects of Antihypertensive Agents on Biochemical Parameters in Diabetes Mellitus Patients

P. Neelaphar ¹, Ashly Elizabeth Sabu^{2*}, Jereena LV³, Kesia Thomas⁴ & Mohammed Bilal KA⁵

¹ *Associate Professor, Department of Pharmacy Practice, Aditya Bangalore Institute of Pharmacy Education and Research, Bangalore-64*

² *Pharm.D, Aditya Bangalore Institute of Pharmacy Education and Research*

³ *Pharm.D, Aditya Bangalore Institute of Pharmacy Education and Research*

⁴ *Pharm.D, Aditya Bangalore Institute of Pharmacy Education and Research*

⁵ *Pharm.D, Aditya Bangalore Institute of Pharmacy Education and Research*

¹ neelaphar@gmail.com,

² ashlyelizabeth67@gmail.com, ³ jereenalv1996@gmail.com, ⁴

thomaskesia19@gmail.com, ⁵ bilalbinnasser@gmail.com

Abstract

Background

As there has been an elevation in patients with both hypertension and T2DM, likewise the number of people on drug therapy for it has increased. This has raised several doubts on the effects of concomitant drug consumption in these patients. Data supporting them are available in numerous articles.

Objective

The study looked into the changes in various lab parameters when antihypertensive drugs are given to diabetic hypertensive patients.

Methodology

A prospective observational study was conducted for six months in a tertiary care hospital. Data from case files and other relevant reports were utilized. Demographics and drug use were depicted as graphs and pie charts with tables recording changes in parameters when concurrent drug use is implemented.

Result

It was observed that consuming antihypertensive agents affects lipid profile (LDL, HDL), liver enzymes (AST, ALT), creatinine and all electrolytes in diabetics. ACE-Is modified LDL and HDL measures in up to 8.27% users, with its combination with biguanides affecting these lipid levels in 69.92%. Insulin when taken with ACE-Is and ARBs deranged creatinine values. Chloride levels were affected by CCBs; 30%. Beta blockers with hypoglycemic agents increased ALT.

Conclusion

Monitoring lab values is advised as changes are seen in several parameters while on therapy for both T2DM and HTN. Continuous monitoring of these parameters is required to avoid such modifications.

Keywords: Hypertension, Type 2 Diabetes Mellitus, Antihypertensive drugs, Hypoglycemic agents, LDL, HDL, Serum creatinine, AST, ALT.

Introduction

Diabetic hypertensive patients on drug therapy are increasing day by day, raising concerns on its combined use. The increased risk of cardiovascular disease in this patient group is another issue to be addressed. Extensive research and evidence reveal alterations in biochemical parameters in this subset.

The relevance of such a scenario in India was a compelling force for this study as the country would soon be titled the diabetic capital. Hence, the study follows closely the alterations in the lab parameters of diabetic hypertensive patients while on antihypertensive agents.

Lipid profile and liver enzymes are affected by drugs like Atenolol and Captopril, with the latter altering creatine kinase, bilirubin and creatinine levels according to Alblihed et al. However, Daoud et al found that ARBs with Insulin changed lipid profile, serum creatinine and liver enzymes in comparison to ARBs with Biguanides. Also, ACE-I with Biguanides elevated the lipid profile relative to ACE-I with Insulin. Hyperkalemia was a notable effect in patients on ARBs than ACE-Is quoting Sadjadi et al. Satia et al found that Atenolol affected triglyceride levels of hypertensive patient with and without DM in comparison to Nifedipine. Another study by Savage et al recorded slight yet transient changes in high density lipoprotein, total cholesterol, uric acid and fasting blood sugar. Shehri et al reported increase in lipids, alanine transaminase, creatinine, urea, platelets and decrease in RBC indices, WBC, high density lipoprotein. Similar results were arrived at when we conducted our study. This calls for continuous monitoring of all aforementioned parameters to ensure better healthcare.

Materials and Methods

This is a Prospective observational study. The study was carried out for 6 months in the general medicine department. The subjects under inclusion criteria like patients who are having 18 to 70 years of age, both genders, patients who are diagnosed with the hypertension along with T2DM, patients on antihypertensive and anti-diabetic drugs, patients with T2DM but no hypertension were completely monitored during the study period. The data supporting the study was collected from authorized standard international and national journals. A properly designed data collection form was used to collect and record the patient data. All relevant data sets for the study were gathered from a variety of sources, including case sheet, case report, treatment chart, laboratory reports (biochemical parameters) and entered into data collection form.

Result

Out of 133 patients studied, 66 (49.6%) were female and 67 (50.3%) were male. The most commonly prescribed drugs were biguanides (69.9%) and calcium channel blockers (30%). In that 88.7% were oral route of administration and 37.59% were sub-cutaneous route of administration. The study was conducted by dividing the patients into two groups, diabetes mellitus only and diabetes mellitus with hypertension.

To study effects on the lipid profile, total count, triglycerides, high density lipoprotein and low-density lipoprotein levels were observed. Significant increase were noted in total count and triglycerides levels when ACE inhibitors (8.27%) and Beta blockers (7.5%) were used. LDL and HDL levels significantly increased in ACE inhibitors + Biguanide (69.92%) compared to ACE inhibitors + Insulin (41.35%) and ACE inhibitors + Biguanide + DPP 4 inhibitors (13.53%). HDL level was significantly increased in ARBs (23.3%) + Insulin in comparison to ARBs+ Biguanides. TC and TG significantly increased with most of the hypoglycemic agents.

To study the effect of electrolytes, sodium (Na⁺), chloride (Cl⁺) and potassium (K⁺) levels were monitored. The effects of ACE inhibitors (8.27%), ARBs (23.3%), Beta blockers (7.5%), CCBs (30%), Alpha antagonists (3.75%) and Diuretics (19.54) on electrolytes were observed when used with hypoglycemic agents. It was found that chloride levels were affected, its values increased with ACE Inhibitors (8.27%) + hypoglycemic agents. Sodium level were significantly increased with ARBs + Biguanide DPP-4 inhibitors (23.3%+69.92%+13.53%) when compared to ARBs + Insulin (23.3%+69.92%+13.53%) > (41.35%). Also, significant increase was seen in case of sodium and potassium levels when ARBs + Insulin was used.

To study changes in renal function, we considered serum creatinine, albumin and urea. In that, serum creatinine was elevated with ACE inhibitors+ Insulin and ARB + Insulin. No change was observed with regard to other parameters.

To study changes in hepatic function, we observed values of AST, ALT, ALP, Total protein and albumin. ALT was significantly increased by Beta blockers and hypoglycemic agents. ALT was also elevated with ARB + Biguanide + DPP4I. There were alterations in the values of AST and ALP.

Altered Biochemical Parameters

Table 1. Lipid Profile Test

Antihypertensive Agents	Antidiabetic Agents	TC (mg/dl) (<200 mg/dL)	HDL (mg/dl) (<60 mg/dL)	LDL (mg/dl) (<100 mg/dL)	TG (mg/dl) (<150 mg/dL)
ACE Inhibitors (Enalapril)	Insulin	Slightly Elevated	Slightly Elevated	Slightly Elevated	Slightly Elevated
ACE Inhibitors (Enalapril)	Biguanides (Metformin)	Elevated	No Change	No Change	Elevated
ARBs (Telmisartan, Losartan)	Insulin	No Change	Slightly elevated	No Change	No Change
ARBs (Telmisartan, Losartan)	Biguanides (Metformin)	No Change	Elevated	No Change	No Change

β Blocker (Metoprolol, Atenolol)	Insulin	Elevated	No Change	No Change	Elevated
β Blocker (Metoprolol, Atenolol)	Biguanides (Metformin)	Elevated	No Change	No Change	Elevated
β Blocker (Metoprolol, Atenolol)	Sulfonylureas (Glimepiride, Glipizide)	Elevated	No Change	No Change	Elevated
β Blocker (Metoprolol, Atenolol)	DPP4 Inhibitors (Vildagliptin, Linagliptin)	Elevated	No Change	No Change	Elevated
β Blocker (Metoprolol, Atenolol)	Alpha-1 GIs (Voglibose)	Elevated	No Change	No Change	Elevated
β Blocker (Metoprolol, Atenolol)	SGLT2 Inhibitors (Dapagliflozin)	Elevated	No Change	No Change	Elevated
β Blocker (Metoprolol, Atenolol)	Meglitinides (Sitagliptin, Repaglinide)	Elevated	No Change	No Change	Elevated
β Blocker (Metoprolol, Atenolol)	Thiazolidined Iones (Pioglitazone)	Elevated	No Change	No Change	Elevated
ARBs + ACE (Telmisartan+Enalapril)	Antidiabetic agents (Metformin, Glimepiride, Voglibose)	Elevated	No Change	No Change	No Change

Table 2. Renal Function Test

Antihypertensive Agents	Antidiabetic Agents	S. Cr (0.74 – 1.35 mg/dL)
ACE Inhibitors (Enalapril)	Insulin	Elevated
ARB (Telmisartan, Valsartan)	Insulin	Elevated

Table 3. Liver Function Test

Antihypertensive Agents	Antidiabetic Agents	ALT (7-55 U/L)
β Blocker (Propranolol)	Insulin	Elevated
β Blocker (Propranolol)	Biguanides (Metformin)	Elevated
β Blocker (Propranolol)	Sulfonylureas (Glimepiride, Glipizide)	Elevated
β Blocker (Propranolol)	DPP4 inhibitors (Vildagliptin, Linagliptin)	Elevated
β Blocker (Propranolol)	Alpha-1 GIs (Voglibose)	Elevated
β Blocker (Propranolol)	SGLT2 inhibitors (Dapagliflozin)	Elevated
β Blocker (Propranolol)	Meglitinides (Sitagliptin, Repaglinide)	Elevated
β Blocker (Propranolol)	Thiazolidinediones (Pioglitazone)	Elevated
ARB (Telmisartan, Valsartan)	Biguanide+DPP4 Inhibitors (Metformin+Vildagliptin)	Elevated

Table 4. Electrolytes

Antihypertensive Agents	Antidiabetic Agents	Chloride (96 - 106 mEq/L)	Potassium (3.7 – 5.2 mEq/L)	Sodium (135 – 145 mEq/L)
ACE Inhibitors (Enalapril)	Insulin	Elevated	No Change	No Change
ACE Inhibitors (Enalapril)	Biguanide (Metformin)	Elevated	No Change	No Change
ACE Inhibitors (Enalapril)	Sulfonylureas (Glimepiride, Glipizide)	Elevated	No Change	No Change
ACE Inhibitors (Enalapril)	DPP4 Inhibitors (Vildagliptin, Linagliptin)	Elevated	No Change	No Change

ACE Inhibitors (Enalapril)	Alpha-1 GIs (Voglibose)	Elevated	No Change	No Change
ACE Inhibitors (Enalapril)	SGLT2 inhibitors (Dapagliflozin)	Elevated	No Change	No Change
ACE Inhibitors (Enalapril)	Meglitinides (Sitagliptin, Repaglinide)	Elevated	No Change	No Change
ACE Inhibitors (Enalapril)	Thiazolidinedione s (Pioglitazone)	Elevated	No Change	No Change
ARBs (Telmisartan, Valsartan)	Insulin	No Change	Elevated	Elevated
ARBs (Telmisartan, Valsartan)	Biguanide + DPP4 Inhibitors (Metformin+Vilda gliptin)	No Change	No Change	Elevated

Discussion

Our study is a novel study concerning the effects of antihypertensive agents on the biochemical parameters in hypertensive type II diabetic patients.

To study effects on the lipid profile, total cholesterol , triglycerides, high density lipoprotein and low- density lipoprotein levels were observed. Significant increase was noted in total cholesterol and triglycerides levels when Enalapril and insulin were used. Enalapril which blocks the substance in the body that causes the blood vessels to tighten. On other side, LDL and HDL levels significantly increased in Enalapril with Metformin when compared to Enalapril with Insulin and Enalapril with Metformin and with Vildagliptin or Linagliptin. HDL level was significantly increased in Telmisartan or Losartan with Insulin in comparison to Telmisartan or Losartan with Metformin .Total cholesterol and Triglycerides significantly increased with most of the hypoglycemic agents. These evidence are shows in the Naveen M.Daoud's study in the literature review. In our study also there were changes in biochemical parameters especially lipid profile. So along with blood glucose monitoring, monitoring of lipid profile is also advised at least twice in a year. This is essential as increase in cholesterol levels may lead to an increased cardiovascular disease risk.

To study the effect of electrolytes, sodium (Na⁺), chloride (Cl⁻) and potassium (K⁺) levels were monitored and these are the most common macro electrolytes correlated with diabetes mellitus. The effects of ACE inhibitors, ARBs, Beta blockers, CCBs, Alpha antagonists and Diuretics on electrolytes were observed when used with hypoglycemic agents. It was found that chloride levels were affected, its values increased with Enalapril and hypoglycemic medications. Sodium level were significantly increased with Telmisartan or Valsartan with Metformin and Vildagliptin when compared to Telmisartan or valsartan with Insulin. Also,

significant increase was seen in case of sodium and potassium levels when Telmisartan or valsartan with Insulin was used. These are mentioned in the Naveen M. Daoud's study.

To study changes in renal function, we considered serum creatinine, albumin and urea. In that, serum creatinine was elevated with Enalapril with Insulin and Telmisartan or valsartan with Insulin. No change was observed with regard to other parameters.

To study changes in hepatic function, we observed values of AST, ALT, ALP, Total protein and albumin. ALT was significantly increased by propranolol and hypoglycemic medications. ALT was also elevated with Telmisartan or valsartan with Metformin + Vildagliptin. There were alterations in the values of AST and ALP.

Conclusion

To reveal our study that biochemical parameters changed when anti-hypertensive agents and hypoglycemic agents taken together. As ACE-I and Beta-Blockers result in changes in biochemical parameters, they should be used with caution when prescribing with hypoglycemic drugs. These are the following changes observed from the patient's laboratory reports. Firstly, HDL and LDL level are elevated with ACE and Biguanides. Also, increased level of HDL when administering with ARBs and Insulin. Furthermore, the chloride amount is raised with ACE-I and hypoglycemic medications. On the other side, Sodium level soared with ARBs, Biguanides and DPP-4 Inhibitors. In addition, sodium and potassium range elevated with ARBs and Insulin. Moreover, serum creatinine is elevated when ACE-I with Insulin and ARBs with Insulin and finally, ALT is elevated with Beta-blockers and hypoglycemic medications, ARB with Biguanides+DPP-4 Inhibitors.

For this complications patient have to take some steps for their better life.

- Frequent monitor of electrolytes, lipid profile, renal function test, liver function test.
- Keep an updated list of all the prescription medications.
- Talk to the respective pharmacist.
- Take an appointment with doctor at-least once in a month.

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