Endocrinology & Diabetes Research

Review Article A SCITECHNOL JOURNAL

Drug-Drug Interactions Between Antihypertensive and Antidiabetics Drugs in Ambulatory Patients

Faheem Ahmed Sheikh*

Department of Pharmacist, Dow University Hospital, Karachi Pakistan

***Corresponding author:** Faheem Ahmed Sheikh, Department of Pharmacist, Dow University Hospital, Karachi Pakistan, E-mail: faheemsheikh210197@gmail.com

Received date: September 07, 2021; **Accepted date:** September 21, 2021; **Published date:** September 28, 2021

Abstract

Drugs are utilized in the prophylaxis and treatment for symptoms and diseases although Drug-Drug interaction are of the main issue in multidrug therapy. Beta-blockers and other hypertensive drugs are frequently used in the treatment of blood pressure in diabetic patients. Literature revealed that probably of retinopathy, cardiovascular diseases and other conditions are high in diabetic hypertension patients, which may root to morbidity and mortality. Consequently, our aim is to check interactions between antihypertensive and antidiabetic drugs and to manage, minimize and control these interactions. The method of study in this article included are cross sectional descriptive study, cohort study, using propensity score matched sample, retrospective study and prospective observational study. Suspected results of these methodologies or studies are enhancing or reduced hyperglycemic effects of antidiabetic drugs, give synergistic/toxicity with antihypertensive drugs, pharmacokinetics and pharmacodynamics interactions, dosing problems, prolong hospital stay and comorbid diseases were the risk factor associated with drug-drug interactions.

Keywords: Methodologies; Antihypertensive; Ant diabetic drugs

Introduction

Drug interaction: There are more opportunities today than ever before to learn about your health and to take better care for yourself. It is also more important than ever to about the medicines you take. If you take several medicines, see more than one doctor or have certain health conditions, youand your doctors need to be aware of all the medicines you take to avoid potential problems, such as druginteractions.

Drug interactions may make your drug less effective, cause unexpected side effects or increase the action of a particular drug some drug interactions even be harmful to you. Reading the label every time you uoe a non-prescription or prescription drug and take the time to learn about drug interactions may be critical to your health, You can reduce the rise of potentially harmful drug ingredients and side effects of little bit knowledge of common sense [1].

Drug-Drug interaction(DDIs)

DDIs is substantially increased when multiple drugs are taken (Juurlink et al. 2003). Therefore, patients with diabetes are especially exposed DDIs. Most of the evidence is derived from case reports or investigation of potential DDIs in patients fromhospitalsorpharmacies(Petersonandbates2001; Halkinetal. 2001;Bacicvrca et al. 2010; Schorr et al. 2014). DDIs can be a serious threat to public health. It is important to frequently observe DDIs is current pharmacotherapy because the prediction of DDIs is of clinical importance for selecting regimens and adjusting doses (Pirmohamed et al. 2004). Likewise, knowledge of DDIs is an important parameter for rational pharmacotherapy (Bacic Vrca et al.2005). We sough to investigate the incidence of potential DDIs including antidiabetic agents in patients with diabetes using records of a communitypharmacy.

Literature Review

Type 2 diabetic mellitus patient with hypertensions often receive many medicines and this can lead to occurrence of drug related problems (DRP). A high vague of DRP has been noticed in type 2 DM patients. DRP may lead substandard blood pressure management which can devote to significant morbidity or mortality, long stay in hospitals and added on the health care amount if left untreated. However, in most seniors, theseDRPs are avoidable. These are the several aspects affecting DRPs in T2DM patients with highblood pressure, some of them on poly pharmacy, age status, multiple diseases condition and renal functions deteriorated patients. This study`s purpose was to give data regarding to DRPs to allow utilization of more efficient management and to lower the mortality and morbidity associated with DRPs.(reff#4)

Drug-Drug interactions are one of the main issues in multi-drug therapy. Beta- blockers are mostly use in the treatment of hypertension in diabetic patients. Literature revealed that risk of retinopathy, cardiovascular diseases, vascular event and other conditions are high in diabetic hypertensions patients, which may root to morbidity and mortality. The purpose of this study to check the safety, accuracy of glipizide (anti-diabetic) and probably interactions with propanolol when they were gives in combinations therapy. To avoid these interactions and managed these interactions the dose and frequency of glipizide are change consequently in order to evade severe hypoglycemia, also monitor the individual glucose levels and other medications.(reff#1)

Identify and evaluate the frequency, severity, mechanism and common pairs of drug- drug interactions in prescription by consultant in medicine out-patients department. The aspect on which contribute to interactions are poly pharmacy, patient`s age, cardiovascular events and other co-morbid conditions. The interactions are of two type, pharmacodynamic and pharmacokinetics interactions. To avoid these interactions, use treatment guideline, diabetics and rationalize knowledge of drugs, computer base screening technique, awareness given to the physicians, health care professionals, patients through the electronics, print and social media. Pharmacist involvement should also necessary to increase the rational prescribing and ensuring the patient safety.(reff#2)

Although the common co-incident of diabetes and Heart failure (HF), the optional treatment of debates in HF patients have no been fine studies.Weneededtoan alysesthe associations between metformin and health out-come in a cohort studies of ambulatory patients with diabetics and heart failure, Metformin treatment was associated with decreased rate of mortality in ambulatory patients with diabetes and heart failure Further prospective studies are required to describe the optimal treatment for diabetic patients with heart failure.(reff#3)

A cross sectional study was performed to determine the prevalence of drug-drug interactions in geriatric patients at the ambulatory care pharmacy at King Abul Aziz medical city in Jeddah, in Saudi Arabia, 2 most common interacting pairs was found, one is atorvastatin and omeprazole with a prevalence of 25% and second is atorvastatin and of calcium with prevalence 22.90%.To avoid these interactions, its necessary the social care when handling their prescriptions, the great number of common interacting pairs were category C, we required more to see for D and X interacting pairs thoroughly.(reff#6)

Drug-drug interaction is the main interest in patients with complex therapeutic regiment. The additions of cardiovascular drugs in drug interactions are greater. This study is use to determine the possible DDIs hospitalized heart patients and also estimate the probable risk factors come from these interactions. Great number of interactions were of moderate severity and pharmacokinetics in nature. But the consequences of these interactionsare increasedthemedicinenumbers,longstayinhospital,increasethecostand other comorbid diseases [2]. Were the risk factors consequences come with DDI. This study indicates the need of therapeutic planning, providing DDI information to the prescriber and medicine interactions alert software to the dispensing pharmacist and pharmacokinetic study to reduce the rate of drug-drug interactions.(reff#5)

The association of hypertensions of hypertension with insulin resistance has been reported. Troglitazone is a newly anti-diabetic drug that enhancing the insulin sensitivity. The purpose of this study was to evaluate whether the betterment of high insulin in blood byTroglitazonereducesthebloodpressurethebloodpressureinascensional hypertension. Troglitazone promote the improvement in both glucose metabolism and blood pressure control in essential hypertension patients with diabetes. The result of this study indicates the insulin resistance or plasma insulin level play a role in the pathogenesis of essential hypertension [3].

Methodology

Effect of propranolol and glipizide individually and in combination were tested in healthy and diabetic rats. Diabetes was induced to a group of animals by injecting 55 mg/kg streptozotocin by ip route in normal saline (pH 5.5). Blood glucose level was monitored periodically and hypoglycemic rats after 10-14 days used for the study. Overnight fasted normal and diabetic rat were used for the study. The changes in blood observedduringthestudy.Bloodsampleswerecollectedfromthetailveinatt imeintervals after drug administration and glucose levels were estimated by using glucose oxidase/peroxidase (GOD/POD) method, which is compared with fasting blood sugar level. Individual effect of propranolol and glipizide on blood sugar level were tested after administration of single dose in animals, whereas the influence of repeated treatment of propranolol for seven days on the hypoglycemic effect of glipizide was studied [4].

This cross sectional descriptive study was conducted after approval from the Research Review Committee and Ethical Review Committee of Bahria University Medical andDentalCollegeasapartofmainproject"Prescribingpatternsinhospitali npatients". Prescriptions of consultants were collected from the patients in the medicine outpatient department, of a private hospital in Karachi, after verbal informed consent. Prescriptions were collected by visiting medicine outpatient setting (OPD) twice weekly for two months from 1st December 2015 to 31st January 2016. Adult male and female patients whose prescription contained at least two drugs and who gave their consent, were included in the study while hospital inpatient, children, pregnant and lactating women, patients with terminal illnesses and those who did not gave consent were excluded from the study. A total of 220 prescriptions were collected, out of which 211 were selected while 09 prescriptions were excluded because of unavailability of the prescribed drugs in the drug interaction checkers. Drugs generic names were obtained from Pharmaguide 20th edition and internet sources. ATC classification system was used for the classification of drugs. The severity of prescribed drugs interactions were analyzed by Medscape Drug Interaction Checker i.e. Serious, Significant and Minor and reconfirmed by drugs. com checker and stockley`s drug interactions index. Results are expressed as mean and percentage [5].

We performed an observational study of a national cohort of veterans with HF treated in ambulatory clinics at Veteran Affairs (VA) medical centers using the VA External Peer Review Program (EPRP) data between October 2000 and September 30, 2002. The VA EPRP was created to assess and improve the quality of care for VA patients and has been described previously. The sampling pool of outpatients for EPRP included ambulatory patients with common chronic diseases such as HF, diabetes, ischemic heart disease (prior myocardialinfarction),andchronicobstructivepulmonary diseaseidentifiedbyspecificICD- 9 codes. Experienced data abstractors then reviewed electronic medical records for validation of sample selection criteria, including a documentation of a diagnosis of HF in the outpatient charts for the EPRP HF cohort. For further validation, 70 patients in EPRP cohort from the Houston VA were reviewed; documentation of a diagnosis of HF by a clinician in the electronic medical records was confirmed in 96% of cases. Patient-level data from the EPRP HF cohort were linked with 5 existing national VA databases to obtain further demographic, laboratory, pharmacy, and outcome data. Individuals from the EPRP HF cohort who had diabetes as identified in the EPRP data and who were prescribed hypoglycemic medications in the pharmacy database were included in this study. Diabetic therapy was ascertained using pharmacy data and was based on prescriptions filled 90 days before the index outpatient visit or 30 days after the index outpatient visit. In addition to diabetic status and therapy, baseline demographics and concomitant cardiac medications were assessed at the index visit. The most recent laboratory data within 1 year before the index visit and up to 2 weeks after the index visit were used. Because of the important potential for confounding between metformin use and renal dysfunction, patients with missing creatinine values were excluded from these analyses (n962), leaving patientsinthetotalcohort.Othermissinglaboratoryvalueswereimputedusi ngthemedian value of the study cohort for that parameter and a dummy variable was used to indicate replacement of missing data. Glomerular filtration rate (GFR) was calculated using the 4- variable Modification of Diet in Renal Disease (MDRD) equation.15 Covariates that reflected diabetes severity included hemoglobin A1C and a variable that documented the presence of a diabetic complication

including neuropathy, nephropathy, retinopathy, or peripheral vascular disease [5].

This was are trospective study conducted in Malaysia's premier teaching hospital with 1000-beds, the University of Malaya Medical Centre (UMMC). A total of 200 patients were included in this study. The sample size was calculated using the Epi Info, Version 6 (Centers for Disease Control and Prevention, Atlanta GA), which provided a minimum sample size of 195 patients. The Pharmaceutical Care Network Europe (PCNE) classification of DRPs version 5.01 was used to categorize DRPs. In this study, the six domains of problems of the PCNE classification were used. The DRPs and their possible causes were identified from the patients'medical records, with reference to the stand ard guidelines and established literatures. Two main references were used to assess the appropriateness of drug indications, appropriateness of drug and dosage, possible drug interactions, adverse drug reactions and contraindications. The authors who are pharmacists were involved in the identification and classification of DRPs. The modified Beers criteria were used in this study. This is a consensus-based drug list that includes a number of drugs which should be avoided or used very cautiously in the elderly. For this study, the criteria were used as a reference to assess and identify the potential drugs that were inappropriately prescribed in the T2DM patients with hypertension who were aged 65 and above. The listed drugs were generally divided into low and high risk. In thisstudy,onlyinappropriateprescriptionsof"Beerscriteriahighseverity"drugswere identified as DRPs because these drugs might pose clinically significant adverse effects when used in the elderly [2].

Cardiac patients aged 18 years or older admitted to the cardiac unit of general medicine wards with a hospital stay of at least 24 h and those prescribed two or more drugs were enrolled for the study. Patient profile form was used for collecting the socio-demographic variables and medication profile of patients. DDI database system (Micromedex × 2.0) was used to identify and analyze the pattern of potential DDIs. Micromedex is an electronic database that contains a separate section on DDI known as the Drug-REAX System. On entering the list of medications, it enlists all the potentially hazardous drug interactions on the basis of severity, onset and documentation status. On the basis of severity Micromedex classifies DDI as major, moderate and minor as follows:

Major: Potentially life-threatening; requires medical intervention to minimize or prevent the serious adverseeffects)

Moderate:
Resultsinpotentialdeteriorationofpatients'clinicalconditionandmay require an alteration intherapy.

Minor: The effects are usually mild and may not require change intherapy.

It also classifies potential DDI as excellent, good, fair, poor or unlikely on the basis of documentation status as mentionedfollows:

Excellent: The existence of the drug interaction has been clearly established by the controlledstudies.

Good: The existence of drug interaction is suggested by documentation, but well- controlled studies arelacking.

Fair: Available documentation ispoor.

Poor: Documentation is scant; however, the possibility of a clinical conflictexists.

Unlikely: Documentation as well as a sound pharmacological basis is lacking.(5).

In this study, we did are trospective review of 310 patients' medication profiles of ambulatory care pharmacy dispensed prescriptions. The assigned pharmacist retrieved the dispensed prescriptions randomly. Ten the baseline characteristic and patient demographics data (including patient age, gender, number of drugs, and chronic illness at the time of dispensing) and the patient drug profile data (including drug, dose, and route) were collected. The drug profile for each patient wasanalyzed by Lexi-Interact (a comprehensive drug-to-drug, drug-to- herb, and herb-to-herb interaction analysis program); Lexi-Interact categorized DDIs into five categories according to its risk rating, category A: data have not demonstrated either pharmacodynamic or pharmacokinetic interactions between the specified medications, B: the specified medications may interact with each other, but there is little to no evidence of clinical concern resulting from their concomitant use, C: the medications agents may interact with each other in a clinically significant manner, but the benefits of concomitant use of these two medications usually outweigh the risks, D: the two medications may interact with each other in a clinically significant manner, a patient-specific assessment must be conducted to determine whether the benefits of concomitant therapy outweigh the risks, and X: the specified medications may interact with each other in a clinically significant manner, but the risks associated with concomitant use of these medications usually outweigh the benefits.

Result

We checked the drug interactions between glyburide and metformin, propanolol (sulfonylureas/beta blockers) through the lexicomp drug interaction - Uptodate. The interactions show the risk category C which means monitor therapy. Beta blockers may enhance the hypoglycemic effect of sulfonylureas. Cardioselective beta blockers (atenolol, metoprolol) may be safer than non-selective beta blockers. All beta blockers appear to mask tachycardia as an initial symptoms of hypoglycemia. Closely monitor blood glucose levels because beta blockers may decrease the efficacy of sulfonylureas type medications. Captopril + Metformin: Captopril increases the toxicity of metformin by unspecifiedinteractionmechanism.Usecaution/monitor.Increasesriskforhypoglycemia and lactic acidosis. Monitor closely these interactions to avoid any worse condition. The drug interactions between pioglitazone and hydrochlorothiazide diminish the therapeutic effect of antidiabetic agents. The interactions risk category is C which means monitor therapy. Increase monitoring of blood glucose when using thiazide diuretics in patients being treated with antidiabetic agents. In particular, monitor closely when starting/stopping a thiazide or when increasing thiazide dose. The drug interactions between sitagliptin and lisinopril enhance the adverse/toxic effects of ACEIs. Specifically, the risk of angioedema may be increased. The interactions risk category is C which means monitor therapy. Educate patients regarding this risk and advise them to report any signs or symptoms of angioedema immediately. Angioedema may appear at any time during concurrent use, including after months or years on the combination. We managed, minimized and controlled drug interactions between antihypertensive and antidiabetic drugs through change the timing of drugs, change the frequency of drug, increase or decrease the dose, use alternatives, monitor patients vital signs and symptoms, take blood pressure/blood glucose levels from time to time, monitor the therapeutic/toxic effects of drugs, use

technology aided software, provide awareness regarding the medicines to the physician, health care professionals, patients and general public involvement pf the pharmacist in the treatment of patients to check patient profile, educate the patient regarding drug, provide information to physician and communicate with consultants.

Conclusion

From methodology, we concluded that there are several drug interactions between these two classes of medications (antihypertensive and antidiabetics) and drug interactions are increases in ambulatory care patients, conventional methods are present to manage, minimize and control these interactions but need of more advancement strategies to overcome and resolve these problems more effectively specially in comorbid class of patient population. The use of technology aided soft-wares latest updated versions, pharmacogenomics, evidence based guidelines and patient drug concentration profile are prevent, control and management of these interactions more quickly and more adequately

References

Rama M, Viswanathan G, Acharya LD, Attur RP, Reddy PN, et al. (2012) Assessment of drug-drug interactions among renal failure patients of nephrology ward in a South Indian tertiary care hospital. Indian J Pharm Sci. 74: 63.

Egger SS, Drewe J, Schlienger RG (2003) Potential drug–drug interactions in the medication of medical patients at hospital discharge. Eur J Clin Pharmacol. 58: 773-8.

Corsini A, Ceska R (2011) Drug–drug interactions with statins: will pitavastatin overcome the statins' Achilles' heel?. Curr Med Res Opin. 27: 1551-62.

Soherwardi S, Chogtu B, Faizal P(2012) Surveillance of the Potential Drug-Drug Interactions in the Medicine Department of a Tertiary Care Hospital. J Clin Diagnostic Res. 6.

Farooqui R, Hoor T, Karim N, Muneer M (2018) Potential drug-drug interactions among patients prescriptions collected from medicine out-patient setting. Pak J Med Sci. 34: 144.