

Drug Associated Complications in Type 2 Diabetes Patients with Hypertension

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Abstract

The main aim of present research work was to study the Type 2 diabetes (T2DM) or non insulin dependent diabetes mellitus patients with hypertension, are at increased risk for experiencing drug-associated complications (DACs) since they commonly receive the multiple medications and have multiple co-morbidities. Now a day, there is a lack of studies conducted in T2DM patients with hypertension and to analyze the DACs and identify factors affecting the DACs in this patient population of varies sex and age groups.

Key Words: Drugs, Type 2 diabetes mellitus, hypertension and drug associated complications

Introduction:

In world the top ten countries that are having the large number of diabetic patients, Malaysia is one among these countries¹. And the percentage has increased magically from 8.3% in 1996 to 14.9% in 2006, affecting around 14 lakhs adults aged 30 years old². As per the results of DiabCare Malaysia 2008, more than 90% of adult are suffered from Type 2 diabetes. Hypertension is a common co-morbidity in T2DM patients and possibilities are up to two-thirds of the population, and it may be present by the time T2DM is diagnosed or even before the onset of hyperglycemia³. Hypertension elevates the risk of

cardiovascular disease in T2DM patients. Hypertension also increases the risk of developing micro vascular complications like diabetic retinopathy and nephropathy T2DM patients with hypertension commonly receive the large number medications and this may cause the drug-associated complications (DACs). A high prevalence of DACs has been seen in T2DM patients⁵. DACs may lead to suboptimal blood pressure control which can contribute to significant morbidity or mortality, prolonged hospitalization, and may be leads to severe complications if the medical attention not given timely, however, in maximum cases, the complications of DACs can be prevent⁶. Many factors are there which promote the

DRPs in T2DM patients with hypertension. The factors like Polypharmacy (the number of drugs is 3 to 20) are an inherent factor as high blood pressure and diabetic complications usually complicate the treatment. Age (65 years old) is another factor, given increased association with multiple medical conditions, multiple drug therapies and age-related changes in the pharmacokinetics and pharmacodynamics of drugs. Multiple medical conditions and renal impairment also have been shown to contribute to DACs⁷. Now a day's, there has been a lack of studies conducted locally and globally to investigate and document DACs in T2DM patients with hypertension.

Diabetes and Hypertension .It is common metabolic path way, they occur frequently together, the causes and mechanism of disease is closely overlapped to each other. Over weight, inflammation, oxidative stress, and insulin resistance are consider as common path way. For the effective treatment and prevention the cause and mechanism of disease should be known⁸.

Literature Review:

1. Mark makowsky, BSP, Pharm-D etal⁹(2012), reviewed that HTN is a common problem in people with

diabetes and several changes may occurred, the joint Canadian Hypertension Education Program and Canadian Diabetes Association recommended over the past 5 years. This article uses a case-based approach to review contemporary issues in hypertension management in the context of diabetes, including: treatment targets, optimal combination therapy, choice of diuretic therapy, the role of aldosterone antagonists, role of aliskiren, bedtime dosing of antihypertensive agents, benefits of sodium reduction, impact of lifestyle interventions, vascular risk reduction with anti platelet therapy, adherence strategies, the role of home blood pressure monitoring, and treatment considerations based on ethno cultural background. Particular emphasis is given to linking the recommendations to practice. Up to 80% of people with diabetes and hypertension will die of CVS disease, especially stroke. The 2012 Canadian Hypertension Education Program, hypertension in diabetes key messages for knowledge translation are that clinicians should: 1) ensure people with diabetes are screened for hypertension, 2) assess blood pressure at all appropriate

healthcare visits, 3) encourage home monitoring with approved devices, 4) initiate pharmacotherapy and lifestyle modification concurrently, 5) access and manage all other vascular risk factors, and 6) enable sustained lifestyle and medication adherence.

2. **Ramond O.Estacio.M.D.et al.**¹⁰, (2010), reported recently the use of CCBs in HTN may increase the CVS risk in IDDM patients, and whereas such complications are less in NIDDM patients, and these issues remain controversial. In the world of patients of diabetes and hypertension we found significantly more incidents of fatal and nonfatal myocardial infarction in those who are getting the therapy of calcium channel blockers (nisoldipine) than the people who are getting the Enalapril, hence these things need close drug monitoring.

3. **Mazzone T, et al**¹¹, (2006), conducted a study on Long-term risk of CVS events with rosiglitazone, including MI, heart failure, and cardiovascular mortality. GSK conducted the clinical trials, through US Food and Drug Administration Web site, and made the product information sheets for randomized

controlled trials. Studied the rosiglitazone used for treatment of DM observe for 12 months and monitored CVS adverse events. Rosiglitazone significantly increased the risk of MI and heart failure without a significant increase in risk of cardiovascular mortality. There was no evidence of substantial heterogeneity among the trials for these endpoints.

Materials:

This is the quantitative study with descriptive quantitative phase; data were collected from medical records of 200 to 300 patients of different families, in cardiology and general medicines department in Princess Asra Hospital a super specialty hospital Shah Ali Banda, Charminar, and Hyderabad. The qualitative phase was individually interviewed and is conducted with 5 physicians and 25 patients every week for two to three months.

Study Design:

1. Single center means OPD
2. Observational pts / IPD or ICU.
3. Non-interventional study
4. . Random patients

5. Prospective observational study to design the prescribing pattern of anti Hypertensive drugs.
6. Patient selection was random
7. Total 200 to 300 patient samples from OPD and IPD were included

Study Criteria

I) Inclusion Criteria

Patients in Princess Asra Hospital, Shah Ali Banda, Charminar, Hyderabad, Andhra Pradesh.

1. Patients diagnosed with T2DM and hypertension.
2. Patients who received at least one antidiabetic drug (oral antidiabetic drug or insulin) and at least one antihypertensive agent in the ward.
3. Under the guidance General physician and associates.
4. Patients (in and out-patients) of both genders with all age.
5. Patients who are willing to give verbal and authentic information and are consent for the study and willing to participate.

II) Exclusion Criteria

1. Patients in I.C.U, and other non-selected departments.
2. Patients with previous history of any disorder or toxicity taking any other drug besides anti-diabetic antihypertensive drugs.

3. Pregnant and lactating mothers.
4. Patient with missing data.

The patients taking other than cardiology and general medicine

Source of Data

Patient data relevant to the study was obtained from the

Following sources

1. Treatment chart or case sheet of patient
2. Patient data collection form
3. Prescription or medications
4. Patients counseling

Data collection:

The author (Pharmacist) who was collected the data based up on many characteristics like Demographic characteristics like sex, age, height, weight, and body mass index were recorded. Clinical characteristics such as duration of hospital stay, duration of T2DM, duration of hypertension, presence of diabetic complications (focusing to diabetic retinopathy, neuropathy or diabetic foot ulcer), presence of comorbidities, laboratory results and concurrent medications or use of many medications at a time were also collected.

Methods

Study design and setting

This was a retrospective study conducted in both inpatients and outpatients units of Princess Asra Hospital, A total number of 300 to 350 patients were included in this study. The study population consist of T2DM patients with hypertension, and the patients who were admitted for the treatment hypertension and diabetes with the demographic details (name, age, education, occupation, income of the patient was collected. Admission, diagnosis and condition of the patient were recorded, the study population consisted of Drug data of all the antihypertensive drugs prescribed, dose frequency, and route of administration and dose were recorded. The results were expressed.

Assessment of Drug Associated Complications (DACs)

For the categorization of DACs version 5.01of Pharmaceutical Care Network of Europe was used ¹², which is a established system and has been revised many times and its validity and reproduced ability have been tested. DRPs and their [possible causes where identified from patients, medical data, with reference to

standard guidelines and literatures. there are several references were used to assess the appropriateness of indications, drugs and possible drug interactions and contraindications. ¹³. The author who was a pharmacist involved in the assessment of DACs.

Modified Beers criteria

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 this study, only inappropriate prescriptions of “Beers criteria high severity” drugs were identified as DRPs because these drugs might pose clinically significant adverse effects when used in the elderly¹⁴.

Table 1 Drug Associated Complications in type 2 diabetes patients with hypertension (n = 300)

Code	Problems	Percentage
P1	Adverse reactions	20(6.6)
P1.1	Side effects suffered (non-allergic)	20(6.6)
P2	Drug choice problems	70 (23.3)

P2.1	Inappropriate drug (not most appropriate for indication)	24(8.3)
P2.2	Inappropriate drug form (not most appropriate for indication)	4 (1.3)
P2.3	Inappropriate duplication of therapeutic group or active ingredient	4 (1.3)
P2.4	Contraindication for drug	29 (7.5)
P2.5	No clear indication for drug use	1 (0.3)
P2.6	No drug but clear indication	9 (3)
P3	Dosing problems	62 (15.6)
P3.1	Drug dose too low or dosage regime not frequent enough	6(2)
P3.2	Drug dose too high or dosage regime too frequent	35(11.6)
P3.3	Duration of treatment too short	6 (2)
P3.4	Duration of treatment too long	4(1.3)
P4	Drug use problems	42 (14)
P4.1	Drug not taken/administered at all	20 (6.6)
P5	Interactions	49 (16.3)
P5.1	Potential interaction	45(15)
P6	Others	70 (23.3)
P6.1	Patient dissatisfied with therapy despite taking drug(s) correctly	4 (1.3)
P6.2	Insufficient awareness of health and diseases (possibly leading to future problems)	71 (23.6)
P6.4	Therapy failure (reason unknown)	4(1.3)

The total of 300 DACs in type 2 diabetes mellitus with hypertension were identified in table.1 There was an average of 1.2 to \pm 1.9 problems and whereas 1.1 to \pm 1.7 causes per patient. A total 89 to 90% of patients had at least one DACs. The more often cause or category for DRPs is **Drug Choice Problems, Dosing Problems, Drug Usage, Interactions and Others.**

The most of drug choice problems were the results of inappropriate drug selection and the use of contraindicated drugs. A

total of **20 adverse reactions** were reported (Table 1). Antidiabetic drugs were associated with about one-third of all the cases. 7 patients suffered hypoglycemia secondary to either oral antidiabetic drugs or insulin. Tremor secondary to insulin was also recorded. The antihypertensive drugs that caused adverse reactions were **calcium channel blockers**, diuretics and ACEIs. It was reported that amlodipine had caused increased heart rate and bilateral leg

swelling, preidopril causes Electrolyte imbalances as adverse reactions and indapamide (hyponatremia). Also, steroids had been associated with two cases of ADRs. The inappropriate choice of antihypertensive drugs resulted in 23% drug choice problems. Eg, ACEIs were used in 4 patients with ESRD, blockers like prazosin and doxazosin were used as second or third addition therapies when other better alternatives were available and not contraindicated. Short-acting nifedipine was used in two elderly patients and spironolactone was prescribed to two renal impairment patients with creatinine clearances of less than 30 mL/minute. Followed by Aspirin causes severe renal impairment who have creatinin clearance less than 10mL/mint

The next drug metformin the mostly common drugs that prescribed in the presence of contraindications For instance, metformin was prescribed in 18 patients for whom it was contraindicated (e.g., creatinine clearance less than 30 mL/minute, more than 80 years old, or recent myocardial infarction).

Also, gliclazide was prescribed to 7 patients with severe liver impairment. simvastatin were not given to some of the patients as secondary prophylaxis of CVD. Of the 35 cases of inappropriate dosing

identified, most of the drugs were prescribed at a higher dose than required, particularly in patients with existing renal or liver impairments. The most common drugs that were involved in wrong dosages were H2-antogonists, antibiotics, antihypertensive agents, antidiabetic drugs and others. Ranitidine was commonly prescribed at a higher dosage than required in patients with creatinine clearances of less than 50 mL/minute.

Durations of treatment were too short in 6 cases whereas longer than required in four cases. Eg, oseltamivir (Tamiflu) was only given for three days for the treatment of H1N1 and oral azithromycin 500 mg was administered once daily that to empty stomach for six days..

In this study, the drugs most implicated in drug interactions were aspirin, clopidogrel ,simvastatin , amlodipine , omeprazole and iron salts.

About one-quarter of the DACs that could not be classified under any other category whereas they are categorized as “Others. The majority of patients had insufficient awareness of health and diseases which could possibly lead to future problems. For example, many patients had a lack of knowledge about T2DM. ¼ of the patients had at least one drug use problem and this

made up approximately 14% of all the DACs.

Conclusions:

In the patient's population of T2DM with hypertension the more commonly used were Amlodipine, Inulin and Simvastatin. And in these patients poly pharmacy and co-morbidities were common. The most common DACs were determined as "others" (i.e., lack of health and disease education or insufficient awareness of health and diseases), drug choice problems, dosing problems, and drug interactions. The most useful drugs were Aspirin, Clopidogrel, Simvastatin, Amlodipine and Metformin. Many factors were found to have statistically significant associations with the DACs, including renal impairment, cardiovascular disease, polypharmacy, elderly age, and duration of hospital stay. Therefore very special attention should be given to the T2DM patients with hypertension and the prescribed drugs are commonly responsible for maximum risk factors, hence keen observation and attention is needed before and after prescription of drugs for T2DM patients with hypertension.

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