ANTIHYPERTENSIVE DRUG UTILISATION PATTERN AMONG CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING MAINTENANCE DIALYSIS IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

BACKGROUND

The world is facing a global epidemic of Chronic Kidney Disease (CKD), a major threat to health in general because of an increasing incidence, high cost of treatment and poor outcome associated with various adverse events and comorbidities. Although improved control of hypertension is known to attenuate progression of Chronic Kidney Disease (CKD), a little is known about the adequacy of treatment of hypertension in patients with CKD in India.

AIM

To analyse the utilisation pattern of anti-hypertensive agents in patients with Chronic Kidney Disease in a tertiary care teaching Hospital.

MATERIAL AND METHODS

A descriptive prospective study was conducted in the Department of Nephrology, S. C. B. Medical College and Hospital, Cuttack, for a period of 6 months from 1st January 2015 to 30th June 2015. Relevant patient information, data regarding Anti-Hypertensive Drugs Utilization pattern entered in a preformed proforma in Microsoft Excel sheet for compilation and subjected to statistical analysis.

RESULTS

Total 100 case records were analysed. Mean age was 55.37 ± 13.41 years. Male-female ratio was 2.7. Maximum number of patients were from age group 51-60 years (43%) followed by age group 41-50 years (29%). All the patients (100%) were hypertensives, among which 42% patients of the study population were diabetic with hypertension and rest of the patients (58%) were non-diabetic with hypertension. Routinely prescribed anti-hypertensives are CCB, β blockers, diuretics, α blockers, ACEI and centrally acting sympatholytics. Among them, Calcium Channel Blockers (32.47%) were most frequently used followed by β Blockers (24.78%), Diuretics (23.50%), Centrally Acting Sympatholytics (10.25%), α Blockers (7.69%) and ACE Inhibitors (1.28%). Hypertension in CKD patients was very difficult to manage. Approximately, two-third of the patients (66%) had BP >140/90 mmHg with anti-hypertensive therapy. Targeted blood pressure control was present in (34%) of the patients.

CONCLUSION

Control of hypertension is poor in participants with CKD and that lack of control is primarily Systolic Hypertension. So a permutation and combination of various anti-hypertensive agents were used in CKD patients undergoing maintenance dialysis.

KEYWORDS

Chronic Kidney Disease, Hypertension, Anti-Hypertensive Drugs, Blood Pressure.

HOW TO CITE THIS ARTICLE: Abhisek PA, Panda R, Mohapatra J, et al. Antihypertensive drug utilisation pattern among chronic kidney disease patients undergoing maintenance dialysis in a tertiary care teaching hospital. J. Evolution Med. Dent. Sci. 2016;5(50):3207-3211, DOI: 10.14260/jemds/2016/744

INTRODUCTION

Drug utilisation study is defined as "the marketing, distribution, prescription and utilization of drugs in the society with special emphasis on the resulting medical, social and economic consequences" and has the main aim of facilitating the rational use of drugs, which is very important in decision making for healthcare.^[1]

Financial or Other, Competing Interest: None. Submission 05-05-2016, Peer Review 30-05-2016, Acceptance 06-06-2016, Published 23-06-2016. Corresponding Author: Dr. P. Ansuman Abhisek, Plot No. 23, Jaya Durga Nagar, Cuttack Road, Bhubaneswar-751006, Odisha. E-mail: ansumanabhisek123@gmail.com DOI: 10.14260/jemds/2016/744 Chronic Kidney Disease (CKD) is a worldwide health problem with adverse events, Cardiovascular Disease (CVD) and premature death.^[2] CKD is characterized by progressive loss of renal mass with irreversible sclerosis and loss of nephrons over a period of months to years, which depends on the underlying aetiology.^[3] Hypertension doubles the risk of cardiovascular diseases including Coronary Heart Disease (CHD), congestive heart failure, ischaemic and haemorrhagic stroke, renal failure and peripheral arterial disease.^[4] So, proper control of BP in hypertensive patients is a must to prevent poor outcome in CKD patients. The utilisation pattern studies are components of prescription auditing in health sector that monitors prescribing practices and commends required modifications to achieve rational drug use.^[5]

Hence, our study was designed keeping in mind that limited numbers of literatures accessible in prescribing

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various anti-hypertensives drug combinations to analyse current prescribing patterns in the management of CKD patients with hypertension and to suggest ways to rationalize drug use, minimise medication error and augment outcome therapeutically.

MATERIAL AND METHODS

A descriptive, prospective and hospital-based study was conducted in the Department of Nephrology in association with Department of Pharmacology in S.C.B. Medical College and Hospital, Cuttack, over a period of 6 months, i.e. 1st Jan. 2015 to 30th June 2015. After obtaining the clearance and approval from the Institutional Ethics Committee, 100 inpatients who gave informed consent were included in the study. The patients were diagnosed of having Chronic Kidney Disease by the consultant Nephrologist according to KDOQI guidelines. Clinical and biochemical parameters were collected at the time of admission and after 3 months.

Inclusion Criteria

Patients diagnosed as CKD stage (III-V) within the age group 18-78 having eGFR varies from 4-28 mL/min/1.73 m² undergoing haemodialysis for the 1^{st} time were included in the study.

Exclusion Criteria

- Terminally ill patients co-infected with HIV or Hepatitis or with any infective conditions or with any autoimmune diseases or continuing medications for the same.
- Patients with any sort of cardiac ailments (i.e., Coronary Artery Disease, Angina, Heart Failure, Arrhythmia).
- Patients with renal transplant.
- Patients less than 18 yrs.
- Pregnant and lactating women.
- Surgical conditions like kidney stone, tumours and trauma.

Demographic, clinical and medication details were collected from patients' case sheets in a specially designed proforma.

STATISTICS

Descriptive statistics is done by measuring different proportions. Statistical measurements were done in SPSS version 21.0. Before and after analysis was done by paired-ttest. Graphical representation was done in using Microsoft Excel.

RESULTS

A total of 100 case records of patients having chronic kidney disease (Stage III, IV, V) and on anti-hypertensive medications were compiled and interpreted. CKD was more prevalent in males 69 (69%) and 31 (31%) females with male-to-female ratio of 2.7:1. Most of the patients (43%) belonged to the age group of 51–60 years followed by (29%) in age group 41–50 years. Among the anti-hypertensive agents, most frequently prescribed was Calcium Channel Blockers (32.47%), in which Amlodipine was prescribed in 51 patients followed by Cilnidipine in 18 and Nifedipine in 07 patients. Second most frequently used anti-hypertensives were β blockers (24.78%) of which Metoprolol and Atenolol was prescribed in 44 and 13 patients respectively; Diuretics prescribed in 23.50% of case records included Torsemide, Furosemide, Metolazone in 28, 15 and 12 patients respectively. Among the α blocker Prazosin was prescribed in 18 patients and centrally acting drugs like Clonidine was prescribed in 24 patients. Angiotensin Converting Enzyme Inhibitors like Enalapril was prescribed in 3 patients.

DISCUSSIONS

Almost one billion people (26% approximately) of the adult population of the world are hypertensives.^[6] Both developed (333 million) and underdeveloped (639 million) countries are affected.^[7] The Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation defines CKD as either kidney damage and/or a decreased glomerular filtration rate of less than 60 mL/min/1.73 m2 for 3 months or more.^[8] Hypertension (HTN) and CKD is cyclic in nature and has been found to occur in 85% to 95% of patients with CKD (stages III-V).^[9] Hypertension increases the risk of various disorders like cardiovascular diseases including coronary arterial diseases, congestive heart failure, ischaemic and haemorrhagic stroke, renal failure and peripheral arterial disease.[4] Elevated blood pressure causes about 54% of CVA and 47% of ischaemic heart disease worldwide.[10] Lowering of systolic blood pressure by 10-12 mmHg and diastolic blood pressure by 5-6 mmHg converse relative risk reduction of 35-40% for stroke and 12-16% for CHD within 5 years of the initiation of treatment. Risk of heart failure is also lowered by >50%. So, proper control of blood pressure in hypertensive patient is a must to prevent many of its complications. Treatment with anti-hypertensive agents reduces the incidence of all types of cerebrovascular accidents by 38% in women by 34% in men, by 36% in older persons and by 34% in persons older than 80 years.[11] Hence, one of the main objectives in CKD patients is to maintain blood pressure in the range recommended in different guidelines and to reduce the progression of renal disease and reduce cardiovascular morbidity and mortality.^[12-14] To achieve and maintain adequate control on blood pressure, most of the patients with CKD require combinations of multiple anti-hypertensive agents.^[15]

Out of the 100 prescriptions evaluated, males were predominant in the study population which is in agreement with the results of various other studies.^[8] The (mean±SD) age of the patients was 55.37 ± 13.41 years with a range between 18 and 74 years. Average number of drugs per prescription was 9 ± 2.28 in the beginning of the study. The practice of polypharmacy is seen as in similar studies in CKD patients with average number of drugs per prescription varying from 8 to $12.^{[16,17]}$

Characteristics	
Mean Age (Years)	55.37±13.41
Gender	
Male	73 (73%)
Female	27 (27%)
Stages of CKD eGFR (mL/min/1.73 m) ²	
Stage v (<15)	71 (71%)
Stage iv (15-29)	24 (24%)
Stage iii (30-59)	5 (16%)
Co-morbidities	
Anaemia	86 (86%)
Hypertension	100 (100%)

U.T.I	38 (38%)			
Type II DM±Proteinuria	42 (42%)			
Glomerulonephritis	8 (8%)			
Chronic Obstructive Pulmonary Disease,	F(F0()) and			
Hypothyroidism, Metabolic Derangements	5 (5%) each			
Table 1: Demographic & Clinical Characteristics				



Fig. 1: Age Wise Distribution of Patients

Clinical Parameters	Mean±SD (Beginning of Study)	Mean±SD (After 3 Months)	T Value	Confidence Interval	P Value
Haemoglobin (gm/dL)	8.595± 2.171	10.451±1.538	-21.446	-2.027 to -1.684	0.000
Systolic Blood Pressure (mmHg)	168.92± 20.996	145.82± 13.994	11.872	19.239 to 26.961	0.000
Diastolic Blood Pressure (mmHg)	94.52± 7.578	89.44± 6.458	6.791	3.596 to 6.564	0.000
Serum Creatinine (mg/dL)	10.835± 4.223	7.639± 3.771	29.232	2.979 to 3.412	0.000
Plasma Urea (mg/dL)	117.89± 30.698	90.36± 29.772	30.072	25.714 to 29.346	0.000
Serum Sodium (mEq/dL)	136.04± 4.127	136.61± 2.538	-1.646	-1.257 to 0.117	0.103
Serum Potassium (mEq/dL)	4.99± 0.787	4.63± 0.553	9.326	.285 to .439	0.000
Table 2: Clinical and Biochemical Parameters					

Prescriptions Analysed	100
No. of different class of drugs prescribed	49
Average number of drugs per prescription in the	
beginning of the study during dialysis and non-	9.49±1.43
dialysis days approx.	
Average number of drugs per prescription after	
6 months of the study during dialysis and non-	6.92±1.10
dialysis days approx.	
No. of Anti-hypertensive agents	6 out of
in EDL 2014, State Odisha	11
No. of drugs prescribed by generic name	00
Table 3: Analysis of Prescriptions	

The target blood pressure in CKD patients should be maintained below 140/90 mmHg. High systolic pressure increases the myocardial work, while low diastolic pressure reduces myocardial circulation and increases the myocardial ischaemia leading to cardiovascular morbidity and mortality.^[18] Calcium Channel Blockers (CCBs) were most frequently prescribed anti-hypertensive drugs in our study

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corroborate with the study of Bailie GR et al^[5] followed by beta blockers (Metoprolol). Among the calcium channel blockers, Amlodipine followed by Cilnidipine and sustained release Nifedipine was most commonly prescribed and among the diuretics it is Torsemide. Cilnidipine though has its longer duration of action of 24 hours, also prevents reflex tachycardia as it selectively acts on both L and N type of calcium channels, still Amlodipine (L type of calcium channel blocker) was prescribed because of free supply by the Government of the State.



Fig. 2: Frequency of Anti-Hypertensive Agents Used



Fig. 3: Individual Classes of Anti-Hypertensive Agents among the Total Anti-Hypertensive Agents Prescribed in Patients of CKD



Fig. 4: Frequency of Individual Anti-Hypertensive: Prescribed in Patients with CKD

Torsemide was preferred over furosemide due to its longer duration of action and increased potency. Beta blockers were less commonly used in diabetics than in nondiabetic with hypertension, because of its known adverse effects in diabetic patients with hypertension because of its negative effect on lipid profiles and hypoglycaemic unawareness. Use of anti-hypertensive drugs such as selective beta blocker, alpha-blocker, CCB and/or other combinations more commonly used in non-diabetic than in diabetics. Beta blocker is preferred in haemodialysis patients due to overactivity of renin-angiotensin-aldosterone system, increased levels of sympathetic activity in haemodialysis patients. Beta blockers have been suggested to be cardioprotective in haemodialysis patients.^[19] But beta blockers are underutilized in type 2 diabetes mellitus cases because of some expected side effects.

In chronic kidney disease, hyperkalaemia is more likely to develop when Angiotensin Converting Enzyme (ACE) inhibitors or Angiotensin Receptor Blockers (ARBs) are prescribed. Unlike CCBs, most of the ACE inhibitors need dose modification in renal failure. Positive results were found primarily in patients with proteinuria, whereas the benefit was less substantial for those without proteinuria. That is the reason probably ACE inhibitors or ARBs were underutilized. One systemic review.^[20] showed that ACE inhibitors or ARBS are very fruitful in CKD grade 1-3 patients, which reduces the ESRD risk. Though most of the patients in our study are CKD stage 5, so prescribing ACE inhibitors and ARBs seems illogical.

Centrally acting Anti-Hypertensives lowers BP without compromising the renal blood flow or glomerular filtration rate.^[8] Sympathetic overactivity is commonly seen in chronic kidney disease and is an important contributor to increasing the risk of cardiovascular events as well as increasing renal disease progression. Many of these agents were orally administered, but in some patients diuretics were also administered by parenteral route.

Blood Pressure	No. of Patients at Time of Admission	% Tage	No. of Patients after 3 Months	% Tage
<130/80	0	0%	11	11%
<140/90- 130/80	5	5%	23	23%
<150/90- 140/90	19	19%	39	39%
>150/90	76	76%	27	27%
Table 4: Control of Blood Pressure in Patients Before and After 3 Months				

The degree of control in blood pressure is shown in Table 1. Control of hypertension in CKD patients was difficult to bring under control. More than two-third of the patients (66%) had BP >140/90 mmHg. About one-third of the patients (34%) had BP control <140/90 mmHg. Intensive BP control was present in around one-tenth of total patients (11%). Despite more efforts with use of more anti-hypertensive agents (2.34±0.81 and 2.93±1.20 vs 1.33±0.50) uncontrolled group had BP >140/90 mmHg in comparison to intensive control group with BP <130/80 mmHg.

Constancy to established target of blood pressure is low for participants with CKD in spite of growing evidence that control of hypertension can slow the decline in GFR, reduce proteinuria and reduce the incidence of cardiovascular complications in CKD.^[21-25] Because the CKD population is characterized by wide pulse pressure and isolated systolic hypertension, more aggressive expeditions focusing on systolic hypertension in this population are necessary and the role of vascular stiffness in the treatment of hypertension in CKD should be evaluated.

CONCLUSION

Data of a total of 100 prescriptions pertaining to CKD patients were analysed. Anti-hypertensive agents have been employed with various permutations and combinations among the dialysis patients. The prevalence of CKD was higher in males. The preferential drugs employed among anti-hypertensives were calcium channel blockers, β blockers, diuretics, centrally acting anti-hypertensives and ACE inhibitors. It provides a framework for continuous prescription audit in a hospital-based setting and suggests possible improvement in prescription practices in patients suffering from chronic kidney disease.

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