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Pattern of Utilization of Anti-Hypertensive Drugs Among Patients With Chronic Kidney Disease Undergoing Maintenance Haemodialysis at a Tertiary Care Hospital of Southern Part of West Bengal

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ABSTRACT

In the present world, Chronic Kidney Disease (CKD) has become a major threat to patients worldwide due to several associated co-morbidities, which renders the use of polypharmacy in these patients. Antihypertensive drugs are prescribed for managing high blood pressure, which is the leading cause of mortality in patients with CKD undergoing maintenance hemodialysis. However, very little information is available regarding proper treatment and drug utilization patterns of hypertension in CKD patients in India. The objective of our study is to study the utilization pattern of antihypertensives in patients suffering from chronic kidney disease undergoing maintenance hemodialysis in a tertiary care teaching hospital. This is an observational prospective hospital-based study conducted at Jagannath Gupta Institute of Medical Sciences and Hospital, Budge Budge, South 24 Parganas, West Bengal from 1st May to 31st October 2020. The data was collected from the prescriptions and bedhead tickets of the patients regarding patient details, antihypertensive and other drugs utilized during treatment, relevant vital parameters and biochemical reports. The data was compiled in Microsoft Excel and the result was expressed as Mean ± Standard deviation. Based on the calculated sample size, a total of 100 prescriptions were analyzed. The study population had male predominance (72%), with a mean age of 48.37±17.41 years. Most of the patients belonged to the age group 41-60 years (71%) followed by those within the age group 61-80 years (21%). All the patients in the study were hypertensive (100). Most of the patients were suffering from Stage 5 (eGFR<5ml/min/1.73m^2) chronic kidney disease (68). All the patients were being prescribed Anti-hypertensive drugs, Haematinics, Proton pump inhibitors, Antibiotics, anti-emetics and 25% Dextrose. Among the anti-hypertensives, Calcium channel blockers (82%) were most commonly used, followed by Beta-blockers (60%), Loop diuretics (55%) and Central sympatholytics (46%). Blood pressure control (<140/90mm Hg) was achieved in 17% of patients, whereas 83% of patients had BP >140/90mm Hg after 6 months of treatment given in the prescriptions analyzed. The pattern of prescription of anti-hypertensive drugs in patients suffering from hypertension associated with advanced stages of Chronic Kidney Disease (undergoing maintenance dialysis) requires rationality during prescribing. Both positive and negative effects of such drugs should be kept in mind before prescription.

OPEN ACCESS

Key Words
Chronic kidney disease, anti-hypertensive drugs, drug utilization pattern

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INTRODUCTION

Drug utilization pattern study is known as "marketing, distribution, prescription, and utilization of drugs in the society with special attention to the resulting medical, social and economic consequences". Its main objective is facilitating the rational use of drugs for proper decision-making in healthcare setup[1]. The study of drug utilization is required continuously over some time, as it changes with the time period, prescribing physicians, disease conditions, and population[2]. Chronic kidney disease (CKD) is a worldwide prevalent non-communicable disease that is responsible for rising mortality and morbidity also in India[3]. According to the World Health Organization, CKD contributes to approximately 850000 deaths per year throughout the world[4]. It is characterized by progressive loss of renal mass along with irreversible renal sclerosis and loss of nephrons over months to years depending on the underlying etiology[5]. The patients suffering from CKD present with many associated co-morbidities like hypertension, diabetes mellitus, coronary artery disease and infections[6,7]. These co-morbidities pose a challenge for the treatment of patients with CKD. They not only increase the risk of developing drug-related adverse reactions due to inappropriate polypharmacy but also cause prolonged hospital stays and increased economic burden on the patient[8]. With an increasing number of such co-morbidities especially among the age groups of middle and elderly patients, hemodialysis has become the mainstay of treatment for patients who develop end-stage renal disease (ESRD)[9].

In patients with ESRD undergoing maintenance hemodialysis, hypertension is one of the leading causes of mortality[10]. Hypertension doubles the risk of cardiovascular diseases including coronary artery disease, congestive heart failure, cerebrovascular accidents (ischemic and hemorrhagic) and peripheral arterial disease[11]. So adequate control of BP in such patients is very important to prevent poor outcomes of their CKD. The practice pattern of anti-hypertensive medication may be variable in CKD patients undergoing chronic hemodialysis, as it may interfere with the pharmacokinetic properties of the drugs[12]. So the utilization pattern and prescribing trends of these drugs in CKD patients need to be studied regularly[4]. However, there is very little evidence on the prescribing trends of antihypertensive drugs in CKD patients from India[13,14]. Keeping that in mind, the objective of our study is to study the utilization pattern of various antihypertensive drugs (used either single or in combination) and try to explore the ways of using them rationally with proper therapeutic outcomes and minimal medicational errors.

MATERIALS AND METHODS

This observational, prospective hospital-based study was conducted at Jagannath Gupta Institute of Medical Sciences and Research, Budge Budge, South 24 Parganas from 1st May 2020-31st October 2020 (6 months) after obtaining approval from the institutional ethical committee. The study involved the collaboration of the Department of Pharmacology and the Department of Nephrology.

Sample Size Calculation: The sample size was calculated based on the approximate population of India suffering from some form of CKD (10%)[15]. Using an epidemiological calculator (with an estimation error of 10% and a 95% confidence interval), 97 patients were required for the study. To avoid any error in follow-up, 100 patients were selected for the study based on inclusion and exclusion criteria.

Inclusion Criteria: All patients (both males and females) between the ages 18-80 years age suffering from chronic kidney disease (Stage 3-Stage 5) having estimated Glomerular Filtration Rate (eGFR) of 4-28 mL/min/1.73m^2 diagnosed by the Nephrologist and undergoing maintenance hemodialysis for the first time were included in the study.

Exclusion Criteria:

- Patients not giving consent to participate in the study
- Terminally ill Patients (associated with HIV, hepatitis, or any infective conditions, with any autoimmune diseases or undergoing medications for the same)
- Patients having renal transplants
- Patients less than 18 years old
- Patients having cardiac co-morbidities like Angina, Cardiomyopathies, Arrhythmias, or Valvular heart diseases
- Pregnant and lactating women
- Patients suffering from Surgical conditions like kidney stones, tumors, and trauma

Data Collection and Statistical Analysis: The prescriptions, case records and investigational reports of the patients under study were evaluated. Demographic, clinical and laboratory findings (e.g. hemoglobin, serum urea, creatinine, sodium, potassium and phosphorus) and medication details were collected from the patient's case sheets in a pre-designed, pre-validated data collection proforma. From the collected data, the parameters like the average number of drugs per prescription, utilization of

different classes as well as individual drugs were analyzed using percentage calculation. The results were expressed as Mean±standard deviation.

RESULTS AND DISCUSSIONS

Based on sample size calculation along with inclusion/exclusion criteria, prescriptions of a total of 100 patients were analyzed, whose mean age was calculated as 48.37±17.41 years within the range of 18-80 years of age. Among the patients, there was male predominance (72%) compared to females (28%) (Fig. 1). Most of the patients belonged to the age group 41-60 years (71%) followed by those in the age group 21-40 years (21%) (Fig. 2). Most of the patients were suffering from Chronic Kidney Disease Stage V (68%), followed by those suffering from Stage IV (26%) (Table 2). The patients were suffering from several co-morbidities, out of which hypertension were common in all of the patients (100%), followed by anemia (78%) and Urinary tract infection (55%). Some patients were found to be suffering from 3-4 co-morbidities together (Table 1). On analysis of 100 prescriptions, the total number of different drugs prescribed was 49. None of the prescriptions had drugs written in generic names. The average number of drugs per prescription during dialysis and non-dialysis days was 11±2.12, which was reduced to 6.34±0.45 after 6 months of the study.

Among all patients, the most common group of drugs used in all patients were Anti-hypertensives followed by Diuretics, Antibiotics, Haematinics, Multivitamins and multimineral, Proton pump inhibitors and Cytoprotective agents, anti-emetics, fluids (25% Dextrose) and Anticoagulants (Fig. 3). Out of all antihypertensives, the group most commonly used was Calcium channel blockers/CCBs (82%), followed by Beta-blockers (60%) and Loop diuretics (55%) (Fig. 4). Talking about individual drugs, the most commonly used was Clonidine (46%) which is a Central sympatholytic, followed by Cilnidipine (44%) which is a Calcium channel blocker and Metoprolol, a Beta blocker (Fig. 5) The average Blood Pressure of all the patients was measured during the admission of the patient before the initiation of hemodialysis. It was measured regularly throughout the study i.e. 6 months. Significant improvement in blood pressure was seen in most of the patients at the end of the study period (Table 4). Similarly, some other laboratory parameters (Hemoglobin, Serum Sodium, Potassium, Urea, Creatinine, and Phosphorus) were estimated at the beginning of the study before the initiation of the maintenance hemodialysis. They also showed significant improvement after being estimated at the end of the study period of six months (Table 3).

Out of 100 patients in the study, there was male predominance (72%) compared to females (28%). This is nearly similar to a few other earlier studies[16,17]

Table 1: Associated co-morbidities

Co-morbidity	Patients
Anaemia	78 (78%)
Hypertension	100 (100%)
Urinary Tract Infection	55 (55%)
Type2 diabetes mellitus and proteinuria	48 (48%)
Heart failure	9 (9%)
Glomerulonephritis	8 (8%)
COPD, Asthma, Hypothyroidism, Metabolic encephalopathy	5 (5%) each

Table 2: Percentage of patients in different stages of CKD

Stages of CKD	No. of patients and percentage
Stage-V	68
Stage-IV	26
Stage III	6

Table 3: Mean value of biochemical parameters at the beginning and end of the study

	Mean±S.D (beginning of study)	Mean±SD (after 6 Months)
Hemoglobin (gm/dl)	6.9±1.22	9.3±1.76
Serum creatinine(mg/dl)	13.18±3.17	9.0±3.01
Plasma urea (mg/dl)	156.37±14.26	124.31±16.07
Serum sodium (meq/dl)	140±6.74	136±6.76
Serum Potassium (meq/dl)	6.24±1.49	5.4±1.71
serum phosphorous (mg/dl)	6.21±1.41	5.72±1.26

but unlike an earlier study by Karmakar *et al*[18], which had female predominance. In our study, the patients included were those suffering from end-stage renal disease undergoing maintenance dialysis. The average age of the patients is around 49 years, with the majority of the patients belonging to the age group 41-60 years, which is nearly comparable to a study conducted by Bajait *et al*[19]. The commonest co-morbidity in all the cases was Hypertension (100%) followed by anemia (78%), which shows a similarity to studies like Al-Ramahi *et al* and Abhishek *et al*[9,20]. The average number of drugs per prescription was 11±2.12 at the beginning of the study, which shows the similarity with some other studies where the average number of drugs per prescription in CKD patients ranges between 8 to 12.8[9,19,21,22]. This practice of polypharmacy (prescribing five or more drugs to one patient at a single time) is common in patients with CKD due to associated co-morbidities[23]. The commonest drug prescribed to all the CKD patients in this study was antihypertensives, which is similar in some other studies[21,24]. Among the anti-hypertensive drugs, the most commonly used were calcium channel blockers (82%) followed by beta-blockers (60%) and Loop Diuretics, which have also been found to be similar in a few other studies[13,21]. On the contrary, some studies have shown that Loop diuretics were most prescribed in such patients followed by CCBs[8, 19,25].

Among the CCBs, the most commonly prescribed was Cilnidipine, followed by Amlodipine and Nifedipine. This is because Cilnidipine has a longer duration of action compared to the other two drugs. Amongst Beta blockers, the most commonly used was Metoprolol, followed by Atenolol. Furosemide was the most common Loop diuretic used followed by

Table 4: Number percentage of patients with blood pressure control

BP control (mm hg)	No of patients at time of admission	Percentage	BP control (mm hg)	No of patients at time of admission	Percentage
<130/80	0	0	<130/80	5	5
<140/90 – 130/80	4	4	<140/90 – 130/80	12	12
<150/90-140/90	11	11	<150/90-140/90	30	30
<160/90 – 150/90	27	27	<160/90 – 150/90	25	25
>160/90	58	58	>160/90	28	28

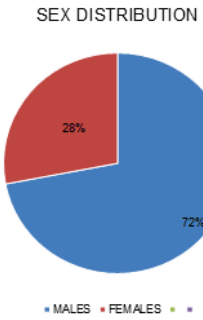

Fig.1: Sex distribution of the patients

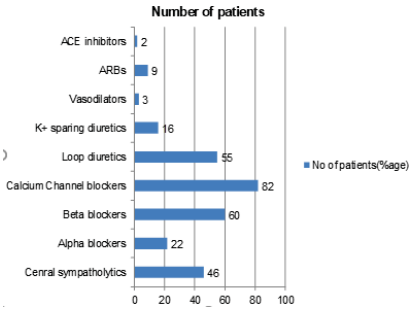

Fig. 4: Classes of anti-hypertensive drugs taken by the percentage of patients

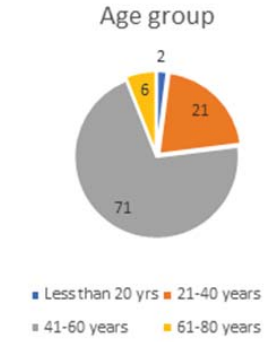

Fig.2: Age group distribution of the patients

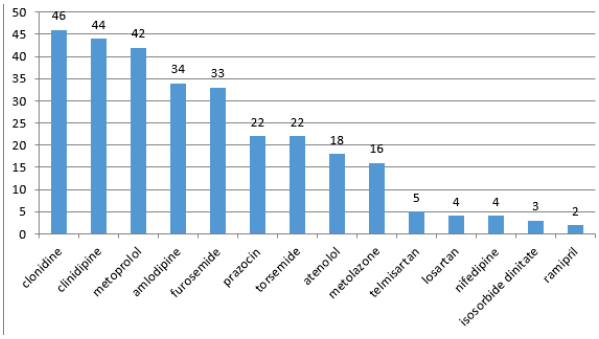

Fig. 5: Individual types of anti-hypertensive drugs taken by the percentage of patients

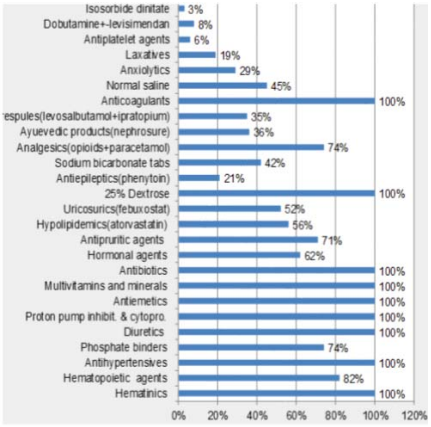

Fig. 3: Types of drugs taken by the percentage of patients

Torsemide, though the latter has higher bioavailability and prolonged half-life compared to the former. Beta-blockers are found to be cardio-protective for hemodialysis patients by reducing the over-activity of the RAAS system and reflex sympathetic over-activity [26]. However, they are avoided in dialysis patients suffering from both hypertension and Type 2 DM as they may cause masking of the hypoglycemic symptoms and negative effects on serum lipid profiles. ACE Inhibitors or ARBs may lead to hyperkalemia in CKD patients. They are more effective in patients with CKD stages 1-3 for reducing the risk of ESRD[27]. However, most of the patients in our study had CKD stage 5, which rendered the ineffectiveness of ACE Inhibitors or ARBs in these patients. In patients with CKD undergoing maintenance dialysis, the target blood pressure should be <140/90mm of Hg, because higher systolic BP leads to increased myocardial workload, whereas low diastolic BP causes increased myocardial ischemia by decreasing the myocardial circulation[28]. At the beginning of this study, only 3% of the study population had BP control of <140/90mm Hg, whereas at the end of 6 months, 17% of the population had BP

control up to <140/90mm Hg. Control of hypertension in CKD patients can reduce cardiovascular complications and proteinuria and prevent a decline in eGFR[29-32].

CONCLUSION

The above study provided a utilization pattern of antihypertensives in patients suffering from CKD and undergoing maintenance hemodialysis. Among 100 patients, most of them were males and the majority of the patients were suffering from Stage 5 CKD. The most common drugs used were Calcium Channel blockers, Beta-blockers, Central Sympatholytics and loop diuretics. There was minimal improvement in BP control and biochemical parameters in most of the patients following the pattern of drug usage seen in the study. This study may help in improving the prescribing pattern of drugs in patients suffering from co-morbidities associated with existing chronic kidney disease in those patients.

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