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Antihypertensive Utilization Study in Patients Undergoing Hemodialysis- in A Tertiary Care Hospital in South Delhi

KEYWORDS: Cyclophosphamide, kidney, peroxisomes, ROS generating enzymes

Razi Ahmad
Department of Pharmacology, HIMSR, Jamia Hamdard, New Delhi, Corresponding author

Anwar Habib
Department of Medicine and Head dialysis unit, HIMSR, Jamia Hamdard, New Delhi.

Sana Rehman
Department of Pharmacology, HIMSR, Jamia Hamdard, New Delhi

Zabeena Saeed
MBBS student, HIMSR, Jamia Hamdard, New delhi

ABSTRACT *Introduction: Chronic kidney disease is a worldwide public health problem with an increasing incidence and prevalence, the scenario of this condition in India is worst for patients and their families due to medical, social and economic problem. Most of the patient on hemodialysis suffers from multiple comorbidity and needs multiple drug that predispose these patients to develop complication leading to morbidity and mortality due to drug-drug interaction.*

The aim of present study was to find out the commonly prescribed medications and to suggest possible solution to avoid drug related complications.

Material and methods: this prospective drug utilization study was conducted on the patients who were on regular hemodialysis therapy in HAHC hospital, they were regularly observed for the drugs they were taking and their efficacy and complications were recorded and possible preventive measures where needed were suggested.

Result: The average number of drugs per prescription was found to be 6.88, antihypertensive agents topped the category with 1.71 per prescription followed by vitamins 1.06, calcium phosphate analogues 0.82, erythropoietin 0.76 and antiulcer drugs having 0.65 per prescription.

Conclusion: calcium channel blocker either alone or in combination of clonidine and/or furosemide were the most commonly used and effective medication for the control of blood pressure in patient on hemodialysis with minimum complications.

Introduction

Chronic kidney disease (CKD) is a progressive loss in kidney function over a period of months or years. CKD is an internationally recognized public health problem affecting 5 to 10% of the world population [1,2]. Cardiovascular diseases are the leading cause of morbidity and mortality in the patients of end stage renal disease (ESRD) leading to hemodialysis. Despite the advances in dialysis therapy the morbidity and mortality from cardiovascular diseases in these patients remains substantially unchanged. Hypertension is both a cause and a consequence of chronic kidney disease and the adequate control of blood pressure is equally difficult that increases the risk of development of left ventricular hypertrophy, congestive heart failure, stroke and other cardiovascular and neurological complications. In a meta-analysis of randomized controlled trials of antihypertensive therapy in hemodialysis patients, blood pressure lowering treatment was associated with a 29% lower relative risk of cardiovascular mortality and a 20% lower relative risk of all-cause mortality [3]. The causes of rise in the blood pressure in these patients are multifactorial such as inappropriately high renin secretion, over activity of sympathetic nervous system, alteration in endothelin and nitric oxide, positive sodium balance due to increased intake, decreased excretion and hypertonic dialysate increasing interdialytic thirst [4]. The uremic metabolites activating chemoreceptors within the kidney, Erythropoietin therapy, and hyperparathyroidism [5,6] are the other causes. In developing countries the high cost of dialysis therapy and the scarcity of state funded health facilities are responsible for inadequate hemodialysis leading to inappropriately high weight gain (fluid accumulation) during interdialytic period and poor control of blood pressure.

Drug utilization study: According to WHO, Drug utilization study is defined as "the marketing, distribution, prescription and use of drugs in society with special emphasis on the resulting medical, social and economic consequences" (WHO, 1977). It is a onetime study to assess the appropriateness of drug therapy. These types of studies are useful for implementation of the rational use of drugs among population in both private and public healthcare. It is important to realize that inappropriate use of drugs represent a potential hazard to the patients along with an unnecessary expense.

Process of drug utilization review: The drug utilization study is grouped into (a) The retrospective drug utilization review where the data on prescribing and dispensing of drugs are evaluated after the drug has been dispensed in a given health care environment (b) the Prospective drug utilization study, evaluates data on drug prescribing and / or dispensing prior to prescribing and dispensing in a given health care environment and can directly influence patient's treatment outcome and (c) Concurrent drug utilization review, evaluates data on prescribing and use of drugs during the course of treatment and involves the ongoing monitoring of drug therapy, that can influence the course of drug therapy [7].

Material and Methods

The study was conducted at dialysis unit of Hakeem Abdul Hameed Centenary Hospital, Jamia Hamdard, New Delhi, India after the approval of IRB (meeting held on July 27, 2016 (13/16). It was a single centered prospective observational study conducted between 1.03.2016 to 30.9.2016 2016 (six months)

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This was an observational prospective drug utilization study on the patients undergoing hemodialysis for chronic renal failure and taking antihypertensive drug. The study population ware the patients attending dialysis unit of HAHC hospital.

Inclusion criteria: All the hypertensive patients of chronic renal failure, will be included in the study (after taking informed consent)

Exclusion criteria: Patients not taking antihypertensive medication will be excluded from the study.

Data Collection

A case record form (CRF), was designed and reviewed by an expert panel, and was pre-tested on 20 patients and was scaled up for study. The data were collected using various data sources as OPD record and dialysis unit record. Relevant clinical information were retrieved through personal interview of patient, patient's attendant, Medical prescribing records, patient's medication profile/treatment chart and Laboratory investigation reports (if available). Informed consent was taken from the patient prior to data collection.

Results

Patient characteristics: out of total 48 patients undergoing hemodialysis 42 (83.33%) were hypertensive and thus enrolled for the study but 40 were followed and completed the study because one patient died during the study period due cardiovascular complications and one left the study due to change of residence. Among the study population 30 (75%) patients were male and 10 (25%) were female, the maximum number of patients were from the age group 41-60 years (60%) followed by the patients of age group 21-40 years (20%) (Table-1).

Table No.1: Age & gender distribution of hemodialysis patients.

Age (years)	Male	Female	Total No. of patients
< 20	0	2	2
21– 40	6	2	8
41 – 60	20	4	24
>60	4	2	6
Total	30	10	40

The body mass index (BMI) of majority of patients were <18.5 (70%) only 20% patients were having BMI within normal limit whereas 7.5% were overweight and 2.8% were obese (Table-2).

Table No.2: Body Mass Index (BMI) of hemodialysis patients.

BMI	Male	Female	Total	% of Patients	Remarks
< 18.5	22	06	28	70	Under weight
18.5 – 25	06	02	08	20	Normal range
25 – 30	02	01	03	7.5	Over weight
>30	00	01	01	2.5	Obese
Total	30	10	40		

The frequency of hemodialysis: The majority of the patients in our study were receiving dialysis therapy twice per week (70%) whereas only 255% were undergoing alternate day dialysis and non-receiving daily dialysis (Table-3).

Table No.3: Frequency of dialysis per week.

Frequency of dialysis per Week	Number of patients	(%) of patients
Less than Once / week or SOS	0	0
Once / week	2	5
Twice /week	28	70
Alternate day (3 times / week)	10	25
Daily	0	0

Primary cause of ESRD leading to dialysis: The most common primary etiology for ESRD leading to dialysis was patient suffering from both diabetes and hypertension 30% followed by hypertension alone 25% and drug induced 1% (Table- 4).

Table No.4: Primary cause of ESRD leading to dialysis.

Primary cause	Number of patients	%
Hypertension	10	25
Diabetes mellitus	4	10
Diabetes mellitus with hypertension	12	30
Smoking	2	5
Drug intake	6	15
Trauma	2	5
Kidney infection	2	5
Others/Unknown etiology	2	5

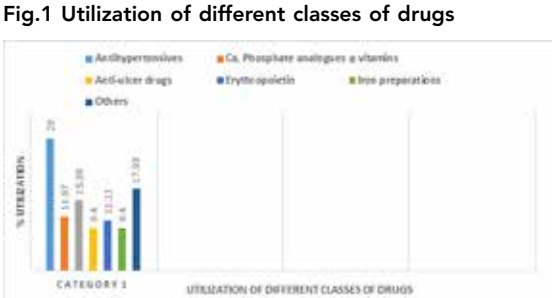
Chronic comorbidity in dialysis patients: Among the presence of co-morbidity, hypertension topped the list (50%) followed by hypertension with diabetes mellitus (40%) and coronary artery disease and hepatitis-B 5% each. (Table-5).

Table No.5: Chronic comorbidity in dialysis patients.

Co-morbid conditions	Number of patients	% of patients
Hypertension only	20	50
Hypertension with Diabetes mellitus	16	40
Hypertension with Cardiovascular disease	2	5
Hepatitis-B	2	5

Category of drugs prescribed: The average number of drugs per prescription was found to be 6.88, antihypertensive agents topped the category with 1.71 per prescription followed by vitamins 1.06, calcium phosphate analogues 0.82, erythropoietin 0.76 and antiulcer drugs having 0.65 per prescription (Fig.1)

Fig.1 Utilization of different classes of drugs



Pattern of antihypertensive agents prescribed: out of total 48 patients receiving hemodialysis 40 were (83.33%) were having high blood pressure and taking antihypertensive medication. Calcium channel blockers (Amlodipine) were the most frequently prescribed agent (72.5%) in the patients on hemodialysis. Amlodipine with clonidine were

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commonest combination (22.5%) followed by Amlodipine + Clonidine + Prazosin combination and Clonidine + Furosemide/Torsemide (15% each) (Table-6).

Table No.6: Pattern of antihypertensive agents prescribed.

Antihypertensive drug / combination of drugs	Number of patients	(%) of patients
Amlodipine	3	7.5
Furosemide/Torsemide	2	5
Amlodipine + Furosemide/ Torsemide	4	10
Clonidine + Furosemide/ Torsemide	6	15
Amlodipine + Clonidine	9	22.5
Amlodipine + Clonidine +Furosemide	5	12.5
Amlodipine + Clonidine + Prazosin	6	15
Amlodipine + Clonidine + Carvedilol	1	2.5
Clonidine + Prazosin + Furosemide	2	5
Amlodipine + Prazosin + Furosemide	1	2.5
Moxonidine + Prazosin + Minoxidil	1	2.5

Intradialytic complications: out of total 40 study patients 27 (67.5%) developed some complications during their dialysis therapy sessions, muscle cramps ranked first (40%) followed by somnolence and shivering 27.5% each (table-7)

Table-7: Common intradialytic complications and their relationship with antihypertensive medications:

Drugs prescribed	no. of patients	Nausea/ Vomiting	Somnolence	Cramps	Shivering	Hypotension	None
Amlodipine	3	-	-	-	-	-	3
Furosemide/Torsemide	2	-	-	-	-	-	2
Amlodipine + Furosemide/Torsemide	4	-	-	-	-	-	4
Clonidine + Furosemide/ Torsemide	6	2	4		4	2	2
Amlodipine + Clonidine	9	2	4	8	2	3	-
Amlodipine + Clonidine +Furosemide/ Torsemide	5	2	2	4	4	2	1
Amlodipine + Clonidine + Prazosin/Tamsulosin	6	-	-	3	1	1	1
Amlodipine + Clonidine + Carvedilol/Labetalol	1	-	-	1	1	-	
Clonidine + Prazosin + Furosemide	2	-	1		1	-	1
Amlodipine + Prazosin + Furosemide	2	-	-	-	-	1	-

Efficacy of the drug combination: the average blood pressure control in all phases of dialysis (inter-dialysis, predialysis and post dialysis) were best provided by a combination of amlodipine with Furosemide/Torsemide followed by a combination of Amlodipine + Clonidine+ Furosemide/Torsemide (table-8).

Table-8: Efficacy of the drug combination prescribed in controlling systolic and diastolic blood pressure.

Drug(s)prescribed	Average pre dialysis BP (in mm Hg) (systolic / diastolic)	Average post dialysis BP (in mm Hg) (systolic/ diastolic)	Average interdialytic BP (in mm Hg) (systolic/diastolic)
Amlodipine	140/86	126/84	112/70
Furosemide/Torsemide	138/74	132/76	122 /78
Amlodipine + Furosemide/Torsemide	130/78	124/76	122 /76
Clonidine + Furosemide/Torsemide	132/72	130/80	124/74
Amlodipine + Clonidine	148/88	160/80	140/80
Amlodipine + Clonidine +Furosemide/Torsemide	142/84	134/76	136/76
Amlodipine + Clonidine + Prazosin/ Tamsulosin	152/84	130/76	126/70
Amlodipine + Clonidine + Carvedilol/Labetalol	180/90	160/70	166/82
Clonidine + Prazosin + Furosemide	144/90	136/72	138/98
Amlodipine + Prazosin + Furosemide	160/100	150/90	158/80
Moxonidine + Prazosin + Minoxidil	160/120	140/90	160/90

Discussion

The mean age of patient in our study was 42.94 ± 15.97, the previous Indian studies reported 47.4 ± 14.9 years (Rizvi et al -2002) and 46.5 ± 16.5 years (Vikrant et al 2004) this indicates that the trend of chronic kidney disease is shifting towards affecting the peoples of younger age group this may be because of adaptation of some unhealthy life style that is responsible for some primary dis-

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eases like hypertension and diabetes mellitus leading to early development of its complication including chronic kidney disease. The average age of development of end stage renal disease (ESRD) and need of renal replacement therapy is much lower in India compare to other countries (Dordevic et al 1999 reported 54.6±12.2 years in Serbia and Bailie et al 2005 reported 60.6 ± 16.0 years in USA). Males predominates the study population which is similar to that reported in other studies (Vikrant et al 2004, Dash et al 2006 and Alebiosu et al 2006) but this study also finds that the chances of developing ESRD in male is almost equal in both age group of 21 to 40 and 41 to 60 but in women the most vulnerable age group is 41 to 60 years.

The most common primary cause of chronic kidney disease leading to ESRD in our study was hypertension followed by diabetes mellitus which was found to be similar as reported in other Indian studies (Modi et al 2006 and Tozawo et al 2007) but we also found a significant number (11.11%) of patient where the cause of ESRD was obstructive nephropathy.

In the present study we found that all CRF patients undergoing hemodialysis were suffering from 2-4 comorbid diseases and the mean number of medications prescribed per prescription was 6.88, the medication prescribing pattern in the study hospital dialysis unit showed that antihypertensive agents were the most prescribed drugs followed by erythropoietin, calcium phosphate analogues, vitamins and iron preparations and anti-peptic ulcer drugs, earlier large studies also shows the similar result which indicates that hyperphosphatemia, renal anemia and hypertension are the common problems in hemodialysis patients during the past few decades. Gastrointestinal symptoms are common in patients with CRF, delayed gastric emptying might be a possible pathological mechanism (Strid et al 2004) leading to the use of anti-peptic ulcer drugs.

Treatment of hypertension in hemodialysis patient: treatment of hypertension is a major issue in the patient undergoing hemodialysis, in our study although all hypertensive patients were receiving antihypertensive drugs yet their blood pressure was high. One reason for poor blood pressure control could be the failure to maintain optimal dry weight as in our study 36.8% of patient were achieving on average 3 Kg, 41.7% were achieving 4 Kg, 7.1% were achieving 6 Kg interdialytic weight only 14.2% were achieving 2 Kg interdialytic weight, the most important reason of this very high interdialytic weight gain was less frequency of hemodialysis (Twice or once per week) for cost cutting and poor compliance of the patients. Data from HEMO study suggest that interdialytic weight gain requiring ultrafiltration of >2.5L per treatment may be associated with hypertension (Rocco et al., 2001). In the present study although we found that amlodipine based combination therapy provides better control of blood pressure in the patients on hemodialysis but most of these patients suffers from intradialytic complication which may be related to these drugs so a long-term study with larger sample size is needed to find out the solution of these problem that can improve quality of life in these patients with increased productivity.

Conclusions

Hypertension is both a cause and a consequence of end stage renal disease leading to dialysis and its management is equally difficult because of inadequate dialysis especially in developing countries like India due to financial problem leading to huge fluid accumulation in interdialytic period that makes the calcium channel blocker (Amlodipine) based combination therapy as chief and effective measure to control blood pressure in these patient. Further study with relatively bigger sample size and long-term study is needed for any comment on long-term morbidity and mortality parameters.

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