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IJPBS |Volume 5| Issue 1|JAN-MAR|2015|72-78

Research Article
Biological Sciences

DRUG UTILIZATION STUDY IN HEMODIALYSIS UNIT IN A TERTIARY CARE CENTRE IN KOLAR

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ABSTRACT

Objective: To assess the prescribing pattern in patients undergoing hemodialysis. Materials and methods: A cross-sectional study was conducted in patients undergoing hemodialysis at R.L.Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Kolar from April to September 2013. The demographic details like age, gender, body weight, biochemical and hematological test values and details of drugs administered were recorded as per predesigned proforma. The observations were expressed as percentage. Results: Data of eighty three patients were analyzed of which 66 were males (79.5%) and 17 females (20.5%). The mean age was 58.61 ± 5.91 and 53.62 ± 4.45 respectively. Mean systolic and diastolic blood pressure were 152.65 ± 15.23 and 88.55 ± 5.44mm Hg respectively. Before hemodialysis the levels of hemoglobin were 7.98 ± 1.74gm/dl, blood urea 100.57 ± 34.93mg/dl and serum creatinine 7.31 ± 2.74mg/dl. Co-morbid conditions were hypertension (75.9%), diabetes mellitus (40.9%), nephropathy (12%) and ischemic heart disease (10.8%). Hemodialysis was carried out twice weekly. On an average, one patient received 5.8 ± 2.5 drugs per day. Most commonly used drugs were anti-hypertensive (75%), calcium salts (71%), phosphate binder-calcium acetate (64%), iron preparations (61%) and erythropoietin (53%). Most frequently used anti-hypertensive was metoprolol. The common adverse event was nausea (14%). Conclusion: Multiple drug use was observed in hemodialysis patients. Most of the patients received five drugs per day, which reflects existence of co-morbid conditions in hemodialysis patients. Precaution should be taken in terms of drug interactions.

KEY WORDS

Drug utilization study, hemodialysis.

INTRODUCTION

Drug utilization study is defined as "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" and has the principal aim of facilitating the rational use of drugs.[1] These studies are powerful exploratory tools to ascertain the role of drugs in society. They create a sound socio-medical and health economic basis for healthcare decision making.

The incidence of End Stage Renal Disease (ESRD) is 100 patients per million population per year, which means more than 100,000 new patients every year for a population of 1 billion in India.[2] Modern societies include increasing proportions of elderly people, with a resulting increase in the incidence and duration of chronic illness like diabetes and hypertension, which are the leading causes of ESRD.[3] The treatment options are dialysis and transplantation.

Polypharmacy is common in chronic kidney disease patients (CKD).[4] ESRD patients who are on hemodialysis have complex drug regimens and receive many medications with multiple doses per day. Frequent medication adjustments on dialysis versus non- dialysis days, medically unstable nature of the disease and restricted life styles, render these patients at high risk for developing drug related problems (DRPs) and non-adherence to treatment.[4] Drug interactions can result in serious adverse events if not detected early. A study of the prescription patterns of drugs with potential interactions would be of interest to prevent drug related adverse effects.

Since there is paucity of Drug Utilization Studies in Haemodialysis, this study was taken to assess the pattern and rates of drug-drug interactions among these patients.

Objective:

To assess the prescribing pattern in patients undergoing hemodialysis.

MATERIALS AND METHODS

This was a cross-sectional study carried out in patients undergoing hemodialysis at R.L.Jalappa hospital and research centre attached to Sri Devaraj Urs Medical College, Kolar over a six-month period from April to September 2013.

Institutional ethics committee approval was obtained, written informed consent was taken from the patients. Patients details like name, age, gender, weight, blood group, occupation, cause for dialysis, kidney transplantation, family history, past medical history, laboratory data, drug data (brand and generic name of all drugs prescribed for haemodialysis patients, dose, frequency and duration of drug administration) were collected.

Patients of either gender above 18years undergoing hemodialysis were included and those with renal tumours receiving chemotherapy were excluded. The demographic data was expressed as mean and standard deviation. Categorical data (gender) was analyzed using chi square test. The drugs prescribed is expressed as frequency and percentage.

RESULTS

Total number of patients suffering from CKD undergoing dialysis during the study period were 83, of which 66 were males and 17 females with their mean age of 58.61 ± 5.91years and 53.62 ± 4.45years respectively. Among 83 patients, 68 patients were undergoing hemodialysis since one year and 15 patients for more than a year.

Systolic blood pressure (SBP) was increased whereas diastolic blood pressure (DBP) was within normal limit, as per Joint National Committee guidelines – 8 (Guideline for CKD patients at all age groups, SBP <140 mm Hg and DBP <90 mm Hg). Mean hemoglobin was decreased, blood urea and serum creatinine were increased which suggests chronic kidney disease as shown in **Table 1**.

Table 1: Demographic characteristics of patients suffering from chronic kidney disease expressed in Mean ± SD

Mean blood pressure (mm Hg)	Systolic : 152.65 ± 15.23 Diastolic : 88.55 ± 5.44
Hemoglobin (g/dl)	7.98 ± 1.74
Blood urea (mg/dl)	100.57 ± 34.93
Serum creatinine (mg/dl)	7.31 ± 2.74
Serum sodium (mEq/L)	136.59 ± 6.5
Serum potassium (mEq/L)	4.89 ± 0.9

Hypertension was the most common co morbid condition seen in patients suffering from renal failure as shown in Table 2.

Table 2: Co-morbid conditions associated with renal failure (n=83)

Co-morbid conditions	No. of patients (%)
Hypertension	63 (75.9)
Diabetes mellitus	34(40.9)
Nephropathy	10 (12)
Ischemic heart disease	9 (10.8)
Bronchial asthma	3 (3.6)

Other co-morbid conditions like pulmonary edema, hypothyroidism, retinopathy, tuberculosis, and gastro-enteritis was seen in two patients each and hydroureteronephrosis, pyelonephritis, hepatitis C virus, epilepsy, pneumonia, hepatorenal syndrome, snake bite , malaria and carcinoma cervix in one patient each. Anti-hypertensives (75%) was most commonly prescribed, followed by calcium salts (71%), phosphate binder (64%), iron preparations (61%) and erythropoietin (53%) as shown in figure-1, Metoprolol was the commonest β-blocker. Clinidipine was the most frequently used calcium channel blocker. Prazosin and Furosemide were the commonest α blocker and diuretic used respectively as shown in Figure 2.

Table 3: Number of drugs received by patients per day

Number of drugs/day	Number of patients
1	3
2	7
3	4
4	6
5	16
6	18
7	9
8	8
9	8
≥ 10	4

Out of 83 patients, 63 received five drugs or more per day as shown in table 3. On an average, one patient received 5.8 ± 2.5 drugs per day.

Most common adverse event observed was nausea (14%), followed by weakness, hypotension, leg cramp, vomiting as shown in **Figure 3**.

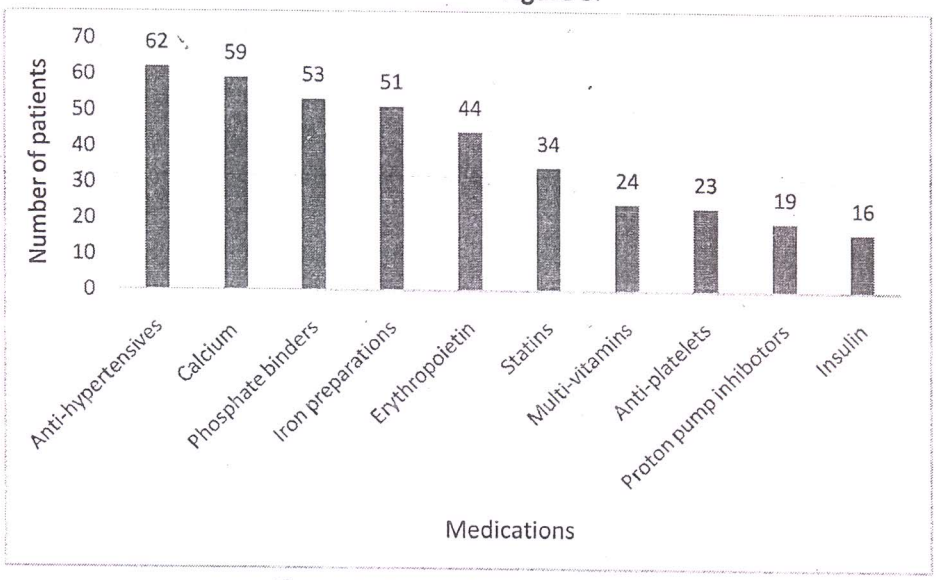

Figure 1. Categories of drugs used

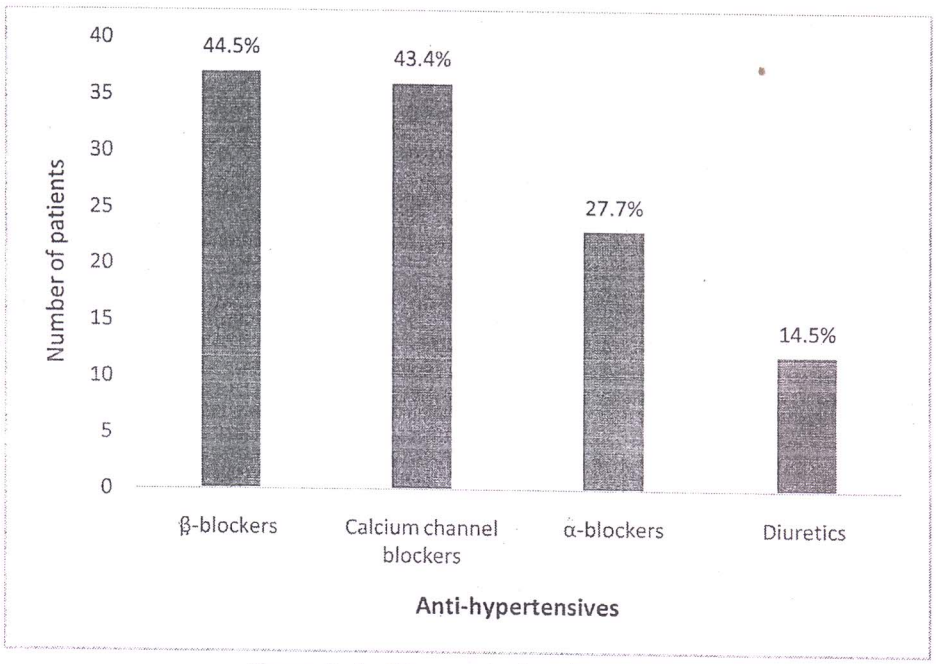

Figure 2. Antihypertensive drugs used

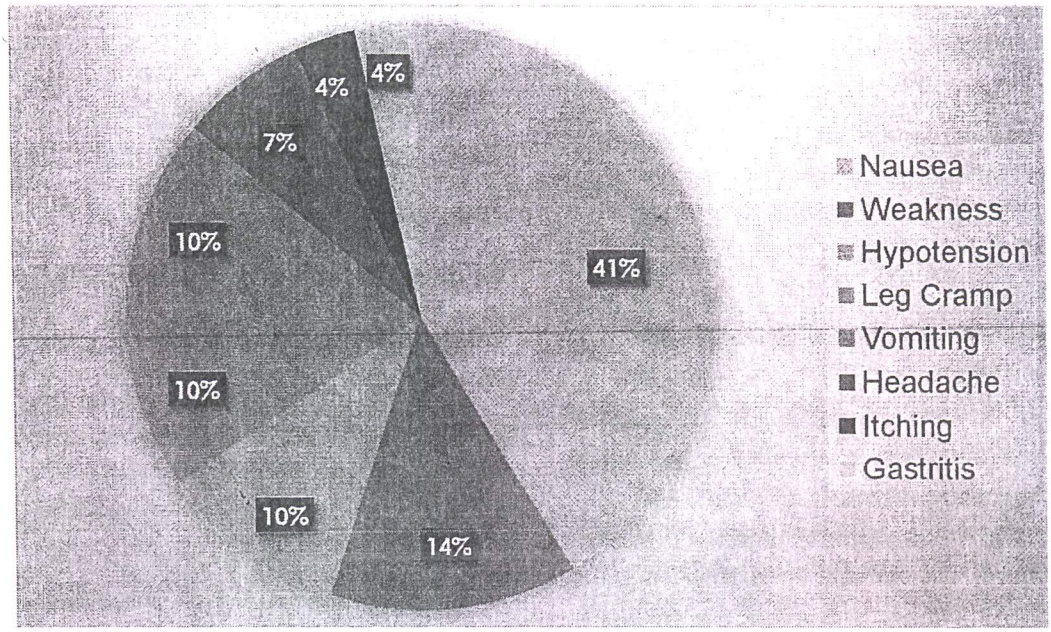

Figure 3. Adverse events

DISCUSSION

The common causes for chronic kidney disease are diabetes mellitus, hypertension and glomerulonephritis. The CKD slowly progresses to End Stage Renal Disease requiring hemodialysis or renal transplantation.[5] Hemodialysis restores the intracellular and extracellular fluid levels which is the function of normal kidney.[6] Patients with chronic kidney disease receive multiple drugs to control the chronic non-communicable diseases like hypertension, diabetes mellitus and for complications due to CKD like anemia, hyperlipidemia and hyperphophataemia.[5]

In our study, 80% of patients were males which are similar to another study. [7] The male predominance of CKD in our study is probably due to hypertension and diabetes, by itself is common in males. Patients in this study underwent hemodialysis in their sixth decade of life, which is observed in another study which may be due to the comorbid conditions.[8] Hypertension and diabetes were the most common co-morbid conditions observed in our study which is similar to another study where 55% were hypertensives and 31% diabetic patients.[8] This explains that these two are the common etiological factors responsible for CKD.

At diagnosis of diabetes 7.3% of patients had microalbuminuria, which increased to 17.3% after 5 years, 24.9% after 10 years and 28% after 15 years. Ten years following diagnosis of diabetes, the prevalence of macroalbuminuria was 5.3% and plasma creatinine elevated in 0.8% of patients.[9] Diabetic patients progress from normal kidney to microalbuminuria at a rate of 2.0% per year, then to macroalbuminuria at 2.8% per year, and then to elevated plasma creatinine at 2.3 % per year. [9] The relative risk for ESRD was 20 fold higher for patients with stage 4 hypertension than for patients with optimal blood pressure.[10]

The target BP 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 ischemia leading to cardiovascular morbidity and mortality.[11] Metoprolol was the most commonly prescribed anti-hypertensive in our study which was similar to a study conducted by Bishu K et al.[12] Beta blocker is preferred in hemodialysis patients due to over activity of renin angiotensin aldosterone system, increased levels of sympathetic activity in hemodialysis patients. Beta blockers have been suggested to be cardioprotective in hemodialysis patients.[13]

In diabetic patients, insulin was used by <50% of them which is similar to another study.[8] Disparity between the number of patients with diabetes and the number of patients treated for diabetes was observed in our study. Deteriorating renal function leads to reduced insulin requirement because kidney is a site of insulin degradation.[3] The cause of death in all age groups (25 to 85+ years) in CKD patients is cardiovascular disease. Hyperlipidemia was observed in CKD patients which is one of the risk factor for cardiovascular disease.

Hence, adequate control of BP, diabetes mellitus, hyperlipidemia and use of anti-platelet drug like aspirin renders protection against CKD complication which has already been documented in Analysis of United States Renal Data System (USRDS), Dialysis Outcome Practice Pattern Study and Henry Ford Health System database.[3] This results in use of multiple drugs.

Calcium acetate was used as phosphate binder in majority of the patients in our study.[8] In CKD patients, phosphorus should be maintained within the target range with dietary phosphorus restriction and use of phosphate binders (PBs). Aluminium-based PBs is currently restricted because of tissue accumulation resulting in use of calcium carbonate and calcium acetate.[8]

More than 50% of the patients received iron supplements and erythropoietin in our study.

Iron is required for formation of red blood cells. Hemodialysis patients lack iron due to loss of small amounts of residual blood discarded in the dialyzer and tubing after each dialysis session.[14] Erythropoietin is a hormone which is synthesized from kidney that stimulates the bone marrow to produce red blood cells.[15] In CKD patients, erythropoietin is not produced in sufficient amount, which leads to renal anaemia.[16] Hence iron supplements (Ferrous fumerate) and erythropoietin should be administered in patients undergoing hemodialysis.

23% of patients were prescribed pantoprazole, a proton pump inhibitor (PPI) to reduce peptic ulcers and gastro-esophageal reflux disease which is more common in CKD patients than in general population. In another study 50% of hemodialysis patients were prescribed PPI.[3] USRDS reported the use of PPI in 30% of hemodialysis patients.[3]

We have observed nausea as the frequent adverse event, study by Jesus et al has reported nausea, vomiting in 15%, headache, itching in 10% of patients.[17] Polypharmacy is prescription of five or more medications to one patient at one time. [8] In our study, 5-6 drugs were received by 34 patients to treat comorbid conditions and complications of CKD. Patients receiving more than 6 drugs have an increased risk of mortality probably due to CKD and medication related problem. More than six drugs was required by 29 patients probably they were severely ill.

CONCLUSION

Hemodialysis patients have multiple comorbid conditions which require several medications for treatment. As the number of prescribed medication increases, patient's compliance decreases so, they require frequent monitoring and dose adjustments. Physicians should be aware of medication related problems.

REFERENCES

1. Shalini S, Ravichandran V, Mohanty BK, Dhanaraj SK, Saraswathi R. Drug utilization studies- An overview. International Journal of Pharmaceutical Sciences and Nanotechnology 2010; 3:803-10.
2. Veerappan I, Arvind M, Ilayabharthi V. Predictors of quality of life of hemodialysis patients in India. Indian J Nephrol 2012; 22: 18-25.
3. Manley HJ, Garvin CG, Drayer DK, Reid GM, Bender WL, Neufeld TK, et al. Medication prescribing patterns in ambulatory haemodialysis patients:comparisons of USRDS to a large not-for-profit dialysis provider. Nephrol dial transplant 2004; 19: 1842-8.
4. Rama M, Viswanathan G, Acharya LD, Attur RP, Reddy PN, Raghavan SV. Assessment of Drug-Drug Interactions among Renal Failure Patients of Nephrology Ward in a South Indian Tertiary Care Hospital. Indian J Pharm Sci 2012;74:63-8
5. Levey AS, Coresh J. Chronic kidney disease. Lancet 2012; 379:165-80.
6. Himmelfarb J, Ikizler TA. Hemodialysis. N Engl J Med 2010; 363:1833-45.
7. Tozawa M, Iseki K, Iseki C, Oshiro S, Higashiuesato Y, Yamazato M, et al. Analysis of drug prescription in chronic haemodialysis patients. Nephrol Dial Transplant 2002 17: 1819–24.
8. Bajait CS, Pimpalkhute SA, Sontakke SD, Jaiswal KM, Dawri AV. Prescribing pattern of medicines in chronic kidney disease with emphasis on phosphate binders. Indian J Pharmacol 2014; 46:35-9.
9. Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR. Development and progression of nephropathy in type 2 diabetes: The United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney International 2003; 63: 225–32.
10. Ravera M, Re M, Deferrari L, Vettoretti S, Deferrari G. Importance of Blood Pressure Control in Chronic Kidney Disease. J Am Soc Nephrol 2006; 17: 98–103.
11. Amaresan MS,Geetha R. Early diagnosis of CKD and its prevention. JAPI 2008; 56: 41-6.
12. Bishu K, Gricz KM, Chewaka S, Agarwal R. Appropriateness of Antihypertensive Drug Therapy in Hemodialysis Patients. Clin J Am Soc Nephrol 2006; 1: 820–24.
13. Levin NW, Kotank P, Eckardt KU, Kasiske BL, Chazot C, Cheung AK et al. Blood pressure in chronic kidney disease stage 5D — report from a Kidney Disease: Improving Global Outcomes controversies conference. Kidney International 2009; 10 :1-12.
14. Feldman HI, Santanna J, Guo W, Furst H, Franklin E, Joffe M et al. Iron Administration and Clinical Outcomes in Hemodialysis Patients. J Am Soc Nephrol 2002; 13: 734–44.
15. Jelkmann W. Regulation of erythropoietin production. Physiol 2011; 6: 1251–58.
16. Pinevich AJ, Petersen P. Erythropoietin therapy in patients with chronic renal failure. West J Med 1992; 157:154-57.
17. Jesus AC, Oliveira HA, Paixao MO, Fraga TP, Barreto FJ, Valenca MM. Clinical description of hemodialysis headache in end-stage renal disease patients. Arq Neuropsiquiatr 2009; 4: 978-81.

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