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Research Article

A STUDY ON DRUG RELATED PROBLEMS AND PHARMACIST INTERVENTION IN PATIENTS UNDERGOING HAEMODIALYSIS IN A TERTIARY CARE HOSPITAL

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Abstract: Chronic kidney disease is a health burden affecting people of all ages and races worldwide. The patients who undergo haemodialysis receive multiple drugs for the treatment of various co-morbid conditions. Due to this, Drug Related Problems (DRP) is common in haemodialysis patients. The aim of the study was to identify the drug related problems in hospitalized haemodialysis patients. It was a prospective interventional study for a period of six months. A total of 37 patients were enrolled in the study. Thirty nine drug related problems were identified in which the most common was drug interaction (25.64%); out of this 3 serious interactions and 7 moderate interactions were identified. Overdose was the next major DRP, which constituted 23.07%. Suggestion by the clinical pharmacist was accepted and changes in drug therapy were made in nine cases.
Key word*:* Haemodialysis, Drug Related Problems, Pharmacist intervention

INTRODUCTION

End-stage kidney disease (ESKD) can be defined by the need for dialysis or kidney transplantation. Worldwide, the number receiving renal replacement therapy (RRT) is estimated at more than 1.4 million.[1] CKD and end-stage renal disease (ESRD) are associated with an increased risk of mortality, increased rate of hospitalisation, and decreased life expectancy[2]. When the number of drug increases, the number of DRPs also increases. Provision of appropriate medication use and management services to patients includes the identification and resolution of real or potential drug-related problems. According to Hepler and Strand, Drug related problems are divided into 8 categories: (1) Indication Without Drug therapy (IWD), (2) Drug use Without Indication (DWI), (3) Improper Drug Selection (IDS), (4) Sub Therapeutic Dosage (STD), (5) Over Dosage (OD), (6) Adverse Drug Reaction (ADR), (7) Drug Interaction (DI), (8) Failure to Receive Drug (FRD) [3]. Our study is designed to identify the DRPs in patients undergoing haemodialysis.

MATERIALS AND METHODS

The study was conducted at Nephrology department of a 1000-bedded private tertiary care teaching hospital located in Dakshina Kannada. It was a prospective interventional study conducted for the period of 6 months. All the patients above 18 years of age undergoing haemodialysis in dialysis unit were included. All the patients were given a brief introduction about the study and the informed consent was obtained. The study was approved by the Institutional Human Ethics Committee. The collected data included age, sex, weight, co morbidities, past and present medication and medical history, fresh complaints, drug treatment regimens and lab reports. Thorough study of patient's case note and daily follow up was carried out. The identified DRPs were documented in DRP documentation form and necessary interventions were made.

RESULTS

During the study period a total of 37 patients had undergone haemodialysis at the dialysis unit and all patients were enrolled in the study. Over a period of six months study, 39 drug related problems were identified in 19 patients. The most common drug related problems identified was the drug interactions that constituted (n=10) 25.64%; out of these 3 serious interactions and 7 moderate interactions were identified. Over dose was the next major drug related problem (n=9) 23.07%. Looking into the 12 dose related issues, the number of sub therapeutic dosage was (n=3) 7.69%. Improper drug selection was observed in few cases (n=3) 7.69% and the patients failed to receive the prescribed drugs was found to be (n=7) 17.94%. The number of adverse drug reaction identified was (n=4) 10.25%. We also noted that there were two drugs prescribed for untreated indication and one drug was used without any indication (Table 1).

Table 1: Types of drug related problems

TYPES OF DRP	N=39	%
Untreated Indication	2	5.12
Improper Drug Selection	3	7.69
Sub Therapeutic Dosage	3	7.69
Failure To Receive Drugs	7	17.94
Over Dose	9	23.07
Adverse Drug Reaction	4	10.25
Drug Interaction	10	25.64
Drug Use Without Indication	1	2.56

Among the identified ten drug-drug interactions three were serious and seven were moderate.

Serious interactions

- Drug-drug interaction between Linezolid and Tramadol (Linezolid increases toxicity of Tramadol and shows increased risk of hypertension, hyperpyrexia, somnolence).
- Concomitant use of Methyl Prednisolone and Ofloxacin may potentiate the risk of tendonitis and tendon rupture.
- Concurrent use of Atenolol and Clonidine increases the risk of sinus bradycardia.

Moderate interactions

- Usage of Aspirin with Insulin where Aspirin may increases the hypoglycemic effect of Insulin,
- Concurrent use of Aspirin and Prednisolone may results in increased of risk of GI ulceration
- Calcium carbonate with Nifedipine decreases the effect of Nifedipine,
- Injection Pantoprazole with Cefuroxim will decrease the effect of Cefuroxime
- Sevelamer with Gabapentin decreases the effect of Gabapentin.

Drug interactions of anti-hypertensives with other anti-hypertensives were not included because most of the patients were on more than one antihypertensive for their uncontrolled hypertension.

One case of drug use without indication was identified. It was found that the phosphate binder was used in patient with normal phosphorous level.

In improper drug selection category three drugs were listed which includes one antihypertensive, one antidiabetic and one antibiotic.

Among 12 (30.75%) drugs identified in improper dose category, 9 (23.07%) were over dosages and 3 (7.69%) were sub therapeutic dosages. Over dosages were observed in 9 cases, it includes six antihypertensives, two antibiotics and one antidiabetic drug. In sub-therapeutic dosages there was one antibiotic, one anticonvulsant and one phosphate binder.

Four adverse drug reactions were reported in our study which includes pain in the back, GI disturbances, constipation and headache. The causality assessment and severity assessment were done by using Naranjo scale and Hartwig severity scale respectively. Among four adverse drug reactions 3 were probable and one was possible.

Clinical Pharmacist Intervention

Based on the identified drug related problems we tried to make necessary interventions in the pattern of drug therapy and attempted 39 interventions. It was observed that nine suggestions were accepted and the drug therapy was changed (Table 2).

Table 2: Clinical pharmacist's intervention

Intervention category	N=39	Percentage
Suggestion accepted and therapy changed	9	23.07
Suggestion accepted but drug therapy not changed	19	48.72
Neither suggestion accepted nor drug therapy changed	11	28.05

On the total 37 patient's prescriptions, only those prescriptions in which drug related problem were detected had been analyzed. A total of 187 drugs were prescribed for 19 patients, ranging from 6-13 medications with a mean of 10.16 ± 1.353 S.D per prescription.

Among 187 drugs, maximum number of drugs prescribed were antihypertensive (n=57) 30.48%. The drugs for treating renal bone disease (n=24) 12.83% was the next widely prescribed drugs and the other drugs included were phosphate binders, calcium salts, anti-emetics, NSAID's, anticonvulsants and antidepressants.

Drugs to treat anemia constituted (n=11) 5.88%, in which Human Recombinant Erythropoietin was prescribed in (n=8) 4.278% patients. Oral and intravenous iron was prescribed for (n=3) 1.60% patients. A total of 17 antibiotics were prescribed which included Cephalosporin (n=6), Piperacillin/Tazobacum (n=4), Rifampicin and Ethambutol two each, Vancomycin, Linezolid, Levofloxacin were prescribed one each. Antidiabetics (n=11) 5.88%, anticoagulants (n= 5) 2.63% and antacids (n=11) 5.88% were also prescribed.

Out of 24 drugs, used to treat renal bone disease alphacalcidol (n=11) 5.88% and phosphate binders (n=13) 6.95% (lanthanum carbonate, sevelamer, calcium acetate and calcium carbonate) were noticed.

Table 3: Types of Medication prescribed

TYPES OF MEDICATION	**N=187**	**%**
Antihypertensives	57	30.48
Renal Bone Disease	24	12.83
Antibiotics	17	9.09
Iron Preparations	3	1.60
Erythropoietin	8	4.27
Folic Acid	1	0.53
Vitamin Supplements	6	3.20
Antidiabetics	11	5.88
Anticoagulants	5	2.67
Antacids	11	5.88
Miscellaneous	44	23.52

Among antihypertensives calcium channel blockers (36.84%) were the most widely prescribed class of drugs in which amlodipine constituted the largest proportion (n=13) 22.80%. Cilnidipine and Nifedipine were found to be prescribed for 3 and 5 times respectively. Another widely prescribed class of drug was loop diuretics (n=12) 21.05%

in which Torsemide (n=9) and Furosemide (n=3) were given. The only prescribed centrally acting drug was Clonidine (n=10) 17.54% which is an alpha-2 adrenergic agonist. Beta adreno-receptor antagonists were prescribed for (n=6)10.53% patients and all were cardioselective beta adreno-receptor antagonist in which three Atenolol and three Metoprolol was noticed. Prazosine which is a selective alpha-receptor antagonist and Minoxidil, direct vasodilator was prescribed in (n=3) 5.26% patients. One prescription had Telmisartan which is an angiotensin receptor blocker and one prescription of Carvedilol (beta blocker with alpha-blocking activity) was also observed.

Table 4: Types of antihypertensives prescribed

Types of Antihypertensives	Number	Percentage
Calcium Channel Blockers	21	36.84
Alpha-1 Blockers	3	5.26
Centrally Acting	10	17.54
Angiotensin II Receptor Blockers	1	1.75
Beta-1 Selective Blocker	6	10.52
Alpha&Beta Blocker	1	1.75
Loop Diuretics	12	21.05
Vasodilators	3	5.26

DISCUSSION

Patients undergoing haemodialysis is a special population and they need extra care especially identification of drug related problems and resolving those problems. Thus, morbidity and mortality can be reduced and improved quality of life can be promoted.

In our study the most common drug related problem identified was the drug interactions that constituted 25.64%. Haemodialysis patients had received more than six drugs to treat different co morbid conditions; this may be the reason for higher number of drug interaction in these patients. Grabe DW and his co-workers in their study revealed that drug interactions were the major DRP in patients undergoing haemodialysis[4]. Over dose (23.07%) was the next major drug related problem. Dosing problems may arise when creatnine clearance is not considered. It is recommended to monitor creatnine clearance regularly in every patient who undergoes dialysis. Similar results were found in a study conducted by HJ Manley et al.[5] The most commonly prescribed drugs were antihypertensive. The study conducted by Masahiko Tozawa et al also presents similar results[6]. Based on the drug related problems the clinical pharmacist played a major role and provided suggestions to physicians in improving the drug therapy where, nine suggestions were accepted and drug therapy was altered.

CONCLUSION

Our study concludes that DRPs were frequently observed in the patients who had undergone haemodialysis. The study reveals that the frequency of drug related problem is directly proportional to the number of drugs. DRPs are prevalent in hemodialysis patients. The clinical pharmacy services points out the inevitable role of clinical pharmacist in identifying, resolving and preventing the drug related problem especially in critical areas of care like hemodialysis where, more than a single drug is prescribed to a patient. Clinicians should be vigilant regarding polypharmacy and the occurrence of DRPs where clinical pharmacy services are not available.

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