Notes

PHARMACIST EFFECTIVENESS IN REDUCING MEDICATION RELATED PROBLEMS IN DIALYSIS PATIENTS

Abdulmalik M. Alkatheri*

يضطر المرضى بمرض الكلية المتقدم إلى أداء مهامهم اليومية المتنوعة بما في ذلك الاستعمال الصحيح للعديد من الأدوية البغيضة والمقيدة لهم. ويعتبر الدور الذي يساهم به الصيدلي في رعاية مريض الديلزة طويلة الأمد دوراً هاماً جداً. ويتركز هذا المقال حول الدور الحالي والمستقبلي للصيدلي في تقليل المشاكل المتعلقة بالدواء في مراكز الديلزة.

Patients with End Stage Renal Disease (ESRD) are required to perform various daily tasks including proper use of multiple medications that are frequently considered restrictive and unpleasant. The role of a pharmacist in contributing to the care of patients receiving long-term haemodialysis is very essential. This article will focus on the current and future role of the pharmacist to minimize drug-related problems at dialysis centers

Key words: Drug-related problems, pharmacist role

Introduction

End Stage Renal Disease (ESRD) is a nationwide disease that affects many people all over the world. The data of the United States Renal Data Systems (USRDS) shows that the number of patients who had been treated increases year by year. The number of patients has increased from 60,000 to 159.800 during 10 years (1986-1995) in Hemodialysis (HD) centers (1). This increment is associated with a high morbidity and mortality rate. Generally, ESRD patients have other concurrent diseases that require intensive patient care and multiple medications that need to be controlled since these diseases are costly to the health care system. Consequently, control of the disease progression becomes difficult and requires more than one professional team to provide the patient with the best care in which the pharmacist can be a key element.

This article will focus on the role of the pharmacist and his/her role in the dialysis units through identifying the need for the pharmacist intervention, recognizing types of drug-related problems that may occur in such patients. Besides discussing the type and area of intervention most suited for the pharmacist. Also, barriers that can hinder the pharmacist's intervention and the best ways to minimize these barriers will be discussed. Other issues of concern such as compliance with medication, factors affecting this compliance, patient's knowledge, and upgrading pharmacist knowledge will be discussed.

In dialysis centers, physician, physician assistant, registered nurses are considered as the corner stone of the dialysis team. Recently, MEDICARE required the involvement of a social worker and a dietitian to be part of the dialysis team. However, the pharmacist's involvement in this team is still not required (2). This brings the question about the importance of the pharmacist as a part of the dialysis team.

Pharmacist's Role:

Several factors may dictate the requirement for the pharmacist to be part of the health professional's team in order to provide the patient with the most comprehensive and advanced care. ESRD patients have multiple diseases that require multiple medications (poly-pharmacy). The average number of medications, which a haeomdialysis patient can receive, is 10 prescription and 2 non-prescription items (3). This makes it quite difficult to control the use of these medications through single health professional team.

*National Guard Health Affairs, King Abdulaziz Medical City, Riyadh, Pharmaceutical Care Department.

Expensive medications that are usually used in dialysis units such as erythropoietin require frequent monitoring of the laboratory tests, drug dosage adjustment, assessment of both drug effectiveness and adverse effects, as well as patient counseling. Availability of new medications that might have a nephrotoxic effect may increase the need for a pharmacist's input. It is important to control these parameters by a drug expert such as a pharmacist in order for the patient to get the maximum benefit.

Since dialysis patients receive up to 12 medications per day, potential of Drug Related Problems (DRP) become an important issue for those patients. Indeed it is essential to give a special attention in order to identify, solve, and prevent the occurrence of those problems. DRP are considered significant in the US and their impact on the health care is estimated to be around 76.6 billion $ each year (4). So it is essential to recognize and solve DRP in order to prevent drug-related morbidity and mortality.

Table 1: Drug-Related Problems(3)

- **Drug selection**
  - Adding drug
  - Deleting drug
  - Alternative product selection
  - Therapeutic duplication
  - Drug therapy management
- **Drug regimen**
  - Drug dosing
  - Treatment regimen
- **Adverse drug reactions**
  - Allergy or intolerance
- **Interactions**
  - Drug-drug
  - Drug-disease
- **Compliance**
  - Under utilization
  - Over utilization
- **Self care**
  - Timing of medication
  - Selection of non-prescription agents
- **Miscellaneous**
  - Physical and sensory barriers
  - Financial impact

Table 2: Comparing Drug-Related Problem Studies.

Study	Number of Patients	Number of Recommend-ations	% of Accep-tance	Types of DRP
Kaplen and Mason	30 (only 24 complete study)	216 (114 recommend-ations, 85 informative comments)	76%	*Drug under utilization 86.7% *Financial impact 66.7% *physical and sensory barrier 56.7%
Grabe	49 (45 included)	126 (102 interventions were made)	81%	*Drug interaction 93% *Dialysis specific group 86.6%
Tang	55	205	91.7%	*Drug selection 32% *Dose selection and therapeutic monitoring 24%
St. Peter	---	872	95%	*Pharmacokin-etic 40% *Adding, stopping, and changing medication 15.4%

In practice, understanding DRP and identifying patients at high risk to develop such problems allow pharmacists to achieve his/her role. Patient's education and counseling, therapeutic intervention, and cost reduction are some but not the pharmacist's entire role. Indeed, the exact role will be discussed in the remaining part of this article.

Drug-Related Problems:

Drug-related problems are significant issues among haemodialysis patients and it includes eight general categories (3,8,9). Based on the previous risk factors, most ESRD patients would be considered at high risk of developing DRP since those patients fulfill most of the above criteria. In part-one of their study, Kaplan and Mason (3) tried to identify DRP (Table-1) through a program that they called the Focused Drug Therapy Review Program (FDTRP). This program obtains the history of intensive medication and reviews drug therapy for haemodialysis outpatients. In 30 patients, 216 DRP were identified and about 76% of the patients reported missing an average of 3.4 (range 1-11) doses of medications per month (Table-2). Those

potential DRP that can be identified in haemodialysis patients include: drug selection, drug regimen, adverse drug reactions, drug interactions, compliance and self-care.

Regarding drug selection, adding or deleting a drug or the use of an alternative product was considered as a major problem. However, adding a drug was rated as the most significant problem (43.3% of patients) since many of those patients were not receiving the renal medications that are used to treat anemia, hypocalemia, and hyperphosphatemia respectively (eg; iron, calcitriol, and phosphate binders). Failure of receiving these medications may result in disease aggravation.

Drug-drug interactions are another problem since poly-pharmacy medications that are taken by those patients can cause many of drug-drug or drug-disease interactions. For example, phosphate binders have a potential harmful interaction with several medications such as phenytoin, digoxin, and iron. Therefore, it is important to provide those patients with the appropriate consultation in order to avoid the undesirable harmful effects of these interactions.

Drug under utilization, which is considered as an inappropriate patient's behavior, is the highest occurring DRP (86.7% of the patients) especially with patients taking anti-hypertensives, iron, and phosphate binders.

Self-care that includes timing of medication, selection and over-use of non-prescription drugs is also considered as another potential DRP, especially in adherence to timing of medications that occurred in about 43.3% of the patients. In addition, financial, physical and sensory barriers may have some effect in the incidence of DRP.

In part-two, Kaplan etal (10) tested and measured the impact of FDTRP in ESRD patients and assessed the impact of the prescriber on the patient behavior through measuring recommendation acceptance. The pharmacist addressed 114 therapeutic recommend-ations and 85 informative comments regarding drug therapy. 76% of those recommendations were accepted since better problem management can be achieved (Table-2). Also, the prescriber considers the informative comment as important and helpful information even though it is not directly applicable to the patient. However, this study did not characterize the significance of the intervention and considered the impression of the prescriber's comment about the recommendation was helpful. Recognizing the significance of the intervention is important in order to identify the potential effect on the patients. Grabe etal (11), in their study, classified the significance of the intervention through ranking the intervention from 1 (less significant and causes an adverse outcome) to 6 (most significant and information considered as a life and death situation). Forty-five patients were included in that study for a period of over one month of chart review for which 126 DRP were identified and only 102 (81%) interventions were made. Most of the interventions were ranked as number 4 (recommendations would bring care to a more acceptable and appropriate level). Both drug interactions (27.5%) and dialysis specific group (26.5%) yielded the most significant result in the DRP study (Table-2).

The pharmacist's intervention for patients on dialysis is important since those patients are receiving multiple-medications and there is a high probability to have a significant interaction among those medications. Recommendations can be delivered to the prescriber through different mechanisms either in writing or verbally depending on the situation and the time of recommendation. However, documentation of the recommendations is also important in order to show the effective role of the pharmacist. In a study done by St. Peter (12), pharmacokinetic consultations accounted for almost 100% of the written nephrology recommendations from 1983 through 1986 (1300 recommendations per year). In 1988 through 1991, written consultations were doubled when compared to 1984 through 1986.

In addition, 95% of the pharmacokinetic recommendations were accepted which indicates the need of a highly trained pharmacist to be present in that area (Table-2).

Other areas for pharmacist's interventions include nephrology medications and areas where antibiotics are heavily prescribed. These areas demonstrate more acceptance of the recommendation than gastrointestinal, antifungal, antihypertensive, and anti-thrombotic medications. The reason for the high acceptance in specific areas as compared to others is not as yet clear. However, since pharmacists are considered to be highly experienced in the area of drug pharmacokinetics, that may be able to explain the reason for the acceptance of such recommendation.

Pharmacist Opportunity:

Based on the multiple medications taken by the ESRD patients and the complexity of the regimen, the pharmacist can perform several activities that are essential for the health professional. These include team rounds, hospital discharge counseling,

medications profile, patient compliance follow up, staff education, preceptor training, quality assurance, protocol development, drug use utilization, and research (13).

Team rounds for the dialysis units are usually done once a week in which the pharmacist is involved and can provide suggestions and recommendations to the prescriber. Also, this clinical round allows the pharmacist to realize pharmaceutical care concerns from the perspective of other members of the health team. Reviewing of the medication profile allows the pharmacist to gain all information regarding the patient's medication even those that were not dispensed by the hospital. Staff education is considered as another opportunity in which the pharmacist can provide an in-service to the nursing staff, pharmacy members, and physicians. This service provides an opportunity to disseminate academic information and to influence staff behavior by the demonstrating correct method or technique for performing a specific task. Also, drug-related information can be explained to the health team. Quality assurance or total quality management allows the pharmacist to document follow-up and short-term plans based on the outcome of patient's treatment. Regarding the medication, quality assurance involves medication monthly or quarterly review that ensures that the guidelines for specific drugs are adhered. Protocol development could be an important issue to reduce cost of some laboratory investigations such as decreasing the number of hematology assays required for each patient. Additionally, creating a protocol for the administration of antibiotics during or after haemodialysis could maximize medication benefit and minimize drug interaction.

Although, the input by a pharmacist is very helpful and effective to the health team, however, determining that input is difficult. Skoutakis etal. (14) tried to assess effectiveness of the pharmacist through evaluating patient knowledge and understanding their drug, diet, dialysis procedure, and disease state. Also, they evaluated patient compliance with medication (antihypertensive drugs, multivitamins, folic acid, and antiacids) and therapeutic response. The pharmacist's in this study include the following activities:

1- Patient consultation regarding disease and compliance.
2- Written reminder for all the instructions that must be recalled.
3- Maintain drug and diet profile.
4- Dosage adjustment.

This study was divided into three phases. The first catered for data collection and patient assessment without the input of a pharmacist (phase-1). In phase 2, patients were divided into two groups. Group-1 consisted of patients who had received a pharmacist's input for 4 months and group-2 were patients who had received traditional services (educational material and consultation) through physician and nurses without any pharmacist's involvement. In phase 3, the patients in group-1 were divided into groups in which group 1-a received another 4 months of pharmacist's input and group 1-b received no further pharmacist's input. The purpose of phase 3 was to evaluate and to measure the need and the importance of continuity of care. The pharmacist's input had a significant effect in improving patient's knowledge, compliance, and therapeutic response ($P<0.001$) when compared to patients that had not received the pharmacist's input. This demonstrates the importance of the involvement of the pharmacist in the continuity of care.

In another study by Tang etal. (15), the role of the pharmacist was assessed and 205 interventions had been made. Almost, the clinical pharmacist initiated 97% of these interventions and only 91.7% were accepted. The reasons for these interventions were; 32% drug selection, 24% dose selection and therapeutic monitoring, and 19% drug discontinue in which most interventions were initiated in response to abnormal laboratory test results (Table-2).

Intervention Barriers:

There are a couple of factors that might be considered as barriers to pharmacist's effectiveness in the dialysis unit. First, the physician-pharmacist relationship is considered as a major barrier for the pharmacist intervention since the physician has the primary responsibility to modify the treatment plan for the patient. Implementation of these changes in the treatment plan requires a great deal of understanding between the pharmacist and the physician. As a result, newly appointed physician in the dialysis unit showed less acceptance to the pharmacist's recommendations. This cleary indicates that the new comers to the dialysis unit can affect the relationship between the pharmacist and the physician. In general, the aim of the treatment of the dialysis patient is to cure or eliminate disease, decrease disease progression or prevent the illness. However, achieving such goals is somewhat difficult

because these patients are of old age, complain of other concurrent diseases, require long periods of time to recover and mostly do not comply with their medications. Therefore, it is not easy to document the benefit that a patient may gain following a pharmacist intervention because it is quite difficult to demonstrate these effects of the pharmacist's role on the clinical outcome of the patient.

Patient Compliance:

Patient compliance is defined as the extent to which an individual chooses behavior that coincides with a clinical prescription. Patient's non-compliance is costly but preventable and the patients take almost over half of 1.8 billion prescriptions incorrectly annually. About 30-50% of these prescriptions fail to produce a desirable effect. Around 10% of hospital and 23% of nursing home admissions are attributed to a patient inability to follow drug therapy. This leads to increasing the cost of the treatment in US by about 100 billion each year. Improving patient's compliance might save more than 80 billion each year (16). This demonstrates the importance of patient's compliance on cost reduction that could be enhanced through the pharmacist's input.

It is estimated that 20-78% of chronic haemo-dialysis patients were non-compliant with diet, about 50% non-compliant with their medication, and 20% of patients take at least one drug holiday per month (16). Cummings etal. (2,17) found that 33% of HD patients fail to comply with their diet and fluid restriction and about 50% of HD patients do not comply with their phosphate binding medication regimen (10,11). Also, Hartmann and Becker (18), reported that only 39% of stable chronic HD patients were compliant with their phosphate binding medication, 74% with diet based on K level, and 78% were compliant with fluid restriction which was based on interdialytic weight gain (IWG). The reasons for the noncompliance in dialysis patients with their medication could be attributed to situational, sociodemographic, knowledge of regimen and regimen rationale, family and staff relationships, psychological, and health belief factors (19-21). Cleary etal. found that dialysis patients were more compliant with their antihypertensive and calcitriol regimens than phosphate binder regimens (22)

Cost benefit:

The pharmacist's role in cost reduction is significant and can be achieved and delivered to the dialysis unit in several ways. Enhancing patient compliance, establishing and developing drug protocols, and implementing drug use evaluation are considered some of the activities that pharmacists can modify in the dialysis unit. As has been discussed before, increase laboratory assay interval in hematology for example by establishing a new protocol might cause an annual cost avoidance of 200,000 US Dollar if compared to a pervious protocol (13). Also, evaluating drug utilization and recommending suitable less costly alternatives that do not affect level of patient care could also reduce cost. For example, over utilization of albumin in a which is less expensive, can provide same benefit to the patient with the minimum cost. In addition, monitoring erythropoietin in the dialysis centers by adopting comprehensive guidelines can result in a tremendous cost reduction. Ultimately, the most significant factor in cost reduction in the dialysis centers is the reduction in the hospitalization admission (4).

Research:

In the dialysis unit, a pharmacist has an excellent opportunity to be involved in research since there are many unsolved questions regarding drugs and dialysis. However, pharmacists should have the ability to respond very well to the questions regarding the use of drugs in patients with renal disease. Within the research group, pharmacist can be the principle investigator or co-investigator for the different studies that require to be investigated. The pharmacist contribution to the literature over the last 20 years is moderate but constant and most of these articles published in the journals that discuss drug-related problems. In the journals that published less information on therapeutic or pharmacology, the pharmacist contribution and publication were few. Ultimately, Most of the pharmacy nephrology research is on pharmacokinetics followed by therapeutic application of drugs (23,24). Other excellent area for research would to establish a protocol for erythropoietin and iron therapy and their effects on quality of life and outcome. Treatment of infection complications is another area of research since there is no consensus of opinion on which is the best therapy option. The stability of drugs in the dialysate is also important to study since few pieces of information are available. Lake of information on drugs removal through the new membrane (high flux) or through the continuous veno-venous haemofiltartion (CVVH) could be another area for research.

Conclusion

It is clear that pharmacist involvements in haemodialysis unit would result in minimizing DRP and reducing total cost for the health care organization. This underscores the essential role of the pharmacist in the proper functioning of the dialysis centers.

References

1. US Renal Data System, USRDS 1997 annual data report. The national institution of health, institute of diabetes and digestive and kidney disease, Bethesda, MD, 1997.
2. Cummings KM, Becker MH, Kirscht JP, and Levin NW. Intervention strategies to improve compliance with medical regimens by ambultory haemodialysis patients. Journal of Behavioral Medicine 1981; 4:111-127.
3. Kaplan B, Mason NA, Shimp LA, and Ascione FJ. Chronic haemodialysis patients. Part I: characterization and drug-related problems. The Annals of Pharmacotherapy 1994; 28:316-319
4. Johnson JA and Bootman JL. Drug-related morbidity and mortality. Arche of Internal Medicine 1995; 155:1994-1956
5. Koecheler JA, Abramowitz PW, Swim SE, and Daniel CE. Indicators for the selection of ambulatory patients who warrant pharmacist monitoring. American Journal of Hospital Pharmacy 1989; 46:729-732
6. Young WW, Bell JE, and Bouchard VE. Clinical pharmacy services: prognostic criteria for selective patient monitoring, part I. Am J Hosp Pharm 1974; 31:562-568
7. Young WW, Bell JE, and Bouchard VE. Clinical pharmacy services: prognostic criteria for selective patient monitoring, part II. Am J Hosp Pharm 1974; 31:667-676
8. Hepler CD and Strand LM. Opportunities and responsibilities in pharmaceutical care. Am J Hosp Pharm 1990; 47:533-543
9. Strand LM, Cipolle RB, and Morley PC. Drug-related problems: their structure and function. Drug Intell Clin Pharm 1990; 24:1093-1097
10. Kaplan B, Mason NA, Shimp LA, and Ascione FJ. Chronic haemodialysis patients. Part II: reducing drug related problems through application of the focused drug therapy review program. The Annals of Pharmacotherapy 1994; 28:320-324
11. Grabe DW, Bailie GR, and Eisele G. Evaluation of drug-related problems in an outpatient haemodialysis unit and the impact of a clinical pharmacist. Clinical Nephrology 1997; 47(2): 117-121
12. St. Peter WL. Clinical pharmacy nephrology consultation and documentation: A comprehensive approach. Journal of Pharmacy Practice 1993; 3:140-147
13. Norwood CE and Paher SN. Clinical pharmacy nephrology practice in the outpatient dialysis center. Journal of Pharmacy Practice.1993; 3:133-139
14. Skoutakis VA, Acchiardo SR, Martinez DR, Lorisch D, and Wood GC. Role effectiveness of the pharmacist in the treatment of haemodialysis patients. American Journal of Hospital Pharmacy 1978; 35:62-66
15. Tang I, Varhnos D, Hatoum H, and Lau A. Effectiveness of clinical pharmacist interventions in a haemodialysis unit. Clinical Therapeutics 1993; 15(2): 495-464
16. Berg SI, Dischler J, and Wagner DI. Patient compliance. The Annals of Pharmacotherapy 1993; 27:S5-S19
17. Cummings KM, Becker MH, Kirscht JP, and Levin NW. Psychological factors affecting adherence to medical regimens in a group of haemodialysis patients. Med. Care 1982; 20:567-580.
18. Hartman PE and Becker MH. Noncompliance with prescribed regimen among chronic haemodialysis patients: a method of prediction and education diagnosis. Dialysis & Transplantation 1978; 7:978-986
19. Blanchard R, Berger W, Bailie G, and Eisele G. Knowledge of haemodialysis and CAPD patients about their prescribed medicines. Clinical Nephrology 1990; 4:173-178
20. Zetin M, Plummer MJ, Vazin ND, and Gramer BA. Locus of control and adjustment to chronic haemodialysis. Clinical Exp Dial Apheresis 1981; 5:319-324
21. Kirilloff LH. Factors influencing the compliance of haemodialysis patients with their therapeutic regimen. AANNT 1981; 8:15-20
22. Cleary DJ, Matzke GR, Alexander AC, and Joy MS. Medication knowledge and compliance among patients receiving long-term dialysis. American Journal of Health System Pharmacy 1995; 52:1895-1900
23. Johnson CA. Clinical pharmacists' involvement in nephrology research. Journal of Pharmacy Practice 1993; 3:118-122.
24. Baili GR. Clinical pharmacy care in continuous ambulatory peritoneal dialysis patients. Journal of Pharmacy Practice 1993; 3:123-132