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DRUG RELATED PROBLEMS AMONGST NEPHROLOGY PATIENTS

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ABSTRACT

Patients receiving a large number of medications are more prone to drug related problems (DRPs). This is especially true for nephrology patients who are prescribed an average of eight medications per day. The complexity of drug therapy can lead to confusion, non compliance, interaction and adverse effects. Nephrology patients are known to be dependent on a large number of medications in view of the severity of the disease. Therefore, this study was performed to evaluate the incidence of DRPs, types of drugs involved, drug risk ratio and risk factors for nephrology patients. The study was performed using the PCNE criteria for identifying DRPs. It was carried out prospectively in a local tertiary hospital. A total of 70 patients were recruited in the study, of which 45 (64.3%) patients reported at least one DRP. There was a total of 118 DRPs reported with a rate of 1.7 DRP per patient. The most common DRP reported based on the PCNE classification was 'drug use problem' (n=57/118, 48.3%) and 'adverse reaction' (n=39/118, 33.1%). The most common class of drugs involved were antianemia (n=23/118, 19.5%), mineral supplements (n=12/118, 10.2%) and lipid modifying agents (n=12/118, 10.2%). The drugs with the highest drug risk ratio were corticosteroid (0.5), lipid modifying agents (0.32) and antianaemia (0.32). Interestingly, risk factors of DRPs were gender (RR=0.105, p=0.030) and number of drugs prescribed (RR=0.130, p=0.015). This work presents the importance of providing appropriate support for nephrology patients to ensure reduced risk of DRPs.

Key Words:- Drug related problems, Nephrology, Medication.

INTRODUCTION

Drug therapy has become more complex with chronic diseases. This is especially true in nephrology patients who receive an average of eight medications per day (Padmini and George 2008). The number of patients who progress to end stage renal disease increases each year (Ngo *et al*., 2008). In patients with renal failure, medication regimens become difficult to adhere to and they are at high-risk of acquiring drug-related problems (DRPs) (Darren, 2000). With the increase in the number of drugs, there is an increase in potential for DRPs to occur (Abdullah *et al*., 2004; Joshua *et al*., 2007). Inappropriate use of drugs is therefore harmful and can evoke worsening of disease.

DRPs are defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health (Pharmaceutical Care Network Europe Foundation, 2006). There are a variety of causes ranging from unneeded medications, adverse effects, inappropriate use, inappropriate dosage regime and poor adherence (Restepo *et al*., 2008). It can lead to an increase in patient morbidity or mortality with approximately 106,000 deaths occurring annually from medication mismanagement (Lazarou *et al*., 1998; Cohen, 1999). Previous work has illustrated the degree of DRPs to be substantially high with 81% of patients reporting at least one DRP (Blix *et al*., 2004). Thus, this study was

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performed to identify the incidence of DRPs in nephrology patients, type of drugs involved and risk factors for DRPs in a local tertiary hospital.

METHODOLOGY

Study design and procedure

The study was performed in a local tertiary teaching hospital. The study was approved by the Committee for Medical Research Ethics. All adult patients in the nephrology ward admitted for six months of the study period were eligible with informed consent. It was performed prospectively in which the patients were interviewed based on a set of questions on admission to obtain a full medication history for review and identification of DRPs. Patient's demographic data, laboratory values and past medical history were retrieved from Patient Medical Records. Patients with incomplete data, readmissions and those who refused to be interviewed were excluded. All data were collected using a standard data collection form. The form was designed, tested and found applicable to be used in the nephrology ward. DRPs that were identified were then discussed with a clinical pharmacist.

Classification of drugs and DRPs

Drugs identified were classified based on the Anatomical Therapeutic Chemical (ATC) classification system (World Health Organization, 2009). The DRPs were defined by the Pharmaceutical Care Network Europe (PCNE) classification (Pharmaceutical Care Network Europe Foundation, 2006). The PCNE provides a set of classification for DRPs which separates problems from causes. The basic classification has six primary domains for problems; P1=Adverse reactions, P2=Drug choice problems, P3=Dosing problems, P4=Drug use problems, P5=Interactions, and P6=Others. One drug may introduce more than one DRP, some which may be independent on each other. For example a drug may cause a side effect for which the drug may be required to be stopped. Thus, two DRPs are recorded.

Drug risk ratio

To calculate the risk of DRP for each drug, a drug risk ratio was calculated. A drug may cause more than one DRP. Therefore, in order to identify the ''drug at risk'', a drug risk ratio was performed as previously described (Blix *et al*., 2010). This was described as the number of DRPs for a given drug divided by the number of times the drug was used. Therefore, the risk ratio definition calculation gave rise to a value between '0' and '1'. A drug risk ratio value of '0' demonstrated a low risk of DRP for a given drug. A value of '1' was considered a high risk of developing DRP for the drug.

Data analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 15.0 for Windows and was tested with the appropriate inferential and descriptive statistics. Linear regression was used to identify the relationship between the occurrences of DRPs with the different types of drugs used and patient factors. Probability values of less than 0.05 ($p < 0.05$) were accepted as statistically significant.

RESULTS

Patient characteristics and DRPs

A total of 70 patients were included in the study. The age of patients in the study was between 20-79 years old, with a mean age of 51.7 (±15.7) years. There were 45 (64.3%) male and 25 (35.7%) female patients. From the 70 patients there were a total of 588 drugs recorded from all patients. This was an average of 8.4 ± 3.0 drugs per patient. Each patient recorded at least one other co-morbidity. The most common co-morbidity was hypertension (n=59, 84.3%) and diabetes mellitus (n=38, 54.3%). Other co-morbidities identified were congestive heart failure (n=12, 17.1%), hyperlipidaemia (n=30, 42.9%), gout (n=5, 7.1%), stroke (n=3, 4.3%).

Altogether there were 45 (64.3%) patients that recorded at least one DRP. The age range of patients that recorded a DRP was 20-76 years old (average 48.4±15.0 years). Of the 45 patients, 29 (64.4%) were female. A Pearson correlation test was conducted in order to measure a relationship between the age, number of drugs taken by patient and number of co-morbidity with the number of DRP occurrence. There was a significant positive relationship between the numbers of drugs taken by patient with the number of occurrence of DRP (R=0.15, p=0.0228). However, no correlation was observed with age and co-morbidities with occurrence of DRPs.

Categories of DRPs

The DRPs were classified based on the PCNE classification. There were a total of 118 DRPs reported from 45 patients. Therefore, an average of 1.7 DRP was recorded per patient. Based on the PCNE classification, the most common DRP observed was drug use problems reported by 29 (64.4%) patients, adverse drug reactions was reported by 22 (48%) patients and 5 (11.1%) patients reported drug choice problem and other DRPs respectively. From these, patients were found to report more than one DRP in each classification. The total

number of DRPs reported by these 45 patients is listed in Table 1.

Table 1. Categories of DRPs reported by patients admitted in the nephrology ward (n=118). The categories of DRP were classified based on the PCNE classifications. The most common DRP observed in the study population was drug use problems, followed by adverse reaction and drug choice problems. Other DRPs were also recorded such as insufficient awareness of disease and dissatisfaction of therapy

Occurrence of DRP	Frequency of DRP n (%)
P1 - Adverse reactions	39 (33.1)
P2 - Drug Choice Problems	5 (4.2)
P3 - Dosing problems	-
P4 - Drug use problems	57 (48.3)
P5 – Interactions	-
P6 – Others	17 (14.4)

Figure 1. Figure illustrating the ten most frequent drugs involved in DRPs and the calculated risk ratio (n=118). The type of drugs identified in each category are; drugs used in diabetes (insulin, gliclazide), vitamins (vitamin C, vitamin B complex), agents acting on the renin-angiotensin (perindopril, enalapril), antithrombotic agents (ticlopidine), calcium channel blockers (amlodipine), antihypertensive (prazosin), mineral supplements (calcium carbonate), antianeamia (iron tablets, folic acid), lipid modifying agents (statins) and corticosteroid (prednisolone)
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Risk ratio of DRPs

The most common drugs involved in DRPs are shown in Figure 1. Drugs with the highest number of DRPs reported were antianaemia (n=23/118, 19.5%), mineral supplements (n=12/118, 10.2%) and lipid modifying agents (n=12/118, 10.2%). The five drugs with the highest risk ratios amongst nephrology patients were found to be corticosteroids (risk ratio = 0.5), antianaemia (risk ratio = 0.32), lipid modifying agents (risk ratio = 0.32), antihypertensives (risk ratio = 0.3) and mineral supplements (risk ratio = 0.3) (Figure 1). Antihypertensive drug (prazosin), antianaemia preparations (folic acid and iron tablets) as well as corticosteroids (prednisolone) and lipid modifying agents (statins) led to DRPs such as adverse reactions and drug use problems. Mineral supplement (calcium carbonate) led to DRPs such as drug use problems.

Patient risk factors of DRPs

All patient factors were analyzed to determine whether there was a relationship with DRP occurrence. Risk factors were analyzed by a log-linear regression with occurrence of DRP as the dependent variable, and age, gender, race, number of drugs taken by patient and number of co-morbidities as independent variables. Number of drugs (RR=0.130, p=0.015) and gender (RR=0.105, p=0.030) were risk factors of DRP (Table 2).

Table 2. Risk factors of DRPs based on demographic characteristics such as age, gender, number of drugs and number of co-morbidities (N=70)

Independent variables	Occurrence of DRP
	RR[b] (p value)
Age (years)	0.003 (0.725)
Gender (male = 1)	0.105 (0.030)
No. of drug	0.130 (0.015)
No. of co-morbidity	0.001 (0.832)

[b]Risk factors were calculated using log-linear regression with significance value of $p<0.05$

DISCUSSION

The occurrence of DRPs in nephrology patients is a ubiquitous problem. The need for appropriate treatment is vital to ensure an increased quality of life. Recent work has demonstrated that pharmacists can play an important role in identifying DRPs in nephrology patients (Belaiche *et al*., 2012). In this study, DRPs were found to occur in a total of 45 (64.2%) patients which was in line with previous reports (Koh *et al.*, 2005). In view of the complexity of the regimen some patients reported more than one DRP. Furthermore, a significant association was demonstrated between higher numbers of medications with the number of DRP occurrence. The correlation between number of medications and DRPs has similarly been shown in previous work (Koh *et al*., 2005) which further substantiates these findings. This is simply due to the difficulty in remembering drug therapy when complex regimens are prescribed. Without proper education and guidance, patients will find the task of adhering to treatment overwhelming.

The DRPs demonstrated here were classified based on the PCNE classification for ease of identification. The PCNE classification has been widely used due to the wide area it addresses such as adverse reactions, problems with drug use, inappropriate drug treatment as well as adherence and lack of understanding of drug treatment (Pharmaceutical Care Network Europe Foundation, 2006). Interestingly, DRPs most commonly observed in patients in this study population was adverse reactions and drug use problems. Adverse reactions have been a major concern in patients with renal dysfunction. Various drugs are known to worsen kidney function if

used inappropriately (Guise *et al*., 2004). The burden of adverse reactions is significant as the time to recovery and hospitalization of nephrology patients has been shown to be longer than patients with normal kidney function (Joshua *et al*., 2007). Similarly, drug use problems were also highly reported in this group of patients. The most common drug use problem was not administering prescribed medication. Non compliance to medication has been reported to be between 20-50% in renal patients (Loghman-Adham, 2003; Kripalani *et al*., 2007). Indeed, this work demonstrates that adverse reaction and drug use problems remain a significant contributor to nephrology patients which should be addressed by healthcare professionals.

There is a lack of knowledge on drug risk ratio in nephrology patients. Here, we present data on the drug risk ratios of patients on renal treatment. The study sample was relatively smaller than previous studies describing drug risk ratio (Blix *et al*., 2004; Blix *et al*., 2010). However, the focus of the study allows an insight on the potential drugs with high risks of DRPs in nephrology patients. Results from this work illustrated that drugs with the highest drug risk ratio were corticosteroids, lipid modifying agents and antianaemia drugs. Most patients were observed to complain of adverse effects with corticosteroids and antianaemia drugs which subsequently led to non compliance. Corticosteroids have been reported to cause a wide range of adverse effects such as weight gain, acne and bruising (Trevitt *et al*., 2012). Complaints of constipation and nausea were noted as the main adverse effects with iron tablets which have also been reported in previous work (Lachance *et al*., 2011). On the other hand, patients taking lipid modifying agents were most likely to not comply due to the lack symptoms. As patients linked lipid modifying agents with obesity, patients were reluctant to take the medication. Therefore, patient support regarding adverse effects and understanding of medication would most likely allow better understanding of drug use. This could potentially improve compliance and reduce DRPs amongst patients on complicated medication regimen.

This study also identified gender and number of medications as risk factors of DRPs in nephrology patients. The number of medication is an important determinant of DRP. The positive relation between number of medication and occurrence of DRP further substantiates this relationship. To that end, focus on patients with a high number of medications is required to ensure better compliancy and efficacy of drugs. Although male patients were found to have a higher number of DRPs compared to their female counterparts, gender may not be as important as medication number in predicting DRPs. Nonetheless, further work could be performed in identifying the cause of the significant effect of gender in DRPs in this group of patients.

CONCLUSION

In conclusion, this work demonstrated that more than half of nephrology patients demonstrated a DRP during treatment. The most common DRPs were adverse effects and drug use problems. The complexity of drug regimens in patients with kidney disease increases the risk of occurrence of DRPs. Important elements regarding drug risk ratio in nephrology patients were also demonstrated in this work. This could potentially guide healthcare professionals towards improving medication therapy in this group of patients.

REFERENCES

Abdullah DC, Ibrahim NS, Ibrahim MM. Medication errors among geriatrics at the outpatient pharmacy in teaching hospital in Kelantan. *Malaysian Journal of Medical Sciences*, 11(2), 2004, 52-58.

Belaiche S, Romanet T, Allenet B, Calop J, Zaoui P. Identification of drug-related problems in ambulatory chronic kidney disease patients: a 6-month prospective study. *J Nephrol*, 25(5), 2012, 782-788.

Blix HS, Viktil KK, Moger TA, Reikvam A. Drugs with narrow therapeutic index as indicators in the risk management of hospitalised patients. *Pharmacy Practice*, 8(1), 2010, 50-55.

Blix HS, Viktil KK, Reikvam A, et al. The majority of hospitalised patients have drug-related problems: results from a prospective study in general hospitals. *Eur J Clin Pharmacol*, 60, 2004, 651–658.

Cohen JS. *Preventing Adverse Drug Reaction before They Occur. Expert Pharmacology Column.*, 1999.

Darren WG. Drug-Related Problems in End-Stage Renal disease population. *The Medscape Journal of Medicine*, 1(2), 2000, 1-7.

Guise JM, McDonagh MS, Osterweil P, Nygren P, Chan BS, Helfand M. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ*, 329, 2004, 15-19.

Joshua L, Padmini DD, Shoba G. Adverse drug reactions in nephrology ward inpatients of a tertiary care hospital. *Indian Journal of Medical Science*, 61, 2007, 562-569.

Koh Y, Moideen Kutty F, Li SC. Drug-related problems in hospitalized patients on polypharmacy: the influence of age and gender. *Ther Clin Risk Manag*, 1(1), 2005, 39-48.

Kripalani S, Yao X, Haynes B. Interventions to enhance medication adherence in chronic medical conditions. *Arch Intern Med*, 167, 2007, 540–550.

Lachance K, Savoie M, Bernard M, Rochon S, Fafard J, Robitaille R, Venditolli PA, Levesque S, Denus Sd. Oral ferrous sulfate does not increase preoperative hemoglobin in patients scheduled for hip or knee arthroplasty. *Surgery*, 45, 2011, 764-770.

Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients. *Journal of American Medical Association*, 270, 1998, 1200-1205.

Loghman-Adham M. Medication non compliance in patients with chronic disease: issues in dialysis and renal transplantation. *Am J Manage Care*, 9(2), 2003, 155-171.

Ngo Ly, Onn LT, Guat LD. 16th Report of the Malaysian Dialysis and Transplant Registry. 2008.

Padmini DD and George J. Diabetic nephropathy: Prescription trends in tertiary care. *Indian Journal of Pharmaceutical Sciences*, 70(3), 2008, 374-376.

Pharmaceutical Care Network Europe Foundation. PCNE Classification for drug related. Version 5.01. *Pharmaceutical Care Network Europe Foundation*, 2006, 5-6.

Restepo RD, Alvarez MT, Wittnebel LD, Sorensen H, Wettsein R, Vines DL, Sikkema-Ortiz J, Gardner DD, Wilkins RL. Medication adherence issues in patients treated for COPD. *Int J Chron Obstruct Pulmon Dis.*, 3(3), 2008, 371–384.

Trevitt R, Whittaker C, Ball EA. Self perception affecting adherence to drug regimen following renal transplantation. *Journal of Renal Care*, 2012, DOI: 10.1111/j.1755-6686.1999.tb00039.x.

World Health Organization. ATC index with DDDs. *WHO Collaborating Centre for Drug Statistics Methodology*, 2009.