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Case Study

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### A case study on essential dosage adjustment in chronic renal insufficiency

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#### ABSTRACT

Renal disease alters the effects of many drugs. Drug doses of certain drugs have to be appropriately adjusted depending upon the degree of renal impairment. Drug dosing errors in patients with renal impairment are common and can lead to accumulation and toxicity leading to adverse effects and poor outcomes. A case of a 72 years old male patient with chronic renal failure with other co morbid disease states like systemic hypertension, diabetes mellitus, osteoporosis and peripheral artery disease has been discussed. Laboratory data revealed both elevated serum creatinine and urea levels. On the day of admission the patient was in end stage renal disease as his calculated GFR was 12ml/min. Modified Diet for Renal Disease equation was used to calculate the GFR and dose adjustments were made accordingly. Drugs prescribed to the patients included ceftriaxone 1 g, Pentoxifylline 400 mg, Tapendadol 50 mg, Levocarnitine 500 mg, Alprazolam 0.5 mg, Alpha calcidiol 0.25 mg, Atorvastatin 20 mg, Cilostazol 50 mg, Tramadol 50 mg, Eesomeprazole 40mg, Calcium 250 mg, A systematic medication chart review revealed that pentoxifylline is the drug of choice with altered dosing recommendations in this patient. Therapeutic duplication in the form of using pentoxifylline and cilostazole to treat peripheral vascular disease was also noted. Alprazolam was started at a higher dose for the geriatric patient.

**Keywords:** Chronic Renal Failure, E GFR, MDRD, Pentoxifylline

#### INTRODUCTION

Kidney disease is a serious health care issue that needs to be taken care of in practice settings. This problem is quite common among geriatrics. Renal disease often leads to alteration of pharmacokinetics of most drugs especially those which are actively excreted by the kidneys. Dosage adjustment in patients based on individuals kidney function is essential to avoid any adverse effects of the drug in the patient.

#### OBJECTIVES

To improve the quality of life of hospitalized patients with chronic kidney disease by appropriately altering the dosage regimen based on individual patient's renal profile. To minimize the incidence of adverse drug effects and drug related issues in such patients.

## METHODS

Demographic data, past medical history, laboratory data and prescribed drugs were recorded in a

customized data entry form. The severity of renal insufficiency was determined by calculating the patient's GFR using MDRD equation as follows:

$$\text{GFR} = 186.3(\text{serum creatinine})^{-1.154} * (\text{age})^{-0.203}$$

Whenever follow up serum creatinine was measured for the patient, Glomerular filtration rate was estimated and dose requirements were calculated once again. A systematic medication chart review was also performed in order to understand the incidence of various Drug related problems such as drug duplication, under dosing, overdosing, drug interactions, adverse drug reactions and other medication errors.

## RESULTS

A male patient of age 72 years was admitted in the general department for 12 days with chief complaints of bilateral legs swelling, pain while walking, inability to walk properly, inability to lift right arm because of

sustained injury in the right arm due to slip and fall at home. He was a known case of Type 2 Diabetes Mellitus, Systemic Hypertension and Chronic Renal Failure. Patients laboratory results showed that mean blood pressure was 140/80 mm Hg and pulse was 80 beats/ minute. Renal function test showed elevated serum urea and creatinine levels of 91mg/dl and 3.47mg/dl respectively on the day of admission. With the above subjective and objective data the patient was diagnosed to have Type2 Diabetes Mellitus, Systemic Hypertension, Chronic Renal failure, Peripheral vascular disease and osteoporosis. The patient also sustained right humeral shaft fracture and so had to undergo IMIL Nailing. The drugs prescribed to the patient given in table no: 1

**Table No 1 Drug prescribed**

Drug prescribed	Dose	Frequency	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12
Inj. Ceftriaxone	1 g	BD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tab. Pentoxifylline	400 mg	TID	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tab. Levocarnitine	500 mg	OD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tab. Alprazolam	0.5 mg	HS	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tab. Alpha calcidol	0.25mg	OD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tab. Cilostazol	50 mg	BD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tab. Atorvastatin	20 mg	BD	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓
Cap. Omega 3 fatty acid	10 mg	BD	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Inj. Tramadol	50 mg	OD	✓	-	-	-	-	✓	✓	✓	✓	-	-	-
Tab. Esomeprazole	40 mg	BD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tab. Clopidogrel + Aspirin	75mg	OD	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓
Tab. Tapentadol	50 mg	BD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

## DISCUSSION

The kidneys play a vital role in the excretion of many drugs. CKD is defined as the presence of kidney damage or a reduction in the glomerular filtration rate (GFR) for three months or longer [1, 2]. The degree of renal

insufficiency and the severity of kidney disease are generally reflected in the reduction of GFR. The Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) established classification of CKD which has been accepted and used worldwide [3].

**Table No 2 Chronic Kidney Disease Staging**

<b>Chronic Kidney Disease Staging</b>		
<b>Stage</b>	<b>Description</b>	<b>GFR (ml per minute per 1.73 m<sup>2</sup>)</b>
1	Kidney damage with normal or increased GFR	≥ 90
2	Kidney damage with a mild decrease in GFR	60 to 89
3	Moderate decrease in GFR	30 to 59
4	Severe decrease in GFR	15 to 29
5	End Stage Renal Disease	< 15 (or dialysis)

The patient had high levels of urea and creatinine in blood. The accumulation of creatinine in blood indicates abnormal or diminished renal function. [5] Most of the time serum creatinine is used to evaluate renal function and equations using serum creatinine concentrations are the bases of most estimates of GFR. [6] The K/DOQI clinical practice guideline advocates using the traditional Cockcroft- Gault equation or the Modification of Diet in Renal Disease (MDRD) study

equation for routine estimation of GFR. [7] In patients with GFR less lower than 60 ml per minute per 1.73 m<sup>2</sup>, the MDRD equation has shown to be superior. [8] More over MDRD equation has been shown to be the best method for detecting GFR lower than 60 mL per minute per 1.73m<sup>2</sup> in older patients. [9] In this case GFR was calculated by using Modification of Diet in Renal Disease (MDRD) formula. [10]

$$\text{GFR} = 186.3(\text{serum creatinine})^{-1.154} * (\text{age})^{-0.203}$$

The patients GFR was calculated and found to be 12 ml/min. Dosing consideration is essential in this case because of high blood levels of urea, creatinine and reduced glomerular filtration rate which can lead to decreased renal drug excretion which may result in prolonged elimination half life of the administered drug. Patient is 72 years old and considered to be a geriatric. As age progresses the normal kidney function also declines due to structural and vascular changes that occur in the kidneys due to ageing. Therefore dosing is very essential in this patient. Drug dosing in these cases can be subjected to interventions. [11, 12, 13] Loading doses usually do not need to be adjusted in patients with chronic kidney disease. Published guidelines suggest methods for maintenance dosing adjustments: dose reduction, lengthening the dosing interval, or both. [14] A detailed medication chart review revealed that pentoxifylline was used to treat intermittent claudication in the patient at a dose of 400 mg TID. But the patient's laboratory reports showed that the patient had end stage renal disease with e GFR of 12ml/min. Dosage adjustment for pentoxifylline has to be made. The drug has to be given at the dose of 400 mg OD. [15] Alprazolam was prescribed at a dose of 0.5mg for the patient. Use of alprazolam at higher doses lead to adverse drug events. [17] Benzodiazepines are associated with confusion, day time sedation memory falls, slips and motor vehicle

accidents in elderly when prescribed at higher doses. [16-19]

## CONCLUSION

A case of a 72 years old male patient with chronic renal failure, systemic hypertension, diabetes mellitus, osteoporosis and peripheral artery disease has been discussed. This article emphasizes the need to consider important variables relevant to prescribing decisions that are quite often not recognized in clinical care especially in lieu with kidney disease. Renal function is a very important physiological variable that affects the pharmacokinetics and clinical efficacy of many drugs. While prescribing the drugs to a patient who has renal impairment, it is essential to consider both the patients and the drugs characteristics. Most of the time renal parameters are not considered before prescribing drugs. Pharmacists play an important role in this aspect of choosing the most empirical dosing regimen for the patient. This can be achieved by active participation of the pharmacists in ward rounds, regular prescription chart review, evaluation of drug dosing based on e GFR or creatinine clearance and altering the dose according to individual patient demands, thereby improving the drug safety in patients with renal impairment.

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