### **Research Article**

## EVALUATION OF THE APPROPRIATENESS OF DRUG DOSAGE IN RENAL IMPAIRED PATIENTS IN A TERTIARY CARE HOSPITAL

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#### ABSTRACT

The main objective is to determine whether appropriate dose adjustment was taken into account by physicians in renal impaired patients and to evaluate the dose adjustment done in patients by following standard guidelines. A prospective observational study was conducted in 60 patients for a period of 6 months in Vivekanandha Medical Care Hospital, Elayampalayam. The drugs prescribed were analyzed and doses were evaluated using a standard guideline (The Renal Drug Handbook). Dose adjustment was required in 195 (37.2%) of 524 prescription entries. Of the 195 prescription entries, 10.25 % (20) were found to be inappropriate and 89.74% (175) were found to be appropriate. Tramadol was the most frequently prescribed drug that required dose adjustment, in the rate of 7 out of 8 cases. Piracetam, Metformin and Tranexamic acid remained unadjusted in all the casesas they were found to be contraindicated in renal patients. The study concludes that appropriate dose adjustment in patients with renal impairment was done in a significant percentage. The presence of clinical pharmacist at physician rounds will help to review all medications as an effective solution to reduce dosing errors and overall improvement in pharmaceutical care.

Key Words: Dose Adjustment, Renal Impairment, Dosing error, appropriate drug dosage.

#### INTRODUCTION

Chronic kidney disease (CKD) is defined as a progressive loss of kidney function occurring over several months to years and is characterized by the gradual replacement of normal kidney architecture with interstitial fibrosis<sup>1</sup>. In India as per recent Indian Council of Medical Research data, the prevalence of CKD as 17.2% with stage 1, 2, 3, 4, 5 as 7%, 4.3%, 4.3%, 0.8% and 0.8% respectively<sup>2</sup>. The overall goal of therapy in individuals with CKD is to delay or prevent progression of the disease, thereby minimizing the development or severity of associated complications and ultimately progression ESRD limitina the when haemodialysis, peritoneal dialysis or kidney transplantation is required <sup>3</sup>.The National Kidney Disease foundation's Kidney Disease Outcome Quality Initiative recommends that planning for dialysis begin when patients reach CKD stage -GFR and creatinine clearance below 30ml/min per 1.73m<sup>24</sup>.

Adjustment of the usual drug dosage regimen is necessary for the patients with renal dysfunction to avoid excessive accumulation of the drug and/or its active metabolite(s) which could result in serious adverse reactions. The dosage

regimen is distinguished by the maintenance dose (DM) and the dosing interval (T). In renal impaired patients, prescriptions requiring dose adjustment are not appropriately adjusted. Inappropriate dosing in patients with renal dysfunction can cause toxicity or ineffective therapy. Therefore, the standard dosage regimen of the drugs have to be adjusted in patients with renal dysfunction. In patients with CKD, several pharmacokinetic factors may be altered. These include bioavailability, volume of distribution protein binding,  $(V_d)$ , biotransformation and excretion<sup>5</sup>. Pharmacist as a full member of the patient care team has been shown to significantly reduce medication errors at prescribing stage. Pharmacists can also offer their expertise in choosing the safest and most efficacious drug to prevent ADRs and help promote the rational use of drugs. The information provided by the pharmacists through the information services can further assist clinicians regarding drug dose adjustment<sup>6</sup>.

#### STUDY DESIGN

The study design used was Prospective Observational study

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# DEPARTMENT SELECTED FOR THE STUDY IN THE HOSPITAL

The study was carried out in General Medicine and Nephrology Department.

#### STUDY DURATION

The study was carried out over a period of 6 months (January 2018 – June 2018)

#### SAMPLEPOPULATION

About 93 renal patients were screened and 60 were included in this study after getting patient's consent.

#### SELECTION OF STUDY SUBJECTS Inclusion criteria:

- 18 years and above.
- Chronic kidney patients with or without comorbidities.
- Patient with GFR <59ml/ min.

#### **Exclusion criteria:**

- Acute renal failure.
- Pregnant and lactating women.
- Patient with insufficient data.

#### STASTICAL ANALYSIS

The statistical analysis was done using Microsoft Excel.2010. Collected data was entered in Microsoft excel spreadsheet for further interpretations.



















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22

#### DISCUSSION

Chronic kidney disease is a common, progressive disease that is becoming a universal public healthproblem<sup>7</sup>.CKD was significant higher in males with 68.3 % and females 31.7 %. This is in concordance with a study conducted by (Getachew et al.2015) where the percentage of male and female was found to be 55% and 45 % respectively<sup>8</sup>.In the present study the occurrence of CKD was highest in patients within the age category (61 - 70) i.e. 21 patients (35 %). Our study tallies The Third National Health and Nutrition Examination Survey (NHANES III), data of populations at increased risk for developing ESRD include the older population, particularly patients65 years of age and older<sup>9</sup>. The classification of CKD staging based on the GFR was found to be ESRD (75 %) and stage 4 (15 %). This is in agreement with the study done by Mohammed A. Hammad et al (2016), which reports that a continued increase incidence rates of ESRD has been observed over the past decade<sup>7</sup>. In our study patients presented with multiple comorbidities. The most common diseases among followed by them were anemia (90%), hypertension (56%), diabetes (50%). cardiovascular disease (17%) and respiratory disorder (5%). This is in agreement with the study conducted by Melissa E. Stauffer et al<sup>10</sup>. The serum creatinine level was found to be within the range of 6 - 10 mg/dl in 28 patients (46.7 %) and in the range of 0-5 mg/dl in 23 patients (38.3%). This is similar to the study done by Nisha R et al (2017) where the mean serum creatinine level was in the similar range<sup>11</sup>. Dose adjustment was required in 195 (37.2%) of 524 prescription entries. Of the 195 prescription entries, 4 % (20) was found to be inappropriate and 32 % (175) was found to be appropriate. A similar study was conducted by Getachew et al (2015) where out of the total number of prescriptions (n = 372) 49 % (57) of the entries appropriate and 51 % (58) were was inappropriate<sup>8</sup>. When type of medication and dose adjustments were evaluated, Tramadol was most frequently prescribed drug that the required dose adjustment, which was appropriately adjusted in 7 out of 8 cases; followed by Aspirin, Levocetrazine and Spiranolactone which were appropriately adjusted in 4 out of 5,2 out of 5 and 1 out of 3 of cases respectively. Piracetam ,Metformin and Tranexamic acid remained unadjusted in all the casesas they were found to be contraindicated .

Medications that were less frequently prescribed were categorised under others.

#### METFORMIN

As the patient's renal function may be unstable, patients whose GFR is under 60 mL/min should be treated with less dangerous alternative drugs, such as the DPP-IV inhibitor sitagliptin, whose dose should be halved if the GFR is under 30 mL/min<sup>12</sup>.

#### TRANEXAMIC ACID

The usual dose is 10 mg/kg three or four a times a day. Recommended dose reduction of TA in patients with renal impairment is as follows: for serum creatinine of 120–250  $\mu$ mol/L 10 mg/kg intravenously twice daily; for serum creatinine of 250–500  $\mu$ mol/L 10 mg/kg intravenously once daily; for serum creatinine above ≥500  $\mu$ mol/L 10 mg/kg intravenously every 48 hr<sup>13</sup>.

#### PIRACETAM

Normal dose is 1200 mg. In mild cases ( $CI_{cr} = 50 - 79 \text{ ml/min}$ ) 800mg ( $2/3^{rd}$  of normal dose) in 2 to 3 divided doses, in moderate cases ( $CI_{cr} = 30 - 49 \text{ ml/min}$ ) 400mg ( $1/3^{rd}$  of normal dose) in 2 divided doses and in severe cases ( $CI_{cr} = <30 \text{ ml/min}$ )200mg( $1/6^{th}$  of normal dose) in a single dose<sup>14</sup>.

#### CONCLUSION

The study concludes that appropriate dose adjustment in patients with renal impairment was done in a significant percentage. The need for providing doctors with information and guidelines for dose adjustment in patients with renal impairment is for optimal clinical outcomes and to prevent toxicity resulting from dosing error. It was found that Piracetam. Metformin and Tranexamic acid remained unadjusted in all the cases as it is contraindicated in renally impaired patients. The presence of clinical pharmacist at physician rounds will help to review all medications as an effective solution to reduce dosing errors and overall improvement in pharmaceutical care.

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