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Research Article

Drug Dose Adjustments in Chronic Kidney Disease Patients

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Abstract

The incidence of Chronic Kidney Disease are extremely increasing world wide due to rise in diabetes, hypertension, cardiovascular diseases. As kidney is a main eliminating organ, its function decreases in renal failure results in build up of drugs which cause toxic effects. The aim is to assess the prescribing drug dose adjustment in chronic kidney disease patients. Objectives are to predict glomerular filtration rate by using Modified diet in renal failure formulae. To assess the drug dose adjustments in renal failure patients. A prospective observational study was carried out in SVRRGGH during October 2016 to March 2017. A total of 125 patients diagnosed with CKD are included in study. Patients who are not willing, below 18 years, special population including pregnant, lactating women were excluded from study. Proforma was used to collect data. Total of 125 patients were included in study, men constituted 86(68.8%) of total population. Most effected age group was 51 - 60 years (29.6%). The study population with stage-4, 44 (35.2%) were higher. In total 1163 studied drugs, only 149 drugs are to be dose adjusted, out of that 102 (68.45%) were not dose adjusted and 47 (31.54%) were adjusted. It is concluded that more than half of drugs was not dose adjusted and there is need of dose adjustment in hospitalized chronic kidney disease patients. Continuous medical education of physicians and collaboration with clinical pharmacist is an important issue for quality improvement regarding renally impaired patients.

Keywords: Chronic Kidney Disease; Dose Adjustments; Renal Failure; Glomerular Filtration Rate

Abbreviations

CKD: Chronic Kidney Disease; GFR: Glomerular Filtration Rate; K/DOQI: Kidney Disease Outcomes Quality Initiative; MDRD: Modified of Diet in Renal Disease; NKF: National Kidney Foundation; SVRRGGH: Sri Venkateswara Ramnarayan Ruia Government General Hospital

Introduction

The Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) defines CKD as either kidney damage or a decreased glomerular filtration rate of less than 60 mL/min/1.73 m^2 for 3 or more months [1]. Chronic Kidney Disease is a world wide public health problem with an increasing prevalence, incidence, poor outcomes and high cost [2]. Chronic kidney disease decreases kidney function, resulting in decrease in elimination of drugs which leads to accumulation of drugs and precipitation of adverse drug reaction [2]. CKD affects the elimination of renally excreted drugs and other pharmacokinetic processes involved in drug disposition [2]. In renal failure patients dosing errors can cause adverse effects and poor outcomes. Dose of drugs should be adjusted according to creatinine clearance or GFR [2]. Inappropriate dosing in patients with chronic kidney disease can cause in effective therapy. In particular, older patients are at high risk of developing adverse events caused by age related decline in reneal function and the use of multiple medications to treat comorbid conditions [2]. Recommended equations for estimation

of glomerular filtration rate (GFR) using serum creatinine concentration (S_{Cr}), age, sex, race, and bodyweight.

Equation from the modification of diet in renal disease study (MDRD): Estimated GFR (mL/min per 1.73 m^2) = 186 x $(S_{Cr})^{-1.154}$ x $(age)^{-0.203}$ x (0.742 for women).

Cockcroft-Gault equation: Estimated creatinine clearance (mL/min).

(140-age) x body weight (kg)

72 x S_{Cr} (mg/dL)

Multiply by 0.85 for women [3].

In this study MDRD equation was considered due to lack of information on body weight of patients.

Aim of the Study

To assess the prescribing drug dose adjustments in chronic kidney disease patients.

Objectives of the Study

- To predict the GFR by using Modified diet in renal failure formulae.
- To assess the drug dose adjustments in renal failure patients.

Methodology

Study design: Prospective Observational study.

Study place: Sri Venkateswara Ramnarayan Ruia Government General Hospital (SVRRGGH).

Study duration: 6 months (October 2016 to March 2017).

Study size: 125 prescriptions.

Study site: Department of General Medicine.

Statistical analysis: Mean, Percentages.

Inclusion criteria

All inpatients with diagnosis of CKD in general medicine department both male and female medical wards.

Exclusion criteria

- Patients below 18 years
- Patients who were not willing.
- Special population including pregnant women and lactating women.

Data collection

A designed proforma and informed consent form was used for collection of data. The proforma contain patient demographics, diagnosis, admission complaints, past medical history, past medication history, family and surgical history, laboratory investigation reports and drugs prescribed. A evaluation proforma was used to evaluate data from proforma. Evaluation proforma contain information on co-morbidities, risk factors in CKD patients, estimation of GFR, CKD stage and dosage adjustment of drugs.

By using Modified Diet in Renal Disease (MDRD) formula Glomerular Filtration Rate (GFR) was estimated. Stage of CKD can classified based GFR value. A specially designed dose adjustment guidelines was prepared by using Myrnay. Munar, Harleen Singh. American family physician guidelines [4] and used for dose adjustments of drugs in prescriptions. The doses of drugs are adjusted based on GFR. The data was collected manually and then entered to Excel sheet data base.

Ethical consideration

Study was carried out from October 2016 to March 2017 after obtaining permission from the Institutional Ethics Committee and after getting consent from all the participating subjects.

Results

Gender	No. of Patients (n=125)	Percentage (%)
Male	86	68.8%
Female	39	31.2%

Table 1: Gender wise distribution in the study population.

Age (Years)	Female (n = 39)	Male (n = 86)	Total (n = 125)	Percentage (%)
21-30	1	3	4	3.2%
31-40	7	4	11	8.8%
41-50	8	18	26	20.8%
51-60	12	25	37	29.6%
61-70	4	27	31	24.8%
71-80	7	8	15	12%
81-90	0	1	1	0.8%

Table 2: Age distribution in study population.

CKD stage	No. of patients (n = 125)	Percentage (%)
Stage-1	5	4%
Stage-2	9	7.2%
Stage-3a	13	10.4%
Stage-3b	7	5.6%
Stage-4	44	35.2%
Stage-5	43	34.4%
None	4	3.2%

Table 3: Stages of CKD in study population.

Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m ^{2})

Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m^2)

Stage 3a: Moderate reduction in GFR (45-59 mL/min/1.73 m^2)

Stage 3b: Moderate reduction in GFR (30-44 mL/min/1.73 m^2)

Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m^2)

Stage 5: Kidney failure (GFR <15 mL/min/1.73 m^2 *or dialysis)*

None: Patients who are not undergone serum creatinine test.

Drugs	Total	Adjusted	Non adjusted
Anti hypertensives			
Enalapril	13	3	10
Atenolol	4	1	3
Clonidine	3	2	1
Spironolactone	18	9	9
Cardiac glycosides			
Digoxin	8	1	7
Antiplatelets			
Aspirin	33	12	21
Antifungals			
Fluconazole	3	3	0
Antibiotics			
Cefixime	1	0	1
Cefoperazone and Sulbactam	1	0	1
Cefotaxime	1	0	1
Amoxicillin/Clavulanate	15	2	13
Meropenem	1	1	0
Piperacillin/tazobactam	6	0	6
Norfloxacin	2	1	1
Azithromycin	4	0	4
Ciprofloxacin	7	0	7
Sulfamethoxazole+ Trimethoprim	3	2	1
Antacids			
Ranitidine	7	2	5
Anagesics			
Tramadol	6	4	2
Antidiabetics			
Metformin	8	1	7
Glimepiride	5	3	2
Total (Percentage)	149	47 (31.54%)	102 (68.45%)

Table 4: Drug dosage adjustments in CKD patients.

Discussion

In this study only drugs need to be dose adjusted in renal failure was considered. Out of 1163 drugs 141 drugs need dose adjustment. Among the 149 drugs 102 (68.45%) were nonadjusted and 47 (31.54%) were adjusted. Were as in Abdulrahaman M Alahdal, Ahmed A: Elberry study [5] 53.1% drugs are nonadjusted. In Ahsan Saleem, Imran Masood study [6] 58.2% are unadjustded and 41.8% are adjustded. The present study shows most drugs requiring dose adjustments was antibiotics especially Amoxicillin/Clavulanate. But in Abdulrahaman M Alahdal, Ahmed A: Elberry study [5] most dose adjustment needed drug is Vancomycin among antibiotics. The dose adjustment can done by reducing the dose of drug or by increasing the dosing interval. Followed by Amoxicillin/Clavulanate, Ciprofloxacin and Piperacillin/tazobactam are antibiotics need dose adjustment.

After antibiotics antihypertensives are drugs needed dose adjustment, especially Spironolactone 9, Enalapril 10 and Atenolol 3. Digoxin is a cardiac glycoside which has narrow therapeutic range (0.8 - 2 mcg per liter), above this level can cause serious toxicity. Higher or lower potassium levels may also lead to toxicity. Digoxin is mostly excreted in unchanged form by kidneys, in normal patients the half life of digoxin is 36 hours, in renal failure patients the elimination is much longer depending on stage of renal dysfunction. Hence in CKD dose adjustment of digoxin is important. In this study digoxin was given to 8 patients among them adjusted are one and unadjusted are seven, so most of patients needed dose adjust- ments. Even though Oral hypoglycemics are less prescribed due to their complications in CKD. Among prescribed drugs some needed dose adjustments.

Metformin was given to 8 patients in that one is adjusted and seven unadjusted. According to FDA metformin should not be used with decreased creatinine clearance or ≥ 1.4 mg/dl in women and serum creatinine ≥ 1.5 mg/dl in men. Because Metformin is renally cleared and may cause lactic acidosis in renal impairment. Glimepiride was prescribed to five patients among them only 2 patients need dose adjustment. Glimepiride and their metabolites are

renally eliminated, leading to increased risk of hypoglycemia as GFR declines. Hence dose adjustments practice in the hospital has to be improved [7-10].

Conclusion

It is concluded that more than half of drugs was not dose adjusted, there is need of dose adjustment in hospitalized chronic kidney disease patients. Continuous medical education of physicians and collaboration with clinical pharmacist is an important issue for quality improvement regarding renally impaired patients.

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