

## DEVELOPMENT OF RENAL DOSING GUIDELINES FOR NONSTEROIDAL ANTI-INFLAMMATORY DRUGS AND ANTIBIOTICS - A PROSPECTIVE STUDY

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### ABSTRACT

**Objectives:** The objectives of this study were to determine the impact of renal dosing guidelines on prescribing pattern for nonsteroidal anti-inflammatory drugs and antibiotic in patients with chronic kidney disease (CKD).

**Methods:** This was a prospective interventional study. The study was divided into two phases, pre-intervention and post-intervention phases. Data regarding the kidney function and the pattern of drug dosing will record in the pre-intervention phase. Pocket guides were prepared for the drug dosing in renal impairment and were distributed to clinicians and the pharmacist as a part of intervention. In the post-intervention phase, the dosing pattern of renal eliminated drugs was observed for any improvement. The patterns of dosing of renal eliminated drugs were compared in both the phases.

**Results:** In pre-interventional phase, a total of 43 cases were reviewed, 20 of them were non-hemodialysis (non-HD) (9 female and 11 male) cases with a mean±standard deviation (SD) age of 56.05±8.22 (56) and 23 were undergoing HD (11 female and 12 male) cases with a mean±SD age of 56.72±6.85 (56). In the post-intervention phase, a total of 41 cases were reviewed, 22 of them were non-HD (12 female and 10 male) cases with a mean±SD age of 55.85±6.87 (57) and 19 were undergoing HD (10 female and 9 male) cases with a mean±SD age of 55.77±8.39 (56.6).

**Conclusion:** Health-care professionals have an important responsibility in monitoring the dose for renal impairment patients. Development of renal dosing guidelines for patients hospitalized with CKD can improve the pattern of prescribing in renal failure population.

**Keywords:** Renal dose, Guidelines, Nonsteroidal anti-inflammatory drugs, Antibiotics.

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### INTRODUCTION

The kidneys are bean-shaped organs found on the left and right sides of the body in vertebrates [1,2]. The nephron is the structural and functional unit of the kidney. Each adult kidney contains around one million nephrons. The nephron utilizes four processes to alter the blood plasma which flows to it: Filtration, reabsorption, secretion, and excretion [3,4]. The kidneys also carry out functions independent of the nephron. For example, they convert a forerunner of Vitamin D to its active form, calcitriol, and synthesize the hormones such as erythropoietin and renin [5,6]. Renal physiology was the study of kidney function. Nephrology is the medical specialty which addresses diseases of kidney function, which include chronic kidney disease (CKD), nephritis and nephritic syndrome, acute kidney injury, and pyelonephritis. Urology addresses diseases of the kidney (and urinary tract) anatomy which include cancer, renal cysts, kidney stones and ureteral stones, and urinary tract obstruction [7,8]. Dialysis and kidney transplantation are used to treat kidney failure; one (or both sequentially) of these are almost always used when renal function drops below 15%. Nephrectomy was frequently used to cure renal cell carcinoma [9,10].

### METHODS

This was a prospective interventional study. Subjects will be recruited according to selection criteria. A structured data collection form is designed to collect the information from the case sheets of the patients. The study was divided into two phases, pre-intervention and post-intervention phases. Data regarding the kidney function and the pattern of drug dosing will record in the pre-intervention phase. Pocket guides were prepared for the drug dosing in renal impairment and were

distributed to clinicians and the pharmacist as a part of intervention. In the post-intervention phase, the dosing pattern of renal eliminated drugs was observed for any improvement. The patterns of dosing of renal eliminated drugs were compared in both the phases. Ethical committee approval no. VISTAS-SPS/IEC/IV/2017/07.

### RESULTS

In the pre-interventional phase, a total of 43 cases were reviewed, 20 of them were non-hemodialysis (non-HD) (9 female and 11 male) cases with a mean±standard deviation (SD) age of 56.05±8.22 (56) and 23 were undergoing HD (11 female and 12 male) cases with a mean±SD age of 56.72±6.85 (56). In the post-intervention phase, a total of 41 cases were reviewed, 22 of them were non-HD (12 female and 10 male) cases with a mean±SD age of 55.85±6.87 (57) and 19 were undergoing HD (10 female and 9 male) cases with a mean±SD age of 55.77±8.39 (56.6) (Table 1). The number of drugs that prescribed was found to be 479. The number of nonsteroidal anti-inflammatory drugs (NSAIDs) and Antibiotics prescribed was found to be 59 for non hemodialytic patients and 57 for hemodialytic patient. The number of NSAIDs that required dose adjustments was found to be 13 for non-HD patients and 11 for HD patients. The number of antibiotics that required dose adjustments was found to be 16 for non-HD patients and 17 for HD patients. (Table 2). As a part of intervention study, pocket guides were prepared for the NSAIDs and antibiotic drug dosing in renal impairment and were distributed to the clinician. Post-intervention, the number of drugs that prescribed was found to be 410. In that, the total number of NSAIDs and antibiotics prescribed was found to be 65 for non-HD patients and 62 for HD patients. The number of NSAIDs that required dose adjustments was found to be 6 for non-HD patients and 9 for HD patients. The number of antibiotics that required dose adjustments was found to

Table 1: Demographic profile of study population

Demographics	Pre-intervention		Post-intervention	
	Non-HD (20)	HD (23)	Non-HD (22)	HD (19)
Gender				
Female (%)	9 (45)	11 (47.82)	12 (54.54)	10 (52.63)
Male (%)	11 (55)	12 (52.17)	10 (45.45)	9 (47.36)
Age				
Mean+SD (median)	56.05+8.22 (56)	56.72+6.85 (56)	55.85+6.87 (57)	55.77+8.39 (56.6)
Serum creatinine				
Mean+SD (median) Serum creatinine	5.03+2.01 (5.2)	5.33+2.37 (5.2)	5.18+1.90 (5.2)	5.00+1.72 (4.9)

Non-HD: Non-hemodialysis, SD: Standard deviation

Table 2: Number of medications prescribed in study population

Category	Pre-intervention		Post-intervention	
	Non-HD	HD	Non-HD	HD
Total number of prescriptions	20	23	22	19
Total number of drug prescribed	212	259	217	203
Total number of NSAIDs and antibiotics prescribed	59	57	65	62
Number of antibiotics dosed appropriately	18	15	28	23
Number of NSAIDs dosed appropriately	12	11	23	24
Number of NSAIDs dosed in appropriately	13 (63.15%)	14 (63.63%)	6 (28.57%)	9 (50%)
Number of antibiotic dose in appropriately	16 (84.21%)	17 (77.27%)	8 (49.76%)	6 (33.33%)

NSAIDs: Nonsteroidal anti-inflammatory drugs, Non-HD: Non-hemodialysis

Table 3: Details of the type of dosing adjustment needed

Type of adjustment	Pre-intervention	Post-intervention
	Number of drugs, n=60 (%)	Number of drugs, n=29 (%)
Dose reduction	28 (46.6)	11 (37.9)
Change in dosing interval	24 (40)	8 (27.5)
not recommended	8 (13.3)	10 (34.4)

Table 4: Impact of pocket guide on dosing adjustments

Parameters	Pre-intervention		Post-intervention		p value
	Total	Inappropriate (%)	Total	Inappropriate (%)	
In non-HD NSAIDs	25	13 (63.15)	29	6 (28.57)	0.0163*
Antibiotics	34	16 (77.27)	36	8 (49.76)	0.0287*
In HD patients NSAIDs	25	14 (63.63)	33	9 (50)	0.0268*
Antibiotics	32	17 (84.21)	29	6 (33.33)	0.0090

NSAIDs: Nonsteroidal anti-inflammatory drugs, Non-HD: Non-hemodialysis

be 8 for non-HD patients and 6 for HD patients. (Table 2). The type of dosage adjustments needed was found to be dose reduction in 46% (28 drugs) of the drugs for pre-intervention phase and 37.9% (11 drugs) in post-intervention, change of dosing interval in 40% (24 drugs) of the drugs in pre-intervention and 27.5% (8 drugs) in post-intervention, and about 13.3% (8 drugs) in pre-intervention and 34.4% (10 drugs) in post-intervention which were not recommended for the prescribing in renal function (Table 3). By comparing the results of post- and pre-intervention phases, it is clear that there is a significant impact of the dosing guidelines in the form of pocket guides in improving the dosing pattern of the renally eliminated drugs. The rate of inappropriateness in dosing was significantly reduced in post-intervention phase as compared to pre-intervention phase. Inappropriateness in dosing was significantly reduced in antibiotics from 77.27% to 49.76% ( $p=0.0287^*$ ) in non-HD patients and NSAIDs reduced its inappropriateness of dosing from 63.15% to 28.57% in non-HD patients ( $p=0.0163^*$ ). Furthermore, inappropriateness in dosing was significantly reduced in antibiotics from 84.21% to 33.33% in HD patients ( $p=0.0090^{**}$ ) and NSAIDs

reduce its inappropriateness in dosing from 63.63% to 50% in HD patients (Table 4).

#### DISCUSSION

By comparing the results of post- and pre-intervention phases, it is clear that there is a significant impact of the dosing guidelines in the form of pocket guides in improving the dosing pattern of the renally eliminated drugs. The rate of inappropriateness in dosing was significantly reduced in post-intervention phase as compared to pre-intervention phase. Inappropriateness in dosing was significantly reduced in antibiotics from 77.27% to 49.76% ( $p=0.0287^*$ ) in non-HD patients and NSAIDs reduced its inappropriateness of dosing from 63.15% to 28.57% in non-HD patients ( $p=0.0163^*$ ). Furthermore, inappropriateness in dosing was significantly reduced in antibiotics from 84.21% to 33.33% in HD patients ( $p=0.0090^{**}$ ) and NSAIDs reduce its inappropriateness in dosing from 63.63% to 50% in HD patients

**CONCLUSION**

The prevalence of CKD is increasing and polypharmacy is common. There is a need to monitor the dosing of drugs in those patients to avoid the adverse effects, to reduce the length of stay in the hospital, and to control the unnecessary cost of medications. Antibiotic and NSAID prescriptions required dosage adjustment based on patient's renal function. Health-care professionals have an important responsibility in monitoring the dose for renal impairment patients. Development of renal dosing guidelines for patients hospitalized with CKD can improve the pattern of prescribing in renal failure population.

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