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OPTIMISATION OF DOSING ANTIBIOTICS IN RENAL IMPAIREMENT PATIENTS

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ABSTRACT

Aims &Objectives: To study the antibiotics dosage adjustment in renal impairement patients. To evaluate the rationalized use of antibiotics in a givenprescription based on renal dysfunction. Drug dosage adjustment in an individual renal impairement patients can maximize therapeutic afficacy and minimize adverse effects.This dosage adjustment also minimize the therapeutic costs, length of hospital stay and mortality as well as therapeutic effectiveness. Methodology: Prospective Observational Study was conducted on 150 Patients in a Teritiary Care Hospitals. Demographic data were extracted and creatinine clearance was calculated by using Cockcroft-Gault equation. Antibiotic dosages were compared with stanford guidelines dose recommendations to judge whether they were correctly adjusted or not. Results: Among 150 patients ,94 were male &56 were female. Out of all the patients,53 patients are done with dialysis .Totally 220 antibiotics were prescribed. Out of that 127 antibiotics require dosage adjustment,94 antibiotics were adjusted correctly and 33 were incorrectly prescribed. Piperacillin +tazobactam was the most frequently prescribed antibiotic requiring dosage adjustment (18.1%)followed by Levofloxacin(14%). Piperacillin + tazobactam was the majorly used antibiotic (63.6%) with inappropriate dose. In most of the cases inappropriate dosage adjustment (60%), guideline's recommended dosing intervals were not followed. Of the unadjusted doses, 18 incorrect interval cases, 5 incorrect dose, and in 10 cases incorrect dose and interval were observed. Conclusion: Approximately 71.3% antibiotics were adjusted appropriately in this study and remaining 28.7% were adjusted inappropriately.Findings indicate that dosing errors were common among hospitalized patients with renal impairment. Improving the quality of drug prescription in patients with renal impairment could be of importance for improving the quality of care.

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INTRODUCTION

To study the antibiotics dosage adjustment in renal impairement patients and to evaluate the rationalized use of antibiotics in a given prescription based on renal dysfunction.

Renal Impairement:

Renal impairment may be acute or chronic - both of which can result in problems with medications. Renal impairment may be the result of a variety of renal or systemic diseases. Normal ageing results in a decline in renal function due to loss of nephrons. When prescribing for elderly patients, it should therefore be assumed that some degree of renal impairment exists. The accumulation and toxicity of many drugs can develop rapidly if dosages are not adjusted in patients with renal impairment. More than half of the adverse drug effects are due to the inappropriate dosage adjustments. Generally Cephalosporins, Carbapenems, Beta lactam antibiotics, Anti hypertensives, Anti emetics, Analgesics and Vitamin supplements are used in renal dysfunction. Even though not common yet, different strategies such as setting automated alerts and dosing checks for physicians'prescribing drugs to patients with renal failure had been conducted, where the latter did not seem to be improved enough to comply with available dosing guidelines especially in the elderly and patients with unstable renal function. [1]

When renal function is impaired any antibiotic which is normally excreted through kidneys will be retained in the body. Continued administration of such a drug in normal dosage will result in abnormally high levels being reached,and dangerous side effects may develop. It has long been appreciated that some modification of dosage was required in patients with renal failure.[2]

Dosage Adjustments:

Drug dosing errors are common in patients with renal impairment and can cause adverse effects and poor outcomes. Dosages of drugs cleared renally should be adjusted according to creatinine clearance or glomerular filtration rate and should be calculated using online or electronic calculators. Recommended methods for maintenance dosing adjustments are dose reductions, lengthening the dosing interval, or both.[3].

In clinical practice, dose adjustments are commonly informed by guidelines which may be based on interpretations of measured TDM concentrations. The dose adjustment strategies depend on the pharmacokinetic properties and the specific PK/PD index of the antibiotic. Generally, for antibiotics with concentration-dependent activity where the goal is to achieve a target peak concentration (Cmax) to MIC ratio (Cmax/MIC) or target ratio of the area under the concentration-versus-time curve (AUC) to the MIC (AUC/MIC), adjustment of the magnitude of the dose may be adequate; whereas for time dependent antibiotics, like the beta-lactams, adjusting the frequency or mode of administration (prolonged infusion in preference to intermittentbolus administration) is the best approach to maximize the time the free drug concentration remains above the MIC[4].

MATERIALS& METHODS

The protocol for the proposed study was submitted to the Institutional Ethics Committee(IEC) of Nirmala College Of Pharmacy, Atmakuru, Guntur district, Andhra Pradesh. The protocol was approved by the IEC.

Study Design: Study was Prospective Observational Study conducted in patients in Teritiary Care Hospitals in the Department Of Nephrology.

Inclusion Criteria:

Renal Impairement patients in between the age group of 10-80years.

Exclusion Criteria:

Pediatric Patients, Pregnancy Patients.

Source Of Data:

All the necessary and relevant data was obtained from Patient / Care taker interview, Demographic details**,** Lab parameters**,** Treatment Chart **,** Other relevant data sources.

Procedure:

In Department of Nephrology 150 renal impairement cases were collected and the content collected was patient demographic graphic details, lab parameters and medications mainly targeting the antibiotic doses and their intervals were collected. Creatinine clearance was calculated by using Cockgroft gault equation.

Males - (140-age)/ serum creatinine x Wt/72

Females - (140-age)/ serum creatinine x Wt/ 72 x 0.85 [5]

Antibiotics doses were adjusted based on the patient age, weight,sex and serum creatinine levels.Recommended methods for mainataining dosage adjustments are dose reductions, lengthening the dosing interval or both.In clinical practice dosage adjustments are commonly informed by guidelines which may be based on interpretations of measured TDM concentrations. Here in this study Stanford guidelines were followed.[6]

RESULTS:

A total of 150 patients were included in the study and the Percentage of diseased population in particular age group were presentented in Table 1

Table-1: Percentage of diseased population in particular age group.

S.no	Creatinine Clearance(ml/min)	Male	Female	Total no.of patients
1	> 50	9	6	15
2	30 to 50	18	7	25
3	10 to 29	48	38	86
4	<10	15	9	24

The diseased population were high in between the age group of 51-60years i.e, 29.3%[n=42] and were less in between 20-30years i.e, 1.3%[n=2].The renal impairement was higher in males [n=94] than in females[n=56],this result was similar with the study performad by Fanak Fahimi which shows males with renal impairement are predominant than females [7]

Figure-1:

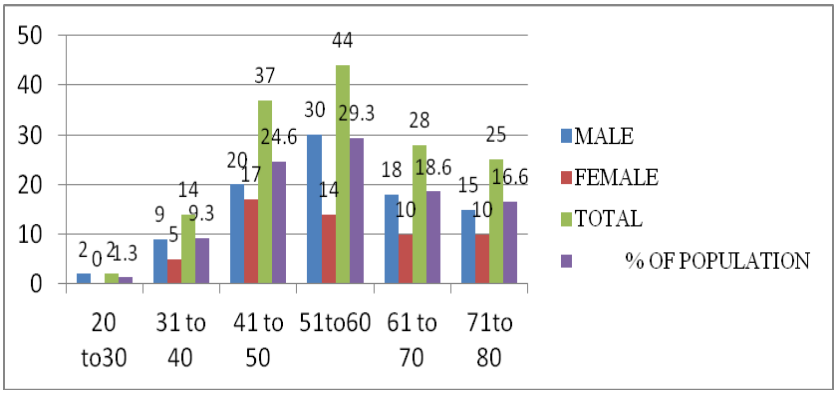

Table -2 : Distribution of patients based on creatinine clearance.

S.no	Age group	Male	Female	Total	% Of Population
1	20 to30	2	0	2	1.3
2	31 to 40	9	5	14	9.3
3	41 to 50	20	17	37	24.6
4	51to60	30	14	44	29.3
5	61 to 70	18	10	28	18.6
6	71to 80	15	10	25	16.6

The above table shows more number of patients were within the range of 10-29 ml/min[n=86] and less patients were ≤ 50 ml/min[n=15].

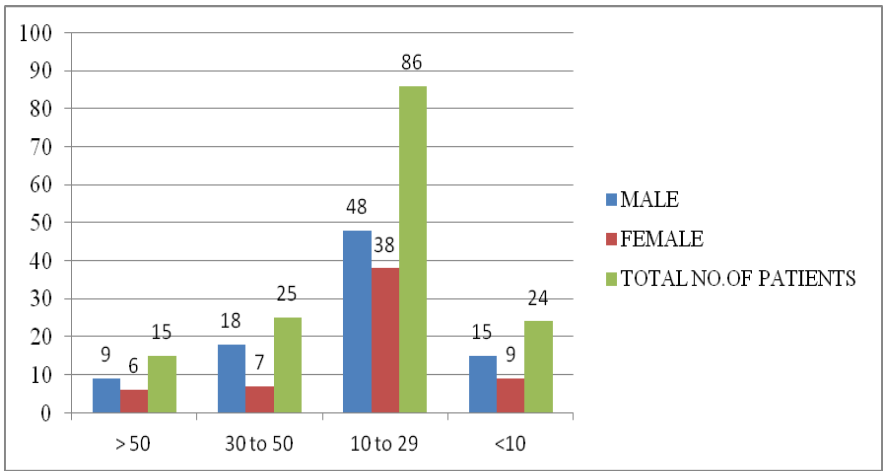

Figure -2 : Distribution of patients based on creatinine clearance.

Table -3: Distribution of patients with particular comorbidities.

S.no	Comorbidities	Number Of Patients
1	Hypertension	28
2	Diabetes	11
3	HTN+DM	46
4	Cardiovascular	13
5	others	24

The above table shows highest number of patients are with comorbities of both hypertension & diabetes [n=46] and less number of patients were with cardiovascular complications [n=13]. [8]

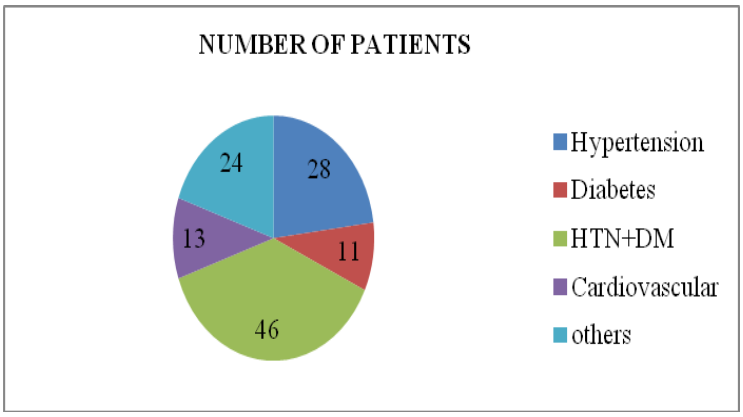

Figure-3: Distribution of patients with particular comorbidities.

Table -4: Distribution of patients with and without dialysis.

S. no	Patients With Dialysis	Without Dialysis
1	53	97

Out of 150 patients, greater number were without dialysis [n=97] and remaining were gone with dialysis [n=53] [9]

Table-5: Total number of Antibiotics prescribed.

S. no	Name Of Antibiotics	Number Of IV antibiotics	Number Of Oral Antibiotics	Total
1	Piperacillin+tazobactam	40	0	40
2	Amoxicillin+clavulonic acid	21	7	28
3	Levofloxacin	10	21	31
4	Cefoperazone+sulbactam	23	0	23
5	Metronidazole	16	3	19
6	Linezolid	---	13	13
7	Ertapenam	10	0	10
8	Ceftriaxone	8	0	8
9	Doxycycline	7	0	7
10	Azithromycin	5	3	8
11	Amikacin	5	0	5
12	Meropenem	3	1	4
13	Imepenam+Cilastatin	4	0	4
14	Cefotaxim	2	0	2
15	Ofloxacin	2	0	2
16	Cefpodoxim	0	1	1
17	Ciprofloxacin	0	2	2

Totally 220 antibiotics were prescribed out of which Piperacillin +tazobactam was the most frequently prescribed antibiotic[18.3%], followed by levofloxacin [14%] and the less frequently prescribed antibiotic was cefpodoxime[0.4%].our result was different with study performed by Fanak Fahimi where Ciprofloxacin (29.1% of cases), and vancomycin (33.6% of cases), were the most inappropriate prescribed antibiotics.

Table-6: Percentage of Antibiotics within particular categories.

S. no	Category Of Antibiotics	Percentage[%]
1	Pencillins	34.9
2	Cephalosporins	26
3	Fluoroquinolones	14.3
4	Carbapenams	8.2
5	Tetracyclines	3.4

Among all the prescribed antibiotics, penicillins [34.9%] were majorly prescribed followed by cephalosporins [26%].

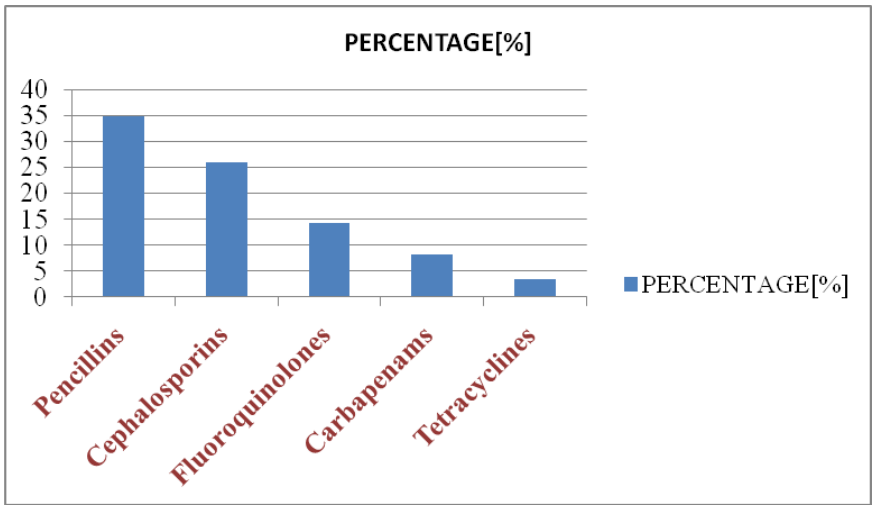

Figure-6: **Percentage of Antibiotics within particular categories.**

Table 7: Dosage adjustment.

S.no	Total no. of antibiotics	No. of antibiotics requiring dosage adjustment	No. of antibiotics prescribed correctly	No. of antibiotics prescribed incorrectly
1	220	127	94	33

Totally 220 antibiotics were prescribed. Out of that 127 antibiotics require dosage adjustment,94 antibiotics were adjusted correctly and 33 were incorrectly prescribed [10]

Table 8: Number of prescriptions with incorrect doses.

S.no	Antibiotics prescribed incorrectly	No. of prescriptions with incorrect doses
1	Piperacillin+ Tazobactum	21
2	Amoxicillin+ Clavulanic acid	3
3	Levofloxacin	2
4	Metronidazole	1
5	Amikacin	1
6	Ertapenem	2
7	Cefoperazone Sulbactum	2
8	Ampicillin + Sulbactum	1

The above table shows, Piperacillin + tazobactam was the majorly used antibiotic i.e, 63.6%[n=21] with inappropriate dose followed byAmoxicillin + Clavulonic acid i.e, 9%[n=3].

Table-9: Dosage Parameters.

S.no	Parameters	Number Of antibiotics
1	In correct doses	5
2	Incorrect dosing interval	18
3	Incorrect dose and dosing interval	10

In most of the cases ,inappropriate dosage adjustment (60%), guideline's recommended dosing intervals were not followed. Of the unadjusted doses, 18 incorrect interval cases , 5 incorrect dose, and in 10 cases incorrect dose and interval were observed. [11], [12]

CONCLUSION

- Clinical Evaluation Of this study will helps to decrease mortality rate, length of stay and further co-morbidities.
- Dosage adjustment study in renal impairement will stabilize the patient condition by giving correct doses based upon their serum creatinine levels.
- In this study approximately 71.3% antibiotic doses were adjusted appropriately and remaining 28.7% antibiotic doses were prescribed inappropriately.
- The findings indicate that dosing errors were common among hospitalized patients with renal impairment. Improving the quality of drug prescription in patients with renal impairment could be of importance for improving the quality of care.
- Further research is needed to monitor the adverse drug reactions due to inappropriate doses in renal impairement patients.

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