



**A PROSPECTIVE OBSERVATIONAL STUDY ON ASSESMENT OF  
NEPHROTOXICITY DUE TO USAGE OF CEFTRIAXONE AND AMIKACIN**

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**ABSTRACT**

**Aim:** This study sought to investigate or assessing the nephrotoxicity in patients who are administered ceftriaxone and amikacin more than 7 days. **Design:** A prospective observational study. **Methods:** All patients receiving ceftriaxone and amikacin were monitored and evaluated over 3 months. Patients who are administered in hospital receiving ceftriaxone and amikacin more than 7 days are recruited. Those patients are requested to undergo renal function test [BUN, SrCr] for assessment of kidney functioning test[RFT]. Based on the Renal function test percentage of occurring nephrotoxicity in those patients can be identified. **Results:** Result showed that amikacin and ceftriaxone-treated patients experienced a rise in the serum creatinine level and BUN that fit the designated definition of nephrotoxicity-i.e., an increase to at least 60 percent. **Conclusion:** Nephrotoxicity due to amikacin and ceftriaxone are confirmed in this present study. Therefore patients under antibiotic therapy, treatment must be done cautiously further in depth long term study is required for proving more information aimed to safer therapeutics, specially for antibiotics.

**KEYWORDS:** Ceftriaxone, Amikacin, Nephrotoxicity, BUN, Serum creatinine.

**INTRODUCTION**

Antibiotics are administered prior to some susceptible infections. Aminoglycosides and cephalosporins have potent activity against Gram negative bacilli and are often used to treat infections caused by these species, especially when resistance to beta lactam antibiotics is suspected. Cephalosporins are Beta-lactam antibiotics that are closely related both structurally and functionally to the penicillins. These are broad spectrum antibiotics and these are classified into three generations based on bacterial susceptibility. Cephalosporins are Administered intravenously because of their poor oral absorption. These are well distributed into body fluids, and elimination occurs through tubular secretion.

Ceftriaxone causes number of adverse effects, those are bleeding, nephrotoxicity, allergic manifestations and disulfiram like effect etc.<sup>[1]</sup> Aminoglycosides have potent activity against Gram negative bacilli and are often used to treat infections caused by these species, especially when resistance to beta lactam antibiotics is suspected. However, use of aminoglycosides is limited by concerns about toxicity, primarily nephrotoxicity and ototoxicity. The drugs are usually administered

intravenously in two to four doses a day in patients with normal renal function. A once daily dose is more convenient and has been proposed to be an equally effective and potentially less toxic mode of administration.<sup>[2,3,4]</sup> The drug is actively concentrated in the renal cortex and proximal tubular cells achieve maximum concentration. After entering the cortical cells AMG bind to lysosomes with formation of myeloid bodies/secondary lysosomes. Thereafter mechanisms are unclear. It is believed that the release of AMG into cytoplasm interferes with the phosphatidyl-inositol pathway. The transport system is a low affinity high capacity system that is not easily saturable. Thus momentary high drug concentrations as achieved immediately after intravenous injection result in saturation of the uptake mechanism. Hence, multiple dosing is more deleterious than single dosing bolus injection.<sup>[5]</sup> Ceftriaxone is a third-generation cephalosporin that is widely used to treat various infections during childhood. Long plasma half-life and single daily dose are the main advantages of this agent. Approximately 33% to 67% of ceftriaxone is excreted unmetabolized in the urine, whereas the remainder is excreted through biliary elimination. Clinical studies

have demonstrated that ceftriaxone can cause biliary pseudolithiasis, nephrolithiasis and bladder sludge, especially in children.<sup>[6,7,8]</sup> Aminoglycosides are antibiotics had been used in the treatment of serious infections due to aerobic gram bacilli. Mode of action of this aminoglycosides are by inhibiting the bacterial protein synthesis. These are bactericidal antibiotics, they are effective only against aerobic organisms. Pharmacokinetics of aminoglycosides are these all must be given parenterally to achieve adequate serum levels achieved. All are rapidly excreted into the urine, predominantly by glomerular filtration. Accumulation occurs in patients with renal failure, and requires dose modification. Aminoglycosides causes number of adverse side effects, it is important to monitor peak and trough plasma levels of gentamycin, tobramycin, netilmycin and amikacin to avoid concentration that cause dose related toxicities. The elderly patients are particularly susceptible to develop nephrotoxicity and ototoxicity. Nephrotoxicity; Retention of aminoglycosides by the proximal tubular cells disrupts calcium-mediated transport processes and results in kidney damage remaining from mild renal impairment to severe acute tubular necrosis which can be irreversible. Ototoxicity; Is directly related to high peak plasma levels and duration of treatment. Deafness may be irreversible and has been known to affect fetuses in utero. Neuromuscular paralysis. The side effect most often results after direct intraperitoneal or intrapleural application of large doses of aminoglycosides.<sup>[2]</sup> The nephrotoxicity of amikacin has been examined in a number of clinical trials.<sup>[8,9]</sup> employing various study designs and definitions of toxicity. An overall compilation of prospective clinical trials of aminoglycosides reported in the period 1975 to 1982 suggested that amikacin may be slightly less nephrotoxic than gentamicin. When the data were limited to those from comparative trials be-nephrotoxicity associated with amikacin was still less than that associated with gentamicin.<sup>[10,11]</sup>

#### AIM

This study sought to investigate or assessing the nephrotoxicity in patients who are administered with Ceftriaxone and amikacin more than 7 days.

#### OBJECTIVES

- To assess or estimate the prevalence pattern of the nephrotoxicity in the patients using Ceftriaxone and amikacin.

- To assess the adverse reactions of the Ceftriaxone and amikacin.

#### RESEARCH METHODOLOGY

##### Study Site

- All general medicine and surgery departments of Rajiv Gandhi Institute of Medical Sciences, a 750 bedded tertiary care teaching hospital, Kadapa.

##### Study Duration

- Study will be performed for approximately 3 months.

##### Study Population

- Approximately 30 patients.

#### PATIENT ENROLLMENT

##### Inclusion Criteria

- In this study we are recruited both age group between 2-70 years.
- The patients who are receiving both ceftriaxone and amikacin more than 7 days.

##### Exclusion Criteria

- We are excluded the patients from the study who are having the age below 2 years.
- We are excluded the patients who are already suffered with renal disease.
- We are excluded pregnancy and lactating women.
- We are excluded non co-operative, mentally retarded [psychiatric etc.] patients.

##### Method of Study

- Patients who are administered in hospital receiving ceftriaxone and amikacin more than 7 days are recruited.
- Those patients are requested to undergo renal function test [BUN, SrCr] for assessment of kidney functioning test [RFT].
- Based on the Renal function test percentage of occurring nephrotoxicity in those patients can be identified.

#### RESULTS

Among 30 patients were collected from general medicine department from this 18 (60%) patients were male and 12 (40%) were female. From that majority of them males are more affected.

**Table: 1 Based on gender wise distribution**

Gender	Number of patients (30)	Percentage %
Male	18	60%
Female	12	40%

**Table: 2 Based on age wise distribution**

Out of 30 patients 19 (63.6%) were of age group between 30-50 years and 11 (36.6%) were about in the age of 50-70years.

Age in years	Number of patients (30)	Percentage %
30-50	19	63.6%
50-70	11	36.6%

**Table: 3 Based on educational status**

A total of 30 patients 25(83.3%) patients were found to be literate and 5 (16.6%) individuals are illiterate.

Educational Status	Number of patients(30)	Percentage %
Literate	25	83.3%
Illiterate	5	16.6%

**Table:4 Based on comorbidity diseases**

A total number of 30 patients 2 (6.66%) patients are found to be CKD with HTN and 4 (13.3%)patients are found to be HTN with DM and 2(6.66%) patients are found to be PEPTIC ULCERS with HTN.

Diseases	Number of patients (30)	Percentage %
CKD with HTN	2	6.66%
HTN with DM	4	13.3%
Peptic ulcers with HTN	2	6.66%

**Table: 5 Frequency of Ceftriaxone induced RFT increased levels of BUN and Serum Creatinine levels.**

A total number of 30 patients 10 (33.3%) patients had experienced increased level of BUN and Serum creatinine levels.

Ceftriaxone [frequency]	Number of patients (30)	Percentage %
BD	10 patients had increased levels of RFT	33.3%

**Table: 6 Frequency of Amikacin associated with increased RFT BUN and SerumCreatinine.**

A total number of 30 patients 2 (6.66%) patients had experienced increased level of BUN and Serum creatinine.

Amikacin [frequency]	Number of patients (30)	Percentage %
BD	2 patients had increased levels of RFT	6.66%

**Table: 7 Frequency of both ceftriaxone and amikacin administration increased levels of BUN and Serum Creatinine.**

A total of 30 patients, respective patients were increased RFT after administration of ceftriaxone and amikacin therapy shown in table: 7.

Amikacin and Ceftriaxone [frequency]	Number of patients(30)	Percentage %
7 days BD	2 patients had increased RFT	6.66%
12 days BD	1 patient has increased RFT	3.33%
6 days BD	3 patients has increased RFT	10%

Increased levels of BUN and SrCr levels of patients; out of 30 patients 18 patients are experienced to be increased levels of RFT and cause the Nephrotoxicity.

## DISCUSSION

This prospective observational study is a component of medical audit which seeks monitoring, evaluation, and necessary modifications in the treatment procedure to achieve rational and cost effective medical care.

In our study we found that the majority of the male population has be affected with increased level of Renal function test BUN and Serum creatinine levels it may be due to over dosage of the treatment they given for above 7 days and also due to immunity of the body, Among the

enrolled subjects most of the individuals from the age group of 30-50 years are more affected with increased RFT levels.

According to our study we found that the majority of the patients are from the poor socioeconomic background, the upper middle class population individuals are less in our study. Among the two group of literate and illiterate, illeterates are found to be more effected with increased levels of RFT, when comparing unemployed are more effected, majority of the individuals affected in our study was observed as known smokers. Involvement of subjects was less in our study with habit of alcoholism when associating with non alcoholic.

Among 30 patients comorbidity disease state condition has been seen, 2 (6.66%) patients are the past history of CKD with Hypertension, 4 (13.3%) patients are the past history of hypertension with diabetes mellitus, 2 (6.66%) patients are found to be peptic ulcers with hypertension, majority of HTN with Diabetes are more patients are present.

Among 30 patients 10 (33.3%) patients are effected with increased level of BUN and Serum creatinine due to administration of ceftriaxone 1gm BD for above 7 days according to their medical condition, Normal range of BUN is 15.0 mg/dl - 45.0 mg/dl and Serum creatinine is 0.5 mg/dl - 1.5mg/dl, And thus the comorbidity disease condition patients are also included in increased level of RFT. Due to this ceftriaxone administration 8 patients has increased SrCr level of 4.5 mg/dl and 2 patients has increased level of BUN 55mg/dl - 60mg/dl.

Among 30 patients 2 (6.66%) patients are mostly effected with increased level of BUN and Serum creatinine levels due to administration of Amikacin BD for above 7 to 8 days according to their medical condition, amikacin administred patients 1 patient has increased SrCr is 3.5 mg/dl and 1 patient has increased BUN of 2.5mg/dl.

Among this patients both drugs ceftriaxone and Amikacin aministration is seen in 6 patients, Increased levels of BUN and Serum creatinine levels are high for both drugs. According to their medical condition in that 1(3.33%) patient has been administered for 12 days BD, 2(6.66%) patients has been administered for 7 days BD and 3(10%) patients has been administered for 7 days BD .Thus the majority of the patients are treated with ceftriaxone other than other amikacin is treated for less individuals.

Our study explains that that nephrotoxicity is the most developed adverse drug reaction in receiving of both drugs ceftriaxone and amikacin and sometimes diarrhoea also seen in some cases.

In our study most of the patients are prone to nephrotoxicity due to usage of ceftriaxone and amikacin. Medication errors are mostly seen in all tertiary care hospitals it is one of the principle causes the therapeutic failure .So clinical pharmacist should be assess the laboratory findings while ceftriaxone and amikacin is prescribed to patient. Clinical pharmacist is one of the key influences who can overhaul for medication errors and can provide the better patient care.

## CONCLUSION

Ceftriaxone and amikacin is frequently used antibiotic in both inpatient and outpatient department for its wide dose range and broad coverage of common susceptible infection but have a common potential adverse reaction nephrotoxicity. Nephrotoxicity due to amikacin and ceftriaxone are confirmed in this present study.

Therefore patients under antibiotic therapy, treatment must be done cautiously further in depth long term study is required for proving more information aimed to safer therapeutics, specially for antibiotics.

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