

# Comparison and Evaluation of Nephrotoxicity with Cisplatin

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## Abstract

**Objective:** Cisplatin is alkylating platinum used as chemotherapeutic agent. Reduced serum Magnesium, Potassium levels, increased serum Creatinine, Blood Urea Nitrogen indicates Cisplatin induced Nephrotoxicity. This study aims to compare and evaluate nephrotoxicity in patients treated with hydration therapy and without hydration therapy.

**Methods:** This is a Cross-Sectional Prospective study conducted in. Patients prescribed with Cisplatin equal or over 50mg/m<sup>3</sup> as chemotherapy. Clinical parameters compared were Serum Creatinine and Blood Urea Nitrogen after administration of cisplatin.

**Results:** Our study reports that there is a significant difference between the patients who were given hydration therapy before and after administration of Cisplatin when compare to the group of patients who were not hydrated.

**Keywords:** CDDP-cis-diamminedichloroplatinum, Cisplatin Induced Nephrotoxicity, Hydration Therapy, Isotonic Saline, Magnesium Sulphate and Potassium Chloride.

## I.Introduction

Cisplatin is a alkylating platinum based compound synthesized by M.Peyrone in 1844, which was approved by FDA in 1978 as chemotherapeutic agent. The chemical name of Cisplatin is CDDP-cis-diamminedichloroplatinum which is used to treat Head and neck cancer, cervical cancer, ovarian cancer, testicular cancer, lung cancer and other solid tumours (1-7). Cisplatin is a simple inorganic molecule that creates inter and intra stand cross-linkages in DNA resulting to form defective DNA templates and arrests DNA replication and synthesis (8-14). Adequate renal function is prerequisite for the administration of Cisplatin. Cisplatin Induced nephrotoxicity can be predicted by several clinical parameters like decreased glomerular filtration rate, hypokalaemia, hypomagnesemia depending on dose and frequency of administration(15-20).Over 90% is the cure rate of Cisplatin in testicular cancer and potent in many types of cancers like non -small cell lung carcinoma, head and neck, testicular, ovarian, cervical(8-14). Cisplatin enters tubular cells via facilitated and/or passive diffusion activating signalling pathways and trigger robust inflammatory response promoting renovascular injury and ischemic tubular cell death leading to acute renal failure. Cisplatin induced caspase-dependent or independent apoptosis is due to activated intrinsic, extrinsic mitochondrial death receptor pathway which includes transcription of apoptotic genes. Tubular cell apoptosis and kidney injury is determined by balance between cytoprotective p21 and cdk2 which promotes apoptosis (21).Reduced serum Magnesium, Potassium levels, increased serum Creatinine, Blood Urea Nitrogen indicates Cisplatin induced Nephrotoxicity. Dose fractionation, Slower infusion Rate, forced diuresis, Hydration, screening for renal abnormalities can prevent Cisplatin Induced Nephrotoxicity (22-29). Our study aimed to assess the efficacy of protective role of short hydration therapy with isotonic saline, Magnesium Sulphate and Potassium Chloride before and after cisplatin administration.

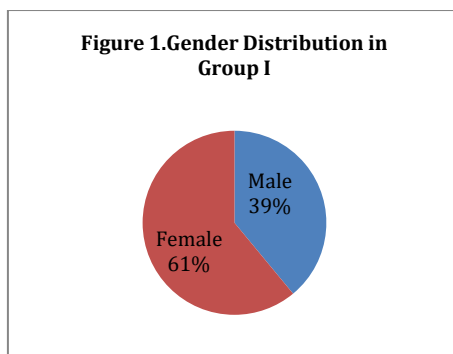
## II. Materials and Methods

This is a Cross-Sectional Prospective study conducted in 126 patients on chemotherapy with Cisplatin between November 2021 to March 2022. Patients prescribed with Cisplatin equal or over 50mg/m<sup>3</sup> as chemotherapy were included in this study. Patients on NSAIDS, Aminoglycosides, higher serum creatinine levels greater than 1.4mg/dl, Hyperkalemia, Heart Failure were excluded. Clinical parameters compared were Serum Creatinine and Blood Urea Nitrogen after administration of cisplatin.Statistical Analysis an Unpaired t-test was performed to assess the statistical significance between the group treated withhydration therapy and without hydration therapy using SPSS version 1.0.0.1406.

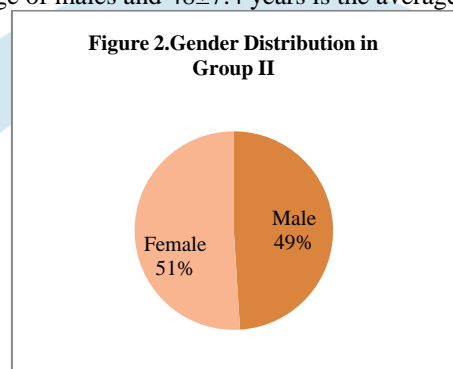
## III. Results

### Demographic Data

A total of 126 patients have been enrolled in the present study, out of which 74 members were on Cisplatin with hydration therapy in Group I and 52 were in Group II without hydration therapy.



Group I Data of 74 patients on Cisplatin with Hydration therapy was collected. Of them 39% were males and 61% were females (Figure 1).  $47.1 \pm 7.6$  years is the average age of males and  $48 \pm 7.4$  years is the average age of females.



Group II Data of 52 patients on Cisplatin without Hydration therapy was collected. Of them 49% were males and 51% were females (Figure 2).  $40.68 \pm 9.24$  years is the average age of males and  $40.7 \pm 8.62$  years is the average age of females.

#### Clinical Parameters

Table.1 Distribution and Clinical Parameters			
		Group I	Group II
1	Total Number of Patients	74	52
2	Percentage of Males	39%	49%
3	Percentage of Females	61%	51%
4	Average age of Males	$47.1 \pm 7.6$ years	$40.68 \pm 9.24$ years
5	Average age of Females	$48 \pm 7.4$ years	$40.7 \pm 8.62$
6	Average Serum Creatinine	$1.008 \pm 0.26$ mg/dl	$1.829 \pm 0.9$ mg/dl
7	Average BUN	$13.24 \pm 3.73$ mg/dl	$27.16 \pm 2.9$ mg/dl

The average level of Serum Creatinine was  $1.008 \pm 0.26$  mg/dl in Group I and  $1.829 \pm 0.9$  mg/dl in Group II. There was a significant difference between two groups with a p-value of  $<0.001$  with a mean difference of  $0.821 \pm 0.64$  mg/dl. The average level of Blood Urea Nitrogen was  $13.24 \pm 3.73$  mg/dl in Group I and  $27.16 \pm 2.9$  mg/dl in Group II. There was a significant difference between two groups with a p-value of  $<0.001$  with a mean difference of  $13.92 \pm 0.83$  mg/dl.

#### IV. Discussion

Our study reports that there is a significant difference between the patients who were given hydration therapy before and after administration of Cisplatin when compare to the group of patients who were not hydrated. Cisplatin induced Magnesium depletion and deficiency increases nephrotoxicity, in a study patients treated with Cisplatin greater than or equal to 50mg/m<sup>2</sup> received 1000ml of isotonic saline plus 20mEq of KCL and 2grams of MgSO<sub>4</sub> over 2-3 hours prior and 500ml over 2 hours after Cisplatin Injection reported a significant decrease in Nephrotoxicity compared with patients who were not hydrated. According to an investigation Saline modifies sensitivity to the cisplatin by releasing a stress response in the cell, which also demonstrated that chloride ion concentration can reduce the formation of reactive species of Cisplatin (30). In two Retrospective studies performed in patients treated with short duration hydration with intermediate to high dose Cisplatin experienced nephrotoxicity in 4.6% to 6% of the patients (31). Another study showed that vigorous administration of saline with MgSO<sub>4</sub> and KCL with capability of producing 100ml/hr of urine output remarkably reduced nephrotoxicity and hematological toxicities due to Cisplatin (32). The rate of Acute Kindney Injury due to Cisplatin is equal to or less than in patients treated with short hydration therapy of outpatients when compared with continuous hydration therapy.

Cisplatin Induced Nephrotoxicity was 22.7% in a study group of patients with hydration therapy (33). According to Common Terminology Criteria for Adverse Events (CTCAE) compared subjects treated with short hydration regimen and traditional hydration concluded no significant differences in renal toxicity, however 17 patients experienced grade 2 toxicity who were on 2.2 L of fluid on cisplatin administration day followed by oral hydration. Another study showed significant increase in serum creatinine in traditional hydration group whereas a stable creatinine clearance and serum creatinine was reported in both groups of a study (34).

**Conclusion:**

Nephrotoxicity is the primary complication of Cisplatin therapy. Hydration therapy decreases the severity of renal complications. This protective effect is well documented through many evidence based studies. More cautions are required in patients with high dose of Cisplatin administration, patients with impaired renal activity. Safety of several types of hydration protocols must be ruled out before administration of Cisplatin for a better clinical outcome.

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**Disclosure of conflict of interest**

The authors of this manuscript declare no conflict of interest.

**Statement of informed consent**

Informed consent was obtained from all individual participants included in the study.

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