A STUDY OF RENAL FUNCTION PROFILE DURING COURSE OF COMBINATION CHEMOTHERAPY OF GERM CELL TUMOR

Abhijit Das¹, Pankaj Kr. Marik², Goutameswar Majumdar³, Avijit Ganguly⁴, Sanatan Banerjee⁵, Anup Kr. Bhattacharya⁶

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ABSTRACT: BACKGROUND & OBJECTIVES: Bleomycin, Etoposide and Cisplatin (BEP) are commonly used combination for the treatment germ cell tumor. Among them cisplatin is a highly nephrotoxic drug. Proper therapy and continuous assessment of renal function is necessary to prevent nephrotoxicity. Our goal is to assess renal function following cisplatin containing combination chemotherapy. **SETTINGS METHODS AND MATERIAL:** This is a nonrandomized, uncontrolled open label prospective observational study carried out in the Department of Radiotherapy and Department of Pharmacology of Burdwan Medical College, West Bengal. Assessment of renal function was done by measurement of serum urea, creatinine, eGFR. Parameters were measured before starting chemotherapy, after 2nd cycle and at the end of chemotherapy **RESULTS:** Analysis was done by using mean, standard deviation and percentage and paired t test. It was found that serum urea and serum creatinine was significantly ($p<0.000$) increased from the pretreatment level and Estimated GFR was decreased from the base line significantly ($p<0.000$) in spite of pretreatment hydration therapy. **CONCLUSIONS:** Cisplatin causes reversible renal failure. Nephrotoxicity can occur in spite of adequate pretreatment hydration therapy. So other measures are required to prevent cisplatin induced renal damage.

KEYWORDS: Renal function, Cisplatin, eGFR.

INTRODUCTION: Germ cell tumor (GCT) of testis is a commonly observed tumor in male in our hospital setting. GCTs of testis are the most common solid tumors in men between the ages of 15 and 35 years. Approximately 90% of GCTs originate in the testis and 10% are extra-gonadal.⁽¹⁾ Germ cell tumor of ovary are much less common than epithelial ovarian neoplasms, accounting for 2-3% of all ovarian cancer, with a peak incidence in women in their early 20s.⁽²⁾ The standard chemotherapy protocol usually used are the combination of three chemotherapeutic agents like Bleomycin-Etoposide-Cisplatin (BEP) combination regimen in testicular as well as ovarian germ cell tumor. Bleomycin, etoposide and cisplatin (BEP) as a first-line treatment was first reported by Professor Michael Peckham in 1983.⁽³⁾

Cisplatin is a widely used and highly effective cancer chemotherapeutic agent. One of the limiting side effects of cisplatin use is nephrotoxicity. Cisplatin gets accumulated in the tubular epithelial cells of proximal kidney tubule, causing nephrotoxicity, characterized by morphological destruction of intra cellular organelles, cellular necrosis, loss of microvilli, alterations in the number and size of the lysosomes and mitochondrial vacuolization, followed by functional alterations including inhibition of protein synthesis, GSH depletion, lipid peroxidation and mitochondrial damage.⁽⁴⁾ The first report of nephrotoxicity in animal studies was in 1971, which demonstrated histopathologic changes of acute tubular necrosis along with azotemia.⁽⁵⁾ Cisplatin-induced

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nephrotoxicity has been largely abrogated by adequate pretreatment hydration and chloride diuresis.⁽⁶⁾ The incidence of renal insufficiency in more recent experience using saline hydration and diuresis, is in the range of 20–30% of patients.⁽⁷⁾ This study was undertaken with an aim to evaluate the renal function during BEP therapy where cisplatin is a component. The objective of this study was to assess and compare the renal function before and after the cisplatin containing combination (BEP) chemotherapy of GCT.

SUBJECTS AND METHODS: This study was carried out in the outpatient department and day care Centre of the department of radiotherapy of Burdwan Medical College. Study period was from January 2012 to January 2013. Study design was nonrandomized, uncontrolled open label prospective observational study. Institutional ethics committee permission was obtained and written informed consent was taken from the patients prior to the study. The patients received cancer chemotherapy as per the assessment of the treating physician. No changes in the treatment decision, schedule or duration were made during the study period.

Patients diagnosed histological as germ cell tumor and treated in the department of radiotherapy with combination chemotherapy containing Bleomycin-Etoposide-Cisplatin (BEP) were taken as study subject considering inclusion and exclusion criteria. All patients of GCTs of both gender and of all ages, who received BEP chemotherapy under standard regimen, were included for the study. Patients who were not willing to give consent and had H/O acute myocardial infraction in recent past, prior renal and hepatic impairment and very poor general condition, were excluded from the study.

Patients were treated with 4 cycles of combination chemotherapy at an interval of 3 weeks. During the course of combination chemotherapy patients were under continuous assessment of different adverse drug events that may occur due to chemotherapy by means of different physical, biochemical and radiological parameters. Serum urea, creatinine, eGFR and routine urine examination were measured before, at the end of 2nd cycle and at the end of chemotherapy. Analysis was done by using mean, standard deviation and percentage change from the base line values. Significance tested by paired t test using spss version 21 software.

RESULTS: During the study period a total of 36 patients were diagnosed as having GCTs and received chemotherapy in the department of radiotherapy. Among these 36 patients 30 were male and 6 were female. Mean age was 31.3 ± 10.51 years with a minimum of 16 years and a maximum of 55 years. Mean body weight 48.36 ± 4.9 kg.

Demographic Profile:

- Mean age- 31.3 ± 10.51 years.
- Mean body weight- 48.36 ± 4.9 kg.

Fig. 1: Showing sex composition of the population

Male: 84.33%, Female: 15.67%.

Parameters	Pre treatment	After 2 nd cycle	At the end of treatment	% of change	Significance (p value)
Serum urea (mg/dl)	25.28±5.5	34.57± 4.96	44.5 ± 7.56	76.03%	0.000
Serum creatinine (mg/dl)	0.68± 0.12	0.92± 0.11	1.04± 0.12	52.94%	0.000
Estimated GFR (ml/min/1.73m ²)	143.88± 35.07	99.24± 19.06	87.72± 15.56	39.03%	0.000

Table 1: Assessment of renal function

Fig. 2: Line diagram showing serum urea at different time

Fig. 3: Line diagram showing serum creatinine at different time points

Fig. 4: Line diagram showing estimated GFR at different time points

DISCUSSION & CONCLUSION: Kidney is the most important organ for excretion of different metabolic product of human body as well as metabolites of different xenobiotics. It also act as an organ of metabolism and serves a hormone releases some hormone and cytokines. It so vital that jeopardisation of which life cannot withstand. So protection renal function is an essential criteria for any exogenous intervention.

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Some chemotherapeutic agent like cisplatin has a tendency to damage the renal structure followed by impairment of renal function. It is an obvious challenge to identify how far renal function is impaired on cisplatin therapy. However cisplatin is an important component of different cancer chemotherapy. Cisplatin induced renal dysfunction also varied from dose to dose, prior protective measures, individual to individual, regime to regime, even institution to institution. Therefore this study was under taken to evaluate the impairment of renal function in a subset cancer patients (GCT) where cisplatin is used as a component in chemotherapy (BEP).

This disease is not so frequent and for that reason we have taken all the patients attended the clinic for evaluation. All the relevant parameters of renal function (serum urea, serum creatinine, eGFR) was measured. It was found that serum urea and serum creatinine was significantly ($p<0.000$) increased from the pretreatment level and absolute increment of that value was 73.81% and 51.47% respectively. Estimated GFR was decreased from the base line significantly ($p<0.000$) with absolute decrement 40.34%. These all patients received pretreatment hydration therapy still they developed such renal impairment. Protection of renal function by these conventional measures is not adequate. It can be concluded that that more stringent action may have to be taken to avoid renal impairment.

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AUTHORS:

1. Abhijit Das
2. Pankaj Kr. Marik
3. Goutameswar Majumdar
4. Avijit Ganguly
5. Sanatan Banerjee
6. Anup Kr. Bhattacharya

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Pharmacology, R. G. Kar Medical College, Kolkata, West Bengal.
2. MD, Department of Pharmacology, Burdwan Medical College, West Bengal.
3. Professor & HOD, Department of Pharmacology, North Bengal Medical College, West Bengal.

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4. Assistant Professor, Department of Pharmacology, R. G. Kar Medical College, Kolkata, West Bengal.
5. Associate Professor, Department of Radiotherapy, Burdwan Medical College, West Bengal.
6. Professor, Department of Medicine, Kishanganj Medical College, Kishanganj, Bihar.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Avijit Ganguly,
BG 116, Rabindrapally,
Krishnapur, P. O.,
Prafullakanan, Kolkata-700101.
E-mail: avijitdec81@gmail.com

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