Original Article

Protective Effect of Withania Somnifera Root Extract Against Cisplatin Induced Nephrotoxicity Through Renal Function Analysis in Albino Wistar Rats

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ABSTRACT

Objective: To observe the nephroprotective effects of W. Somnifera root extract against cisplatin induced nephrotoxicity through biochemical parameters in albino Wistar rats.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Baqai Medical University, Karachi fromNovember 2018 till February 2019.

Materials and Methods: For this study 80 adult male Albino Wistar rats were divided in to four groups, 20 rats in each group. Group A served as control group,group B received inj. Cisplatin(1mg/kg intraperitoneally) for 7 days, group C received W. Somnifera root extract (500mg/kg) for 15 days before cisplatin treatment and thereafter concurrently with cisplatin for last 7 days. Whereas group D was given only W. Somniferaroot extract (500mg/kg) for 22 days. 1st blood samples of all the groups were collected at the start of the study. Second blood samples of group A, C and D were taken on 23rd day and of group B was taken on day 8th of experiment. Estimation of serum urea and creatinine levels were done by using standard Laboratory kits.

Results: In this study mean (± SD)serum urea level of group A, B, C & D were 31.853± 8.3258 mg/dl, 251.495 ± 95.4603 mg/dl, 35.570± 22.1801 mg/dl and 30.700± 6.2149mg/dl respectively. While mean (± SD) serum creatinine level of group A, B, C & D were 0.538± 0.0656 mg/dl, 2.109± 0.9247 mg/dl, 0.606± 0.1911 mg/dl and 0.521± 0.0495mg/dl respectively. Significant ($p<0.05$) mean serum urea and creatinine level differences were observed when WS pretreated and cisplatin treated Group C was compared with cisplatin group B indicative of correction of raised serum urea and creatinine level. While comparison with group A & D showed insignificant changes.

Conclusion: It is concluded from our study that Cisplatin induced renal toxicity in albino Wistar rats may be corrected by W. Somnifera root extract through the renal function analysis (serum urea and creatinine levels).

Key Words: Cisplatin, W. Somnifera, Nephrotoxicity

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INTRODUCTION

Renal failure primarily means failure of excretory functions of kidney, which results in retention of nitrogenous waste products of metabolism in blood along with inability to regulate fluid and electrolyte balance and endocrine dysfunction.

Some proven medicines which include some antibiotics and chemotherapeutic drugs causes nepthrotoxicity.[1,2,3]

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Chemotherapeutic agents are cytotoxic and have severe side effects.[4]Cisplatinis widely used for the treatment of carcinomas and sarcomas. Its common side effects includes bone marrow suppression and nephrotoxicity.[5,6] Main mechanism for Cisplatin induced acute kidney injury is Oxidative stress.[7]Acute kidney injury (AKI) includes rise in serum creatinine level (decrease in creatinine clearance), rise in blood urea nitrogen (BUN) and low serum Na, K, Mg and Ca.[8] Creatinine is produced by the non-enzymatic conversion of creatinine and phosphocreatinine in the muscles. Normal serum creatinine ranges from 0.5-1.0mg/dl. Urea is an organic compound and normal BUN level is 20-40mg/dl.[9]

Withania Somnifera(WS) is known for its nephroprotective effects.[10]Active ingredients in the roots of this herb has proven nephroprotective effects.[11]

Keeping in view of the above, the current study was designed to analyze the potential nephroprotective

effect of Withania Somnifera root extract on Cisplatin induced biochemical changes in albino Wistar rats' renal biomarkers.

MATERIALS AND METHODS

This study was an experimental study conducted in Baqai Medical University, Karachi, fromNovember 2018 till February 2019.For this study80 healthy adult, male Albino Wistar rats of 14-16 weeks, weighing180-250gm were purchased. Whereas female and diseased animals were excluded from the study. After 1 week of acclimatization, rats were randomly divided into four groups (A, B, C & D), 20 rats in each group.

Cisplatin injections were purchased from local pharmacy and W. somnifera root extract was prepared.

Group A was a control group and received normal saline orally for 22 days through gastric gavage and 0.5ml normal saline injection (intraperitoneally) for 7 days.

Group B received Inj. Cisplatin only in a dose of 1mg/kg, intraperitoneally for 7 days.[12]

Group Creceived ethanolic extract of W. somnifera roots in a dose of 500mg/kg via gastric gavage for 15 days before cisplatin treatment and thereafter concurrently with cisplatin (1mg/kg intraperitoneally) for 7 days.[13]

Group D received ethanolic extract of W. somnifera roots in a dose of 500mg/kg via gastric gavage for 22 days, to evaluate any harmful effect of W. somnifera on rat kidneys.Dosing was done around 9am in morning after overnight fasting.

At the start of the study blood samples were collected from all groups through tail venipuncture to assess the kidney functions. Second blood samples of group A, C and D were taken on 23rd day and of group B was taken on day 8th of experimentand stored in sterile EDTA tubes for renal function analysis (serum urea and serum creatinine).

Blood samples were centrifuged and serum was separated by using standard Auto Analyzer (Architect c8000).

Data was statistically analyzed on(SPSS) version 22. Mean comparison of blood parameters of group C with group A, B and D were analyzed by independent sample T test. P value of less than 0.05 was considered significant ($p<0.05$).

RESULTS

Mean ± SD of Serum urea level of group A, B, C & D were 31.853± 8.3258 mg/dl, 251.495 ± 95.4603 mg/dl, 35.570± 22.1801 mg/dl and 30.700± 6.2149mg/dl respectively. Significant mean serum urea level difference was observed when Group C was compared with Group B (P = 0.000) whereas insignificant changes were seen in comparison with group A & D (P values 0.487 & 0.350) respectively as shown in Table I and Figure I.

Table I: Comparison of mean serum urea level of group C with groups A,B & D

Groups	Mean ± SD (mg/dl)	P Value
C & B	35.570 ± 22.1801	0.000*
	251.495 ± 95.4603	
C & A	35.570 ± 22.1801	0.487
	31.853 ± 8.3258	
C & D	35.570 ± 22.1801	0.350
	30.700 ± 6.2149	

*(P value ≤ 0.05 is considered statistically significant)

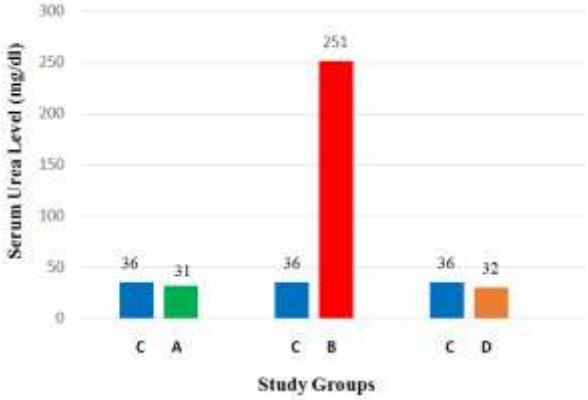

Figure No.1: Showing comparison of mean ± SD of serum urea level of group C with groups A, B & D

Mean ± SD of serum creatinine level of group A, B, C & D were 0.538± 0.0656 mg/dl, 2.109± 0.9247 mg/dl, 0.606± 0.1911 mg/dl and 0.521± 0.0495mg/dl respectively. Significant mean serum creatinine level difference was observed when Group C was compared with Group B (P value 0.035) whereas insignificant changes were seen in comparison with group A & D (P values 0.141 & 0.347) respectively as shown in Table 2 and Figure 2.

Table No.2: Comparison of mean serum creatinine level group C with groups A, B & D

Groups	Mean ± SD (mg/dl)	P Value
C & B	0.606 ± 0.1911	0.035*
	2.109 ± 0.9247	
C & A	0.606 ± 0.1911	0.141
	0.538 ± 0.0656	
C & D	0.606 ± 0.1911	0.347
	0.521 ± 0.0495	

(P value ≤ 0.05 is considered statistically significant *)

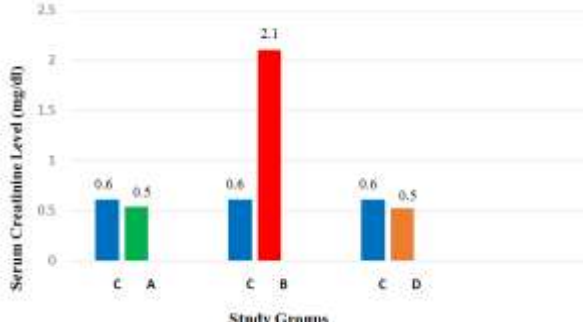

Figure No.2: Showing comparison of mean ± SD of serum creatinine level of group C with groups A, B & D

DISCUSSION

Serum urea and Creatinine are the hall mark and have been measured to recognize acute kidney injury. Creatinine is generated by muscles from non-enzymatic conversion of creatinine and phosphocreatinine and Urea plays an important role in metabolism of nitrogenous compounds.[14]Inthe current study, biochemical parameters confirmed the nephroprotective effects of W. somnifera root extract against these renal changes.

In our study cisplatin treated group B showed marked elevation of serum and creatinine levels as compared to control groups which is in accordance to the results of (Cheng etal:2018) who stated that elevation of biochemical parameters might be due to cisplatin induced oxidative stress.[15] In line with our study, results of (Hossenianetal:2016) also revealed cisplatin induced renal injury which was evident by significant increase in renal biomarkers (BUN & Cr). He reported that elevation of renal biomarkers after cisplatin administration might be due to decrease glomerular filtration rate (GFR) which occurs as a result of production of reactive oxygen species (ROS). ROS increases the production of vasoconstrictors which leads to glomerular vasoconstriction and reduced GFR.[16] Similar changes in renal parameters were reported by (Bamietal: 2017) and (Vasaikaretal: 2018) due to cisplatin induced glomerular and tubular damage.[17,18]

However biochemical parameters were significantly decreased, almost near to normal values, in W. somnifera pretreated and cisplatin treated group C. These findings were in agreement with the previous studies reported by (Govindappaetal: 2019) and (Kushwahaetal: 2016).[19,20] (Jeythanietal: 2014) also mentioned similar renal biomarker changes after pretreatment with W. somnifera along with gentamicin administration. He stated that nephroprotective effect of W. somnifera could be due to anti-oxidant properties of its bio active constituents.[21]

CONCLUSION

It is concluded from our studythat Cisplatin induced renal toxicity in albino Wistar rats may be corrected by W. Somnifera root extract through the renal function analysis (serum urea and creatinine levels).

Author's Contribution:

Concept & Design of Study:	Aaqiba Rasheed
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Revisiting Critically:	Aaqiba Rasheed, Nadia Younus
Final Approval of version:	Aaqiba Rasheed

Conflict of Interest: The study has no conflict of interest to declare by any author.

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