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Research Article

EFFECT OF VARIABLE DOSES OF CISPLATIN ON MICROANATOMY OF KIDNEY IN ALBINO RATS

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A R T I C L E I N F O

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A B S T R A C T

Cisplatin is an inorganic metal complex, and its cytotoxic properties were discovered serendipitously. Cisplatin interferes with DNA replication and kills the fastest proliferating cells. It causes apoptosis in view of the fact that the growth of normal cells is also affected. These toxic effects alter the metabolic function of certain tissues and organs. 60 albino rats weighing on an average 100 grams were taken. The animals were divided into three groups. Group A animals received no drug. Group B were injected with 1.3mg/ m^2 of cisplatin by intraperitoneal route and group C 2.5mg/^{2}. The process of drug administration was continued for 12 weeks. The animals were sacrificed in five sittings, after interval of 1,3,6,9 and 12 weeks after drug administration. At the termination of experiments the kidneys were fixed and stained with H&E. In kidney no apparent gross change was found in any of the groups. Histologically it was found that renal corpuscles were affected in high dose group from 3rdweek onwards. Odeama of bowmans space and tubules was seen in high dose group from 6th week onwards .Necrosis of tubular epithelium was profound in high dose group at 12th week. Therefore careful kidney function monitoring is required in patients who are on cisplatin therapy.

INTRODUCTION

Cisplatin is a metallic coordination compound with a square planar geometry. Cisplatin is one of the most potent chemotherapy drugs widely used for cancer treatment.[1,2] including those of the head, neck, lung, testis, ovary, and breast. Cisplatin interferes with DNA replication, which kills the fastest proliferating cells, which in theory are carcinogenic[3,4]Cisplatin represents a perfect example of how a small alteration in chemical structure can significantly affect biological activity in target cell[5].Whiletoxicities include ototoxicity, gastrotoxicity, myelosuppression, and allergic reactions[6,7], the maindose-limiting side effect of cisplatin is nephrotoxicity[8,9]

MATERIALS AND METHODS

The present randomised controlled trial (RCT) study was conducted in the Postgraduate Department of Anatomy, Government Medical College Srinagar. Sixty male albino rats weighing on an average 100gms (0.1kg) were taken for the present study.

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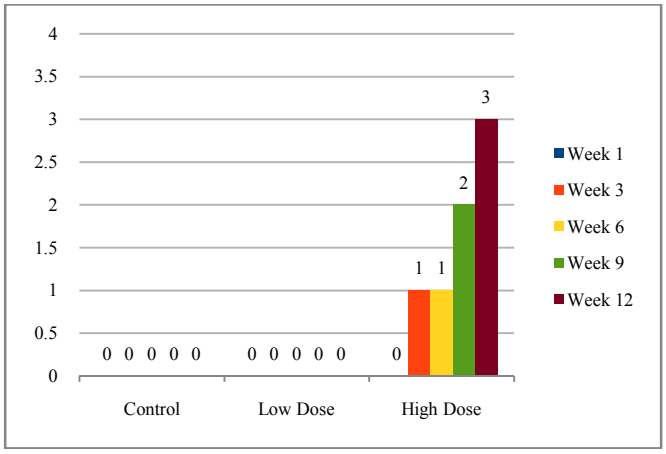
The animals (rats) were obtained from animal house Govt medical college Srinagar. This study was conducted following the guidelines of the Animal Ethical committee, Government Medical College Srinagar. Animals were divided into three groups. Group A (control group) contain twenty (20) rats. These rats were fed normal diet which include grains, vegetables and tap water. Group B (low dose group) contain twenty (20) rats. This group was given low dose of cisplatin at the dose of 1.3mg/ m^2. The drug was given intraperitoneally besides this. The rats received normal diet which includes grains, vegetables and tap water. Group C (high dose group) contained twenty rats (20). This group was given high dose of cisplatin at the dose of 2.5mg/ m^2 intra peritoneally. The rats were sacrificed in five sittings at 1st week, 3rd week, 6th week, 9th week and 12th week. In each, sitting five rats were sacrificed from each group. After anaesthetizing with chloroform, midline abdominoperineal incision was given. Kidneys were identified, dissected and cleaned, and were put on blotting paper. The tissues were processed manually for block making and the slides were stained with haematoxyline and eosin under various steps. Then these prepared slides were seen under electronic microscope.

RESULTS AND DISCUSSION

Macroscopically: no significant change was seen after Administration of cisplatin.

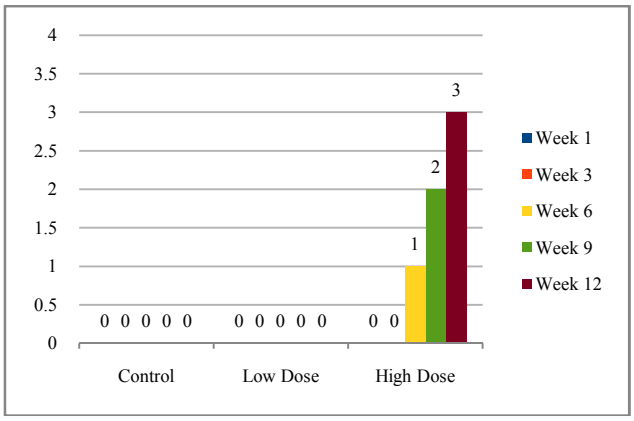
Microscopically

Renal corpuscles affected (K.RCA): No change in control group and low dose group was seen, but in high dose group, small numbers of renal corpuscles were affected at 3rd and 6th week while as moderate numbers of renal corpuscles were affected at 9th week and large numbers of renal corpuscles were affected at 12th week.



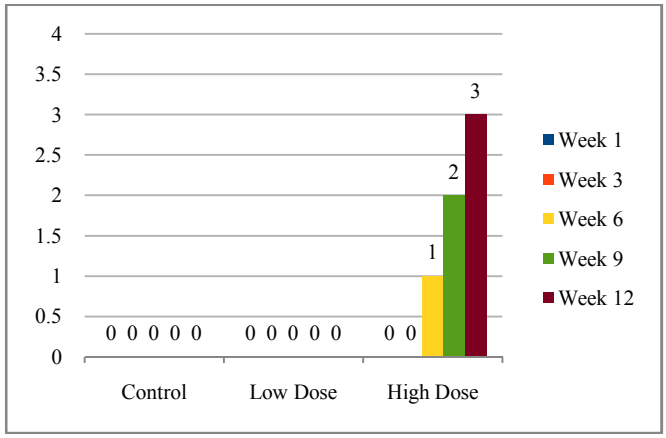
Oedema of bowmans space (K.OBS)

In control and low dose group there was no edema seen after drug administration at any week, while as high dose group showed mild oedema at 6th week, moderate at 9th week and severe oedema at 12th week.



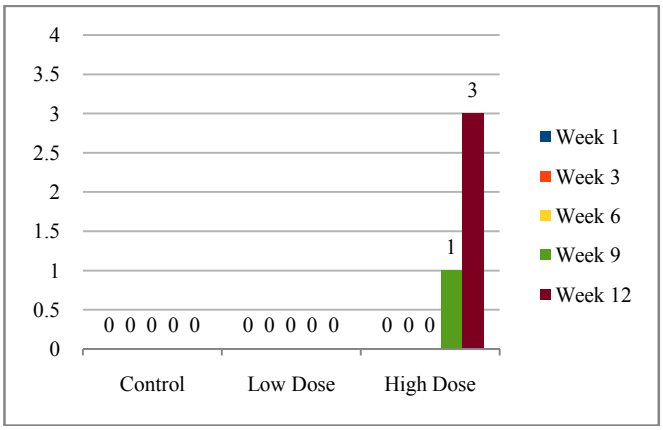
Renal tubular oedema (K.TO)

There was no tubular oedema in control and low dose group, while as high dose group showed mild tubular oedema at 6th week, moderate tubular oedema at 9th and severe tubular oedema at 12th week.



Necrosis of tubular epithelium (K.NTE)

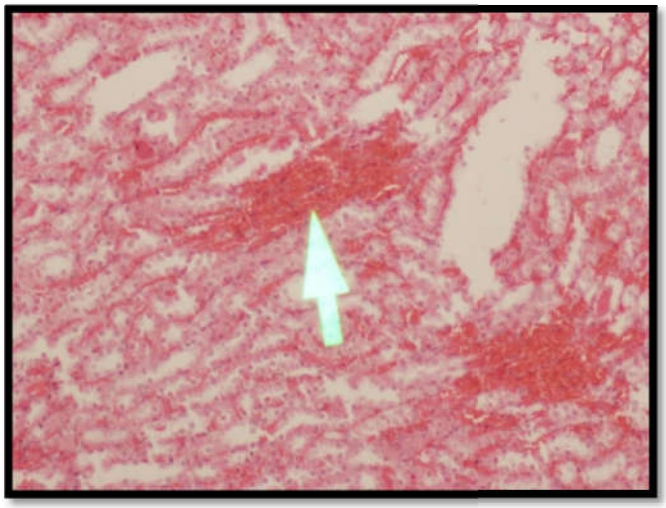
In control and low dose group, there was no necrosis of tubular epithelium seen, however high dose group showed mild necrosis of tubular epithelium at 9th week and severe necrosis of tubular epithelium at 12th week.



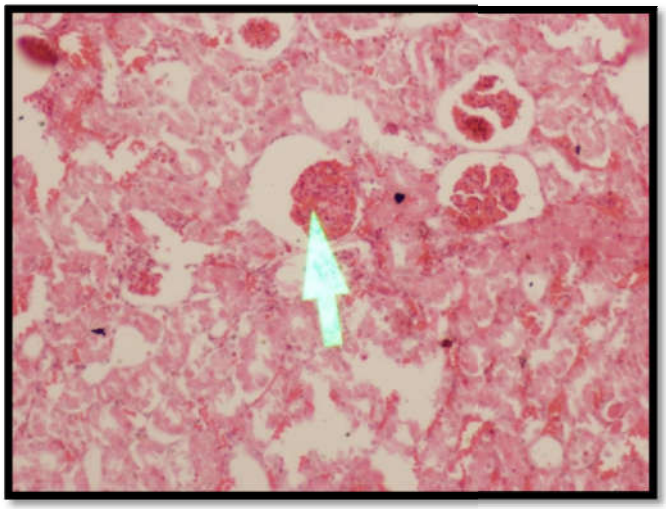
In our study it was found that there was no apparent gross macroscopic change found in any of the groups. Histologically it was found that renal corpuscles were affected in high dose group from 3rd week onwards, oedema of bowmans space and tubular oedema was seen in high dose group from 6th week onwards, necrosis of tubular epithelium was profound in high dose group at 12th week. Constantin Crăciun and Cristina Pașca 2014[10] while working on effect of cisplatin on liver, kidney and spleen found similar results. Cisplatin injured the structures involved in both the ultrafiltration process (glomerular capillaries, Bowman capsule, mesangium) and in the absorption and excretion processes (epithelium of the proximal convoluted tubule, loop of Henle and distal tubule) - Light microscopy examination showed that Cisplatin induced necrosis processes of the tubular epithelium, urinary stasis, proliferation of the mesangial cells, the appearance of some granular protein material inside the lumen of the tubules, a few epithelial cells getting an abnormal, peculiar aspect, and a significant monocyte infiltration. Narinder Singh, Ashwani K. Sharma et al 2015[11] had comparable results while working on Histomorphological Effects of Cisplatin on Kidney of Male Wistar Albino Rats. The rats were divided into 4 groups where 3 groups were given the test drug Cisplatin I. P. (Intraperitoneally) in doses of 0.2mg/kg body weight for 7 days, 1 mg/kg body weight for 7 days and 45 mg/kg body weight as a single dose respectively, whereas in the 4th group or control group normal saline of same volume was injected intraperitoneally. The changes were congestion and

haemorrhage of glomeruli, tubular changes in PCT &DCT (loss of microvilli with sloughing of epithelium, vacuolisation of cells leading to focal tubular atrophy and presence of RBC's in tubules). These changes were evidently more marked in PCT as compared to DCT.

Pictures



Necrosis of Tubular Epithelium and Intertubular Haemmorhage in Cisplatin Treated Rats



Renal Corpuscles Showing Haemorrhage Treated with Cisplatin

CONCLUSION

Undoubtly cisplatin is an important and potent anti cancer drug, but its significant antitumor action is often limited by the development of toxicity, which is evident in various animal species. It was found that the effect of cisplatin was dose dependent on kidneys. Renal corpuscles were greatly affected in high dose group with oedema of renal tubules and bowmen space. Necrosis of tubular epithelium was found in high dose group. However low dose group doesn't show any significant change and on gross examination kidney was apparently normal. Any proposed strategy, however, must be carefully studied in tumor-bearing animals to ensure that the chemotherapeutic efficacy of cisplatin is not compromised.

Acknowledgement

All praises to Almighty Allah Who Has Guided Me from Darkness to Enlightenment, " I express my gratitude to my loving husband - Dr Ubaid ali and my darling son Mohammad Mahir for their immense love and patience.

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