PROTECTIVE EFFECT OF PLATELET-RICH PLASMA ON CISPLATIN INDUCED NEPHROTOXICITY IN ADULT MALE ALBINO RATS: (HISTOLOGICALAND IMMUNOHISTOCHEMICAL STUDY)

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Introduction

Drug induced nephrotoxicity is the presence of any kidney injury caused by medications.This nephrotoxicity may be manifested as acute kidney injury (AKI), chronic kidney injury (`CKI), or any other clinical renal manifestations. Cisplatin is one of the most common drugs documented to cause nephrotoxicity. It causes nephrotoxicity by many mechanisms. First, it is mainly excreted by the kidney through tubular secretion. Within the tubular cells, cisplatin conjugate with water forming hydrates which cause DNA damage, oxidative stress, and apoptosis. Also, Cisplatin induces renal cell apoptosis via three ways; death receptors exogenous pathway, endoplasmic reticulum stress pathway (ERS), and mitochondria mediated endogenous pathway. Platelet –rich plasma (PRP) is an autologous human plasma. It is a mixture of highly concentrated platelets, growth factors, and bioactive molecules. It may play a major protective role in cases of cIt activates the tissue regeneration through cell proliferation and differentiation cisplatin –induced nephrotoxicity because of its high content of growth factors.

Aim of the work

Studythe possible protective effect of platelet-rich plasma (PRP) on the kidney in cisplatin - induced nephrotoxicity in adult male albino rats by morphometric, histological and immunohistochemical study.

Materials and Methods

Thirty adult male albino rats were randomly assigned to three groups; control, cisplatin treated group, PRP-treated group, the control groupincludes ten adult male albino rats received sterile sodium chloride solution 0.9% (1mL, single dose) by intraperitoneal injection on the first day as a placebo. Cisplatin-treated groupincludes ten rats received cisplatin (7,5 mg/kg, single dose) by intraperitoneal injection on the first day, the last group includes ten adult male albino rats received cisplatin (7,5 mg/kg, single dose) by intraperitoneal injection on the first day of experiment and received platelet –rich plasma (1 ml, single dose) by intraperitoneal injection after injection of cisplatin by 24 hours.All the rats were kept for 14 days from the start of the experiment and then wereeuthanized under anaesthesia. The kidney specimens were studied anatomically, histologically, immunohistochemically, and with morphometric studies.

Results

The kidneys of the cisplatin treated group showed massive injuries at the level of the tubules, glomeruli, and even renal interstitium. There was severe tubular necrosis in addition to severe interstitial infiltrations. The PRP treated group showed nearly restoration of the normal renal structure.

Table1: Comparison between the three studied groups according to change in creatinine (14^{th} day – 1^{st} day)

Change in creatinine	Control (n = 10)	Cisplatin treated (n = 10)	PRP treated (n = 10)	H	p
Min. – Max.	-0.21 – 0.10	0.16 – 2.20	-0.15 – 0.20	19.665*	<0.001*
Mean ± SD.	-0.04 ± 0.12	1.17 ± 0.59	0.03 ± 0.11		
Median	-0.04	1.16	0.0		
p_1		<0.001*	0.358		
p_2			0.001*		

Table2: Comparison between the three studied groups according to change in BUN (14^{th} day – 1^{st} day)

Change in BUN	Control (n = 10)	Cisplatin treated (n = 10)	PRP treated (n = 10)	H	p
Min. – Max.	-3.0 – 5.0	32.0 – 107.0	-12.0 – 32.0	21.422*	<0.001*
Mean ± SD.	0.80 ± 2.97	71.40 ± 22.17	13.60 ± 13.80		
Median	1.0	72.0	16.50		
p_1		<0.001*	0.137		
p_2			0.002*		

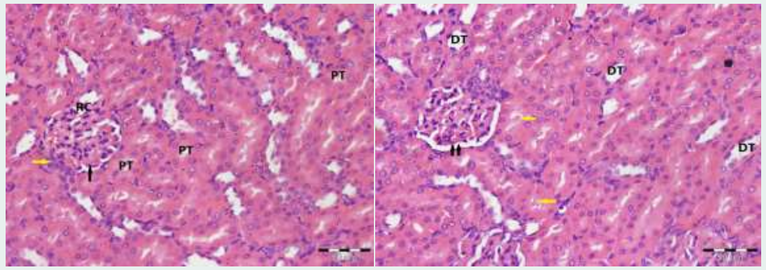

Figure 1: Higher magnification of the control group showing the renal corpuscle (**RC**). The proximal convoluted tubules pyramidal cells deeply eosinophilic with rounded basal nuclei (**PT**). (H&E. Mic. Mag x 400).

Figure 2: Higher magnification of the control group showing the bowman space of the (⬆⬆). Proximal convoluted tubules showing prominent brush border (⬅) . The distal convoluted tubules (**DT**) appeared with wider lumen and cuboidal cells. (H&E. Mic. Mag x 400)

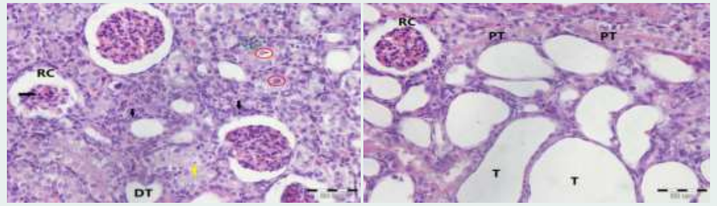

Figure 3: photomicrograph of section of cisplatin treated group showing the cortex in which there are abnormal renal corpuscles (**RC**). Distorted distal convoluted tubules with flattened cells are seen (**DT**). (H&E. Mic. Mag x 400)

Figure 4: photomicrograph of the same group showing abnormal renal corpuscles (**RC**) and many of the tubules showing severe ballooning (**T**). (H&E. Mic. Mag x 400)

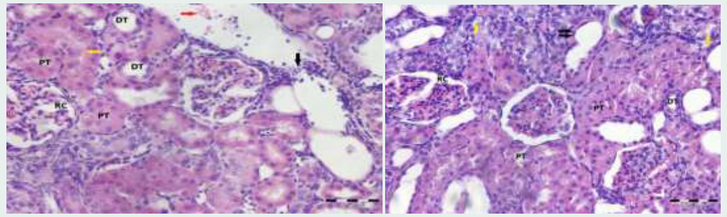

Figure 5: photomicrograph of section of the PRP treated group showing nearly normalrenal corpuscles with bifurcated glomerular tuft (**RC**), many normal proximal convoluted tubules (**P**) with eosinophilic cytoplasm, intact epithelial lining. (H&E. Mic. Mag x 400)

Figure 6: photomicrograph of the same group showing normal renal corpuscles with bifurcated glomerular tuft (**RC**) and distal convoluted tubules appear with cuboidal epithelial lining (**DT**). (H&E. Mic. Mag x 400)

Conclusion

The present work revealed the following:

1-Cisplatin has destructive effects on renal tissues and functions.

2-PRP seems to have protective effects on renal tissues and functions

Concomitant use of PRP with cisplatin helps to preserve the renal tissues and functions.