THE THERAPEUTIC EFFECT OF PLATELET-RICH PLASMA ON GENTAMICIN INDUCED NEPHROTOXICITY IN ADULT MALE ALBINO RATS

Ayman Ahmed Khanfour, Nehal Mohamed Nabil, Atef Nazmy Boulos, Dina Mohamed Youssef Rostom*, Nouran Khamis Ismail Soffar

Department of Human Anatomy and Embryology, Department of Histology and Cell biology*, Faculty of Medicine, Alexandria University

Introduction

Gentamicin (GM) is an antibiotic of aminoglycoside group. Aminoglycosides are broad-spectrum antibiotics. The aminoglycosides are particularly effective against aerobic Gram-negative bacteria. Most common side effects of GM are ototoxicity and nephrotoxicity. A rise in serum ccreatinine (Cr) level is the typical sign of GM -induced nephrotoxicity. The proximal tubule is specifically targeted in GM-induced nephrotoxicity. After glomerular filtration, about 5% of the given dosage accumulates within the proximal tubules. Megalin, a multi-ligand receptor, has been shown to be the primary mechanism for this accumulation by endocytosis. GM is then distributed to the lysosomes, Golgi apparatus, and endoplasmic reticulum. It binds to phospholipids and suppresses phospholipase activity, which leads to phospholipidosis. In the pathophysiology of GM-induced nephrotoxicity, oxidative stress is one of the important factors that plays a significant role. Oxidative stress leads to the production of toxic free radicals, increased cellular lipid peroxidation, decreased cellular antioxidants and finally tubular necrosis. Platelet-rich plasma (PRP) is an autologous blood concentrate with a higher platelet concentration than whole blood, ranging from 200,000 to 1,000,000 platelets/μL in a 5 mL plasma. The α-granules found in platelets contain a variety of substances, such as proteins, cytokines, and growth factors, which help to control the healing process. The α-granules also contain the transforming growth factor β1 (TGF-β1), the fibroblastic growth factor (FGF), the epidermal growth factor (EGF), the vascular endothelial growth factor (VEGF), the platelet-derived growth factor (PDGF) and the insulin-like growth factor (IGF).

Aim of the work

The aim of the present work was to: Study the possible protective effect of platelet rich plasma (PRP) on renal structure (proximal convoluted tubules) in gentamicin- induced renal failure in adult male albino rats.

Material and Methods

This study was carried out on thirty-seven adult male albino rat obtained from the animal house center of physiology department, faculty of medicine, Alexandria university. The rats were divided into: • Five healthy male rats (weighing about 300 ± 50 g), to obtain the PRP. • Thirty-two adult male rats (weighing about 200 ± 20 g), were considered as the experimental group. The rats of the experimental group were further subdivided into 4 groups (8 rats in each group) as following; **Group I:** Negative control group: without any treatment.**Group II:** Positive control group, received single intraperitoneal injection of 1 ml PRP.**Group III:** as GM group received GM (80 mg/kg/day, intraperitoneal, 8 consecutive days). **Group IV:** as GM+ PRP group received GM for 8 days, and 24 hours later, 1 mL PRP was injected intraperitoneal once. At the end of induction by GM and 3 days after PRP therapy, blood samples were collected to determine levels of blood urea nitrogen (BUN) and Cr in serum and the kidneys were removed for tissue processing.

Results

1- Biochemical results

Table (1): Comparison between the different studied groups according to serum Cr level (mg/dl)

Cr (mg/dl)	Control (n = 8)	PRP only (n = 8)	GM (n = 8)	GM+PRP (n = 8)	F	p
Min. – Max.	0.38 – 0.55	0.32 – 0.52	1.35 – 1.52	0.40 – 0.64	342.072	<0.001*
Mean ± SD.	0.45 ± 0.06	0.43 ± 0.08	1.42 ± 0.06	0.51 ± 0.09		
Median (IQR)	0.44(0.40 – 0.51)	0.46(0.35 – 0.49	1.41(1.4 – 1.5)	0.51(0.44 – 0.58		
p_0		0.933	<0.001*	0.377		
Sig. bet. grps.		p_1<0.001*,p_2=0.145,p_3<0.001*				

Table (2):Comparison between the different studied groups according to BUN level

Biochemical	Control (n = 8)	PRP only (n = 8)	GM (n = 8)	GM+PRP (n = 8)	F	p
BUN (mg/dl)						
Min. – Max.	15.0 – 26.0	13.60 – 23.0	49.0 – 71.0	18.0 – 27.0	118.170*	<0.001*
Mean ± SD.	19.65 ± 3.46	18.58 ± 3.81	59.88 ± 8.51	21.51 ± 3.10		
Median (IQR)	20.10(17.0 – 21.0)	20.0(14.5 – 21.5)	59.0(52.5 – 68.0)	20.50(19.4 – 23.7)		
p_0		0.976	<0.001*	0.890		
Sig. bet. grps.		p_1<0.001*,p_2=0.676,p_3<0.001*				

2- Histological results

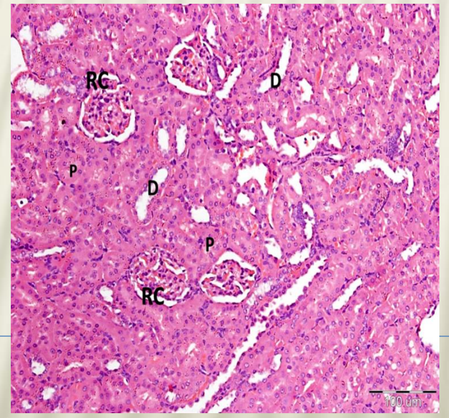

Figure (1): A photomicrograph of section of rat's renal cortex from control group (group I) showing normal structure and architecture. It shows normal appearance of the renal corpuscle (**RC**), proximal convoluted tubules (**P**), and distal convoluted tubules (**D**). H&E Stain (Mic.Magx200).

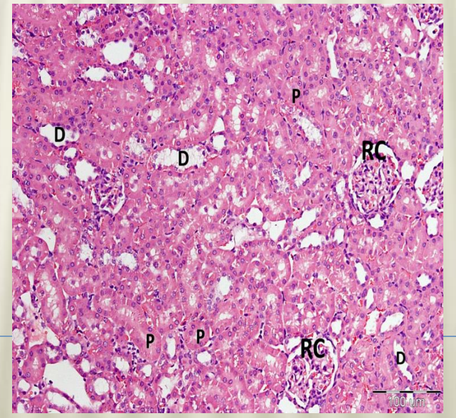

Figure (2) A photomicrograph of section of rat's renal cortex from PRP group (group II received single intraperitoneal injection of 1 ml PRP) showing normal structure and architecture of renal cortex. It shows normal appearance of the renal corpuscle (**RC**), proximal convoluted tubules (**P**), and distal convoluted tubules (**D**). H&E Stain (Mic.Magx200).

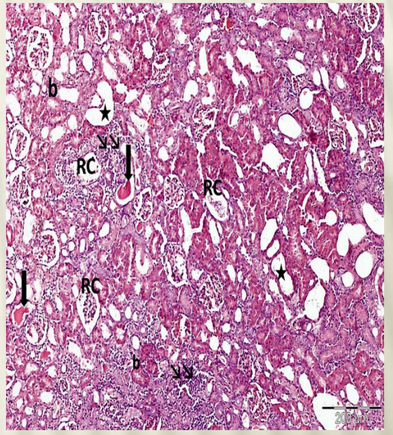

Figure (3) A photomicrograph of section of rat's renal cortex from the gentamicin treated group (group III received 80 mg/kg/day gentamicin for 8 consecutive days) illustrating loss of normal architecture. Most proximal tubules show defective brush border (**b**). Some tubules show pink homogenous hyaline casts within their lumen (↓). Extensively dilated distal convoluted tubules with attenuated lining cells are seen (**star**). Renal corpuscles (**RC**) are distorted with shrunken or absent glomeruli. Interstitial mononuclear cellular infiltration (↘↘) presents all around. H&E Stain (Mic.Magx100).

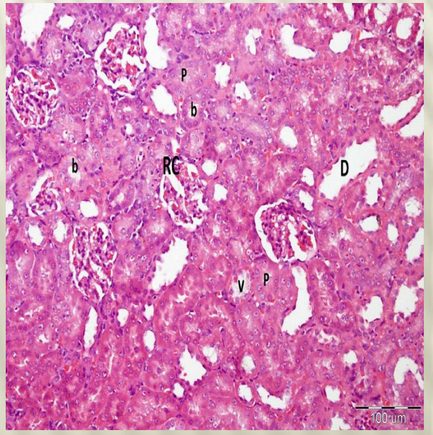

Figure (4) A photomicrograph of section of rat's renal cortex from GM+PRP group (group IV received GM for 8 days, and 24 hours later, 1 mL PRP was injected intraperitoneally once) showing many normal proximal convoluted tubules (**P**) with intact brush border, few proximal tubules show loss of brush border (**b**), few show slight vacuolations (**V**). Distal tubules (**D**) appear dilated lined by attenuated cells. Renal corpuscles (**RC**) appear nearly normal. H&E Stain (Mic.Magx200).

Conclusion

After the completion of the present work, it was concluded the following: Gentamicin therapy caused marked histological alterations in the kidneys of adult male albino rats, in addition to deterioration of the renal functions. PRP displayed effective protection against gentamicin-induced kidney damage and fibrosis, as evidenced by improvements in renal function and histological characteristics.