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Evaluation of the Protective Effect of Rosuvastatinin Attenuating Contrast-Induced Acute Renal Injury in the Adult Albino Rat

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Abstract: Background: Contrast-induced nephropathy (CIN) is one of important causes of hospital-acquired acute renal failure and is responsible for about 10–12% of the cases. Rosuvastatin is a new generation of statins which reduces levels of circulating LDL-C. In addition to its beneficial cholesterol lowering effects, rosuvastatin has been shown to protect against inflammatory, oxidant, and thrombotic effects, and may improve endothelial function. **Objective:** This study is suggested to explore and evaluate the renoprotective effect of rosuvastatin against contrast-induced acute kidney injury (CI-AKI) in adult albino rat using light microscopy. **Methods:** Fourty adult albino rats were used in this study each of which weighs about 200 – 250 gm. The rats were acclimatized for 7 days prior to the start of study. Rats were divided randomly into four equal groups each of which was formed of 10 rats. Group **I (control group):** rats were able to access normal diet and normal amounts of water without any medication. Group **II (dehydration group) (dehydration + furosemide, without CM administration)**: rats were deprived of water for 72 hours and then were given 10 mg/kg furosemide by intramuscular injection. Group **III (CI-AKI group):** rats will were treated in the same manner as group II, then after 20 minutes they were given a low-osmolar CM, Ultravist 50 ml injectable solution (Iopromide 300mg/mL) by intravenous injection (10 mL/kg) via the tail vein over the course of 5 minutes once then they were sacrificed. Group **IV (CI-AKI + rosuvastatin group):** rosuvastatin was administered by oral gavage once daily for 5 consecutive days prior to CM injection and once at 4 hours after CM injection. Rats were allowed to recover for 24 hours after the CM injection and then they were sacrificed. By the end of the experiment, kidney specimens were processed for light microscope examination using H & E and PAS stains. **Results:** group II showed average renal capsule, mildly congested glomeruli with average Bowman's spaces, proximal tubules showed partial loss of brush borders and markedly edematous and apoptotic epithelial lining with intra-tubular debris, and renal medulla showed collecting tubules with markedly edematous and apoptotic epithelial lining with markedly congested peri-tubular capillaries compared to group I. Group III showed disrupted renal capsule, partially necrotic glomeruli with patent Bowman's spaces, scattered completely necrotic proximal tubules and others with markedly apoptotic epithelial lining and complete loss of brush borders, and areas of hemorrhage with inflammatory infiltrate, and renal medulla showed collecting tubules with markedly apoptotic and edematous epithelial lining with congested peri-tubular capillaries. While when rosuvaststin was administered before CM in group IV, there was a significant improvement in the histological picture towards the normal. Conclusion: the results of the current study showed that rosuvastatin has some protective role against contrast-induced acute kidney injury.
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Keywords: rosuvastatin, contrast-induced, acute kidney injury.

1. Introduction

Contrast-induced nephropathy (CIN) is one of important causes of hospital-acquired acute renal failure. Contrast-induced acute kidney injury (CI-AKI) is defined as an increase of > 25% or > 0.5 mg / dL (44 μmol / L) serum creatinine (sCr) from baseline within 48−72 hours following intravenous injection of iodine-based radio contrast material (RCM) if other causes of renal impairment can be excluded (**Schilp et al., 2014**).

CI-AKI is the third most common cause of hospital acquired acute renal failure **(Nicola et al., 2015)** and is responsible for about 10–12% of the cases **(Filiopoulos et al., 2014).** The pathogenic mechanism of CI-AKI is multifactorial and previous studies have shown that it is mainly associated with oxidative stress, renal ischemia and direct nephrotoxicity **(Seeliger et al., 2015)**. Statins are 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors that reduce both total and LDL

cholesterol. Studies have found that lowering LDL-C, particularly with statins, decreases the risk of cardiovascular deaths and events **(Lancet 2002)**.

Recently, there has been increasing interest in the role of statins in decreasing CIN risk in patients receiving contrast media. This is owing to both their anti-inflammatory effect and their ability to improve endothelial function, also their anti-apoptotic and anti-oxidant effects **(Rappy et al., 2011) (Luvai et al., 2012)**.

Rosuvastatin is a new generation of statin which reduces levels of circulating LDL-C. In addition to its beneficial cholesterol lowering effects, rosuvastatin has been shown to protect against inflammatory, oxidant, and thrombotic effects, and may improve endothelial function **(Luvai et al., 2012)**.

These effects of rosuvastatin have been translated into beneficial effects on atherosclerosis and have resulted in a significant reduction in cardiovascular events. Recent study suggests that rosuvastatin reduces the risk of CIN in DM patients **(Leoncini et al., 2014)** and another study shows that patients with renal dysfunction benefited from rosuvastatin therapy **(Han et al., 2014)**.

2. Material and methods:

1. Chemicals:

A. Ultravist: low-osmolarradio contrast media to induce acute kidney injury in rats in the form of ultravist 50 ml injectable solution (Iopromide 300mg/ml), was purchased from Scherring pharmaceutical company.

B. Rosuvastatin: 10 mg tablets as a member of HMG-CoA reductase inhibitors was obtained from Borg Company for pharmaceutical industries.

C. Furosemide: in the form of Lasix 20mg/2ml ampule to induce dehydration, was purchased from SANOFI pharmaceutical company.

2. Experimental animals:

Fourty adult albino rats were used in this study each of which weighs about 200 – 250 gm. They were obtained from animal house of Faculty of Medicine, Azhar University. Rats were kept in individual fan ventilated wide polypropylene cages with stainless steel top and wood shavings for bedding under controlled hygienic conditions at 20◦ C–24◦ C on a 12: 12-hour light/dark cycle. They had free access to tap water and a standard laboratory diet. The rats will be acclimatized for 7 days prior to the start of study. All rats were handled according to the standard guide for care and use of laboratory animals.

3. Experimental design:

Rats were divided randomly into four equal groups each of which was formed of 10 rats as follows:

•Group I (control group):

Rats will be able to access normal diet and normal amounts of water without any medication.

•Group II (dehydration group): (dehydration + furosemide, without CM administration)

Rats will be deprived of water for 72 hours and then given 10 mg/kg furosemide by intramuscular injection.

•Group III (CI-AKI group):

Rats will be treated in the same manner as group II, then after 20 minutes they will be given low-osmolar CM ultravist 50 ml injectable solution (iopromide 300mg/mL) by intravenous injection (10 mL/kg) via the tail vein over the course of 5 minutes once then they will be sacrificed **(Sun et al., 2014).**

•Group IV (CI-AKI + rosuvastatin group):

Statins will be administered by oral gavage once daily for 5 consecutive days prior to CM injection and once at 4 hours after CM injection. Rats will be allowed to recover for 24 hours after the CM injection and then they will be sacrificed **(Bae et al., 2010).**

Tissue processing for ordinary histological examination:

Each kidney was cut into two halves across the renal pelvis along its longitudinal axis to expose cortex, medulla and papilla. The specimens were immediately immersed in 10% formol saline for 48 hours to be processed and embedded in paraffin according to **Bancroft and Gamble (2008)** as follows: the kidneys were fixed in 10% formol saline for 48hours. The solution was prepared at least one day before being used, to allow time for depolymerization of formaldehyde polymers. Samples were dehydrated in ascending grades of alcohol (50%, 70%, 90%, and 95%) each for one hour then absolute alcohol (100%) for two changes one hour for each then they were cleared in xylol for two hours. Samples were embedded in soft paraffin wax at 55°C for two hours and in hard paraffin at 60°C for another 2 hours. Sectioning**:** 5 um thick paraffin sections were obtained. Finally they were stained with haematoxylin and eosin and PAS stains.

3. Results:

Histopathological results:

Group I (Control):

H & E stain: kidney showed average renal capsule, average glomeruli with average Bowman's spaces, average proximal tubules with preserved brush borders, average distal tubules, and renal medulla showed average collecting tubules with average interstitium **(Fig 1, 2,). PAS stain:** kidney showed average glomerular basement membrane, average proximal tubular basement membrane with preserved brush borders, and preserved collecting tubular basement membrane **(Fig 3, 4).**

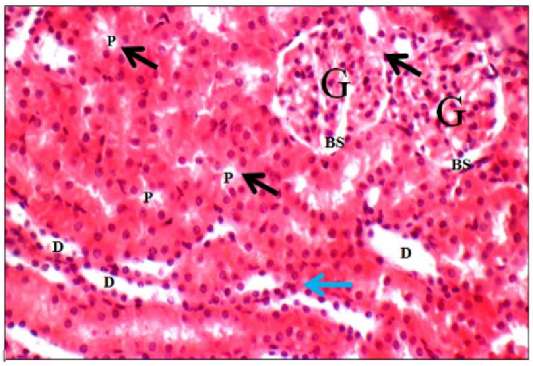

Fig (1): (Control): A photomicrograph of a section of adult albino rat kidney (Control) showing average glomeruli (G) with average Bowman's space (BS), average proximal tubules (P) with preserved brush borders (black arrows), average distal tubules (D), and average interstitium (blue arrow) (H & E x 400)

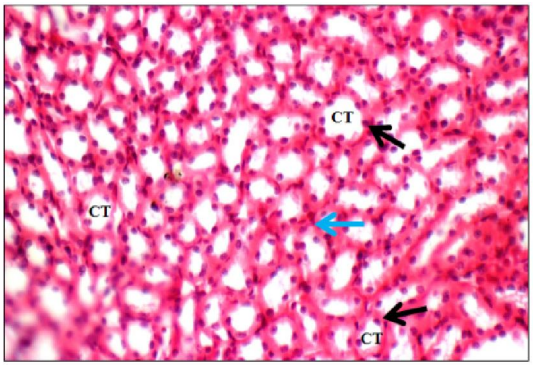

Fig (2): A photomicrograph of a section of adult albino rat kidney (Control) with another view in renal medulla showing average collecting tubules (CT) with average epithelial lining (black arrows) and average interstitium (blue arrow) (H & E x 400)

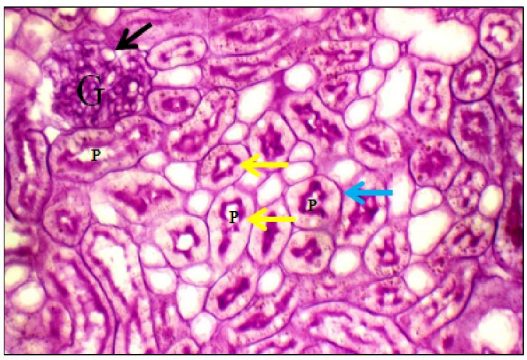

Fig (3): A photomicrograph of a section of adult albino rat kidney (Control) showing average glomerular basement membrane (black arrow), average proximal tubular basement membrane (blue arrow), and preserved brush borders (yellow arrow) (PAS stain X 400)

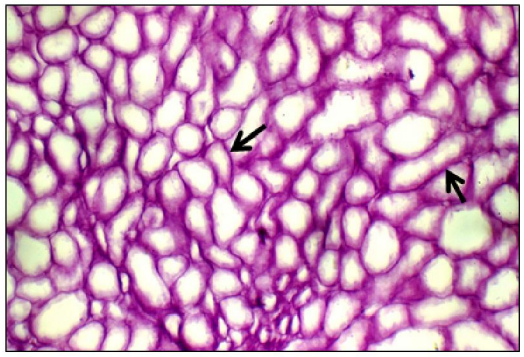

Fig (4): A photomicrograph of a section of adult albino rat kidney (Control) with another view in renal medulla showing average collecting tubular basement membrane (black arrows) (PAS x 400)

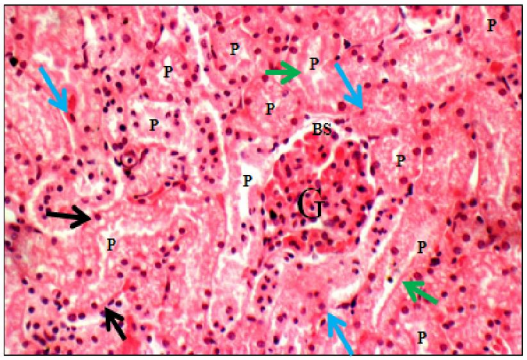

Fig (5): A photomicrograph of a section of adult albino rat kidney (group II): another view showing mildly congested glomerulus (G) with average Bowman's space (BS), and proximal (P) tubules showing markedly edematous (black arrows) and apoptotic epithelial lining (blue arrow) with partial loss of brush borders (green arrow) (H & E x 400)

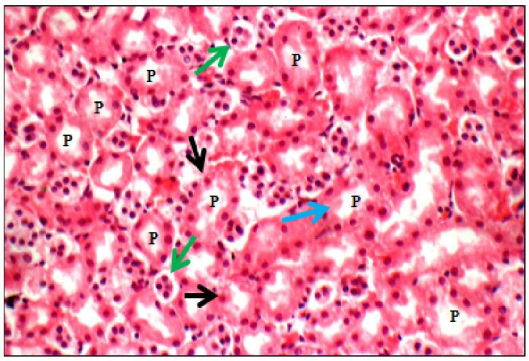

Fig (6): A photomicrograph of a section of adult albino rat kidney (group II): another view showing proximal (P) tubules showing with apoptotic epithelial lining (black arrow) and partial loss of brush borders (blue arrow), and intra-tubular debris (green arrow) (H & E x 400)

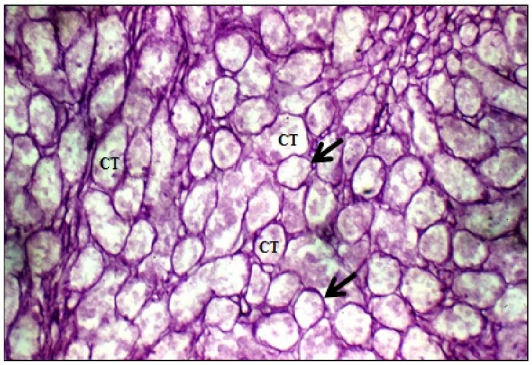

Fig (7): A photomicrograph of a section of adult albino rat kidney (group II): another view in renal medulla showing average collecting tubular basement membrane (black arrows) (PAS x 400)

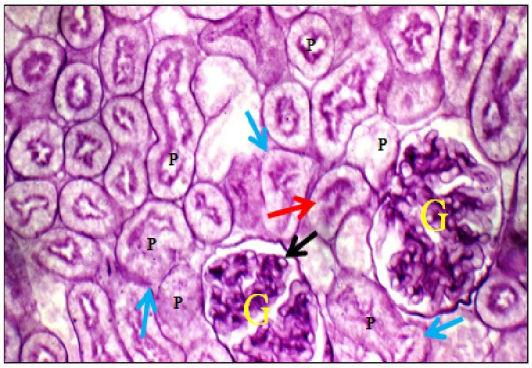

Fig (8): A photomicrograph of a section of adult albino rat kidney (group II): another view showing average glomerular basement membrane (black arrow), scattered proximal tubules showing destructed basement membrane (blue arrow), and partial loss of brush borders (red arrow) (PAS x 400)

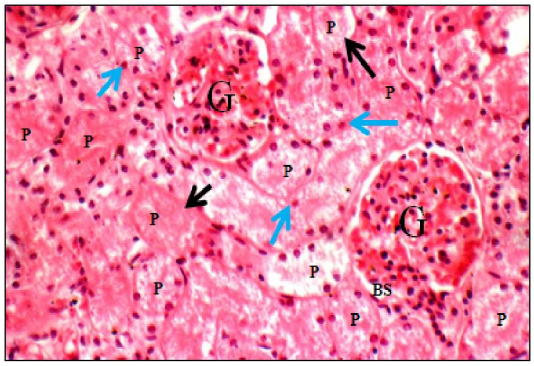

Fig (9): A photomicrograph of a section of adult albino rat kidney (group III): high power view showing partially necrotic glomeruli (G) with patent Bowman's space (BS), scattered completely necrotic proximal (P) tubules (black arrows), and other tubules showing markedly apoptotic epithelial lining (blue arrows) (H & E x 400).

Group II (Dehydration + Furosemide):
H & E stain:

Kidney showed average renal capsule, mildly congested glomeruli with average Bowman's spaces, proximal tubules showed partial loss of brush borders and markedly edematous and apoptotic epithelial lining with intra-tubular debris, and renal medulla showed collecting tubules with markedly edematous and apoptotic epithelial lining with markedly congested peri-tubular capillaries **(Fig 5, 6).**

PAS stain:

Kidney showed average glomerular basement membrane, scattered proximal tubules showed destructed basement membranes and partial loss of brush borders, and average collecting tubular basement membrane **(Fig 7, 8).**

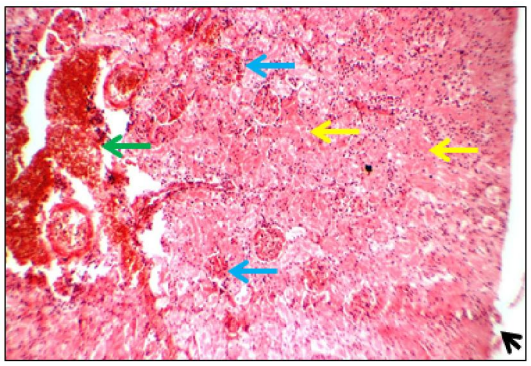

Fig (10): A photomicrograph of a section of adult albino rat kidney (group III): another view showing disrupted renal capsule (black arrow), markedly necrotic glomeruli (blue arrows), markedly necrotic tubules (yellow arrow), and areas of hemorrhage (green arrow) (H & E x 200).

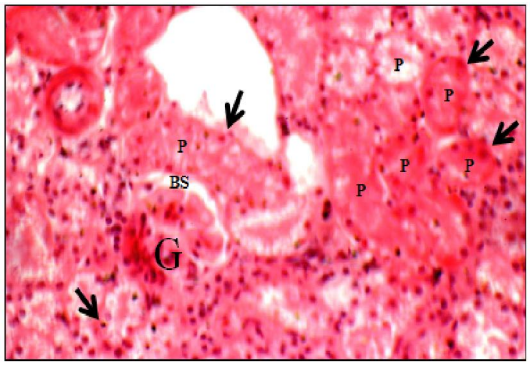

Fig (11): A photomicrograph of a section of adult albino rat kidney (group III): another view showing partially necrotic glomerulus (G) with patent Bowman's space (BS), and proximal (P) tubules showing markedly apoptotic epithelial lining (black arrows) (H & E x 400).

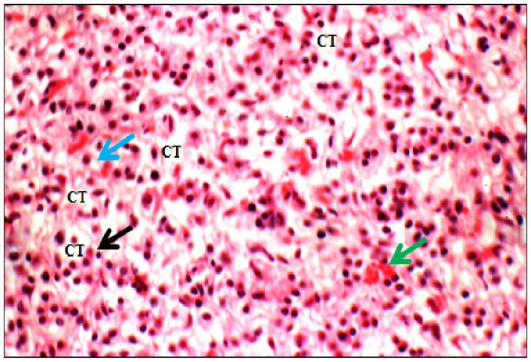

Fig (12): A photomicrograph of a section of adult albino rat kidney (group III): another view in renal medulla showing collecting tubules (CT) with markedly apoptotic (black arrow) and edematous epithelial lining (blue arrow), and congested peri-tubular capillaries (green arrow) (H & E x 400).

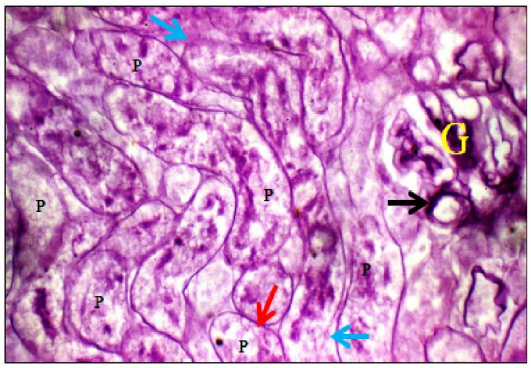

Fig (13): A photomicrograph of a section of adult albino rat kidney (group III): another view showing markedly thickened glomerular basement membrane (black arrow), destructed proximal tubular basement membrane (blue arrow), and complete loss of brush borders (red arrow) (PAS x 400).

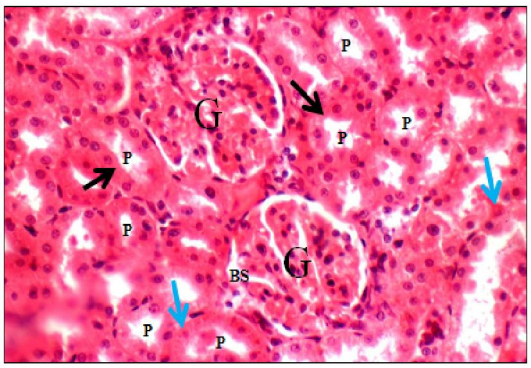

Fig (14): A photomicrograph of a section of adult albino rat kidney (group IV): high power view showing average glomeruli (G) with average Bowman's space (BS) and proximal (P) tubules showing preserved brush borders (black arrows) and mildly apoptotic epithelial lining (blue arrows) (H & E x 400).

Group III (Dehydration + Furosemide + Ultravist):

H & E stain: kidney showed disrupted renal capsule, partially necrotic glomeruli with patent Bowman's spaces, scattered completely necrotic proximal tubules and others with markedly apoptotic epithelial lining and complete loss of brush borders, and areas of hemorrhage with inflammatory infiltrate, and renal medulla showed collecting tubules with markedly apoptotic and edematous epithelial lining with congested peri-tubular capillaries **(Fig 9, 10, 11, 12).**

PAS stain: kidney showed markedly thickened glomerular basement membrane, destructed proximal tubular basement membrane with complete loss of brush borders, and destructed collecting tubular basement membrane **(Fig 13).**

Group IV (Dehydration + Ultravist +Rosuvastatine):

H & E stain: kidney showed average renal capsule, average glomeruli with average Bowman's spaces, proximal tubules showed partial loss of brush borders and mildly edematous and apoptotic epithelial lining, and renal medulla showed collecting tubules with markedly edematous epithelial lining and intra-tubular hyaline casts **(Fig 14, 15).**

PAS stain: kidney showed average glomerular basement membrane, most of proximal tubules showed average basement membranes with preserved brush borders, and average collecting tubular basement membrane **(Fig 16, 17).**

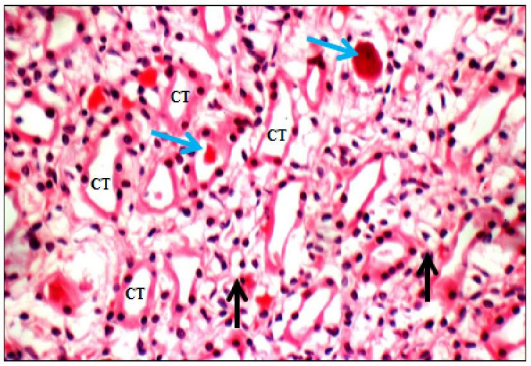

Fig (15): A photomicrograph of a section of adult albino rat kidney (group IV): another view in renal medulla showing collecting tubules (CT) with markedly edematous epithelial lining (black arrow), and intra-tubular hyaline casts (blue arrow) (H & E x 400).

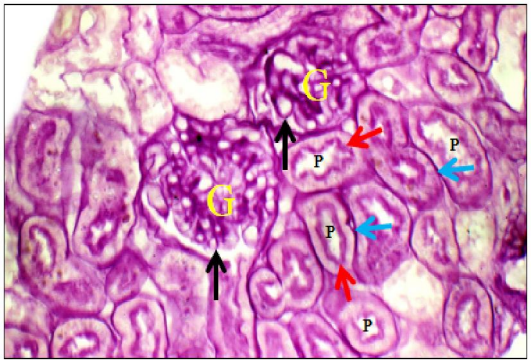

Fig (16): A photomicrograph of a section of adult albino rat kidney (group IV): kidney showing average glomerular basement membrane (black arrow), most of proximal tubular showing average basement membrane (blue arrow), and preserved brush borders (red arrows) (PAS x 400).

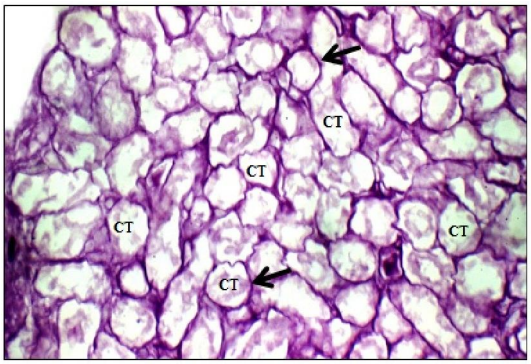

Fig (17): A photomicrograph of a section of adult albino rat kidney (group IV): another view in renal medulla showing average collecting tubular basement membrane (black arrows) (PAS x 400).

4. Discussion:

Contrast-induced acute kidney injury (CI-AKI) is a serious clinical complication, associated with increased use of iodinated contrast media (CM) in diagnostic and interventional procedures. It is now the third most important cause of hospital-acquired acute kidney injury and accounts for 12% of all cases **(Itoh Y. et al., 2005).** Although the use of low-osmolar CM (LOCM) reduces the risk of CI-AKI, the incidence of CI-AKI remains high following intravascular administration of LOCM in high-risk patients with renal insufficiency **(Aspelin P. et al., 2003).**

The pathogenic mechanism of CI-AKI is multifactorial, and previous studies have shown that it is mainly associated with oxidative stress, renal ischemia and direct nephrotoxicity **(Seeliger E. et al., 2015).**

As RCM administration in patients with high risk of CI-AKI such as preexisting renal problems or the use of large RCM doses is often unavoidable, which underscores the need for effective prevention strategies **(Pavlidis et al., 2015).**

There are some measurement that are suggested to protect against CI-AKI and one of them is rosuvastatin therapy due to their anti- inflammatory, anti-apoptotic and anti-oxidant effects (**Luvai et al., 2012).**

In this study we explore the reno-protective effect of rosuvastatin against CI-AKI in the adult albino rat.

In this study the rat was chosen in agreement with **Al-Samawy (2012)** who said that the rat is one of the most widely used research animals. The rat is also useful in the assessment of toxicological insult to the urinary system.

In this work, control animal renal tissue examination with H & E showed that the renal cortex was formed of renal corpuscles and tubules. Renal corpuscle is formed of glomerulus surrounded by Bowman's capsule. Distal convoluted tubules had wider lumen than proximal convoluted tubules. The distal tubules are lined by small cuboidal cells and eiosinophilic cytoplasm. Proximal convoluted tubules have narrow lumen and lined by cuboidal cells with apical brush border and more eosinophilic cytoplasm. The normal present results were similar to those of **Salem et al., (2015).**

In this work, sections of the control group stained with PAS, showing strong reaction in the basement membrane of the glomeruli, Bowman's capsule, DCT and the brush borders of the PCT. These results are close to those of **Zaghlol, (2012)** and **Ahmed et al., (2015).**

The renal lesions were graded according to **Yamasowa et al., (2005).** Tubular necrosis and proteinaceous casts were graded as follows: 0 = no damage, 1 = mild (unicellular, patchy isolated damage), 2 = moderate (50% damage). Medullary congestion was graded as follows: 0 = no congestion, 1 = mild (vascular congestion with identification of erythrocytes by ×400 magnification), 2 = moderate (vascular congestion with identification of erythrocytes by ×200 magnification), 3 = severe (vascular congestion with identification of erythrocytes by ×100 magnification), or 4 = very severe (vascular congestion with identification of erythrocytes by ×40 magnification).

In group II which treated with furosemide 10mg/kg B.W. IM after 72hours of dehydration, sections stained with H & E showed average renal capsule, mildly congested glomeruli with average Bowman's spaces, proximal tubules showed partial loss of brush borders and markedly edematous and apoptotic epithelial lining with intra-tubular debris, and renal medulla showed collecting tubules with

markedly edematous and apoptotic epithelial lining with markedly congested peri-tubular capillaries.

Sections stained with PAS stain showed average glomerular basement membrane, scattered proximal tubules showed destructed basement membranes and partial loss of brush borders, and average collecting tubular basement membrane.

We assigned this group specially to demonstrate the pathogenic effect of dehydration without CM as well as to augment the pathogenic effect of CM on the renal tissue which is reported to be augmented with dehydration **(Topark et al., 2008 and Norbert Kiss and PéterHamar 2016).**

Yoshioka et al., (1992) reported that dehydration alone significantly reduced renal cortical antioxidant expression in rats and produces remarkable renal damage. That made us to think about assigning this group treated only with dehydration.

Our result was similar to that reported by **Schley et al., (2013)** who reported that 72h dehydration resulted in mild tubular necrosis with cast formation and medullary vascular congestion.

Also **Topark et al., (2008)** reported that dehydration for 72h resulted in mild medullary congestion and tubular necrosis.

The pathogenic effect of dehydration on the kidney can be explained by volume depletion with circulatory compromise will result in acute renal ischemia. Uncorrected, this leads to a type of ischemic tubular injury usually known as acute tubular necrosis (ATN), which is the most common cause of acute kidney injury in the setting of volume depletion **(Schiffl et al., 2008 and Marcedo et al., 2008).**

Furthermore, **Roncal-Jimenez et al., (2015)** reported that dehydration has multiple effects on the kidney, leading to urinary concentration due to activation of vasopressin that occurs as a result of increase in serum osmolarity due to the loss of body water. Classically dehydration results in a 'pre-renal state' associated with intrarenal vasoconstriction but with relative maintenance of glomerular filtration rate (GFR). If volume depletion is severe, GFR falls that results in acute kidney injury (AKI).

Group III sections stained with H & E showed disrupted renal capsule, partially necrotic glomeruli with patent Bowman's spaces, scattered completely necrotic proximal tubules and others with markedly apoptotic epithelial lining and complete loss of brush borders, and areas of hemorrhage with inflammatory infiltrate, and renal medulla showed collecting tubules with markedly apoptotic and edematous epithelial lining with congested peri-tubular capillaries which is similar to the result of **Wang et al., (2017)** who treated the group with the same manner and reported that sections showed severe tubular necrosis and medullary congestion.

Kidney sections with PAS stain showed markedly thickened glomerular basement membrane, destructed proximal tubular basement membrane with complete loss of brush borders, and destructed collecting tubular basement membrane.

In 2016 **Norbert Kiss and Péter Hamar** reported a similar result as they stated that CI-AKI group sections stained with H & E showed tubular casts, congestion in renal medulla and tubular necrosis.

In the present study, the result was close to the result of **Yang et al., (2014)** who observed tubular epithelial cell shedding and basement membrane nudity, degeneration of tubular epithelial cells, protein cast, tubular dilatation, loss of tubular brush border, and necrosis of partial tubular epithelial cells was observed in CM‐injected rats.

However, **Anderucci et al., (2014)** reported that kidney sections in the CM group revealed the significantly severe damage consisting of tubular necrosis, proteinaceous cast formation, PTC congestion and interstitial edema in the outer stripe of the outer medulla (OSOM) and cortex.

Also, **Toprak et al., (2008)** reported a similar result as they observed that CM group developed tubular necrosis, proteinaceous casts and medullary congestion although they used a high-osmolar CM (urograffin) in a dose of 6mg/kg B.W.

Buyuklu et al., (2014) observed tubular necrosis and degenerative changes but also they observed inter tubular heamorrage.

The pathological changes in the renal tissue of the CI-AKI group are suggested to be due to endothelial damage, tubular hypoxia and tubular damage.

Norbert Kiss and PéterHamar (2016) explained that vascular endothelial injury has been suggested to be due to contrast-induced vasoconstriction. Same explanation was suggested by **Andreucci et al., (2014)** that added that the endothelial cells are the first to come in contact with intravenously injected RCM and Endothelial damage in peritubular capillaries by RCM directly or through ROS can be an important driving force of the medullary hypoxia.

Renal tubular epithelial cells affection is as they are the most sensitive to hypoxia due to their high metabolic demand as mentioned by **Norbert Kiss and PéterHamar (2016).** They added, furthermore, due to the countercurrent circulatory system of the kidney, the oxygen supply decreases towards the medulla as the oxygen demand increases. Thus, tubular epithelial cells are the first to suffer from hypoxic damage. Necrosis was present only if RCM was combined with other hypoxia triggers like dehydration. **Golchahi et al., (2014)** added that the suggested mechanism of

RCM-induced cytotoxicity is apoptosis induced by oxidative damage to the tubular epithelial cell membrane.

In another study by **Zhao et al., (2015)** they used Ioversol (3g/kg organically bound iodine) a low owosmolar CM instead of ultravist (iopromide) and they observed severe tubular damage and edematous basement membrane which is in an agreement with our result.

In the present study we planned to augment contrast effect in inducing nephropathy by dehydration 72 h followed by furosemide IM injection (10mg\kg B.W.) while another study However, a more recent study by **Linkermann et al., (2013)** reported that in rats with unilateral nephrectomy + indomethacin (100 μg/kg) + LNAME (100 μg/kg) + water deprivation (16 h) + iomeprol (low osmolar CM) (250 μL) induced only minimal changes. While in study of **Buyuklu et al., (2105)** they induced renal injury by Dehydration (24 h) + Indomethacin + furosemide and that resulted in moderate necrotic and degenerative tubular cells.

Another study by **Saritemur et al., (2015) and Zurovsky et al., (2011)** used dehydration (24 h) + glycerol rhabdomyolysis to augment the effect of CM and observed average tubular necrosis and glomerular affection.

In our study we used the protocol of dehydration of rats for 24 h followed by furosemide in agreement with **Schley et al., (2013) and Toprak et al., (2008).**

The whole idea is to induce a relevant and an obvious CI-AKI in rats and mice a combination of injuries is required beside CM injection. This injury can be done through inhibition of vasodilators, dehydration, surgical kidney injury, diabetic nephropathy or long term cholesterol feeding **(Norbert Kiss and PéterHamar (2016).**

Group IV in which animals were treated with rosuvasatin before CM injection sections stained with H & E kidney showed average renal capsule, average glomeruli with average Bowman's spaces, proximal tubules showed partial loss of brush borders and mildly edematous and apoptotic epithelial lining, and renal medulla showed collecting tubules with markedly edematous epithelial lining and intra-tubular hyaline casts.

In sections stained with PAS stain: kidney showed average glomerular basement membrane, most of proximal tubules showed average basement membranes with preserved brush borders, and average collecting tubular basement membrane.

These results are similar to these of **Wang et al., (2017)** as they reported that histopathological alterations were attenuated in CI-AKI rats treated with rosuvastatin. They reported that Compared with untreated CIAKI, treatment with rosuvastatin lowered the tubular necrosis by 20% and medullary congestion by 20%.

Deng et al., (2015) also reported similar results as he stated that the degree of injury was less severe in rosuvastatin treated CM group, compared with DCM group, as they showed less tubular injury and less medullary congestion, suggesting that rosuvastatin therapy significantly protected the kidney from the contrast media. They explained that rosuvastatin has potent anti-inflammatory properties: it increases nitric oxide synthetase bioavailability, and reduces oxidative stress independent of its cholesterol-lowering effect. They also demonstrated that rosuvastatin decreased oxidative damage, inflammatory responses, kidney injury and apoptosis.

Wang et al., (2017) studied the effect of different statins on CI-AKI and reported that histopathological alterations were attenuated in CI-AKI rats treated with rosuvastatin and atorvastatin as they showed mild to moderate tubular necrosis and medullary congestion. While simvastatin treated CM group, tubular necrosis or medullary congestion were not attenuated.

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