THE RENAL EFFECTS OF CARNOSINE IN AN EXPERIMENTAL SEPTIC SHOCK MODEL

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Introduction: We aimed to investigate the renal function and histological findings in experimental septic rat models with AKI by cecal ligation and puncture (CLP) and observed the pathological changes in renal tissues and the renal functions in the septic rats with or without carnosine intervention

Material and Methods: 24 Sprague Dawley rats were used. Rats were examined into 3 groups of 8 rats for each including control group, septic shock group and septic shock group treated with carnosine. Femoral vein and artery catheterization was applied in all rats. Rats in control group underwent laparotomy and catheterization. The other two groups with septic shock underwent laparotomy,(CLP) cecal ligation- puncture, catheterization and bladder cannulation. Rats in treatment group received intraperitoneal (IP) injection of 250 mg/kg carnosine at 60 min after cecal ligation- perforation. Rats were monitored for blood pressure, heart rate and fever to assess the postoperative septic responses and extensive fluid replacement was introduced. At the end of24 hours, rats were sacrificed and blood and renal samples were collected.

Results: As conclusion, statistically significant improvements were observed on renal functions, tissue and serum MDA levels, routine blood tests, biochemical indexes and pathological features group treated with carnosine compared to the other sepsis group. Meanwhile, sepsis-induced damages in renal functions and tissue were also markedly ameliorated by carnosine treatment.

Discussion: We concluded that carnosine may be effective on oxidative damage due to renal tissue perfusion defect in septic shock.

Key Words: Carnosine, Septic shock, Rat, Renal.

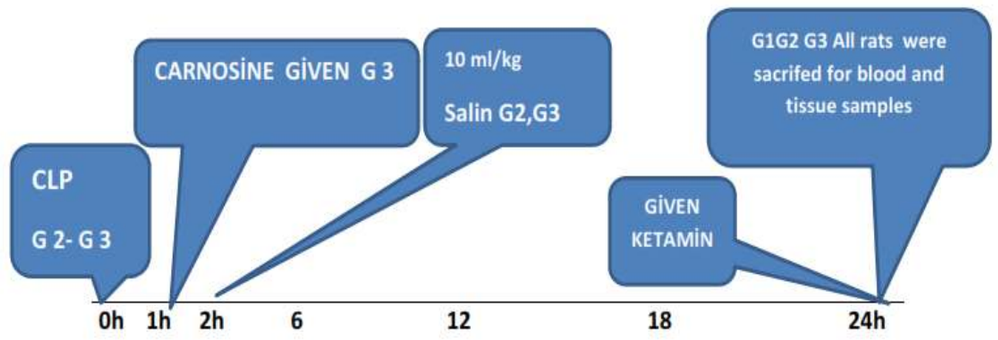
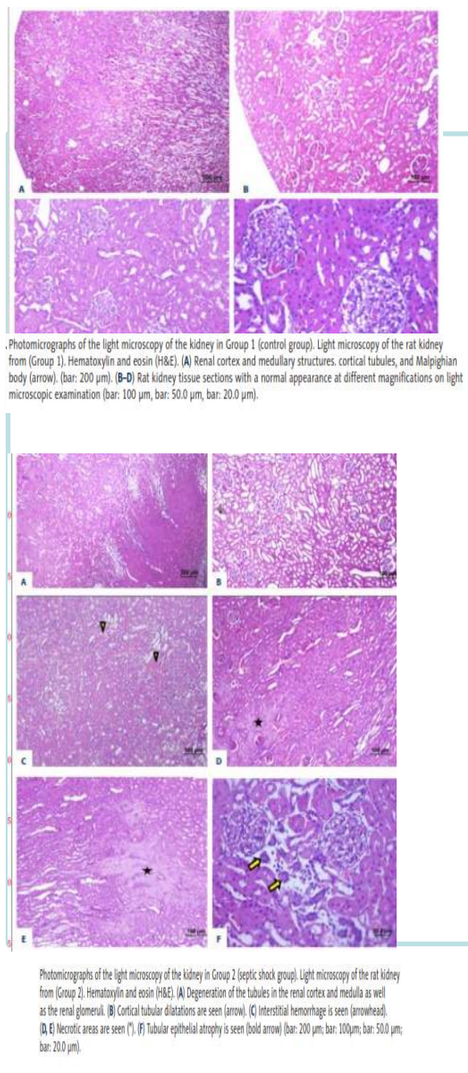


Table 5. Laboratory results of Groups 1, 2, and 3.

	Grup 1		Grup 2		Grup 3		KW	p
	Ort	Ss	Ort	Ss	Ort	Ss		
WBC 1 (preop)	7.102	842	7.228	1.281	7.370	1254	0.184	0.912
WBC 2 (postop)	11.470	2.008	16.656	1.767	14.957	1242	16.293	**0.000**
BUN 1 (preop)	22.000	2.777	24.625	2.973	26.000	2.673	6.203	**0.045**
BUN 2 (postop)	35.625	4.596	93.875	12.005	62.000	8.435	20.348	**0.000**
Cr 1 (preop)	0.513	0.155	0.550	0.131	0.625	0.183	1.762	0.414
Cr 2 (postop)	0.625	0.149	0.950	0.288	0.775	0.205	6.156	**0.046**
CLcr	0.888	0.247	0.190	0.130	0.575	0.128	18.582	**0.000**
CK	43.375	2.774	417.250	2.053	223.875	2.748	20.401	**0.000**
MDAS	2.390	0.551	7.533	1.380	3.723	0.563	19.314	**0.000**
MDAT	11.300	1.225	19.975	1.676	12.494	1.430	16.758	**0.000**

* p<0.05, ** p<0.001 (Kruskal-Wallis test for multiple comparisons), aMean ±SD (ANOVA used for multiple comparisons). G1 – Control; G2 – sepsis; G3 – sepsis+carnosine. WBC – white blood cell; BUN – blood urea nitrogen; Cr – creatinine; CL cr – creatinine clearance; CK – creatine kinase; MDAS – malondialdehyde serum; MDAT – malondialdehyde tissue.



Photomicrographs of the light microscopy of the kidney in Group 2 (septic shock group). Light microscopy of the rat kidney from (Group 2). Hematoxylin and eosin (H&E). (**A**) Degeneration of the tubules in the renal cortex and medulla as well as the renal glomeruli. (**B**) Cortical tubular dilatations are seen (arrow). (**C**) Interstitial hemorrhage is seen (arrowhead). (**D, E**) Necrotic areas are seen (*). (**F**) Tubular epithelial atrophy is seen (bold arrow) (bar: 200 µm; bar: 100µm; bar: 50.0 µm; bar: 20.0 µm).

Table 6. Histology of the renal tissue of rats in of Groups 1, 2, and 3.

	Groups	Median (25%–75%)	Multiple comparison results		
			G1	G2	G3
Glomerular injury	G1	0.00 (0.0–0.0)		*	
	G2	3.000 (1.5–3.0)	*		*
	G3	1.500 (1.0–2.0)	*	*	
	H=13.506 DF=2 P=0.003 (P<0.05)				
Tubular atrophy	G1	0.000 (0.0–0.0)		**	*
	G2	2.500 (1.5–3.0)	**		**
	G3	1.000 (1.0–2.0)	*	**	
	H=14.82 DF=2 P<0.001				
Necrosis	G1	0.000 (0.0–0.0)		**	*
	G2	3.000 (3.0–3.0)	**		**
	G3	1.500 (1,0–2,0)	*	**	
	H=13,506 DF=2 P<0.001				
Inflammation	G1	0.000 (0.0–0.0).		**	*
	G2	3.000 (3.0–3.0)	**		**
	G3	1.000 (0.5–1.0)	*	**	
	H=13,82 DF=2 P<0.001				
Hemorrage	G1	0.000 (0.0–0.0).		**	*
	G2	3.000 (3.0–3.0)	**		**
	G3	2.000 (2.0–2.0)	*	**	
	H=14.82 DF=2 P<0.001				

* p<0.05; ** p<0.001 Kruskal-Wallis H. G1 – Control; G2 – sepsis; G3 – sepsis+carnosine. Histological Findings: Absent (0 degree), mild (1 degree), moderate (2 degree) or severe (3 degree).

Photomicrographs of the light microscopy of the kidney in Group 1 (control group). Light microscopy of the rat kidney from (Group 1). Hematoxylin and eosin (H&E). (**A**) Renal cortex and medullary structures. cortical tubules, and Malpighian body (arrow). (bar: 200 µm). (**B–D**) Rat kidney tissue sections with a normal appearance at different magnifications on light microscopic examination (bar: 100 µm, bar: 50.0 µm, bar: 20.0 µm).