Pancreatic Injury Induced by Renal Ischemia-Reperfusion(I/R) Injury: Possible Role of Oxidative Stress

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Introduction

Renal ischemia-reperfusion injury (I/R) is an inevitable consequence of kidney transplantation, partial nephrectomy and aortic cross-clamping[1]. Reactive oxygen species (ROS) play an important role in mediating cell damage during I/R injury[2] and the I/R induced-tissue injury is caused by an imbalance between production of ROS and antioxidant capacity[3].

Renal ischemia-reperfusion (I-R) elicits tissue damage in a number of organs: heart, lung, and liver. In the pancreas, although, a recent invitro study demonstrated impairment of kidney function by pancreatic I/R injury through xanthine oxidase enzyme[4], there is no study, up to the best of our knowledge, investigated the impact of renal I/R injury on pancreatic function and histology.

Aim

the aim of this study was to investigate the impact of renal I/R injury on the functions and histology of pancreas as well as on the oxidative stress state in pancreas.

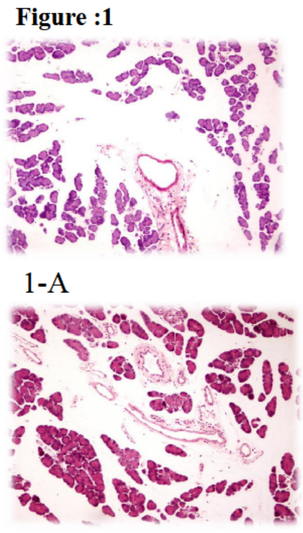
Method

Experimental study:
twenty-four mice were assigned to the following equal four groups
1- sham control early (SH E)
2- AKI model early (AKI E)
3- shame control delayed (SH D)
4- AKI model delayed (AKI D)
where experimental bilateral RI were induced for 45 minutes , released for 2 hours then scarified for (SH E , AKI E)
bilateral R.I for 45 minutes , released then scarified on 7th day (SH D , AKI D)

Laboratory investigations:
1) Renal functions:
serum creatinine and BUN
2) Pancreatic functions:
Blood glucose level , serum amylase , serum lipase and serum insulin
(MDA - catalase - GSH)

Histological examination
Evaluation of renal tissues for congestion. Tubules for degenerative changes , tubular dilatation, luminal debris, cast formation, and loss of brush borders from proximal tubules.
Pancreatic sections were taken for congestion, cellular degenerative changes, cytoplasmic vacuolization and leukocyte infiltration .

Figure :1

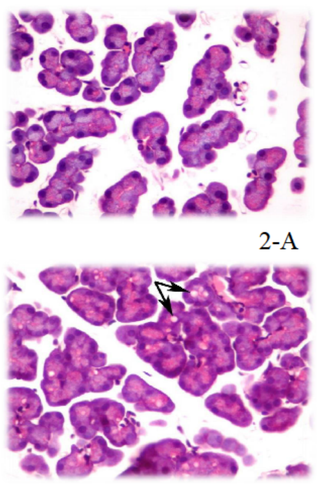


1-A

1-B

Fig. (1)
Oedema expanding the interstitial tissue separating pancreatic acini and lobules (H&E, X200) (A) and, (H & E, X400) (B)

Figure :2



2-A

2-B

Fig. (2):
Pancreatic acinar cell vacuolization (A). Vacuoles appear as unstained "holes" within the cytoplasm (Arrows) (B) (H & E, X400

Figure :3

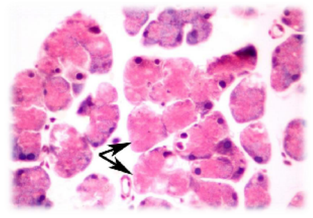


Fig. (3):
Groups of necrotic acinar cells (Arrows) (H & E, X400)

Results

Table (1) shows :
Effects of 45 min bilateral renal ischemia on renal functions (serum creatinine , BUN). And on pancreatic functions (serum amylase, lipase, fasting insulin) and fasting blood glucose

Table (1): *Effect of 45 min bilateral renal ischemia on renal functions, pancreatic functions and blood glucose*

	Group	2 hr	1 day	3 days	7 days
Renal functions:					
-Serum creatinine (mg /dl)	Sh D	0.41 ± 0.05	0.77 ± 0.12	0.500 ± 0.05	0.44 ± 0.01
	AKI D	0.82* ± 0.07	1.066 ± 0.15*	1.57 ± 0.12*	0.66 0.15
-Serum BUN (mg/dl)	Sh D	19.85 ± 1.91	34.95 ± 4.69	46.64 ± 1.68	24.10 ± 3.22
	AKI D	47.08 ±4.29*	134.55 ± 18.48*	104.78 ± 8.91*	29.68 ± 4.31
Pancreatic functions :					
-Serum amylase (mg /dl)	Sh D	264.0 ± 44.43	255.0 ± 22.53	249.17 ± 33.06	383.67± 40.82
	AKI D	287.67 ± 44.68	315.83 ± 62.26*	498.33 ± 103.84 *	459.5 ± 54.38
-Serum lipase (U/L)	Sh D	32.00 ± 5.51	18.67 ± 6.47	24.0 ± 9.18	29.83 ± 10.05
	AKI D	36.00 ± 8.03	54.67 ± 12.25*	74.83 ± 5.56*	42.33 ± 15.38
-Fasting insulin (mIU/ml)	Sh D	9.61± 1.41	13.50 ± 2.85	8.72 ± 0.58	9.88 ± 1.19
	AKI D	8.68 ± 1.69	8.25 ± 1.36*	8.40 1.77	7.95 ± 1.26
Fasting blood glucose (mg/dl):					
	Sh D	105.17 ±13.60	125.67 ± 7.97	109.67± 7.86	109.00 ± 4.42
	AKI D	116.20 ±28.35	123.67± 20.43	129.33 ± 25.82	99.33 ± 8.89

All data expressed as Mean ± SD. Independent T- test.* significant vs sham group ($p < 0.05$). BUN= blood urea nitrogen

groups at 2hrs, day 1, day 3 and day 7 after ischemia.
Compared to sham group, serum creatinine and BUN were significantly high in ischemic group at 2 hrs, day 1, and day 3 only after ischemia ($p< 0.05$). At day 7 there was no significant difference between sham and ischemic group.
Compared to sham group, serum amylase showed significant increase in ischemic
group at 2 hrs, day 1 and day 3 after ischemia ($p< 0.05$), while serum lipase
showed significant increase in control group only at days 1 and 3 (table 1).

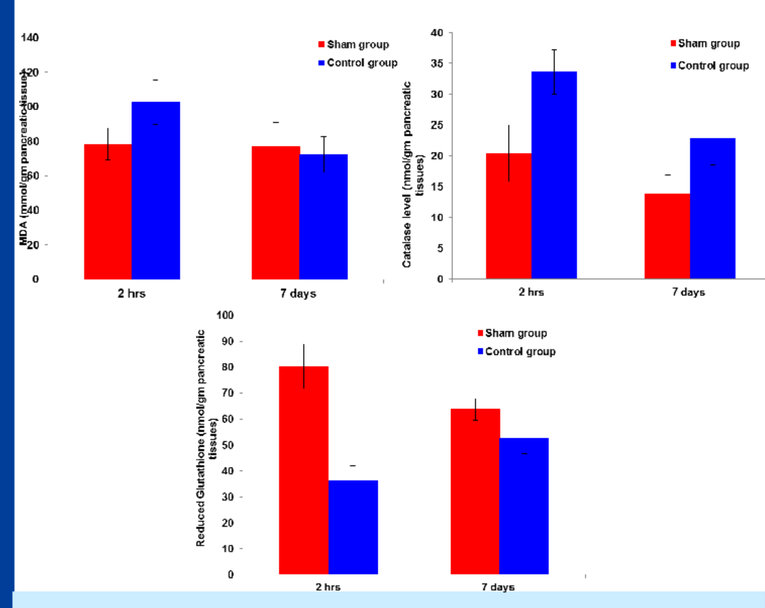
Compared to sham group, fasting insulin showed significant decrease in ischemic group only at day 1 ($p< 0.001$).
Fasting blood glucose showed no statistically significant difference
between sham group and control group at different periods of follow up .

Table (2): Effects of 45 min bilateral renal ischemia on pancreatic weight and histopathological damage score

	Group	Weight	Oedema	Leucocytic infiltration	Vacuolization	Necrosis	Haemorrhage
2 hrs	SH E	120.50 ± 30.31	0.50 ± 0.22	0.50 ± 0.22	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
	AKI E	98.80 ± 29.40*	1.14 ± 0.26*	0.714 ± 0.18*	0.143 ± 0.142*	0.143 ± 0.14*	0.00 ± 0.00
7 days	SH D	120.17 ± 81.55	0.67 ± 0.21	1.00 ± 0.25	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
	AKI D	174.00 ± 56.39*	1.67 ± 0.21*	1.500 ± 0.34*	0.833 ± 0.307*	0.00 ± 0.00	0.00 ± 0.00

All data expressed as Mean ± SD. Independent T- test.* significant vs sham group ($p< 0.05$).

Table 2 shows the results of pancreatic weight and damage score. Compared to sham group, the weight of pancreas was significantly increased in ischemic group at the end of experiment.
Also, compared to sham group, pancreatic oedema, leucocytic infiltration, and vacuolization were significantly high in ischemic group at 4 hrs after ischemia and at the end of the experiment.
However, pancreatic necrosis was present only in control ischemic group at 2 hrs after ischemia (figure 3), as well as both groups showed no pancreatic haemorrhage



Conclusion

We conclude that 45 minutes bilateral renal ischemia causes detrimental changes in pancreatic exocrine functions and morphology as well as it enhances oxidative stress and inflammatory states in pancreas.
We recommend, care should be taken to protect other organs such as pancreas remote from I/R sites, especially during renal surgery

References

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