LIPID METABOLISM AND THE EXPRESSION OF PROTEINS FOR LIPID REGULATION IN EXPERIMENTAL CHRONIC RENAL FAILU

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OBJECTIVES

The uremic dyslipidemia might be associated with the altered regulation of proteins for lipid metabolism. We assessed the changes in level of sterol regulatory element binding protein-1 (SREBP-1) and liver X-receptor (LXR) and the effect of angiotensin II receptor blocker (ARB) on the lipid metabolism using a murine 5/6 nephrectomy model.

METHODS

Male Sprague-Dawley rats (*n*=30) were randomly assigned to CRF and c groups. The CRF group underwent 5/6 nephrectomy and randomized to untr (CRF group, *n*=11) and losartan-treated (ARB group, *n*=9) groups. The control (*n*=10) underwent sham operation. After 4 weeks later, we collected physiologic such as blood pressure, amount of proteinuria, BUN, serum creatinine, triglyc and LDL levels. We investigated histologic findings and examined the express TGF-β1 by immunohistochemistry in renal tissues. Quantitative real-time PCR performed to evaluate the mRNA expression of LXRα, TGFβ and fibronectin western blotting and confocal microscopic examination were done to examin SREBP-1 expression in the kidney of each group.

RESULTS

Blood pressure, amount of proteinuria, serum triglyceride and LDL levels increased in CRF rats compared to control rats, and were down-regulated in ARB treated rats. The expression of LXR was up-regulated in CRF rats compared with control and ARB group as assessed by real-time PCR [Figure 1]. SREBP-1 was up-regulated in CRF group as evaluated with western blot [Figure 2] and confocal microscopy [Figure 3]. In control and ARB groups, the regulation of SREBP-1 showed the reciprocal patterns compared to that of CRF rats. The expressions of TGF-β and fibronectin were coincided with the changes of renal function and ARB treatment [Figure 4].

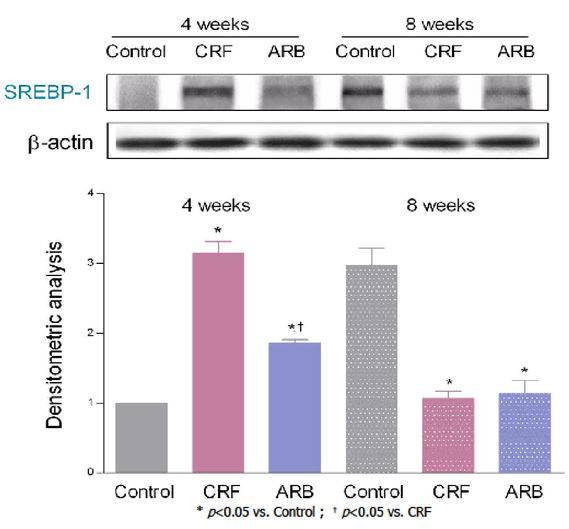

Fig. 2 Western blot analysis for SREBP-1 proteins in control, CRF, and ARB group

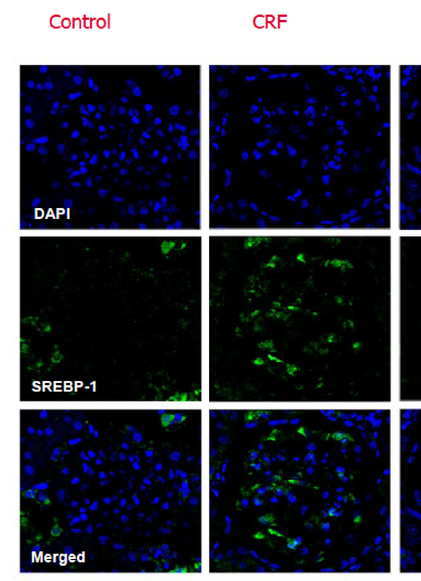

Fig. 3 Confocal microscopic local of SREBP-1 (green color). ×800

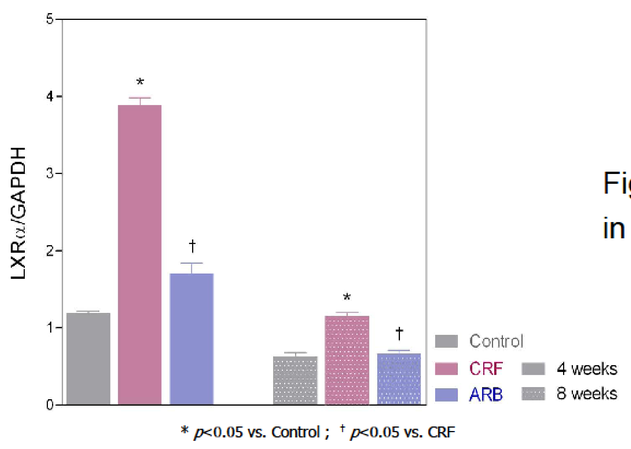

Fig.1 Renal LXRα mRNA expression in control, CRF, and ARB group

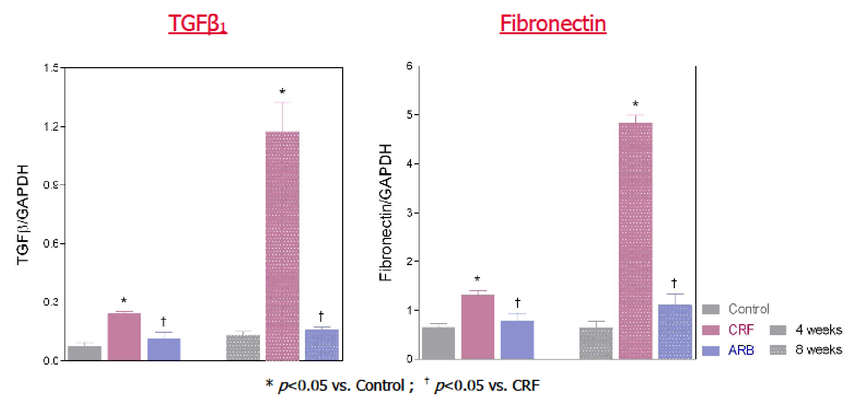

Fig.4 Renal TGF-β1 and fibronectin mRNA expression in control, CRF, and ARB g

CONCLUSION

Chronic renal failure was directly related with the development of dyslipidemia through the differential expression of proteins for lipid regulation, and ARB may halt the deleterious process of dyslipidemia via normalization of regulators.

REFERENCES

1. Muntner P, Coresh J, Smith JC, Eckfeldt J, Klag MC: Plasma lipids and risk of developing renal dysfunct atherosclerosis risk in communities study. *Kidney Int* 58:293-301, 2000
2. Wanner C, Krane V: Uremia specific alteration in lipid metabolism. *Blood Purif* 20:451-453, 2002
3. Batista MC, Welty FK, Diffenderfer MR, Sarnak MJ, et al.,: Apolipoprotein A-I, B-100, and B-48 metab subjects with chronic kidney disease, obesity and the metabolic syndrome. *Metabolism* 53:1255-1261, 2004
4. Abrass CK: Cellular lipid metabolism and the role of lipids in progressive renal disease. *Am J Nephrol* 24:46-5
5. Sun L, Halaihel N, Zhang W, Rogers T, Levi M: Role of sterol regulatory element-binding protein 1 in regu renal lipid metabolism and glomerulosclerosis in diabetes mellitus. *J Biol Chem* 277:18919-18927, 2002
6. Horton JD, Goldstein JL, Michael SB: SREBPs: activators of the complete program of cholesterol and fa synthesis in liver. *J Clin Invest* 109:1125-1131, 2002
7. Wu J, Zhang Y, Wang N, Davis L, Yang G, Wang X, Zhu Y, Breyer MD, Guan Y: Liver X receptor-alpha m cholesterol efflux in glomerular mesangial cells. *Am J Physiol Renal Physiol* 287:F866-895, 2004