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Lipidomic study of kidney in a mouse model with urine flow obstruction

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Obstructed urine flow is known to cause structural and functional kidney damage leading to renal fibrosis. However, limited information is available on the change in kidney lipids during urinary tract obstruction. In this study, we investigated the change in lipidome in a mouse model with unilateral ureteral obstruction (UUO). The establishment of the UUO model was confirmed by histopathological examination using transmission electron microscopy. Untargeted liquid chromatography/mass spectrometry was carried out over a time course of 4 and 7 days. Compared to the sham control, the UUO kidney at 7 days showed dilatation of the renal tubule with loss of brush borders and thickening of the capillary endothelium. In the kidney lipidomes obtained from the UUO 7 days group compared to the control, a significant decrease of ceramide, sphingomyelin, phosphatidylcholine, lysophospholipids, and phosphatidylethanolamine was observed, whereas cholesteryl esters, free fatty acids, phosphatidylglycerol, and cardiolipins were significantly increased. The present study revealed the disturbed lipid metabolism in the UUO model, which may provide a clue to potential lipid pathways and therapeutic targets for the early stage of renal fibrosis.

Keywords Lipid, Liquid chromatography, Mass spectrometry, Kidney injury, Unilateral ureteral obstruction, Renal tubulointerstitial lesion

Lipids consist of the most abundant metabolites in circulation and serve as an integral part of cell structure and function[1]. Lipidomics refers to the global study of lipid species and their biological functions within biological systems[2]. Their alterations are linked with disease severity and outcome[3], therefore, an abundance of individual lipid molecular species in plasma may be indicative of the variety of specific human diseases[4]. The utility of large-scale lipidomic profiling has been shown in several systemic disorders[1]. Recent, promising data indicate lipid profiling is a powerful discovery tool in nephrology research[5,6]. Obstructive nephropathy, also known as uropathy is a common clinical case[7] it's serious and irreversible consequences as it can lead to renal failure and interfere with the maturation of the kidneys. Additionally, it may also result in acute kidney injury (AKI) or chronic kidney disease (CKD)[8].

Ureteral obstruction is known as one of the prevalent clinical renal disorders that can occur at any age[9]. Studies have demonstrated that prolonged ureteral obstruction can lead to nephropathy and chronic kidney injury[10]. Early detection enables effective treatment and reversal[9]. One commonly used model for studying obstructive nephropathy is a unilateral ureteral obstruction (UUO). In this experimental procedure, the left ureter is typically ligated using a silk thread[11]. UUO occurs in approximately 1 in 1000 adults[12]. This condition causes an increase in hydrostatic pressure due to urine stagnation. Which then triggers the renin-angiotensin system (RAS) via the production of angiotensin II (Ang II)[13]. Ang II activates nicotinamide adenine dinucleotide phosphate

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