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Effects of Nutritional Ketosis Induced by Ketogenic Diet on Kidney Function and Metabolism in a Mouse Model of Diabetic Kidney Disease

Sol Been Park, Joo Young Park, Ji Woo Kim, Seeun Lee, Soo Jin Yang
Department of Food and Nutrition, Seoul Women's University, Korea, Republic of

Objectives : Nutritional ketosis is a physiological condition that ketone concentration is within 0.5~3.0 mmol/L, and can be induced by ketogenic diet (KD) ingestion. Recent studies suggest that induction of nutritional ketosis may improve kidney function by regulating molecular or metabolic pathways. This study aims to investigate whether KD-induced nutritional ketosis improves kidney function and to identify underlying mechanisms.
Methods : The mouse model of diabetic kidney disease was established by a single intraperitoneal injection of streptozotocin and nicotinamide combined with a high-fat diet feeding to male C57BL/6J mice. The subset of mice was assigned to the KD group, and fed with KD for 6 weeks after the induction of diabetic kidney disease condition for 8 weeks.
Results : The mouse model of diabetic kidney disease was established as shown by hyperglycemia, hyperinsulinemia, reduced urinary albumin creatinine ratio (UACR), and disorganized kidney tissue morphology. KD ingestion for 6 weeks induced nutritional ketosis with about 1.3 mmol/L of beta-hydroxybutyrate in serum. Also, KD feeding enhanced glycemic control and insulin sensitivity. Moreover, the kidney weights were restored and UACR was significantly reduced by KD feeding. This was accompanied by decreases in serum concentrations of corticosterone, insulin, and c-peptide, as well as increases in pyruvate dehydrogenase activity and acetyl-CoA concentrations in the kidney.
Conclusions : Collectively, the KD-induced nutritional ketosis status improved kidney function with alterations in nutrient metabolism.