Impressive weight loss induced by a very low-calorie ketogenic diet in a morbidly complex obese patient with a recent episode of acute kidney injury and advanced chronic kidney disease: a case report

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ABSTRACT

The very low-calorie ketogenic diet (VLCKD), characterized by a marked energy restriction that induces rapid weight loss, has recently been proposed as a valid nutritional strategy for managing obesity. VLCKD is commonly considered dangerous for the kidneys due to the misconception that it is high in protein, beyond the risk of electrolyte imbalances and an increase in diuresis. We report a case of safe and effective weight loss induced by VLCKD in a 43-year-old Caucasian woman with a recent episode of acute kidney injury on advanced chronic kidney disease. Surprisingly, we observed that after the diet-induced weight loss, not only did renal function not worsen, but proteinuria also improved. The principal value of this case report is its singular demonstration of impressive weight loss induced by VLCKD in a complex obese patient that was apparently not accompanied by the development of serious adverse sequelae.

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Key words: ketogenic diet, chronic kidney disease, obesity, acute kidney injury, case report.

Contributions: MCP, VT, FA, conceptualization; MCP, VT, methodology; MCP, VT, MC, NC, CV, FC, MM, MRN, FG, GA, writing - original draft preparation; MCP, VT, FA, writing - review and editing; FA, supervision. All authors have read and agreed to the published version of the manuscript.

Conflict of interest: the authors declare no potential conflict of interest.

Ethics approval and consent to participate: not applicable.

Patient consent for publication: the patient gave her consent to use her personal data for the publication of this case report.

Funding: none.

Availability of data and materials: all data underlying the findings are fully available.

Received: 10 August 2024.
Accepted: 29 August 2024.

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Licensee PAGEPress, Italy
Italian Journal of Medicine 2024; 18:1787
doi:10.4081/itjm.2024.1787

Introduction

Obesity is a complex, multifactorial disease that affects approximately one-third of the world's population, resulting in an increasing health and societal burden. Obesity is defined by the World Health Organization as a chronic disease characterized by excess body fat that can lead to medical, psychological, physical, social, and economic problems. However, obesity appears to be one of the most visible yet neglected public health problems. Despite countless efforts, the treatment of obesity remains one of the most difficult challenges, with often disappointing results. A very low-calorie ketogenic diet (VLCKD) is characterized by a marked restriction of carbohydrate intake, usually less than 30 g/day, with an increase in fat (30-40 g/day) and a protein intake of about 1.2 to 1.5 g/kg ideal body weight per day, with a daily energy intake <800 Kcal that induces rapid weight loss.[1] VLCKD has recently been proposed as a valid nutritional strategy for the treatment of obesity. Ketone bodies (acetoacetate, D-ß-hydroxybutyrate, and L-ß-hydroxybutyrate) are metabolites produced in the liver and catabolized in extrahepatic organs with pleiotropic effects. Ketone bodies play a fundamental role in the heart and have multiple roles in the regulation of cellular processes such as metabolism, inflammation, and cellular crosstalk. Obesity is an independent risk factor for the progression of chronic kidney disease (CKD).[2] Furthermore, CKD is a global health

problem as it is associated with an increased risk of cardiovascular mortality.[2] CKD is characterized by a reduced estimated glomerular filtration rate (eGFR) (<60 mL/min/1.73 m^2) and albuminuria (≥30 mg/day) persisting for at least 3 months.[2] Obesity is associated with low eGFR.[2] In addition to its role in storing and providing energy in the fasting state, adipose tissue is an endocrine organ that can produce adipocytokines that influence systemic homeostasis.[2] Excessive production of pro-inflammatory adipocytokines causes chronic low-grade systemic inflammation and oxidative stress, which can lead to the development of obesity-related diseases, including CKD. Specifically, pro-inflammatory adipocytokines can damage the kidney by altering renal hemodynamics, resulting in glomerular hyperfiltration, proteinuria and ultimately impaired eGFR.[2] Here we report a case of the effect of VLCKD on body weight resulting in improved renal function in an obese woman with multiple sclerosis and a recent episode of acute kidney injury (AKI) on CKD.

Case Report

This case is about a 43-year-old Caucasian woman who presented to our hospital with a complaint of chronic fatigue, hypertension (blood pressure from 140/80 to 160/80 mmHg), and deterioration of renal function (creatinine from 1.53 to 2.85 mg/dL and proteinuria from 0.13 g/24 h to 2.24 g/24 h). Her past medical history included class III obesity [weight 179.5 kg; body mass index (BMI) 70 kg/m^2], multiple sclerosis, and chronic renal failure. Physical examination revealed a vesicular murmur in the absence of wet crackles and peripheral smear. Her eGFR assessed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was 19.4 mL/min/1.73 m^2, her serum albumin was 3.2 g/dL, her blood urea nitrogen was 77 mg/dL, her glycated hemoglobin A1c was 6%, her intact parathyroid hormone (iPTH) was 122.5 pg/mL, her adrenocorticotropic hormone was 29 pg/mL, and her serum electrolytes were in the normal range. Blood chemistry showed normocytic normochromic anemia with a hemoglobin of 8.0 g/dL. Urinalysis was positive for protein (+3) and blood (+2) and showed 5-10 white blood cells/high power field (HPF), 20-40 red blood cells/HPF, and no casts. AKI was diagnosed as CKD with proteinuria, and several tests were performed to understand the etiology. Autoimmunity tests and complement levels were performed and were all negative. Similarly, immunofluorescence studies for immunoglobulin (Ig) G, IgA, IgM, and serum immunofixation were negative. Renal ultrasound showed normal-appearing kidneys. Although percutaneous renal biopsy was indicated, it was decided to postpone the procedure because of her anemia and severe obesity, which would have complicated the technical approach. The patient was started on irbesartan 300 mg/day.

After 2 months from AKI, she started the VLCKD because she needed to lose weight quickly before bariatric surgery. At the start of the diet, her creatinine was 1.3 mg/dL (eGFR with CKD-EPI: 50 mL/min/1.73 m^2). During the treatment period, the medical team carried out weekly check-ups for the first month and twice a week for the remaining months, monitoring the rate of diuresis, proteinuria, urinalysis, electrolyte levels, creatinine, azotemia, uric acid, anthropometric assessments, and blood pressure. In about 6 months we got a great result: she lost about 40 kg, reaching a BMI of 48.9 kg/m. Besides, she showed both neurological and cardiometabolic improvement, improving her quality of life. Electrolyte levels were maintained within the normal range during treatment (data not shown). Surprisingly, we found that not only renal function but also proteinuria improved after diet-induced weight loss (Table 1).

Discussion

In general, there was little data in the literature about VLCKD in patients with impaired renal function. The use of the ketogenic diet in CKD has raised several theoretical concerns. Firstly, the high levels of lipids, phosphate, acids, and animal proteins in the ketogenic diet could exacerbate

Table 1. Renal function, hemoglobin values and body mass index during the disease course.

Parameter	Before hospitalization	At the time of hospitalization	1 month after hospitalization	At the beginning of VLCKD	3 months after beginning of VLCKD	At the end of VLCKD	1 year later
Days to relative VLCKD (day)	-120	-60	-30	0	+90	+180	+365
Creatinine (mg/dL) (n.v. 0.5-1.0)	1.53	2.85	1.4	1.3	1.19	0.92	0.76
eGFR (mL/min/1.73m^2) (n.v. 90-120)	40	19	46	50	59	76	96
Azotemie (mg/dL) (n.v. 10-50)	54	77	57	56	60	72	39
Urine protein (gr/24 h) (n.v. 0-150)	0.130	2.24	2.80	2.50	1.20	0.90	0.90
Uric acid (mg/dL) (n.v. 2.4-5.7)	6.9	6.5	6.1	5.9	5.9	6.0	5.0
Hemoglobin (gr/L) (n.v. 12-16)	8.7	8.0	9.7	10.7	9.3	10.4	10.8
MCV (fL) (n.v. 81-99)	83.8	81.7	84	77	88	92.7	90.2
Body weight (kg)	179.5	179.5	171.0	165	133	125.5	131
BMI (kg/m^2) (n.v. 20-24.9)	70	70	66.8	64.5	51.9	48.9	51
β-hydroxybutyrate (capillary blood) (millimolar) (up to 3 mmol/L)	-	-	-	0.2	1.5	1.0	-

VLCKD, very low-calorie ketogenic diet; n.v., normal value; eGFR, estimated glomerular filtration rate; MCV, mean corpuscular volume; BMI, body max index.

some of the metabolic changes observed in CKD, such as hyperphosphatemia, hyperlipidemia, metabolic acidosis with concomitant hyperkalemia, and increased release of uremic toxins by the gut microbiota. Secondly, the relatively high protein intake of the ketogenic diet could cause glomerular hypertension and hyperfiltration, renal damage, proteinuria, and worsening renal function.[3] The ketones usually produced during the active phase of VLCKD are excreted through frequent and increased urination. This can lead to decreased effective circulating volume and electrolyte loss. The most common electrolyte abnormalities observed during the active phase of VLCKD are hyponatremia and hypomagnesemia, which may be related also to low intake of these micronutrients.[1]

However, when supervised by experienced health professionals with an appropriate micronutrient supplementation, VLCKD could then be a safe option for weight loss in obese patients, including those with mild kidney failure.[1] Indeed, although moderate and severe renal failure is an absolute contraindication,[1] there are data in the literature showing that in VLCKD there was no significant change in eGFR from baseline to the end of the ketogenic phase.[2] Another study where subjects that followed a VLCKD were stratified according to renal function into normal renal function and mild CKD (eGFR between 60 and 89 mL/min/1.73m^2) showed that in the subgroup with mild CKD, eGFR improved (p=0.002).[4]

However, the evidence for kidney-specific effects of ketogenic diets is limited and controversial. In our case, we reported the singular demonstration of safe and effective weight loss induced by VLCKD in a complex morbidly obese patient with a recent episode of AKI on advanced CKD. VLCKD is a highly effective dietary strategy in patients who require rapid weight loss over a short period of time, such as those with severe obesity and associated comorbidities.[1] VLCKD can be dangerous in CKD patients because the diet can exacerbate complications of kidney disease such as metabolic acidosis, which, if left untreated, has been associated with a more rapid decline in kidney function,[5] which is why the concomitant use of sodium-glucose co-transporter 2 inhibitor therapy is an absolute contraindication.[1] However, several studies have shown that the ketogenic diet does not adversely affect renal function,[4,6,7] and one of these showed that VLCKD can normalize glomerular filtrate in patients with mild renal failure.[4] High protein intake is thought to induce hyperfiltration with increased glomerular blood flow and long-term damage in patients with chronic kidney failure.[8] In contrast, low protein intake has been associated with a reduction in the rate of decline in renal function compared with high protein diets.[9] Current guidelines are equivocal regarding daily protein intake in patients with early stages of CKD, with some suggesting 0.8 g/kg ideal body weight per day and others up to 1.4 g/kg ideal body weight per day. Protein intake in VLCKD is less than 1.5 g/kg ideal body weight per day.[10] Recent literature data shows that the effect of dietary protein on renal function depends on the source of the protein. Red meat may be dangerous in a dose-dependent way, whereas proteins from poultry, fish, eggs, and dairy products are less harmful.[10] Vegetable proteins also seem to play a role in protecting the kidneys.[10] The protein of the meal replacements used in the VLCKD source is whey and plant, and during re-introduction, it is recommended to favor fish and poultry. Thus, VLCKD does not seem to have a negative impact on patients with stage 2 CKD in the early stages. A Mexican team has shown that a ketogenic diet in male Wistar rats causes increased renal resistance to ischemia and reperfusion injury with reduced tubular damage and improved renal function. In addition, ketone bodies act as signaling molecules influencing several cellular processes,[11] and thus the ketogenic diet can attenuate oxidative damage, increase antioxidant defenses, reduce inflammatory intermediates (interleukin-6, tumor necrosis factor α, monocyte chemoattractant protein-1), p50 Nuclear Factor κB expression, and cellular infiltration.[11] Finally, VLCKD positively changes the microbiota, but this change is greater when probiotics and prebiotics are supplemented during the diet.[12] Indeed, Simeoni *et al*. demonstrated that the administration of high-quality probiotics in patients with an eGFR between 60 and 45 mL/min/1.73 m^2 (these patients have a demonstrably reduced fecal Lactobacillales and Bifidobacteria concentration) reduces dysbiosis and improves inflammatory indices, iron, and iPTH levels compared to the placebo group.[13] Therefore, the addition of probiotics would allow the ketogenic diet to be further tailored to this specific patient population, making it even safer and more effective. Recently, a case report reported an improvement in renal function in a patient with class III obesity and AKI treated with VLCKD, without side effects such as electrolyte or fluid worsening.[14] However, a higher-than-normal intake of dietary protein can lead to higher levels of urea and other nitrogenous waste products.[15] Consistent with this hypothesis, the higher levels of urea nitrogen in our patient can be attributed to upper protein intake compared to the prescribed normoprotein diet, subsequently normalized with the improvement in glomerular filtrate that has facilitated the excretion of increased amounts of protein-derived nitrogenous waste. Overall, the potential impact of the ketogenic diet on CKD patients with obesity is still poorly understood. The existing evidence on the efficacy of the ketogenic diet in CKD is limited, involving heterogeneous patient populations and different interventions. However, two studies conducted with CKD patients confirmed the safety and efficacy of VLCKD in CKD.[4,7]

This case report has several limitations. First, this is a complex case with multiple potential confounding comorbidities. The presence of multiple comorbidities reduces the ability to attribute specific causal relationships. Second, the absence of a definitive histopathologic diagnosis. Third, the eGFR was evaluated using the CKD-EPI equation. In obese patients, the result may be incorrect because it is influenced by a higher body surface area than in normal-weight people. To have a realistic assessment of kidney damage, we use proteinuria, one of the best markers of kidney damage.[2] In fact, this marker showed a reduction in its value. Fourth, it is important to emphasize that this is a single case, so the ability to extrapolate this experience to other cases is limited. The apparent absence of adverse events in this single case also suggests but does not prove the safety of VLCKD in this patient.

Conclusions

The principal value of this case report is its singular demonstration of safe and effective weight loss induced by

VLCKD in a complex morbidly obese patient with a recent episode of AKI on advanced CKD that was apparently not accompanied by the development of serious adverse sequelae. Further studies are needed to clarify the potential benefits and risks of the ketogenic diet in CKD patients with obesity.

References

1. Barrea L, Caprio M, Camajani E, et al. Ketogenic nutritional therapy (KeNuT)-a multi-step dietary model with meal replacements for the management of obesity and its related metabolic disorders: a consensus statement from the working group of the Club of the Italian Society of Endocrinology (SIE)-diet therapies in endocrinology and metabolism. J Endocrinol Invest 2024;47: 487-500.
2. Verde L, Lucà S, Cernea S, et al. The fat kidney. Curr Obes Rep 2023;12:86-98.
3. Joshi S, Kalantar-Zadeh K, Chauveau P, et al. Risks and benefits of different dietary patterns in CKD. Am J Kidney Dis 2023;81:352-60.
4. Bruci A, Tuccinardi D, Tozzi R, et al. Very low-calorie ke togenic diet: a safe and effective tool for weight loss in patients with obesity and mild kidney failure. Nutrients 2020;12:333.
5. Joshi S, Shi R, Patel J. Risks of the ketogenic diet in CKD – the con part. Clin Kidney J 2023;17:sfad274.
6. Brinkworth GD, Buckley JD, Noakes M, et al. Renal function following long-term weight loss in individuals with abdominal obesity on a very-low-carbohydrate diet vs high-carbohydrate diet. J Am Diet Assoc 2010;110: 633-8.
7. Zainordin NA, Warman NAE, Mohamad AF, et al. Safety and efficacy of very low carbohydrate diet in patients with diabetic kidney disease-A randomized controlled trial. PLoS One 2021;16:e0258507.
8. Kalantar-Zadeh K, Fouque D. Nutritional management of chronic kidney disease. N Engl J Med 2017;377: 1765-76.
9. Yan B, Su X, Xu B, et al. Effect of diet protein restriction on progression of chronic kidney disease: a systematic review and meta-analysis. PLoS One 2018;13: e0206134.
10. Watanabe M, Tuccinardi D, Ernesti I, et al. Scientific evidence underlying contraindications to the ketogenic diet: an update. Obes Rev 2020;21:e13053.
11. Puchalska P, Crawford PA. Multi-dimensional roles of ketone bodies in fuel metabolism, signaling, and therapeutics. Cell Metab 2017;25:262-84.
12. Gutiérrez-Repiso C, Hernández-Garcıa C, García-Almeida JM, et al. Effect of synbiotic supplementation in a very-low-calorie ketogenic diet on weight loss achievement and gut microbiota: a randomized controlled pilot study. Mol Nutr Food Res 2019;63: e1900167.
13. Simeoni M, Citraro ML, Cerantonio A, et al. An open-label, randomized, placebo-controlled study on the effectiveness of a novel probiotics administration protocol (ProbiotiCKD) in patients with mild renal insufficiency (stage 3a of CKD). Eur J Nutr 2019;58:2145-56. Erratum in: Eur J Nutr 2018;58:2157.
14. Parra Guasca M, Manafi M, Parnham A, Angus R. Use of a very low calorie diet for weight loss in a patient with acute kidney injury and class III obesity: a case study. J Ren Nutr 2023;33:698-702.
15. Frank H, Graf J, Amann-Gassner U, et al. Effect of short-term high-protein compared with normal-protein diets on renal hemodynamics and associated variables in healthy young men. Am J Clin Nutr 2009;90:1509-16. Erratum in: Am J Clin Nutr 2010;91:494.