



Keto Flu: A Friend or Foe?

Divya R¹, Ashok V² and Rajajeyakumar M^{3*}

¹Assistant Professor, Department of Physiology, Karpagam Faculty of medical sciences and research, Coimbatore, India

²Assistant Professor, Biochemistry, Karpagam Faculty of medical sciences and research, Coimbatore, India

³Assistant Professor, Department of Physiology, Trichy SRM Medical College Hospital and Research Centre, Trichy, India

***Corresponding Author:** Rajajeyakumar M, Assistant Professor, Department of Physiology, SRM Medical College Hospital and Research Centre, Trichy, MGR Medical University, Chennai, Tamil Nadu, India.

Received: March 26, 2019; **Published:** April 13, 2019

Introduction

Ketosis denotes the creation of ketone bodies, from fats and amino acids used as an alternative to glucose during fasting or extreme carbohydrate restriction. Limiting carbohydrate, by fasting or by decreased dietary intake, leads to decreased insulin levels, thus reduces fat buildup and lipogenesis. Insufficient glycogen reserves leads to decreased supply of glucose which is essential for normal β -oxidation. Instead Acetyl-CoA is used in the production of ketone bodies via acetoacetyl-CoA and β -hydroxy- β -methylglutaryl-CoA that acts as fuel to the Central Nervous System (CNS), which regularly depends on glucose. This method of ketogenesis allows coenzymes to be unfettered for continued fatty-acid β -oxidation [1-8].

The normal levels of ketone bodies is very low (<0.3 mmol/L) related to glucose (approx. 4 mmol). As ketone bodies and glucose have a similar K_m , the CNS begins to utilize the ketone bodies as an energy source when they reach a concentration of about 4 mmol/L which is close to the K_m for the monocarboxylate transporter [9,10].

'keto-flu'

While shifting from a standard, complex carbohydrate diet to 'keto-induction' may lead to unlikable side effects. Due to increased urinary sodium, potassium and water loss in response to lowered insulin levels, keto-induction leads to headache, constipation, halitosis, diarrhoea muscle cramps, fatigue during 1-4 days of ketogenic diet as decreased glucose supply to brain occurs during 1-3 days. Blood glucose normalises after fourth day. Constipation is due to decreased food volume or decrease intake of fibre. These symptoms are called as 'keto-flu'. These effects diminish the efficacy, amenability and acceptability of the Keto diets [11].

Adverse effects are classified as mild, moderate, and severe or short term and long term. KD may also lead to GI discomfort mainly abdominal cramps, diarrhoea, and vomiting [12]. The moderate adverse effects are metabolic acidosis, dyslipidemia, mineral deficiencies, risk of renal stones. It may even raise triglycerides in 6 months [13,14]. Reduced protein intake may lead to hypoproteinemia [15]. The severe effects are due to raised levels of ketones such as redox imbalance which leads to increased risk of mortality and morbidity in diabetic patients [16].

Long-term effects of KD

In mice, due to insufficient insulin, insulin resistance, and reduced beta and alpha cell mass lead to glucose intolerance due to effects on pancreatic endocrine cells [17]. Other risks are raised in bone marrow and visceral fat, reduced insulin-like growth-factor 1, increased leptin, reduced transcription factors promoting osteoblastogenesis, reduced bone mineral density and decreased bone formation [18]. Plasma markers associated with inflammation and dyslipidemia triglycerides, leptin, cholesterol, monocyte chemoattractant protein-1, Interleukin [IL]-1, and IL-6 were increased, and KD-fed mice showed signs of hepatic steatosis after 22 weeks of KD [17].

Conclusion and recommendations

Keto Diet is gaining attention but it has to be performed under strict medical supervision of dietitians and physicians to be operative and require hospital settings for its initiation. The diet protocols have to be modified to facilitate the patient tolerability, acceptability and palatability. The knowledge of clinical impacts, safety, tolerability, efficacy, duration of treatment, and prognosis after discontinuation of the diet is provocative and necessitates further

research to recognize the disease-specific mechanisms. Exercise, smaller meals, increased fiber intake, increased sodium and fluid intake can often prevent or alleviate the complaints. To minimize complications, regular follow-ups has to be done. Future studies are mandatory to assess the long-term effects on health and reversing of diabetic complications in humans.

Bibliography

1. Bueno NB, *et al.* "Very-low-carbohydrate ketogenic diet v. Low- fat diet for long-term weight loss: a meta-analysis of randomised controlled trials". *British Journal of Nutrition* 110 (2013): 1178-1187.
2. Paoli A, *et al.* "Beyond weight loss: A review of the therapeutic uses of very-low-carbohydrate (ketogenic) diets". *European Journal of Clinical Nutrition* 67 (2013): 789-796.
3. Kossoff EH, *et al.* "Ketogenic diets: An update for child neurologists". *Journal of Child Neurology* 24 (2009): 979-988.
4. Al-Khalifa A, *et al.* "Therapeutic role of low-carbohydrate ketogenic diet in diabetes". *Nutrition* 25 (2009): 1177-1185.
5. Dashti HM, *et al.* "Beneficial effects of ketogenic diet in obese diabetic subjects". *Molecular and Cellular Biochemistry* 302 (2007): 249-256.
6. Sharman MJ, *et al.* "A ketogenic diet favorably affects serum biomarkers for cardiovascular disease in normal-weight men". *Journal of Nutrition* 132 (2002): 1879-1885.
7. Krebs and Krebs HA. "The regulation of the release of ketone bodies by the liver. *Advances in Enzyme Regulation* 4 (1966): 339-353.
8. Lehninger, Cox., *et al.* "Lehninger principles of biochemistry". Sixth Edition. New York: Macmillan Learning (2008): 650-642.
9. Veech R.L. "The therapeutic implications of ketone bodies: The effects of ketone bodies in pathological conditions: Ketosis, ketogenic diet, redox states, insulin resistance, and mitochondrial metabolism. Prostaglandins Leukot". *Essential Fatty Acids* 70 (2004): 309-319.
10. Leino RL, *et al.* "Diet-induced ketosis increases monocarboxylate transporter (MCT1) levels in rat brain". *Neurochemistry* 38 (2001): 519-527.
11. Cliff J, *et al.* "The use of nutritional supplements to induce ketosis and reduce symptoms associated with keto induction: a narrative Review". *Peer Journal* 6 (2018): 4488.
12. Kossoff EH, *et al.* "Optimal clinical management of children receiving the ketogenic diet: Recommendations of the International Ketogenic Diet Study Group". *Epilepsia* 50 (2009): 304-317.
13. Caraballo R, *et al.* "Long-term follow-up of the ketogenic diet for refractory epilepsy: Multicenter argentinean experience in 216 pediatric patients". *Seizure* 20 (2011): 640-645.
14. Dressler A, *et al.* "Long-term outcome and tolerability of the ketogenic diet in drug-resistant childhood epilepsy - The Austrian experience". *Seizure* 19 (2010): 404-408.
15. Moriyama K, *et al.* "Protein-losing enteropathy as a rare complication of the ketogenic diet". *Pediatric Neurology* 52 (2015): 526-528.
16. Kanikarla-Marie P and Jain SK. "Hyperketonemia and ketosis increase the risk of complications in type 1 diabetes". *Free Radical Biology and Medicine* 95 (2016): 268-277.
17. Ellenbroek JH, *et al.* "Long-term ketogenic diet causes glucose intolerance and reduced β - and α -cell mass but no weight loss in mice". *American Journal of Physiology-Endocrinology and Metabolism* 306 (2014): 552-558.

Volume 3 Issue 5 May 2019

© All rights are reserved by Rajajeyakumar M., et al.