



## Review

### Why Ketogenic Diet is Beneficial in the Type Two Diabetes During Ramadan Fasting

Hanadi M Beydoun<sup>1</sup> and Sami T Azar<sup>1\*</sup>

<sup>1</sup>*Medicine in Endocrinology, Diabetes and Metabolism, American University of Beirut, Beirut, Lebanon*

#### Introduction

It is estimated that around 400 million people will have diabetes by the end of the year 2030 [1]. An association between overweight and Type Two Diabetes (T2D) have been well established. [2]. During Ramadan, more than 50 million people with T2D choose to fast since fasting is considered one of the main pillars of Islam. Muslims, who fast in Ramadan, should refrain from eating and drinking for one month from sunrise till sunset, around 11 to 19 hours according to their geographical location and the time of year in which Ramadan occurs [3]. Moreover, it is estimated that around 50 % of the U.S population are overweight and 55 % of each, are in the obesity range [2].

There are few interventions that help in weight loss in T2D such as bariatric surgery, increase energy expenditure through physical activity and restricting caloric intake, and medications [4]. However, most of the obesity interventions in T2D failed in upon long follow up [5]. Nevertheless, recent studies have shown a beneficial effect of ketogenic diet on overweight people with diabetes [4-14]. It is believed that prolonged day time fasting such as Ramadan fasting, followed by low carb diet intake, lead to increase of ketone bodies that may have on a beneficial effect on weight in overweight diabetic patients.

#### Discussion

##### Physical Aspect of High Ketone During Fasting

With prolonged fasting or a diet low in carbohydrates less than 30 g/day, fat oxidation, through Krebs cycle will be halted, primary due to the lack of production of oxaloacetate. Glucose is important for the function of pyruvate carboxylase in order of causing oxidative decarboxylation of pyruvic acid resulting in oxaloacetate [6].

So it is believed that a prolonged period of fasting during Ramadan followed by low carbohydrate intake can mimic a state of ketonemia. In fact, during fasting, glucose level in blood circulation tends to decrease and thus leading to low insulin secretion levels. Thereby, gluconeogenesis and breakdown of glycogen occurs. After fasting for more than couple of hours, stores of glycogen are depleted and thus leading to increase of fatty acids. The oxidation of fatty acids leads to the release of ketone bodies that are used as an alternative source of energy [6].

Usually the brain requires glucose as the main source of energy. However, with a diet resulting in an increase of ketone production, the brain will use these ketone bodies as an alternative source

of energy. Acetoacetate,  $\beta$ -hydroxybutyric acid and acetone, are the essential ketone bodies. This process takes place in the mitochondrial matrix from hepatocytes of the liver and is called ketogenesis. Under normal food intake, the ketone body concentration is usually less than 0.3 mmol/l and they will not be used as an energy source by the central nervous system. They are believed to be a source of energy of the brain only when their concentration reaches levels above 4mmol/l.  $\beta$ -hydroxybutyric acid specifically will get transferred into acetoacetyl-coA that will be used in the Krebs cycle. The maximum reported ketone bodies concentration in people on ketogenic diet is 8 mmol/l. We should also mention that glucose is produced from two other sources glycerol and glycogenic amino acid, and it is believed that after several hours of fasting, glycerol can produce around 60 % of total body glucose [5].

##### Benefits of Ketogenic Diet in People with Type Two Diabetes Fasting Ramadan.

Studies have shown that ketogenic diet and T2D may have several benefits such as weight reduction, decrease in HbA1c, improvement of nephropathy, cardiovascular benefits, improvement in dyslipidemia, and even amelioration of diabetic retinopathy and neuropathy [7].

##### Weight Loss Due to Low Carbohydrate Diet and Ramadan Fasting.

People who reduce their carbohydrate intake during Ramadan have a positive effect on weight loss due to high ketone body production. Samaha et al. (2003), compared the efficiency of ketogenic diet to low fat diet and demonstrated that ketogenic diets are three times more effective in weight reduction than low fat diet

**\*Corresponding author:** Sami Azar, Diabetes and Metabolism. American University of Beirut, Beirut, Lebanon, E-mail: sazar@aub.edu.lb

**Rec Date:** February 7, 2017, **Acc Date:** February 27, 2017, **Pub Date:** February 28, 2017.

**Citation:** Hanadi M Beydoun and Sami T Azar (2017) Why Ketogenic Diet is Beneficial in the Type Two Diabetes During Ramadan Fasting. BAOJ Obe Weigt Manage 3: 011.

**Copyright:** © 2017 Hanadi M Beydoun and Sami T Azar. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

[8]. One explanation of their weight loss is the increase of fatty acid metabolism in the presence of ketone bodies. Another explanation for their weight loss in a diet inducing ketonemia, could be the hunger reduction effect on the hypothalamus of the ketone bodies. However, this mechanism is still not very clear since ketone bodies were shown to have both anorexigenic and orexigenic effect.

Leonetti et al. (2015), have demonstrated that a very low carbohydrate ketogenic diet was safe and effective in obese patients with T2D prior to bariatric surgery. Moreover, the introduction of this kind of diet prior to surgery resulted in significant pre-operative weight loss that is translated in the reduction of pre-operative risk of anesthesia [9].

As such we can propose that a low carbohydrate diet for most of T2D when they break their fast during the holy month of Ramadan, results in a beneficial weight reduction.

### Glucose Control

The benefit of carbohydrate restriction in patients with T2D has been well established independent of weight loss. However, the long term efficacy and safety have never been established [10]. Yet, it is believed that during Ramadan fasting, low carbohydrate diet may increase ketone body formation which may have a beneficial effect on glucose reduction. A study by Al-khalifa et al. (2009), on rats showed that a very low caloric ketogenic diet resulted in a significant improvement in glucose control by improving Beta cell function [11].

Talib et al. (2012), showed that a ketogenic diet was more significant than a low calorie diet on HBA1c in diabetic population. This effect is believed to be due to the ability of ketone bodies to decrease glucose metabolism. The mechanism is yet not well understood [12].

A review by Feinman et al. (2015), supports the use of ketogenic diet in the management of T2D and as an adjunct to therapy in type one diabetes. [10]

All of the above confirms that a low carbohydrate diet after fasting results in ketonemia that would be beneficial for glucose control in T2D.

A note of caution should be mentioned that with T2D patient on oral agent hypoglycemic medications, who are fasting Ramadan on low carbohydrate diet, may be at risk of hypoglycemia due to the prolonged fasting and ketosis. Thus reduction of the dose of hypoglycemic agents should be highly considered with close blood sugar monitoring during the fasting hours.

### Improved Nephropathy

Diabetic nephropathy is a common complication of T2D. Poplawski et al. (2011), studied rats which were put on a ketogenic diet and showed reversal of diabetic secondary nephropathy to the increase level of 3-beta-hydroxybutyric acid that reduced glucose metabolism in the kidneys. It was only after one week of initiation of a ketogenic diet that the blood sugar normalized in the diabetic rats. Two months later the albumin/creatinine ratio dropped back to normal and the diabetic nephropathy was completely reversed. It

was found that normalization of certain genes induced by oxidation and other form of stress were responsible for this amelioration [7]. Talib et al (2012), showed that ketogenic diet in human decreases creatinine level compared to low caloric intake diet, since ketones could be used as an alternative energy-efficient fuel [12]. Little et al. (1971), showed that infusion of B-hydroxybutyric acid in dogs resulted in utilization of the ketones for more than 50% of Qo2 [13]. As such we can conclude that low carbohydrate diet in people fasting Ramadan may result in mild ketosis which may be beneficial in T2D patients with nephropathy.

### Cardiovascular Benefits of Ketogenic Diet

Studies revealed an increased risk of cardiovascular disease in the diabetic populations. Myocardial dysfunction in diabetic patients is blamed to be due to cardiomyopathy, hypertension, and myocardial Ischemia. Many factors were implicated in diabetic cardiomyopathy; namely, autonomic dysfunction, increase in oxidative stress, mitochondrial dysfunction, interstitial fibrosis and myocardial stiffness. All this is believed to be secondary to interstitial protein glycosylation caused by hyperglycemia. It is well known that around 95 % of the cardiac muscle energy is obtained from the myocardial oxidation metabolism. Studies have shown that during fasting, as during states of insulin resistance, free fatty acids are the main fuel for myocardial oxidative metabolism. This reliance on the free fatty acid as a main fuel for the myocardium of the left ventricle would decrease the cardiac efficiency and increase the propensity for heart failure. Yet, when the serum ketone level increases, the ketone bodies become the main contributors to the energy metabolism of the myocardium and as such decrease the effect of free fatty acids [14-15]. In a study performed on rat hearts, ketone body infusion resulted in increased cardiac work efficiency by around 25% [14]. On the other hand, Aubert et al. (2016), did a proteomic analysis on mouse models of heart failure and they showed that ketone bodies are the major fuel of failure heart. A similar study was performed by Bedi et al. (2016), on humans, confirmed that ketone bodies were the fuel in heart failure [14-15]. The recent EMPA-REG study (empagliflozin) showed cardiovascular beneficial effect of Sodium glucose co transporter. Moreover, it also showed decrease in mortality and hospitalization for heart failure. One possible mechanism of improved function of failing myocardium was attributed to the use of ketone bodies that are increased in the circulation for people taking empagliflozin [16]. We can conclude that a low carbohydrate diet coupled with fasting during the month of Ramadan resulting in the release of ketone bodies, would have a beneficial cardiovascular outcome in diabetes T2D and would increase cardiac work efficiency, improve myocardial contractility, and decrease the incidence and progression of diabetic heart failure.

### Improved Dyslipidemia with Ketogenic Diet

It is well established that people with T2D with or without metabolic syndrome may suffer from high triglyceride and low HDL cholesterol along with small dense cholesterol molecules that are considered risk factors for cardiovascular disease in diabetes. Several studies

demonstrated that a ketogenic diet may improve lipid profile in T2D patients. In a Study done by Talib et al. (2014), high ketone bodies resulted in decrease in Low density lipoprotein , triglyceride, and increase High density lipoprotein levels [12]. The study conducted by Samaha et al. (2003), also revealed that ketogenic diet induced a better reduction in triglyceride compared to low fat diet. These benefits of ketosis induced diet may be extrapolated to the state of ketosis that is typically present in patients who fast Ramadan and break their fast in a low carbohydrate diet meal plan [8].

## Conclusion

Finally , a low carbohydrate diet during Ramadan fasting resulting in serum ketosis should have several beneficial effects in T2D. These benefits include a better glycemic control, weight loss, improved Dyslipidemia profile along with a beneficial cardiovascular outcome and possible amelioration of micro vascular complications such as nephropathy and probably neuropathy and retinopathy. In conclusion, a low carbohydrate diet inducing a state of mild ketosis is safe and efficacious in overweight diabetic patients who fast the Holy month of Ramadan.

## References

1. Wild S, Roglic G, Green A, Sicree R, King H (2004) Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care* 27(5): 1047-1053.
2. Campbell RK (2009) Type 2 diabetes: where we are today: an overview of disease burden, current treatments, and treatment strategies. *J Am Pharm Assoc* 49(supp 1): S3-S9.
3. Kadiri A, Nakhi A, Ghazali SE, Jabbar A, Arouj MA, et al. (2001) Treatment of type 1 diabetes with insulin lispro during Ramadan. *Diabetes Metab* 27(4 Pt 1): 482-486.
4. Thompson WG, Cook DA, Clark MM, Bardia A, Levine JA (2007) Treatment of obesity. *Mayo Clin Proc* 82(1): 93-101.
5. Paoli A (2014) Ketogenic diet for obesity: friend or foe? *Int J Environ Res Public Health* 11(2): 2092-2107.
6. Arouji M, Khalil S, Buse J, Fahdil B, Fahmy M, et al. (2010) Recommendations for Managements of Diabetes During Ramadan. *Diabetes Care* 33(8): 1895–1902.
7. Poplawski MM, Mastaitis JW, Isoda F, Grosjean F, Zheng F, et al. (2011) Reversal of diabetic nephropathy by a ketogenic diet. *PloS One* 6(4): e18604 doi: 10.1371/journal.pone.0018604.
8. Samaha FF, Iqbal N, Seshadri P, Chicano KL, Daily DA, et al. (2003) A low-carbohydrate as compared with a low-fat diet in sever obesity. *N Engl J Med* 348(21): 2074-2081.
9. Leonetti F, Campanile F, Coccia F, Capoccia D, Alessandrini L, et al. (2015) Very Low- Carbohydrate Ketogenic Diet Before Bariatric Surgery: Prospective Evaluation of a Sequential Diet. *OBES SURG* 25(1): 64-71.
10. Feinman RD, Bernstein RK, Westman EC, Accurso A, Frassetto L, et al. (2015) Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. *Nutrition* 31(1): 1-13.
11. Khalifa A, Mathew TC, Zaid NS, Mathew E, Dashti HM (2009) Therapeutic role of low-carbohydrate ketogenic diet in diabetes. *Nutrition* 25(11-12): 1177-1185.
12. Talib H, Mathew Tc, Dashti AA, Asfar S, Al-Zaid N, et al. (2012) Effect of low-calorie versus low-carbohydrate ketogenic diet in type 2 diabetes. *Nutrition* 28(10): 1016-1021.
13. Little JR, Spitzer JJ (1971) Uptake of ketone bodies by dog kidney in vivo. *Am J Physiol* 221(3): 679–683.
14. Aubert G, Martin OJ, Horton JL, Lai L, Vega RB, et al. (2016) The Failing Heart Relies on Ketone Bodies as a Fuel. *Circulation* 133(8): 698-705.
15. Bedi KC, Snyder NW, Brandimarto J, Aziz M, Mesaros C, et al. (2015) Evidence for Intramyocardial Disruption of Lipid Metabolism and Increased Myocardial Ketone Utilization in Advanced Human Heart Failure. *Circulation* 133(8): 706-716.
16. Mudaliar S, Alloju S, Henry R (2016) Can a Shift in Fuel Energetics Explain the Beneficial Cardiorenal Outcomes in the EMPA-REG OUT-COME Study? A Unifying Hypothesis. *Diabetes Care* 39(7): 1115-1122.