Keto-diets: Good, Bad or Ugly?

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Type 2 diabetes is a rapidly growing disease carrying potentially devastating complications. Despite its apparent inexorable increase, type 2 diabetes can be reversible with weight loss. (Lean) Current official dietary recommendations for diabetes are generally to adjust calorie intake to control energy balance/ body weight, limit fat (especially saturated) and sugar but not to restrict carbohydrates with advice to aim for 40—60% of total calories as latter. Conversely, low carbohydrate diets, particularly ketogenic diets which are low enough in carbohydrates to induce ketosis (typically < 30g carbohydrates daily termed “keto-diets”) continue to grow in popularity in the general population. Many report significant weight loss with low carbohydrate diets and it is hardly surprising that some with diabetes become frustrated with attempts to control weight and blood glucose on conventional diets and turn to these. Additionally, in type 1 diabetes, lower carbohydrate intake might reduce the potential for error when calculating insulin doses based on carbohydrate intake.

Despite reports of success from individuals, controlled studies in diabetes examining whether low carbohydrate diets can benefit glycaemia have given mixed outcomes for both type 1 and type 2 diabetes. (Turton, Forouhi) Parenthetically, extreme caloric restriction *per se* has long been known to result in “starvation diabetes”. Randomised dietary studies in humans are particularly challenging for obvious reasons. Studying animal models allows more experimental control- animals cannot choose to break their diet and usually their only choice is to eat greater or lesser amounts of a fixed ratio of macronutrients.

To date, ketogenic diet studies in rodents have also resulted in mixed outcomes for glycaemic measures when examined over a few weeks. One of the challenges of examining integrated biological systems is that initial changes often lead on to secondary alterations in physiology. Addressing this, in a paper in this edition of the journal, Grandl and colleagues examine the initial effects (3 days) of a ketogenic (0.6% carbohydrates/ 67% fat by weight/volume) vs high fat diet (23% carbohydrate/ 35% fat) and chow (58% carbohydrate /7% fat). (Grandl et al., 2018) At face value, comparing a ketogenic diet popularly used for weight loss with an obesegenic high fat diet might appear curious but from the physiological viewpoint, this three-way comparison allows the effects of varying dietary macronutrients on glucose physiology to be examined.

As expected, even three days of high fat diet resulted in impaired glucose tolerance and insulin resistance. This is consistent with previous reports in rodents and indeed humans and is thought to be mediated by changes in hepatic insulin sensitivity.

At face value, the ketogenic diet appeared beneficial with lower plasma glucose after a six hour fast compared with the other two diets. More detailed physiological testing though revealed glucose intolerance and impaired (hepatic) insulin sensitivity compared with chow. In fact, the ketogenic diet appeared metabolically less healthy than even the high fat diet. Although the focus of this paper was on glycaemia, another interesting point was that energy intake was also higher, albeit only over 3 days.

What then should we make of this? These were by design short-term studies designed to shed light on the initial metabolic effects of a ketogenic diet. Extrapolating to human physiology and disease carries the usual warning about cross-species differences and, for clinical interpretation, potential differences between healthy individuals and those with diabetes. Another note of caution is that diets labelled as being low carbohydrate vary from 4% of total caloric value up to about 40% with the lower end of the spectrum being those that induce ketosis. Here the ketogenic diet selected provided < 0.5% calories from carbohydrates.

Analogous to the three gunslingers in Sergio Leone’s classic film, the “good” here perhaps is the lower plasma glucose seen in the ketogenic diet group, an important aim in diabetes and probably in broader metabolic health. The “bad” here is hepatic insulin resistance, although difficult to know how to interpret this in the face of a lower plasma glucose. What about the “ugly”. Not addressed here, critics of ketogenic diets raise concerns about the potential adverse effects on circulating lipids

Spaghetti or not in Western diets, the keto diet discussion continues.

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