Céto Santé

L'alimentation cétogène est une alimentation mise au point à l'origine pour les enfants épileptiques, oubliée pendant des décennies et réétudiée depuis une dizaine d'années.

En cétose, le corps ne fonctionne plus en brûlant les glucides (via le glucose) mais en brûlant les lipides (via les cétones). Ce fonctionnement apporte, selon les études, de nombreux bienfaits et est susceptible d'améliorer les symptômes voire d'entraîner la guérison de nombreuses maladies.

La diminution drastique des glucides (5% des calories), la modération des protéines (15 à 20% des calories) et l'augmentation des lipides (75 à 80 % des calories) permettent de conserver tous les macros et micro-nutriments essentiels tout en apportant l'ensemble des bienfaits des corps cétoniques.

L'alimentation cétogène rétablit le fonctionnement hormonal optimal : les personnes souffrant de résistance à l'insuline (état de pré-diabète) peuvent à nouveau rétablir un niveau d'insuline bas, guérissant ainsi des maladies liées au syndrome métabolique (1)(2), telles que :

- le diabète (3). Cette étude indique que la diète cétogène devrait être le traitement de première intention pour les personnes souffrant de diabète de type 1 et 2. Cette seconde étude concerne spécifiquement le diabète de type 2 (4), alors que celle-ci concerne le diabète de type 1 (5). Elle peut être bénéfique pour les futures mères obèses souffrant de diabète gestationnel (6).
- les maladies cardio-vasculaires. Cette étude indique que la réduction des lipides alimentaires entraîne une aggravation des risques coronaires (7) :
- l'obésité. Cette étude met en avant la meilleure efficacité sur le long terme de la diète cétogène par rapport à un régime basses calories, ainsi que son innocuité (8).

Selon les études, la diète cétogène est indiquée et pourrait permettre d'améliorer l'état de santé des personnes souffrant :

- d'épilepsie (9) : La diète cétogène a fait l'objet de beaucoup d'études, et notamment sur les enfants et adolescents sur lesquels la pharmacopée ne produisait aucun effet positif (10).
- de maladies neurologiques en général (Alzheimer, Parkinson,…) (11) :
- de cancer, et notamment de tumeur au cerveau (12), et autres cancers (13).

La diète cétogène est susceptible de priver les cellules cancéreuses de leur carburant essentiel, le glucose. Lorsque la glycémie est réduite via l'alimentation, les cellules saines du corps utilisent les cétones alors que les cellules cancéreuses sont privées du seul carburant qu'elles peuvent utiliser. Les études montrent trois avantages au recours à la diète cétogène en complément des traitements classiques du cancer :

1. La diète cétogène n'est pas toxique pour le reste du corps, elle est même bénéfique et permet au patient de mieux supporter les effets de la chimiothérapie et radiothérapie.
2. La diète cétogène augmente l'efficacité des traitements classiques. Les cellules cancéreuses deviennent plus sensibles à la radiothérapie et à la chimiothérapie.
3. La diète cétogène semble forcer les cellules cancéreuses à se comporter selon une expression génétique semblable aux cellules saines.
4.

Source : http://www.ketogenic-diet-resource.com/cancer treatments.html

Autres affections : cet article très complet répertorie toutes les indications de la diète cétogène (acné, trauma neurologique, syndrome des ovaires polykystiques, syndrome de Stein-Leventhal, sclérose latérale amyothropique) (14).

Comment adopter l'alimentation Céto/LCHF ?

- Connaître les aliments qui entraînent une production d'insuline et les éviter (sucres, amidons).
- Choisir tous les jours de bonnes sources de lipides, notamment l'huile de coco, les sources d'oméga 3 (poissons gras, huile de colza, graines de lin), ainsi que les lipides saturés d'origine animale (graisses animales, beurre cru, fromage au lait cru). Cette méta-analyse avance l'innocuité des lipides saturés et l'absence de lien avec des maladies cardiovasculaires (15).
- Modérer les protéines à une portion par repas (soit 30 gr de protéines).
- S'assurer de choisir des aliments contenant suffisamment de micro-nutriments (il n'existe aucun micro-nutriment que l'alimentation cétogène ne puisse apporter. Toutes les vitamines et les polyphénols des fruits se retrouvent aussi dans les légumes).

L'alimentation Céto/LCHF présente-t-elle des contre indications ou effets secondaires indésirables ?

Pour les patients étudiés, la diète cétogène ne connaît que peu de contre-indications (16) et les effets secondaires répertoriés ne sont le plus souvent que transitoires (17) : constipation, haleine fruitée, fringales sucrées liées au sevrage du sucre, perte de minéraux transitoire entraînant fatigue, maux de tête, diarrhée, augmentation de la quantité d'urine, perte de cheveux, palpitations cardiaques).

Par ailleurs, outre le poids perdu plus ou moins vite selon les personnes, le métabolisme et l'état hormonal de chacun, elles bénéficient aussi d'amélioration de leur santé :

- une humeur stable et positive (18) ;
- plus d'énergie pendant la journée (grâce à un approvisionnement constant en cétones)
- une baisse d'inflammation, entraînant de meilleures défenses immunitaires (19) ;
- une plus belle peau (les peaux acnéiques peuvent redevenir normales) et de plus beaux cheveux (20) ;
- de meilleures capacités cognitives (le cerveau est un grand consommateur de cétones) (21) ;

- une meilleure absorption des vitamines liposolubles
- de meilleurs bilans sanguins (abaissement des triglycérides, du cholestérol LDL) (22).

Carbohydrate Restriction has a More Favorable Impact on the Metabolic Syndrome than a Low Fat Diet

Abstract

We recently proposed that the biological markers improved by carbohydrate restriction were precisely those that define the metabolic syndrome (MetS), and that the common thread was regulation of insulin as a control element. We specifically tested the idea with a 12-week study comparing two hypocaloric diets (~1,500 kcal): a carbohydrate-restricted diet (CRD) (%carbohydrate:fat:protein = 12:59:28) and a low-fat diet (LFD) (56:24:20) in 40 subjects with atherogenic dyslipidemia. Both interventions led to improvements in several metabolic markers, but subjects following the CRD had consistently reduced glucose (−12%) and insulin (−50%) concentrations, insulin sensitivity (−55%), weight loss (−10%), decreased adiposity (−14%), and more favorable triacylglycerol (TAG) (−51%), HDL-C (13%) and total cholesterol/HDL-C ratio (−14%) responses. In addition to these markers for MetS, the CRD subjects showed more favorable responses to alternative indicators of cardiovascular risk: postprandial lipemia (−47%), the Apo B/Apo A-1 ratio (−16%), and LDL particle distribution. Despite a threefold higher intake of dietary saturated fat during the CRD, saturated fatty acids in TAG and cholesteryl ester were significantly decreased, as was palmitoleic acid (16:1n-7), an endogenous marker of lipogenesis, compared to subjects consuming the LFD. Serum retinol binding protein 4 has been linked to insulin-resistant states, and only the CRD decreased this marker (−20%). The findings provide support for unifying the disparate markers of MetS and for the proposed intimate connection with dietary carbohydrate. The results support the use of dietary carbohydrate restriction as an effective approach to improve features of MetS and cardiovascular risk.

Carbohydrate restriction improves the features of Metabolic Syndrome. Metabolic Syndrome may be defined by the response to carbohydrate restriction

Abstract

Metabolic Syndrome (MetS) represents a constellation of markers that indicates a predisposition to diabetes, cardiovascular disease and other pathologic states. The definition and treatment are a matter of current debate and there is not general agreement on a precise definition or, to some extent, whether the designation provides more information than the individual components. We consider here five indicators that are central to most definitions and we provide evidence from the literature that these are precisely the symptoms that respond to reduction in dietary carbohydrate (CHO). Carbohydrate restriction is one of several strategies for reducing body mass but even in the absence of weight loss or in comparison with low fat alternatives, CHO restriction is effective at ameliorating high fasting glucose and insulin, high plasma triglycerides (TAG), low HDL and high blood pressure. In addition, low fat, high CHO diets have long been known to raise TAG, lower HDL and, in the absence of weight loss, may worsen glycemic control. Thus, whereas there are numerous strategies for weight loss, a patient with high BMI and high TAG is likely to benefit most from a regimen that reduces CHO intake. Reviewing the literature, benefits of CHO restriction are seen in normal or overweight individuals, in normal patients who meet the criteria for MetS or in patients with frank diabetes. Moreover, in low fat studies that ameliorate LDL and total cholesterol, controls may do better on the symptoms of MetS. On this basis, we feel that MetS is a meaningful, useful phenomenon and may, in fact, be operationally defined as the set of markers that responds to CHO restriction. Insofar as this is an accurate characterization it is likely the result of the effect of dietary CHO on insulin metabolism. Glucose is the major insulin secretagogue and insulin resistance has been tied to the hyperinsulinemic state or the effect of such a state on lipid metabolism. The conclusion is probably not surprising but has not been explicitly stated before. The known effects of CHO-induced hypertriglyceridemia, the HDL-lowering effect of low fat, high CHO interventions and the obvious improvement in glucose and insulin from CHO restriction should have made this evident. In addition, recent studies suggest that a subset of MetS, the ratio of TAG/HDL, is a good

marker for insulin resistance and risk of CVD, and this indicator is reliably reduced by CHO restriction and exacerbated by high CHO intake. Inability to make this connection in the past has probably been due to the fact that individual responses have been studied in isolation as well as to the emphasis of traditional therapeutic approaches on low fat rather than low CHO.

We emphasize that MetS is not a disease but a collection of markers. Individual physicians must decide whether high LDL, or other risk factors are more important than the features of MetS in any individual case but if MetS is to be considered it should be recognized that reducing CHO will bring improvement. Response of symptoms to CHO restriction might thus provide a new experimental criterion for MetS in the face of on-going controversy about a useful definition. As a guide to future research, the idea that control of insulin metabolism by CHO intake is, to a first approximation, the underlying mechanism in MetS is a testable hypothesis.

Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base

Abstract

The inability of current recommendations to control the epidemic of diabetes, the specific failure of the prevailing low-fat diets to improve obesity, cardiovascular risk, or general health and the persistent reports of some serious side effects of commonly prescribed diabetic medications, in combination with the continued success of low-carbohydrate diets in the treatment of diabetes and metabolic syndrome without significant side effects, point to the need for a reappraisal of dietary guidelines. The benefits of carbohydrate restriction in diabetes are immediate and well documented. Concerns about the efficacy and safety are long term and conjectural rather than data driven. Dietary carbohydrate restriction reliably reduces high blood glucose, does not require weight loss (although is still best for weight loss), and leads to the reduction or elimination of medication. It has never shown side effects comparable with those seen in many drugs. Here we

present 12 points of evidence supporting the use of low-carbohydrate diets as the first approach to treating type 2 diabetes and as the most effective adjunct to pharmacology in type 1. They represent the best-documented, least controversial results. The insistence on long-term randomized controlled trials as the only kind of data that will be accepted is without precedent in science. The seriousness of diabetes requires that we evaluate all of the evidence that is available. The 12 points are sufficiently compelling that we feel that the burden of proof rests with those who are opposed.

Effect of low-calorie versus low-carbohydrate ketogenic diet in type 2 diabetes.

Abstract

OBJECTIVE:

Effective diabetic management requires reasonable weight control. Previous studies from our laboratory have shown the beneficial effects of a low-carbohydrate ketogenic diet (LCKD) in patients with type 2 diabetes after its long term administration. Furthermore, it favorably alters the cardiac risk factors even in hyperlipidemic obese subjects. These studies have indicated that, in addition to decreasing body weight and improving glycemia, LCKD can be effective in decreasing antidiabetic medication dosage. Similar to the LCKD, the conventional low-calorie, high nutritional value diet is also used for weight loss. The purpose of this study was to understand the beneficial effects of LCKD compared with the low-calorie diet (LCD) in improving glycemia.

METHODS:

Three hundred and sixty-three overweight and obese participants were recruited from the Al-Shaab Clinic for a 24-wk diet intervention trial; 102 of them had type 2 diabetes. The participants were advised to choose LCD or LDKD, depending on their preference. Body weight, body mass index, changes in waist circumference, blood glucose level, changes in hemoglobin and glycosylated hemoglobin, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, uric acid, urea and creatinine were determined before and at 4, 8, 12,

16, 20, and 24 wk after the administration of the LCD or LCKD. The initial dose of some antidiabetic medications was decreased to half and some were discontinued at the beginning of the dietary program in the LCKD group. Dietary counseling and further medication adjustment were done on a biweekly basis.

RESULTS:

The LCD and LCKD had beneficial effects on all the parameters examined. Interestingly, these changes were more significant in subjects who were on the LCKD as compared with those on the LCD. Changes in the level of creatinine were not statistically significant.

CONCLUSION:

This study shows the beneficial effects of a ketogenic diet over the conventional LCD in obese diabetic subjects. The ketogenic diet appears to improve glycemic control. Therefore, diabetic patients on a ketogenic diet should be under strict medical supervision because the LCKD can significantly lower blood glucose levels.

Low carbohydrate diet in type 1 diabetes, long-term improvement and adherence: A clinical audit

Abstract

BACKGROUND

Reduction of dietary carbohydrates and corresponding insulin doses stabilizes and lowers mean blood glucose in individuals with type 1 diabetes within days. The long-term adherence for persons who have learned this technique is unknown. To assess adherence over 4 years in such a group the present audit was done retrospectively by record analysis for individuals who have attended an educational course. Adherence was assessed from HbA1c changes and individuals' own reports.

FINDINGS

Altogether 48 persons with diabetes duration of 24 ± 12 years and HbA1c > = 6.1% (Mono-S; DCCT = 7.1%) attended the course. Mean

HbA1c for all attendees was at start, at 3 months and 4 years 7.6% ± 1.0%, 6.3 ± 0.7%, 6.9 ± 1.0% respectively. The number of non-adherent persons was 25 (52%). HbA1c in this group was at start, at 3 months and 4 years: 7.5 ±1.1%, 6.5 ± 0.8%, 7.4 ± 0.9%. In the group of 23 (48%) adherent persons mean HbA1c was at start, at 3 months and 4 years 7.7 ± 1.0%, 6.4 ± 0.9%, 6.4 ± 0.8%.

CONCLUSION

Attending an educational course on dietary carbohydrate reduction and corresponding insulin reduction in type 1 diabetes gave lasting improvement. About half of the individuals adhered to the program after 4 years. The method may be useful in informed and motivated persons with type 1 diabetes. The number needed to treat to have lasting effect in 1 was 2.

Hypocaloric diets and ketogenesis in the management of obese gestational diabetic women.

Abstract

The extent to which given levels of caloric restriction will improve glycemic status but increase plasma ketone bodies in gestational diabetic women has received little attention. After reviewing the underlying physiology, we present data on two feeding studies investigating the question. In the first, a weight-maintaining approximately 2400-kcal/day diet was fed on a metabolic ward to 12 gestational diabetic women for 1 week. In the second week, subjects were randomized to a continuation of the 2400-kcal/day diet or to a 1200-kcal/day diet. Twenty-four-hour mean glucose levels remained unchanged in the control group but declined in the calorie-restricted group (6.7 mM or 121 mg/dl in week 1 vs 5.4 mM or 97.3 mg/dl in week 2) (p less than 0.01). Nine-hour overnight fasting plasma insulin also declined but oral glucose tolerance did not improve with caloric restriction. Fasting plasma beta-hydroxybutyrate rose in the calorie-restricted group, along with an increase in ketonuria, but not in the control group. A second study compared the impact of a 33% calorie-restricted diet or insulin to a full-calorie diet in a similar 2-week experimental design and measured hepatic glucose output and insulin sensitivity with dideuterated glucose

before and during an insulin clamp. Diet in three subjects improved fasting and 24-hr mean glucose by 22 and 10%, respectively, whereas prophylactic insulin in three subjects produced 0 and 4% reductions, respectively. On average, ketonuria after a 9-hr fast declined to an equivalent degree with both treatments. Hepatic glucose output and insulin sensitivity were not statistically significantly altered by gestational diabetes or the therapeutic interventions compared to nondiabetic normal weight or obese pregnant controls. In conclusion, 50% caloric restriction improves glycemic status in obese women with gestational diabetes but is associated with an increase in ketonuria, which is of uncertain significance. An intermediate 33% level of caloric restriction (to 1600-1800 kcal daily) may be more appropriate in dietary management of obese woman with gestational diabetes mellitus and more effective than prophylactic insulin. Further studies are required to confirm these findings.

Saturated fat, carbohydrate, and cardiovascular disease

Abstract

A focus of dietary recommendations for cardiovascular disease (CVD) prevention and treatment has been a reduction in saturated fat intake, primarily as a means of lowering LDL-cholesterol concentrations. However, the evidence that supports a reduction in saturated fat intake must be evaluated in the context of replacement by other macronutrients. Clinical trials that replaced saturated fat with polyunsaturated fat have generally shown a reduction in CVD events, although several studies showed no effects. An independent association of saturated fat intake with CVD risk has not been consistently shown in prospective epidemiologic studies, although some have provided evidence of an increased risk in young individuals and in women. Replacement of saturated fat by polyunsaturated or monounsaturated fat lowers both LDL and HDL cholesterol. However, replacement with a higher carbohydrate intake, particularly refined carbohydrate, can exacerbate the atherogenic dyslipidemia associated with insulin resistance and obesity that includes increased triglycerides, small LDL particles, and reduced HDL cholesterol. In summary, although substitution of dietary polyunsaturated fat for saturated fat has been

shown to lower CVD risk, there are few epidemiologic or clinical trial data to support a benefit of replacing saturated fat with carbohydrate. Furthermore, particularly given the differential effects of dietary saturated fats and carbohydrates on concentrations of larger and smaller LDL particles, respectively, dietary efforts to improve the increasing burden of CVD risk associated with atherogenic dyslipidemia should primarily emphasize the limitation of refined carbohydrate intakes and a reduction in excess adiposity.

A Low-Carbohydrate as Compared with a Low-Fat Diet in Severe Obesity

Abstract

BACKGROUND

The effects of a carbohydrate-restricted diet on weight loss and risk factors for atherosclerosis have been incompletely assessed.

METHODS

We randomly assigned 132 severely obese subjects (including 77 blacks and 23 women) with a mean body-mass index of 43 and a high prevalence of diabetes (39 percent) or the metabolic syndrome (43 percent) to a carbohydrate-restricted (low-carbohydrate) diet or a calorie- and fat-restricted (low-fat) diet.

RESULTS

Seventy-nine subjects completed the six-month study. An analysis including all subjects, with the last observation carried forward for those who dropped out, showed that subjects on the low-carbohydrate diet lost more weight than those on the low-fat diet (mean [±SD], –5.8±8.6 kg vs. –1.9±4.2 kg; P=0.002) and had greater decreases in triglyceride levels (mean, –20±43 percent vs. –4±31 percent; P=0.001), irrespective of the use or nonuse of hypoglycemic or lipid-lowering medications. Insulin sensitivity, measured only in subjects without diabetes, also improved more among subjects on the low-carbohydrate diet (6±9 percent vs. –3±8 percent, P=0.01). The amount of weight lost (P<0.001) and

assignment to the low-carbohydrate diet (P=0.01) were independent predictors of improvement in triglyceride levels and insulin sensitivity.

CONCLUSIONS

Severely obese subjects with a high prevalence of diabetes or the metabolic syndrome lost more weight during six months on a carbohydrate-restricted diet than on a calorie- and fat-restricted diet, with a relative improvement in insulin sensitivity and triglyceride levels, even after adjustment for the amount of weight lost. This finding should be interpreted with caution, given the small magnitude of overall and between-group differences in weight loss in these markedly obese subjects and the short duration of the study. Future studies evaluating long-term cardiovascular outcomes are needed before a carbohydrate-restricted diet can be endorsed.

The ketogenic diet and epilepsy.

Abstract

PURPOSE OF REVIEW:

The ketogenic diet has long been used to treat medically refractory epilepsy. The mechanisms underlying its clinical effects, however, have remained a mystery. The evidence to date suggests that a fundamental shift from glycolysis to intermediary metabolism induced by the ketogenic diet is necessary and sufficient for clinical efficacy. This notion is supported by a growing number of studies indicating that glucose restriction, ketone bodies and polyunsaturated fatty acids may all play mechanistic roles, possibly by enhancing mitochondrial respiration and ATP production, and decreasing reactive oxygen species production.

RECENT FINDINGS:

Recent reports indicate that ketone bodies can reduce oxidative stress and that fatty acid-induced mitochondrial uncoupling may also yield similar protective effects. Ketone bodies may attenuate spontaneous firing of ATP-sensitive potassium channels in central neurons, and pharmacological inhibition of glycolysis has been shown to retard epileptogenesis in a rat kindling model.

SUMMARY:

While the mechanisms underlying the broad clinical efficacy of the ketogenic diet remain unclear, there is growing evidence that the ketogenic diet alters the fundamental biochemistry of neurons in a manner that not only inhibits neuronal hyperexcitability but also induces a protective effect. Thus, the ketogenic diet may ultimately be useful in the treatment of a variety of neurological disorders.

The ketogenic diet in children, adolescents and young adults with refractory epilepsy: an Italian multicentric experience.

Abstract

PURPOSE:

This collaborative study by three Italian groups of child neuropsychiatrists was carried on to evaluate the efficacy and safety of the classic 4:1 ketogenic diet as add-on treatment in refractory partial or generalized epilepsy in children, adolescents and young adults.

METHODS:

We performed a prospective add-on study in 56 refractory epilepsy young patients (age 1-23 years, mean 10.4 years), all with both symptomatic and cryptogenic, generalized or partial epilepsies. Child neuropsychiatrists worked with nutritional team for sample selection and patients management. The ketogenic diet was added to the baseline antiepileptic drugs and the efficacy was rated according to seizure type and frequency. During treatment, seizure frequency, side effects, urine and blood ketone levels and other parameters were systematically evaluated.

RESULTS:

Patients have been treated for 1-18 months (mean 5 months). A >50% reduction in seizure frequency was gained in 37.5 and 26.8% of patients after 3 and 6 months, respectively, at 12 months, this number fell by 8.9%. No significant relationship between diet efficacy and seizure or epilepsy type, age at diet onset, sex and etiology of epilepsy was noted.

Nevertheless, it seems noteworthy that 64% of our patients with neuronal migration disorders improved on this diet. Adverse effects occurred, mainly in the first weeks of treatment, in 32 patients (57.1%), but were generally mild and transient. In seven patients (12.5%) it was possible to withdraw one to two AED after 3-4 months on ketogenic diet.

CONCLUSION:

This initial experience with the ketogenic diet was effective in difficult-to-treat patients with partial and generalized epilepsies, though its efficacy dropped significantly by 9-12 months.

Neuroprotective and disease-modifying effects of the ketogenic diet

Abstract

The ketogenic diet has been in clinical use for over 80 years, primarily for the symptomatic treatment of epilepsy. A recent clinical study has raised the possibility that exposure to the ketogenic diet may confer long-lasting therapeutic benefits for patients with epilepsy. Moreover, there is evidence from uncontrolled clinical trials and studies in animal models that the ketogenic diet can provide symptomatic and disease-modifying activity in a broad range of neurodegenerative disorders including Alzheimer's disease and Parkinson's disease, and may also be protective in traumatic brain injury and stroke. These observations are supported by studies in animal models and isolated cells that show that ketone bodies, especially β-hydroxybutyrate, confer neuroprotection against diverse types of cellular injury. This review summarizes the experimental, epidemiological and clinical evidence indicating that the ketogenic diet could have beneficial effects in a broad range of brain disorders characterized by the death of neurons. Although the mechanisms are not yet well defined, it is plausible that neuroprotection results from enhanced neuronal energy reserves, which improve the ability of neurons to resist metabolic challenges, and possibly through other actions including antioxidant and anti-inflammatory effects. As the underlying mechanisms become better understood, it will be possible to develop alternative strategies that produce similar or even improved

therapeutic effects without the need for exposure to an unpalatable and unhealthy, high-fat diet.

Acetoacetate reduces growth and ATP concentration in cancer cell lines which over-express uncoupling protein 2

Abstract

BACKGROUND

Recent evidence suggests that several human cancers are capable of uncoupling of mitochondrial ATP generation in the presence of intact tricarboxylic acid (TCA) enzymes. The goal of the current study was to test the hypothesis that ketone bodies can inhibit cell growth in aggressive cancers and that expression of uncoupling protein 2 is a contributing factor. The proposed mechanism involves inhibition of glycolytic ATP production via a Randle-like cycle while increased uncoupling renders cancers unable to produce compensatory ATP from respiration.

METHODES

Seven aggressive human cancer cell lines, and three control fibroblast lines were grown in vitro in either 10 mM glucose medium (GM), or in glucose plus 10 mM acetoacetate [G+AcA]. The cells were assayed for cell growth, ATP production and expression of UCP2.

RESULTS

There was a high correlation of cell growth with ATP concentration ($r = 0.948$) in a continuum across all cell lines. Controls demonstrated normal cell growth and ATP with the lowest density of mitochondrial UCP2 staining while all cancer lines demonstrated proportionally inhibited growth and ATP, and over-expression of UCP2 ($p < 0.05$).

CONCLUSION

Seven human cancer cell lines grown in glucose plus acetoacetate medium showed tightly coupled reduction of growth and ATP concentration. The findings were not observed in control fibroblasts. The observed over-expression of UCP2 in cancer lines, but not in controls, provides a plausible molecular mechanism by which acetoacetate spares normal cells but suppresses growth in cancer lines. The results bear on the hypothesized potential for ketogenic diets as therapeutic strategies.

Targeting insulin inhibition as a metabolic therapy in advanced cancer: a pilot safety and feasibility dietary trial in 10 patients.

Abstract

OBJECTIVE:

Most aggressive cancers demonstrate a positive positron emission tomographic (PET) result using ^{18}F-2-fluoro-2-deoxyglucose (FDG), reflecting a glycolytic phenotype. Inhibiting insulin secretion provides a method, consistent with published mechanisms, for limiting cancer growth.

METHODS:

Eligible patients with advanced incurable cancers had a positive PET result, an Eastern Cooperative Oncology Group performance status of 0 to 2, normal organ function without diabetes or recent weight loss, and a body mass index of at least 20 kg/m^2. Insulin inhibition, effected by a supervised carbohydrate dietary restriction (5% of total kilocalories), was monitored for macronutrient intake, body weight, serum electrolytes, β-hydroxybutyrate, insulin, and insulin-like growth factors-1 and -2. An FDG-PET scan was obtained at study entry and exit.

RESULTS:

Ten subjects completed 26 to 28 d of the study diet without associated unsafe adverse effects. Mean caloric intake decreased 35 ± 6% versus baseline, and weight decreased by a median of 4% (range 0.0-6.1%). In

nine patients with prior rapid disease progression, five with stable disease or partial remission on PET scan after the diet exhibited a three-fold higher dietary ketosis than those with continued progressive disease (n = 4, P = 0.018). Caloric intake (P = 0.65) and weight loss (P = 0.45) did not differ in those with stable disease or partial remission versus progressive disease. Ketosis was associated inversely with serum insulin levels (P = 0.03).

CONCLUSION:

Preliminary data demonstrate that an insulin-inhibiting diet is safe and feasible in selected patients with advanced cancer. The extent of ketosis, but not calorie deficit or weight loss, correlated with stable disease or partial remission. Further study is needed to assess insulin inhibition as complementary to standard cytotoxic and endocrine therapies.

Beyond weight loss: a review of the therapeutic uses of very-low-carbohydrate (ketogenic) diets

Abstract

Very-low-carbohydrate diets or ketogenic diets have been in use since the 1920s as a therapy for epilepsy and can, in some cases, completely remove the need for medication. From the 1960s onwards they have become widely known as one of the most common methods for obesity treatment. Recent work over the last decade or so has provided evidence of the therapeutic potential of ketogenic diets in many pathological conditions, such as diabetes, polycystic ovary syndrome, acne, neurological diseases, cancer and the amelioration of respiratory and cardiovascular disease risk factors. The possibility that modifying food intake can be useful for reducing or eliminating pharmaceutical methods of treatment, which are often lifelong with significant side effects, calls for serious investigation. This review revisits the meaning of physiological ketosis in the light of this evidence and considers possible mechanisms for the therapeutic actions of the ketogenic diet on different diseases. The present review also questions whether there are still some preconceived ideas about ketogenic diets, which may be presenting unnecessary barriers to their use as therapeutic tools in the physician's hand.

Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease

Abstract

BACKGROUND

A reduction in dietary saturated fat has generally been thought to improve cardiovascular health.

OBJECTIVE

The objective of this meta-analysis was to summarize the evidence related to the association of dietary saturated fat with risk of coronary heart disease (CHD), stroke, and cardiovascular disease (CVD; CHD inclusive of stroke) in prospective epidemiologic studies.

DESIGNE

Twenty-one studies identified by searching MEDLINE and EMBASE databases and secondary referencing qualified for inclusion in this study. A random-effects model was used to derive composite relative risk estimates for CHD, stroke, and CVD.

RESULTS

During 5–23 y of follow-up of 347,747 subjects, 11,006 developed CHD or stroke. Intake of saturated fat was not associated with an increased risk of CHD, stroke, or CVD. The pooled relative risk estimates that compared extreme quantiles of saturated fat intake were 1.07 (95% CI: 0.96, 1.19; *P* = 0.22) for CHD, 0.81 (95% CI: 0.62, 1.05; *P* = 0.11) for stroke, and 1.00 (95% CI: 0.89, 1.11; *P* = 0.95) for CVD. Consideration of age, sex, and study quality did not change the results.

CONCLUSIONS

A meta-analysis of prospective epidemiologic studies showed that there is no significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD. More data are needed to elucidate whether CVD risks are likely to be influenced by the specific nutrients used to replace saturated fat.

Low Carb Diet Side Effects

Low carb diet side effects are manageable if you understand why they happen and how to minimize them. Understanding your physical reactions will help you avoid the worst of the symptoms, and keep you from quitting before you get out of the chute, so to speak. After several weeks, these side effects will subside as you become "keto-adapted" and able to burn fat instead of glucose for fuel. The list below includes the most common low carb diet side effects, and I've included tips on how to handle them.

The only caveat is that you have no contraindicated health conditions. I have detailed here who should NOT follow a ketogenic diet.

- Frequent Urination
- Fatigue and Dizziness
- Hypoglycemia (Low Blood Sugar)
- Headaches
- Constipation
- Sugar Cravings
- Diarrhea
- Shakiness or Weakness
- Muscle Cramps
- Sleep Disturbances
- Kidney Stones
- Lowered T3 Thyroid Hormone Levels
- Heart Palpitations or a "Racing" Heart
- Hair Loss
- Low Carb Diet Side Effects Are Temporary

The effects of a low-carbohydrate ketogenic diet and a low-fat diet on mood, hunger, and other self-reported symptoms.

Abstract

OBJECTIVE:

To investigate the effects of weight loss diets on mood, food cravings, and other self-reported symptoms.

RESEARCH METHODS AND PROCEDURES:

Mood and other symptoms were evaluated by participant self-report using the Atkins Health Indicator Test (AHIT) in individuals undergoing weight loss following either a low-carbohydrate, ketogenic diet (LCKD) or a low-fat diet (LFD). Participants were 119 overweight community volunteers randomized to an LCKD or an LFD. An additional 51 participants who had completed an earlier trial contributed data for the psychometric analyses but were not included in the prospective analyses. Self-reported symptom levels on seven scales factor-analytically derived from the AHIT (negative affect, fatigue, somatic symptoms, physical effects of hunger, insomnia, hunger, and stomach problems) were acquired during 12 visits.

RESULTS:

After adjusting for the change in BMI over the course of the trial, participants experienced significant improvements in most symptoms regardless of diet. Diet group x visit interactions were observed for negative affect [$F(9,803) = 2.30$, $p = 0.015$] and hunger [$F(9,803) = 3.62$, $p < 0.0002$]. Examination of means indicated that the LCKD group reported less negative affect and hunger, compared with the LFD group.

DISCUSSION:

Regardless of diet, participants experienced significant improvement in a broad range of symptoms. Symptoms of negative affect and hunger improved to a greater degree in patients following an LCKD compared with those following an LFD. Whether these symptom changes explain the greater short-term weight loss generally experienced by LCKD followers deserves further research.

The ketone metabolite β-hydroxybutyrate blocks NLRP3 inflammasome-mediated inflammatory disease.

Abstract

The ketone bodies β-hydroxybutyrate (BHB) and acetoacetate (AcAc) support mammalian survival during states of energy deficit by serving as alternative sources of ATP. BHB levels are elevated by starvation, caloric restriction, high-intensity exercise, or the low-carbohydrate ketogenic diet. Prolonged fasting reduces inflammation; however, the impact that ketones and other alternative metabolic fuels produced during energy deficits have on the innate immune response is unknown. We report that BHB, but neither AcAc nor the structurally related short-chain fatty acids butyrate and acetate, suppresses activation of the NLRP3 inflammasome in response to urate crystals, ATP and lipotoxic fatty acids. BHB did not inhibit caspase-1 activation in response to pathogens that activate the NLR family, CARD domain containing 4 (NLRC4) or absent in melanoma 2 (AIM2) inflammasome and did not affect non-canonical caspase-11, inflammasome activation. Mechanistically, BHB inhibits the NLRP3 inflammasome by preventing K(+) efflux and reducing ASC oligomerization and speck formation. The inhibitory effects of BHB on NLRP3 are not dependent on chirality or starvation-regulated mechanisms like AMP-activated protein kinase (AMPK), reactive oxygen species (ROS), autophagy or glycolytic inhibition. BHB blocks the NLRP3 inflammasome without undergoing oxidation in the TCA cycle, and independently of uncoupling protein-2 (UCP2), sirtuin-2 (SIRT2), the G protein-coupled receptor GPR109A or hydrocaboxylic acid receptor 2 (HCAR2). BHB reduces NLRP3 inflammasome-mediated interleukin (IL)-1β and IL-18 production in human monocytes. In vivo, BHB or a ketogenic diet attenuates caspase-1 activation and IL-1β secretion in mouse models of NLRP3-mediated diseases such as Muckle-Wells syndrome, familial cold autoinflammatory syndrome and urate crystal-induced peritonitis. Our findings suggest that the anti-inflammatory effects of caloric restriction or ketogenic diets may be linked to BHB-mediated inhibition of the NLRP3 inflammasome.

Beyond weight loss: a review of the therapeutic uses of very-low-carbohydrate (ketogenic) diets.

Abstract

Very-low-carbohydrate diets or ketogenic diets have been in use since the 1920s as a therapy for epilepsy and can, in some cases, completely

remove the need for medication. From the 1960s onwards they have become widely known as one of the most common methods for obesity treatment. Recent work over the last decade or so has provided evidence of the therapeutic potential of ketogenic diets in many pathological conditions, such as diabetes, polycystic ovary syndrome, acne, neurological diseases, cancer and the amelioration of respiratory and cardiovascular disease risk factors. The possibility that modifying food intake can be useful for reducing or eliminating pharmaceutical methods of treatment, which are often lifelong with significant side effects, calls for serious investigation. This review revisits the meaning of physiological ketosis in the light of this evidence and considers possible mechanisms for the therapeutic actions of the ketogenic diet on different diseases. The present review also questions whether there are still some preconceived ideas about ketogenic diets, which may be presenting unnecessary barriers to their use as therapeutic tools in the physician's hand.

Diet-induced ketosis improves cognitive performance in aged rats.

Abstract

Aging is associated with increased susceptibility to hypoxic/ischemic insult and declines in behavioral function which may be due to attenuated adaptive/defense responses. We investigated if diet-induced ketosis would improve behavioral performance in the aged rats. Fischer 344 rats (3- and 22-month-old) were fed standard (STD) or ketogenic (KG) diet for 3 weeks and then exposed to hypobaric hypoxia. Cognitive function was measured using the T-maze and object recognition tests. Motor function was measured using the inclined-screen test. Results showed that KG diet significantly increased blood ketone levels in both young and old rats. In the aged rats, the KG diet improved cognitive performance under normoxic and hypoxic conditions; while motor performance remained unchanged. Capillary density and HIF-1alpha levels were elevated in the aged ketotic group independent of hypoxic challenge. These data suggest that diet-induced ketosis may be beneficial in the treatment of neurodegenerative conditions.

Effect of a low-carbohydrate, ketogenic diet program compared to a low-fat diet on fasting lipoprotein subclasses.

Abstract

BACKGROUND:

Low-carbohydrate, ketogenic diets (LCKD) are effective for weight loss, but concerns remain regarding cardiovascular risk. The purpose of this study was to determine the effect of an LCKD program on serum lipoprotein subclasses.

METHODS:

This was a randomized, two-arm clinical trial in an outpatient research clinic involving overweight, hyperlipidemic community volunteers motivated to lose weight. Subjects were randomized to either an LCKD (n = 59) and nutritional supplementation (including fish, borage and flaxseed oil), or a low-fat, reduced-calorie diet (LFD, n = 60). The main outcomes were fasting serum lipoprotein subclasses determined by nuclear magnetic resonance analysis.

RESULTS:

The mean age of subjects was 44.9 years, the mean BMI was 34.4 kg/m(2), and 76% were women. Comparing baseline to 6 months, the LCKD group had significant changes in large VLDL (-78%), medium VLDL (-60%), small VLDL (-57%), LDL particle size (+2%), large LDL (+54%), medium LDL (-42%), small LDL (-78%), HDL particle size (+5%), large HDL (+21%), and LDL particle concentration (-11%). Compared with the LFD group, the LCKD group had greater reductions in medium VLDL (p = 0.01), small VLDL (p = 0.01) and medium LDL (p = 0.02), and greater increases in VLDL particle size (p = 0.01), large LDL (p = 0.004), and HDL particle size (p = 0.05).

CONCLUSIONS:

The LCKD with nutritional supplementation led to beneficial changes in serum lipid subclasses during weight loss. While the LCKD did not lower total LDL cholesterol, it did result in a shift from small, dense LDL to large, buoyant LDL, which could lower cardiovascular disease risk.

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