Dieta chetogenica : reale efficacia e sicurezza

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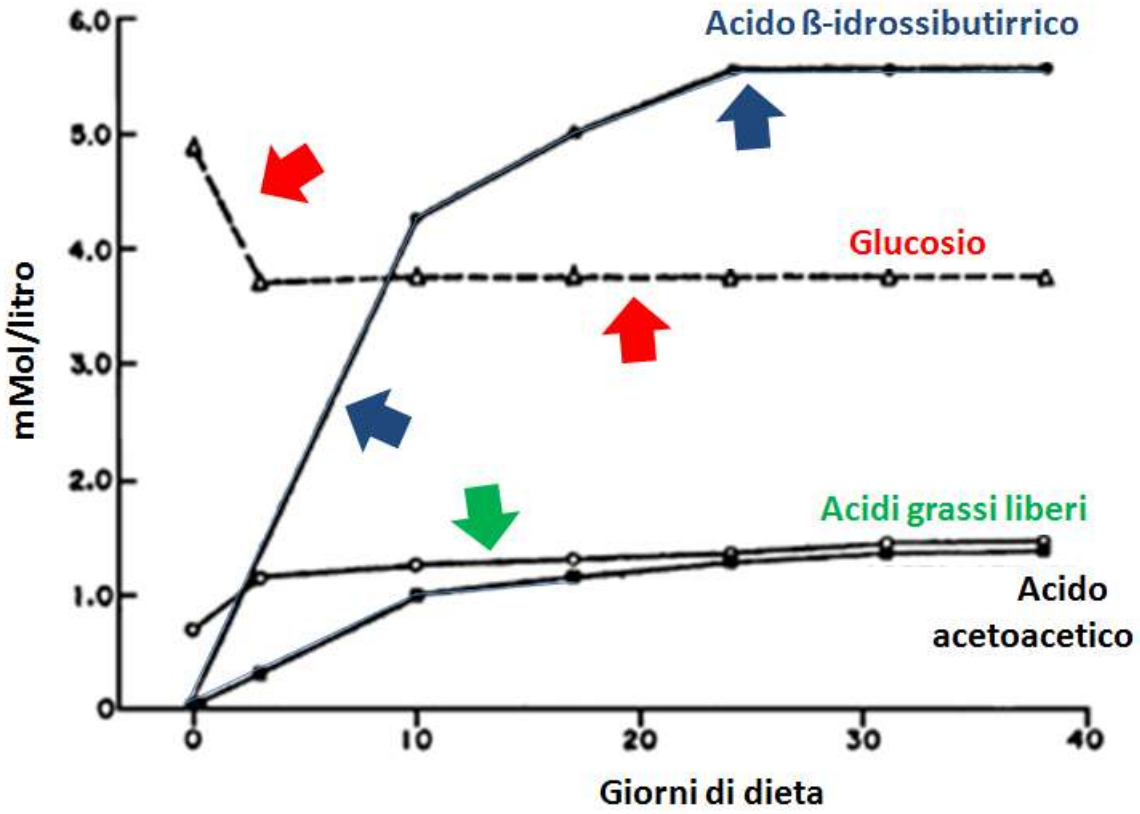
Definizione

- ✓ **L**OW-**C**ARBOHIDRATE **D**IET : intake di CHO tra 50 e 150 gr / die
- ✓ **V**ERY – **L**OW – **C**ARBOHIDRATE **K**ETOGENIC **D**IET : intake di CHO tra 20 e 50 gr /die

Dieta Chetogenica

Si definisce chetogenico un regime dietetico in grado di indurre e mantenere uno stato cronico di **chetosi** cioè **una condizione metabolica in cui vengono utilizzati corpi chetonici come fonte energetica**.

I corpi chetonici sono tre composti denominati acetone, acido acetoacetico e acido beta-idrossibutirrico normalmente presenti nel sangue in quantità trascurabile.



LA DIETA CHETOGENICA: QUALE RAZIONALE?

- Quando si riduce drasticamente l'apporto di glucidi, la modificazione del rapporto tra la concentrazione di insulina e quella di glucagone promuove la mobilizzazione dei lipidi dai depositi tissutali, promuovendone l'ossidazione a scopo energetico.

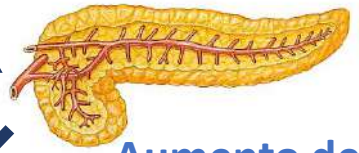
- Essendo rallentata la conversione del glucosio in piruvato, l'acetil-Co-A viene prevalentemente shiftato verso la produzione di corpi chetonici che, perdurando la condizione di chetoacidosi, vengono utilizzati a livello del sistema nervoso centrale, dove forniscono energia e contribuiscono alla comparsa di senso di sazietà, e dal muscolo cardiaco: la loro eliminazione avviene a livello polmonare (alito acetosico) e renale (tamponati dai cationi Na, K, Ca e Mg).

ADI 2014;6:38-43 Fondazione ADI: POSITION PAPER

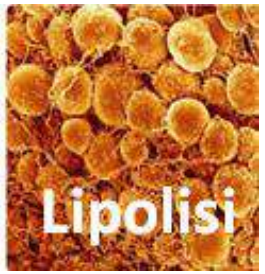
Ridotto apporto glucidico

Riduzione dei livelli d'insulina:
inibizione delle attività glicolitica e liposintetica

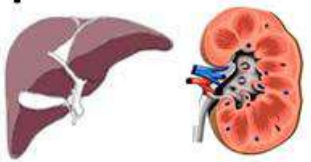
Apporto normoproteico



Aumento dei livelli di glucagone:
attivazione delle attività gluconeogenica e lipolitica



Gluconeogenesi epatica e renale



Glicerolo

Catabolismo dei trigliceridi

Beta ossidazione muscolare

Acidi grassi liberi

60%

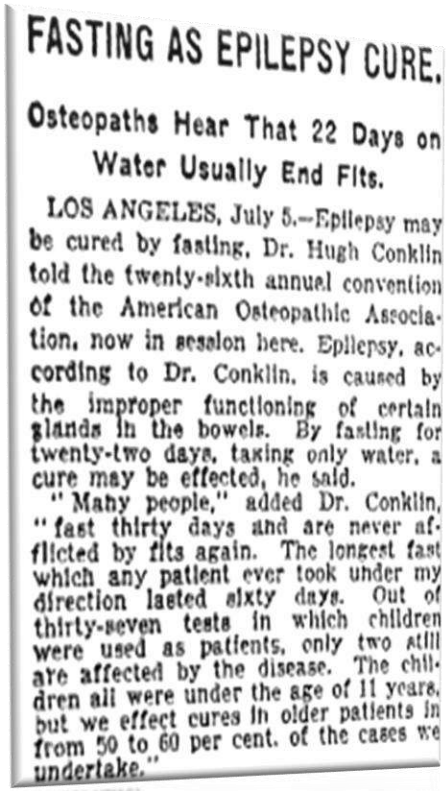
40%

Glicemia stabile

Meccanismo reciproco di controllo dei corpi chetonici e dell'insulina circolanti

Corpi chetonici

Insulina



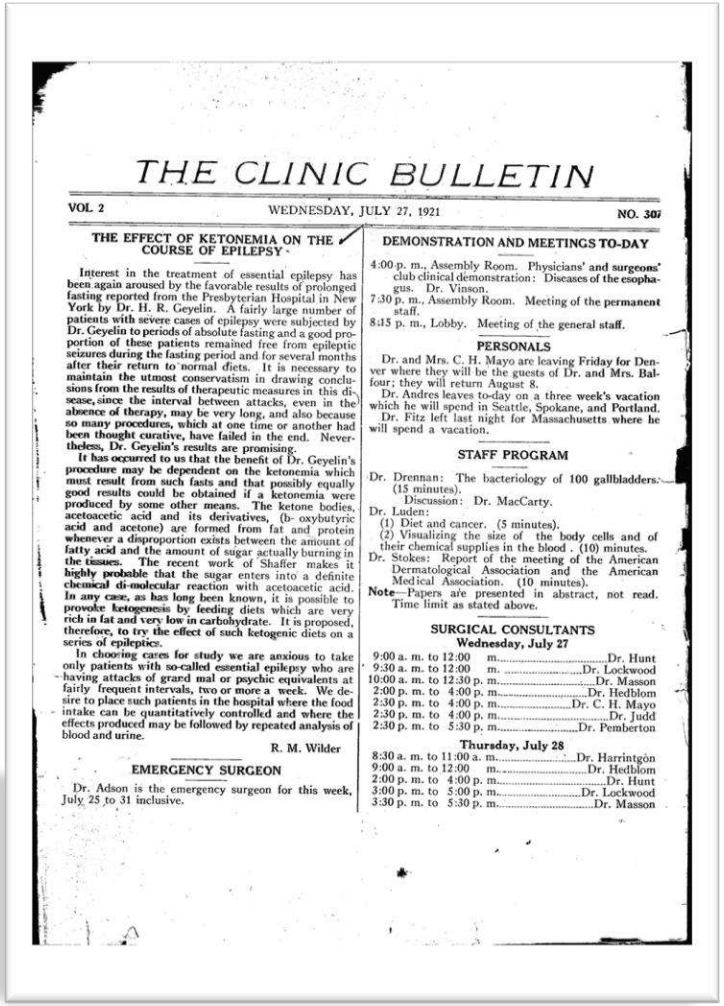
FASTING AS EPILEPSY CURE.

Osteopaths Hear That 22 Days on Water Usually End Fits.

LOS ANGELES, July 5.—Epilepsy may be cured by fasting, Dr. Hugh Conklin told the twenty-sixth annual convention of the American Osteopathic Association, now in session here. Epilepsy, according to Dr. Conklin, is caused by the improper functioning of certain glands in the bowels. By fasting for twenty-two days, taking only water, a cure may be effected, he said.

"Many people," added Dr. Conklin, "fast thirty days and are never afflicted by fits again. The longest fast which any patient ever took under my direction lasted sixty days. Out of thirty-seven tests in which children were used as patients, only two still are affected by the disease. The children all were under the age of 11 years, but we effect cures in older patients in from 50 to 60 per cent. of the cases we undertake."

La dieta chetogenica inizialmente è nata come trattamento per l'epilessia.
Negli anni venti il dottor *Hugh Conklin*, osteopata nel Wisconsin, scoprì che facendo digiunare per 25 giorni bambini epilettici poteva controllarne gli attacchi epilettici.
***Conklin* inizialmente pensò che questo effetto fosse correlato ad un minor lavoro da parte del sistema gastrointestinale.**



THE CLINIC BULLETIN

VOL. 2 — WEDNESDAY, JULY 27, 1921 — NO. 307

THE EFFECT OF KETONEMIA ON THE COURSE OF EPILEPSY

Interest in the treatment of essential epilepsy has been again aroused by the favorable results of prolonged fasting reported from the Presbyterian Hospital in New York by Dr. H. R. Geyelin. A fairly large number of patients with severe cases of epilepsy were subjected by Dr. Geyelin to periods of absolute fasting and a good proportion of these patients remained free from epileptic seizures during the fasting period and for several months after their return to normal diets. It is necessary to maintain the utmost conservatism in drawing conclusions from the results of therapeutic measures in this disease, since the interval between attacks, even in the absence of therapy, may be very long, and also because so many procedures, which at one time or another had been thought curative, have failed in the end. Nevertheless, Dr. Geyelin's results are promising.

It has occurred to us that the benefit of Dr. Geyelin's procedure may be dependent on the ketonemia which must result from such fasts and that possibly equally good results could be obtained if a ketonemia were produced by some other means. The ketone bodies, acetoacetic acid and its derivatives, (b- oxybutyric acid and acetone) are formed from fat and protein whenever a disproportion exists between the amount of fatty acid and the amount of sugar actually burning in the tissues. The recent work of Shaffer makes it highly probable that the sugar enters into a definite chemical di-molecular reaction with acetoacetic acid. In any case, as has long been known, it is possible to provoke ketogenesis by feeding diets which are very rich in fat and very low in carbohydrate. It is proposed, therefore, to try the effect of such ketogenic diets on a series of epileptics.

In choosing cases for study we are anxious to take only patients with so-called essential epilepsy who are having attacks of grand mal or psychic equivalents at fairly frequent intervals, two or more a week. We desire to place such patients in the hospital where the food intake can be quantitatively controlled and where the effects produced may be followed by repeated analysis of blood and urine.

R. M. Wilder

EMERGENCY SURGEON

Dr. Adson is the emergency surgeon for this week, July 25 to 31 inclusive.

DEMONSTRATION AND MEETINGS TO-DAY

4:00 p. m., Assembly Room. Physicians' and surgeons' club clinical demonstration: Diseases of the esophagus. Dr. Vinson.
7:30 p. m., Assembly Room. Meeting of the permanent staff.
8:15 p. m., Lobby. Meeting of the general staff.

PERSONALS

Dr. and Mrs. C. H. Mayo are leaving Friday for Denver where they will be the guests of Dr. and Mrs. Balfour; they will return August 8.

Dr. Andres leaves to-day on a three week's vacation which he will spend in Seattle, Spokane, and Portland.

Dr. Fitz left last night for Massachusetts where he will spend a vacation.

STAFF PROGRAM

Dr. Drennan: The bacteriology of 100 gallbladders. (15 minutes).
Discussion: Dr. MacCarty.
Dr. Luden:
(1) Diet and cancer. (5 minutes).
(2) Visualizing the size of the body cells and of their chemical supplies in the blood. (10) minutes.
Dr. Stokes: Report of the meeting of the American Dermatological Association and the American Medical Association. (10 minutes).
Note—Papers are presented in abstract, not read. Time limit as stated above.

SURGICAL CONSULTANTS

Wednesday, July 27

9:00 a. m. to 12:00 m. ..... Dr. Hunt
9:30 a. m. to 12:00 m. ..... Dr. Lockwood
10:00 a. m. to 12:30 p. m. ..... Dr. Masson
2:00 p. m. to 4:00 p. m. ..... Dr. Hedblom
2:30 p. m. to 4:00 p. m. ..... Dr. C. H. Mayo
2:30 p. m. to 4:00 p. m. ..... Dr. Judd
2:30 p. m. to 5:30 p. m. ..... Dr. Pemberton

Thursday, July 28

8:30 a. m. to 11:00 a. m. ..... Dr. Harrington
9:00 a. m. to 12:00 m. ..... Dr. Hedblom
2:00 p. m. to 4:00 p. m. ..... Dr. Hunt
3:00 p. m. to 5:00 p. m. ..... Dr. Lockwood
3:30 p. m. to 5:30 p. m. ..... Dr. Masson

Nel 1921 il Dr Wilder della Mayo Clinic scoprì che in realtà erano i metaboliti prodotti durante il digiuno a far sì che il sistema nervoso centrale mettesse in atto meccanismi di controllo sulle crisi epilettiche.

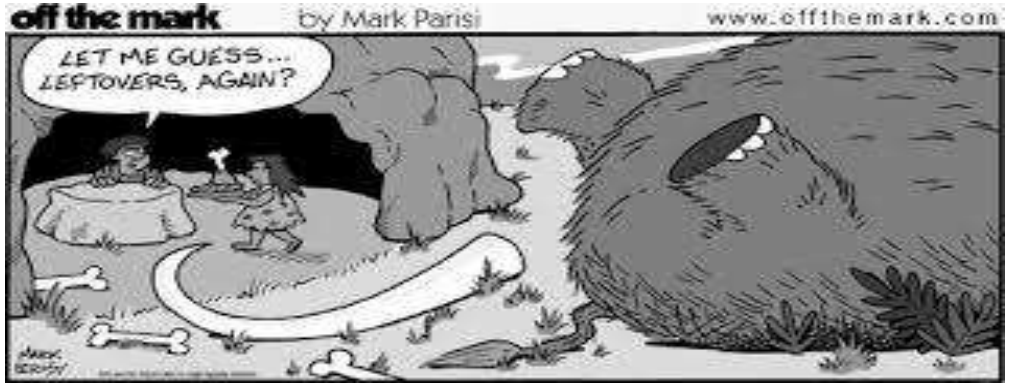
Wilder ipotizzò che il digiuno, cosi come elaborato da *Conklin*, poteva essere in realtà simulato da una dieta vera e propria denominata *chetogenica* dai prodotti finali di questo processo metabolico.

Nel 1938, tuttavia, la dieta *chetogenica* fu medicalmente accantonata dopo l'immissione sul mercato della *Fenitoina*, farmaco definito 'gold standard' per il trattamento dell'epilessia.

Solo negli anni '90 la dieta *chetogenica* fu ripresa, quando ci fu un caso di un bambino epilettico, resistente ai farmaci, il cui padre dopo ricerche accuratissime sulle diete chetogeniche ed i vari trattamenti farmacologici per l'epilessia, riuscì a permettere un trattamento 'alternativo' per il figlio.

Dieta chetogenica

Pur con le diversità legate alle differenze climatiche e ambientali, si possono così riassumere le caratteristiche dell'alimentazione durate da circa 2 milioni di anni fa a 8.000 anni fa (periodo paleolitico e mesolitico, o dei fruttivori e carnivori cacciatori e raccoglitori)



- Necessità di gestire la giornata prevalentemente in funzione della ricerca di cibo
- Ciclica comparsa di periodi di scarsa disponibilità del cibo stesso, alternando periodi di maggior alimentazione ed altri di quasi digiuno
- Ciclica assunzione di elevate quantità di proteine di origine animale in caso di caccia favorevole, con contenuto di grassi medio-basso (consumo di soli animali selvatici), da consumare in pochi giorni
- Apporti medi stimati di circa 70-80 gr di proteine e 1800-2000 kcalorie, con grassi non superiori al 20% delle calorie totali
- Nella scarsità di carboidrati, gli zuccheri semplici erano pressochè assenti
- L'apporto di fibre era molto elevato

(Fondazione ADI ; POSITION PAPER : LA DIETA CHETOGENICA 2014;6 : 38-41)

Queste fluttuazioni hanno condizionato il nostro pattern metabolico, gradualmente disorientato dalla costante disponibilità di cibo, già apparsa con l'avvento dell'agricoltura circa 8.000 anni fa e molto amplificata nell'era moderna industriale e post-industriale.
Il «gene risparmiatore», influenzando fortemente la selezione della specie ed incrementando la sopravvivenza anche in funzione delle capacità metaboliche sviluppate, è diventato co-protagonista della pandemia di obesità, diabete mellito tipo 2 e malattie cronico-degenerative correlate allo stile di vita.
Infatti, l'aumento di resistenza insulinica è stata correlata in vari studi con la sospensione di questa alternanza tra digiuno e sazietà, con conseguente ridotta capacità di preservare il glucosio per le funzioni vitali, quali attività cerebrale e la riproduzione.

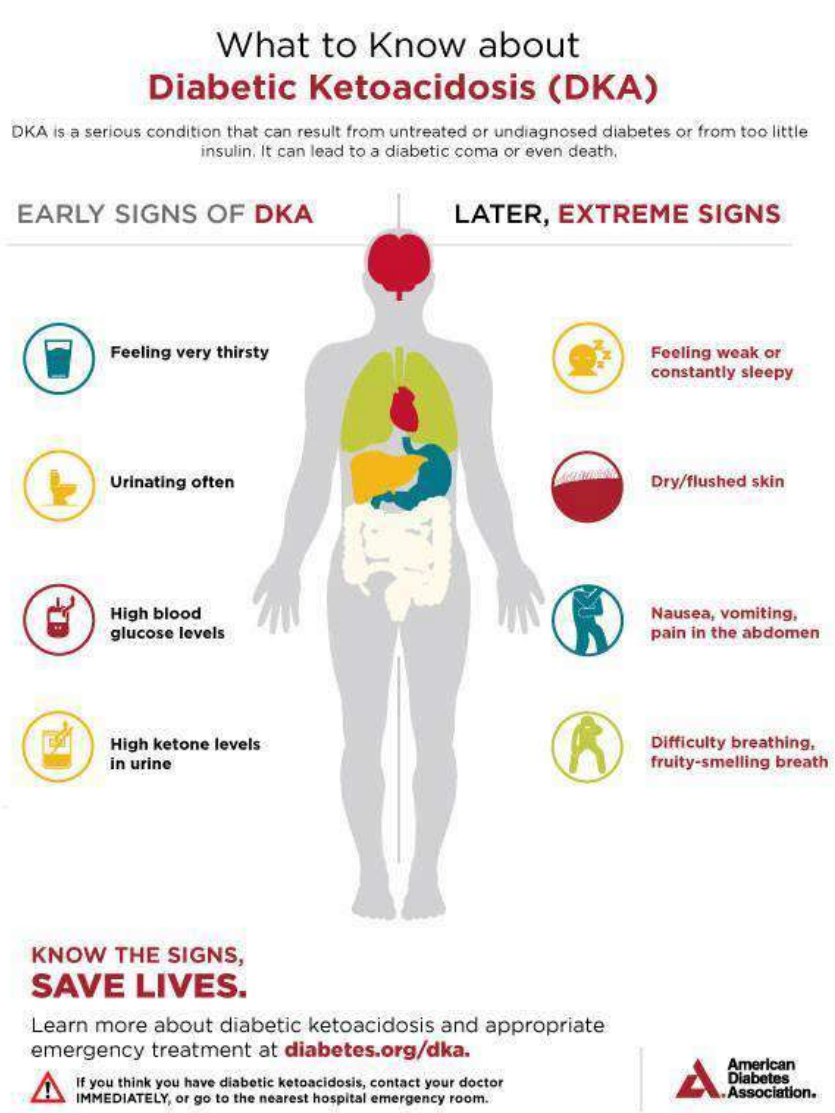
Le cosiddette « paleo-diete», le diete chetogeniche fortemente ipocaloriche e alcune diete «commerciali» come ad es. l'Atkins, condividono quindi il recupero di capacità metaboliche sviluppatesi nel periodo precedente la comparsa dell'agricoltura.

(Fondazione ADI; POSITION PAPER : LA DIETA CHETOGENICA 2014;6 : 38-43)

CHETOSI = CHETOACIDOSI?

Diabetic Ketoacidosis

Blood glucose 300 to 500 mg/dL ↑	PH <7.3 ↓
Ketones Positive +	Total C O 2 ↓
Na ↓	K ↑
Anion gap ↑	HCO 3<15 meq/L ↓



CHETOSI ≠ CHETOACIDOSI

Table 1. Blood levels during a normal diet, ketogenic diet and diabetic ketoacidosis[11]

Blood levels	*Normal diet*	*Ketogenic diet*	*Diabetic ketoacidosis*
Glucose (mg/dl)	80–120	65–80	>300
Insulin (μU/l)	6–23	6.6–9.4	≅ 0
KB conc (mM/l)	0.1	7/8 x 70	>25 x 300
pH	7.4	7.4	<7.3

Diete Chetogeniche

Questi approcci dietetici poiché inducono chetosi vengono spesso annoverati in un unico gruppo, ma in realtà differiscono molto per apporto di carboidrati e di proteine

Ripartizione in nutrienti (espressi in percentuale sull'apporto calorico totale giornaliero) di diete ipoglucidiche a confronto con una dieta equilibrata

%	Atkins inizio	Atkins 6 mesi	Scarsdale	Dukan	Equilibrata
Carboidrati	10	37	34	15	**55-60**
Lipidi	60	41	22	26	**25-30**
Proteine	30	22	43	59	**15**

Very Low Calorie Ketogenic Diet (VLCKD)

Kcal	600 – 800
CHO	< 50 gr
Proteine	1 – 1,2 gr/kg/peso id
Lipidi	10 – 15 gr
Acqua	1,5 – 2 Lt/die

IPOCALORICA
NORMOPROTEICA
IPOGLUCIDICA
IPOLIPIDICA

Microelementi (Vitamine, Sali Minerali), **Fibre, Omega 3**

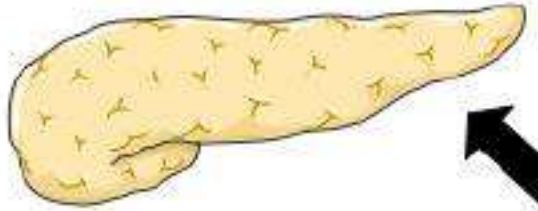
Effetti della Dieta Chetogenica

Rodents :

- ↑ insulin resistance
- ↑ glucose intolerance

Humans :

- ↓ blood glucose level
- ↑/↓ insulin resistance
- ↓ HbA1c
- ↓ glycemic variability
- ↓ antidiabetic medications



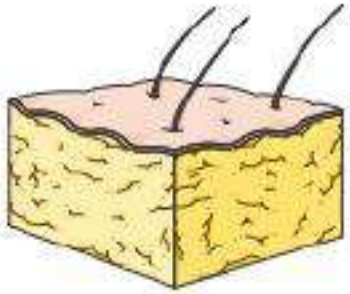
Rodents :

- ↑ total cholesterol
- ↑ LDL-cholesterol
- ↓ HDL-cholesterol
- ↑ triglycerides

Humans :

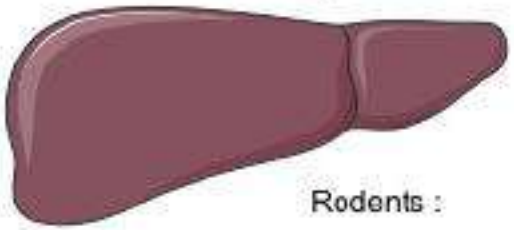
- ↓ total cholesterol
- ↓ LDL-cholesterol
- ↑ HDL-cholesterol
- ↓ triglycerides

KETOGENIC DIETS



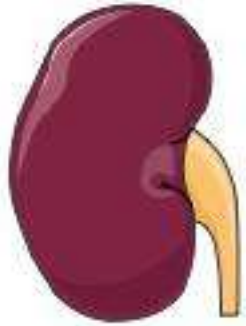
Rodents & humans :

- ↓ weight
- ↓ lean and fat mass



Rodents :

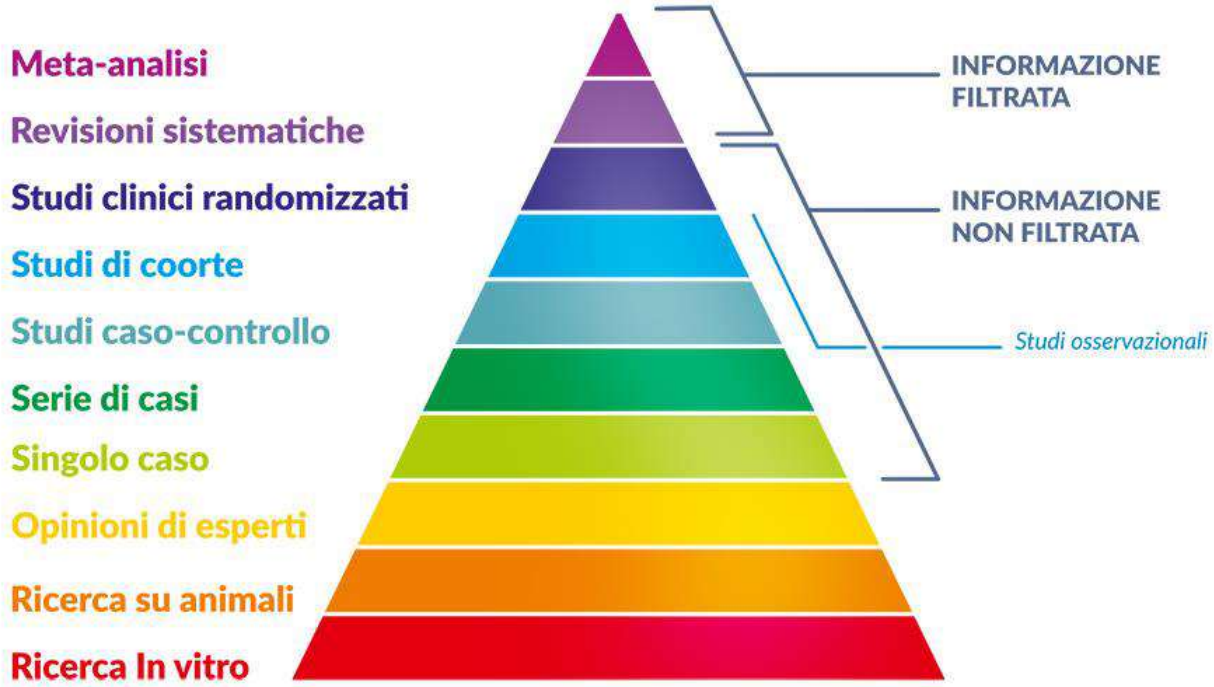
- ↑ hepatic inflammation
- ↑ liver fat content (NAFLD)



Humans :

- ↓ systolic and/or diastolic blood pressure

EVIDENZE SCIENTIFICHE



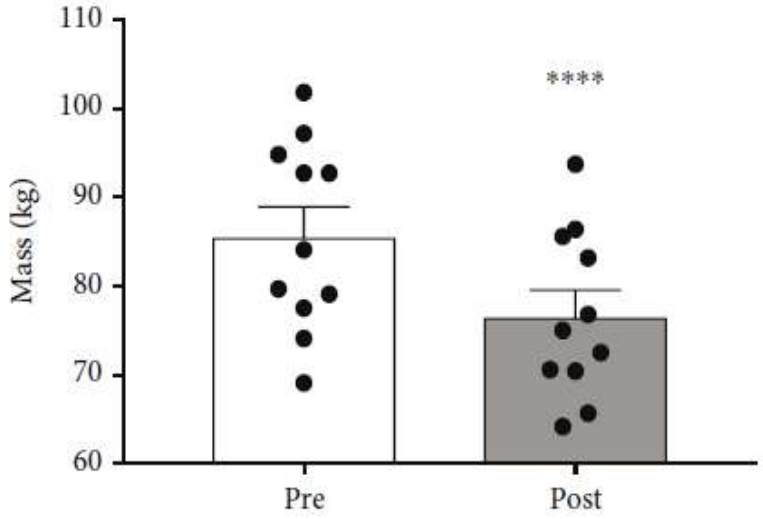
Hindawi
Journal of Diabetes Research
Volume 2019, Article ID 8681959, 6 pages
https://doi.org/10.1155/2019/8681959

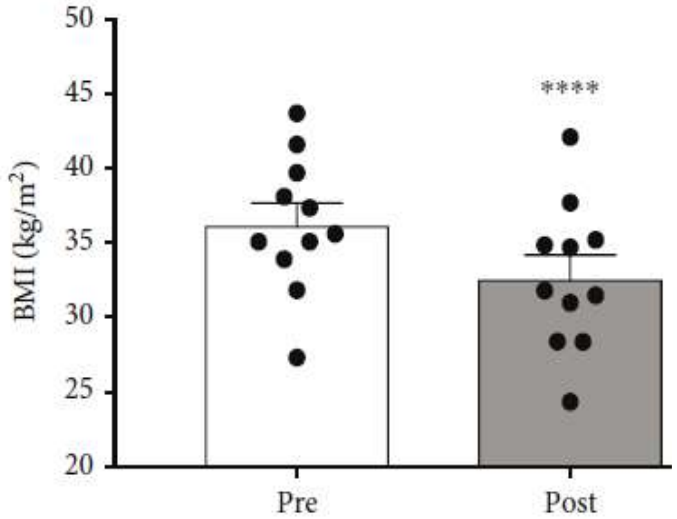
Research Article

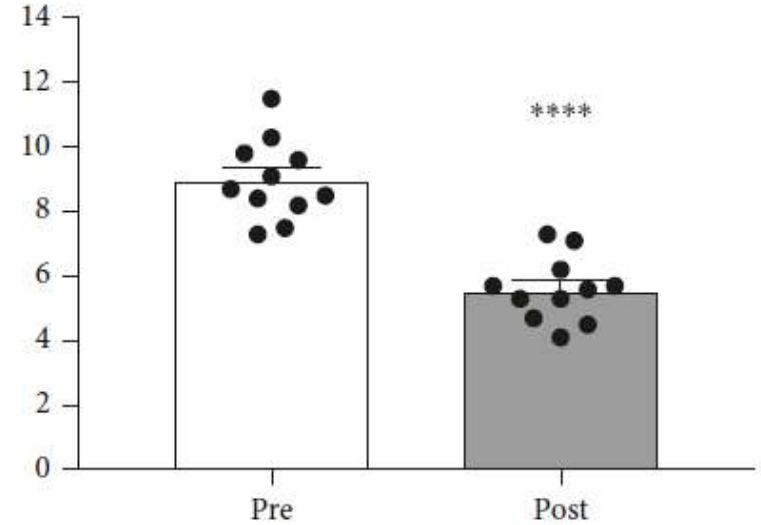
Improvement in Glycemic and Lipid Profiles in Type 2 Diabetics with a 90-Day Ketogenic Diet

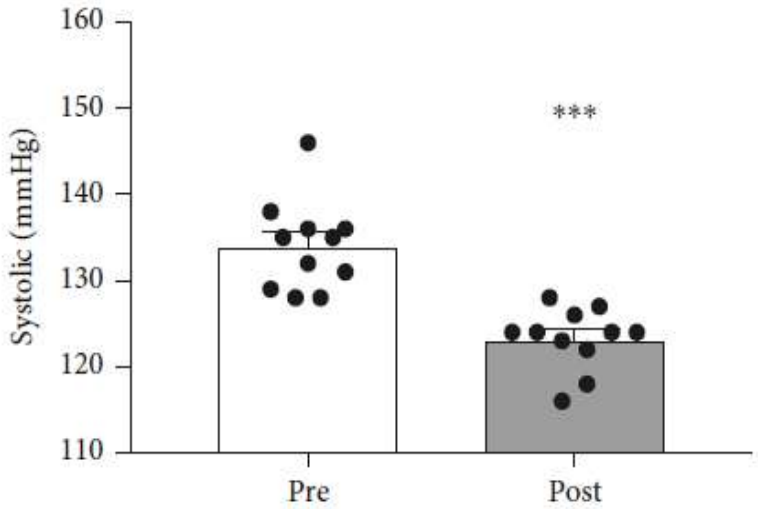
Chase M. Walton,[1] Katelyn Perry,[1] Richard H. Hart,[2] Steven L. Berry,[2,3] and Benjamin T. Bikman[1,2]

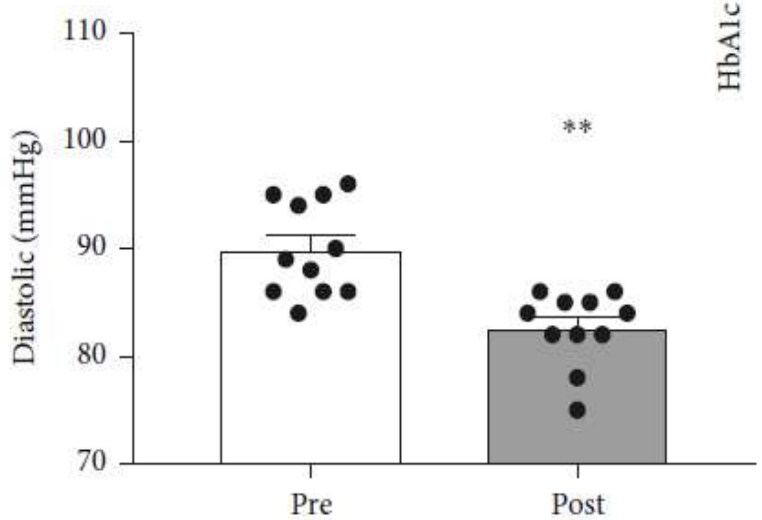
Because low-carbohydrate diets are effective strategies to improve insulin resistance, the hallmark of type 2 diabetes, the purpose of reporting these clinical cases was to reveal the meaningful changes observed in 90 days of low-carbohydrate (LC) ketogenic dietary intervention in female type 2 diabetics aged 18-45. Eleven women (BMI 36.3 kg/m^2) who were recently diagnosed with type 2 diabetes based on HbA1c over 6.5% (8.9%) volunteered to participate in an intensive dietary intervention to limit dietary carbohydrates to under 30 grams daily for 90 days. The main outcome was to determine the degree of change in HbA1c, while secondary outcomes included body weight, blood pressure, and blood lipids. The volunteers lost significant weight (85.7 ± 3.2 kg to 76.7 ± 2.8 kg) and lowered systolic (134.0 ± 1.6 to 123.3 ± 1.1 mmHg) and diastolic (89.9 ± 1.3 to 82.6 ± 1.0 mmHg) blood pressure. HbA1c dropped to 5.6%. Most blood lipids were significantly altered, including HDL cholesterol (43.1 ± 4.4 to 52.3 ± 3.3 mg/dl), triglycerides (177.0 ± 19.8 to 92.1 ± 8.7 mg/dl), and the TG : HDL ratio (4.7 ± 0.8 to 1.9 ± 0.2). LDL cholesterol was not significantly different. AST and ALT, plasma markers of liver health, were reported for eight patients and revealed no significant changes. These findings indicate that a short-term intervention emphasizing protein and fat at the expense of dietary carbohydrate functionally reversed the diabetes diagnosis, as defined by HbA1c. Furthermore, the intervention lowered body weight and blood pressure, while eliciting favorable changes in blood lipids.


Mass (kg)
110
100
90
80
70
60
****
Pre
Post


BMI (kg/m2)
50
45
40
35
30
25
20
****
Pre
Post


HbA1c (%)
14
12
10
8
6
4
2
0
****
Pre
Post


Systolic (mmHg)
160
150
140
130
120
110
***
Pre
Post


Diastolic (mmHg)
110
100
90
80
70
**
Pre
Post

Nutrition & Metabolism

The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus

Eric C Westman*[1], William S Yancy Jr[1,2], John C Mavropoulos[1], Megan Marquart[1] and Jennifer R McDuffie[1,2]

Address: [1]Department of Medicine, Duke University Medical Center, Durham, NC, USA and [2]Center for Health Services Research in Primary Care, Department of Veterans' Affairs Medical Center, Durham, NC, USA

Published: 19 December 2008

Nutrition & Metabolism 2008, 5:36 doi:10.1186/1743-7075-5-36

Abstract

Objective: Dietary carbohydrate is the major determinant of postprandial glucose levels, and several clinical studies have shown that low-carbohydrate diets improve glycemic control. In this study, we tested the hypothesis that a diet lower in carbohydrate would lead to greater improvement in glycemic control over a 24-week period in patients with obesity and type 2 diabetes mellitus.

Research design and methods: Eighty-four community volunteers with obesity and type 2 diabetes were randomized to either a low-carbohydrate, ketogenic diet (<20 g of carbohydrate daily; LCKD) or a low-glycemic, reduced-calorie diet (500 kcal/day deficit from weight maintenance diet; LGID). Both groups received group meetings, nutritional supplementation, and an exercise recommendation. The main outcome was glycemic control, measured by hemoglobin A_{1c}.

Results: Forty-nine (58.3%) participants completed the study. Both interventions led to improvements in hemoglobin A_{1c}, fasting glucose, fasting insulin, and weight loss. The LCKD group had greater improvements in hemoglobin A_{1c} (-1.5% vs. -0.5%, $p = 0.03$), body weight (-11.1 kg vs. -6.9 kg, $p = 0.008$), and high density lipoprotein cholesterol (+5.6 mg/dL vs. 0 mg/dL, $p < 0.001$) compared to the LGID group. Diabetes medications were reduced or eliminated in 95.2% of LCKD vs. 62% of LGID participants ($p < 0.01$).

Conclusion: Dietary modification led to improvements in glycemic control and medication reduction/elimination in motivated volunteers with type 2 diabetes. The diet lower in carbohydrate led to greater improvements in glycemic control, and more frequent medication reduction/elimination than the low glycemic index diet. Lifestyle modification using low carbohydrate interventions is effective for improving and reversing type 2 diabetes.

Effects of the Ketogenic Diet on Glycemic Control in Diabetic Patients: Meta-Analysis of Clinical Trials

Raghad A. Alarim [1], Faris A. Alasmre [1], Hammam A. Alotaibi [2], Mohammed A. Alshehri [1], Sara A. Hussain [1]

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Cureus
Publishing Beyond Open Access

2020 Oct;12(10):e10796

Abstract

Introduction

The ketogenic diet is a diet that relies on reducing carbohydrate intake to a minimum while increasing fat intake. This induces a state of ketosis where it is hypothesized to favor fat metabolism for energy instead of carbohydrates. The diet is used to treat pediatric patients with seizures to control their symptoms. Today, it is used by many to help in weight loss. Extensive research is being conducted on the benefits of the diet, as it gains popularity among patients with diabetes and obesity, to evaluate its effects on glycemic control.

Methods

This review looks at the published literature and summarizes the interventional trials that use the ketogenic diet for glycemic control. Emphasis was on pooling the results of selected variables such as weight, glycemic control, and lipid profile. The meta-analysis was conducted by a trained statistician using the Cochrane software review manager (Revman version 5.4; Cochrane, London, UK). Results were reviewed by an independent reviewer adhering to the Cochrane Collaboration's guidelines.

Results

The findings of this review show a significant effect of the ketogenic diet as compared to controls in terms of weight reduction, glycemic control, and improved lipid profile. A noticeable improvement was seen in glycated hemoglobin (HbA1c) and in high-density lipoprotein (HDL), favoring the ketogenic diet as compared to control.

Conclusion

This review concludes that the ketogenic diet is superior to controls in terms of glycemic control and lipid profile improvements, and the results are significant enough to recommend it as an adjunctive treatment for type two diabetes.

Study ID	Design/sample	Intervention	Findings	Conclusion
Yancy et al., 2005 [9]	Single-arm 16-week interventional trial. n=28 obese diabetic patients	Patients received LCKD counseling. Target carbohydrates: <20 g/day	HbA1c decreased by 16% from 7.5 ± 1.4% to 6.3 ± 1.0% (p<0.001). Fasting serum triglycerides dropped by 42% from 2.69 ± 2.87 mmol/L to 1.57 ± 1.38 mmol/L (p=0.001)	LCKD significantly improved glycemic and lipid control. Medication discontinued in seven patients; reduced in 10.
Dashti et al., 2007 [10]	A 56-week randomized clinical trial. Sample: 64 healthy obese subject. High blood glucose n=31. Normal blood glucose n=33.	Patients received an LCKD diet. Target carbohydrates: <20 g/day. Protein: 80-100 g/day.	Fasting blood glucose level decreased significantly from 10.481 ± 3.026 mmol/L to 4.874 ± 0.556 mmol/L (p=<0.0001). Fasting serum triglycerides significantly decreased from 4.681 ± 2.468 mmol/L to 1.006 ± 0.205 mmol/L (p=<0.0001).	LCKD was very effective for improving glycemic and lipid control. Also, it helps in reducing medications in patients with type II diabetes.
Westman et al., 2008 [11]	A 24-week interventional study. Sample: 84 obese diabetic patients.	Patients received an LCKD diet. Target carbohydrates: <20 g/day (n=38). Patients received a low glycemic index diet (LGID) (n=46). Low glycemic, low calories by 500 kcal 55% of daily caloric intake from carbohydrates.	The LCKD group had a greater reduction of mean ± SD HbA1c (8.8 ± 1.8% to 7.3 ± 1.5%, p=0.009, within-group change, n=21) compared to the LGID group (8.3 ± 1.9% to 7.8 ± 2.1% p=NS, within-group change, n=29; between groups comparison p=0.03). The group that received LCKD had better results with serum triglycerides (210.4 ± 10.3 mg/dL to 142.9 ± 76.9 mg/dL) by a mean change of -67.5 as compared to the group that received LGID (167.1 ± 125.7 mg/dL to 147.8 ± 128.5 mg/dL) with a mean change of -19.3.	In the LCKD, glycemic control was greater than the LGID. Twenty of 21 (95.2%) LCKD group participants had an elimination or reduction in medication, compared with 18 of 29 (62.1%) LGID group participants (p<0.01).



Hussain et al., 2012 [12]	A 24-week diet intervention trial. Sample: 363 overweight and obese, 102 of them had diabetic patients.	Patients received LCKD and LCD and chose an LCD or LCKD counseling. Target carbohydrates: 20 g/day.	HbA1c decreased with LCKD more than LCD. Fasting serum triglycerides: decreased with LCKD more than LCD. Total cholesterol: decreased with LCKD. Blood glucose level: decreased in the two groups but LCKD had a greater effect than LCD.	LCKD had significant positive effects on serum triacylglycerol and glycemic control; there was an improvement in HbA1c.
Goday et al., 2016 [13]	A multi-centric randomized clinical trial with a duration of 4 months. Sample: 89 obese diabetic patients aged between 30 and 65 years.	Patients received LCKD and LCD. Target carbohydrates: <50 g/day.	HbA1c decreased from 6.9% to 6 % (p<0.0001) in LCKD. LCKD decreased serum triglycerides from 150.5 mg/dl to 114 mg/dl (p=0.004). Fasting glucose decreased from 136.9 mg/dl to 108,9 mg/dl (p<0.0001). Decreased oral anti-diabetic medication from 33 (73.3%) to 20 (50.0%) (p=0.0267).	LCKD is most effective in reducing body weight and improving glycemic control than a standard low-calorie diet with safety and good tolerance for T2DM patients.
Saslow et al., 2017 [14]	A 32-week randomized controlled trial. Sample: 25 obese diabetic patients, intervention group n=12, control group n=13.	Patients received VLCKD counseling. Target carbohydrates: 20-50 g/day.	HbA1c decreased in 16 weeks about -0.9% and -0.8% in 32 weeks. LCKD decreased serum triglycerides in 16 weeks about -35.5 g/dl and -60.1 g/dl in 32 weeks.	LCKD had positive effects on serum triacylglycerol and glycemic control. There was an improvement in HbA1c.

TABLE 1: Summary of included studies

HbA1c: glycated hemoglobin, Kcal: kilocalorie, LCD: low carbohydrate diet, LCKD: low carbohydrate ketogenic diet, LGID: low glycemic index diet, SD: standard deviation, T2DM: type two diabetes mellitus, VLCKD: very low carbohydrate ketogenic diet, mg/dl: milligram per deciliter, mmol/l: millimole per liter, n: number of patients, p: p-value

Study ID: refers to included studies [9-14]

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Article

Very-Low-Calorie Ketogenic Diet as a Safe and Valuable Tool for Long-Term Glycemic Management in Patients with Obesity and Type 2 Diabetes

Eleonora Moriconi [1,2], Elisabetta Camajani [2,3], Andrea Fabbri [4], Andrea Lenzi [5] and Massimiliano Caprio [1,3,*]

Nutrients **2021**, *13*, 758.

Abstract: Obesity-related type 2 diabetes represents one of the most difficult challenges for the healthcare system. This retrospective study aims to determine the efficacy, safety and durability of a very-low-calorie ketogenic diet (VLCKD), compared to a standard low-calorie diet (LCD) on weight-loss, glycemic management, eating behavior and quality of life in patients with type 2 diabetes (T2DM) and obesity. Thirty patients with obesity and T2DM, aged between 35 and 75 years, who met the inclusion criteria and accepted to adhere to a VLCKD or a LCD nutritional program, were consecutively selected from our electronic database. Fifteen patients followed a structured VLCKD protocol, fifteen followed a classical LCD. At the beginning of the nutritional protocol, all patients were asked to stop any antidiabetic medications, with the exception of metformin. Data were collected at baseline and after 3 (T1) and 12 (T2) months. At T1 and T2, BMI was significantly reduced in the VLCKD group ($p < 0.001$), whereas it remained substantially unchanged in the LCD group. HbA1c was significantly reduced in the VLCKD group ($p = 0.002$), whereas a slight, although not significant, decrease was observed in the LCD group. Quality of life and eating behavior scores were improved in the VLCKD group, whereas no significant changes were reported in the LCD group, both at T1 and T2. At the end of the study, in the VLCKD group 26.6% of patients had stopped all antidiabetic medications, and 73.3% were taking only metformin, whereas 46.6% of LCD patients had to increase antidiabetic medications. The study confirms a valuable therapeutic effect of VLCKD in the long-term management of obesity and T2DM and its potential contribution to remission of the disease.

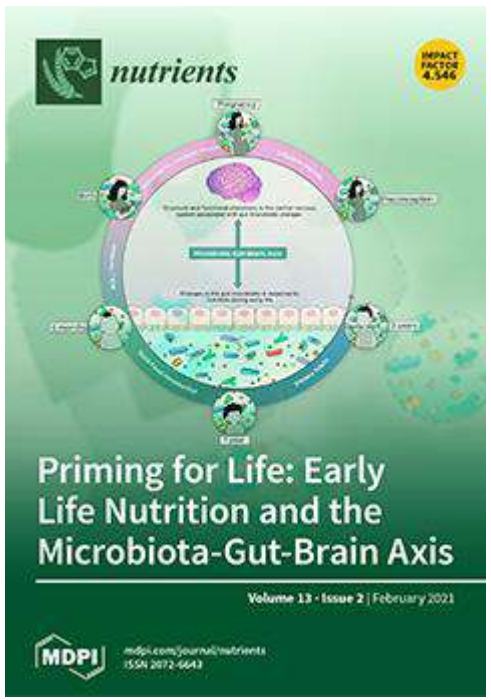


Table 1. Baseline characteristics (± SD) of very-low-calorie ketogenic diet (VCLKD) and low-calorie diet (LCD) group.

Parameters	VLCKD (n = 15)	LCD (n = 15)	p-Value
Age (years)	60.5 ± 10.2	64.4 ± 8.8	0.271
Sex	Female 7 (47%), Male 8 (53%)	Female 7 (47%), Male 8 (53%)	NA
Weight (kg)	111.6 ± 19.8	91.6 ± 18.7	**0.008**
BMI (kg/m^2)	39.5 ± 6.0	32.2 ± 4.3	**0.001**
WC (cm)	118.2 ± 9.0	103.1 ± 11.6	**0.000**
HC (cm)	119.4 ± 14.9	105.5 ± 9.3	**0.005**
WHR	1.00 ± 0.11	0.97 ± 0.05	0.452
BPsys (mmHg)	143.2 ± 16.3	139.6 ± 13.1	0.512
BPdias (mmHg)	85.4 ± 6.9	81.2 ± 7.0	0.105
Glycemia (mg/dL)	118.2 ± 18.8	129.3 ± 33.6	0.273
HbA1c (%)	6.6 ± 0.84	6.7 ± 0.69	0.642
Tot Chol (mg/dL)	203.4 ± 35.0	196 ± 26.7	0.518
HDL chol (mg/dL)	42.4 ± 13.6	42.3 ± 8.6	0.975
LDL chol (mg/dL)	126.0 ± 38.3	117.7 ± 29.2	0.509
Trig (mg/dL)	188.2 ± 36.4	179.8 ± 20.3	0.444
Creatinine (mg/dL)	0.89 ± 0.25	0.83 ± 0.20	0.517

BMI: Body Mass Index; WC: Waist circumference; HC: Hip circumference; WHR: Waist–hip ratio; BPsys: systolic blood pressure; BPdiast: diastolic blood pressure; Tot Chol: total cholesterol; HDL chol: high-density lipoprotein cholesterol; LDL chol: low-density lipoprotein cholesterol; LCD, low-calorie diet; Trig: triglycerides; VLCKD, Very-low-calorie ketogenic diet. All values are presented as mean ± standard deviation. Differences were considered statistically significant when p was <0.05. NA, not applicable. Significant p values are highlighted in bold.

Graphical representation of mean weight loss and BMI reduction (±SE) throughout the entire study in the VLCKD and LCD groups is shown in Figures 1 and 2.

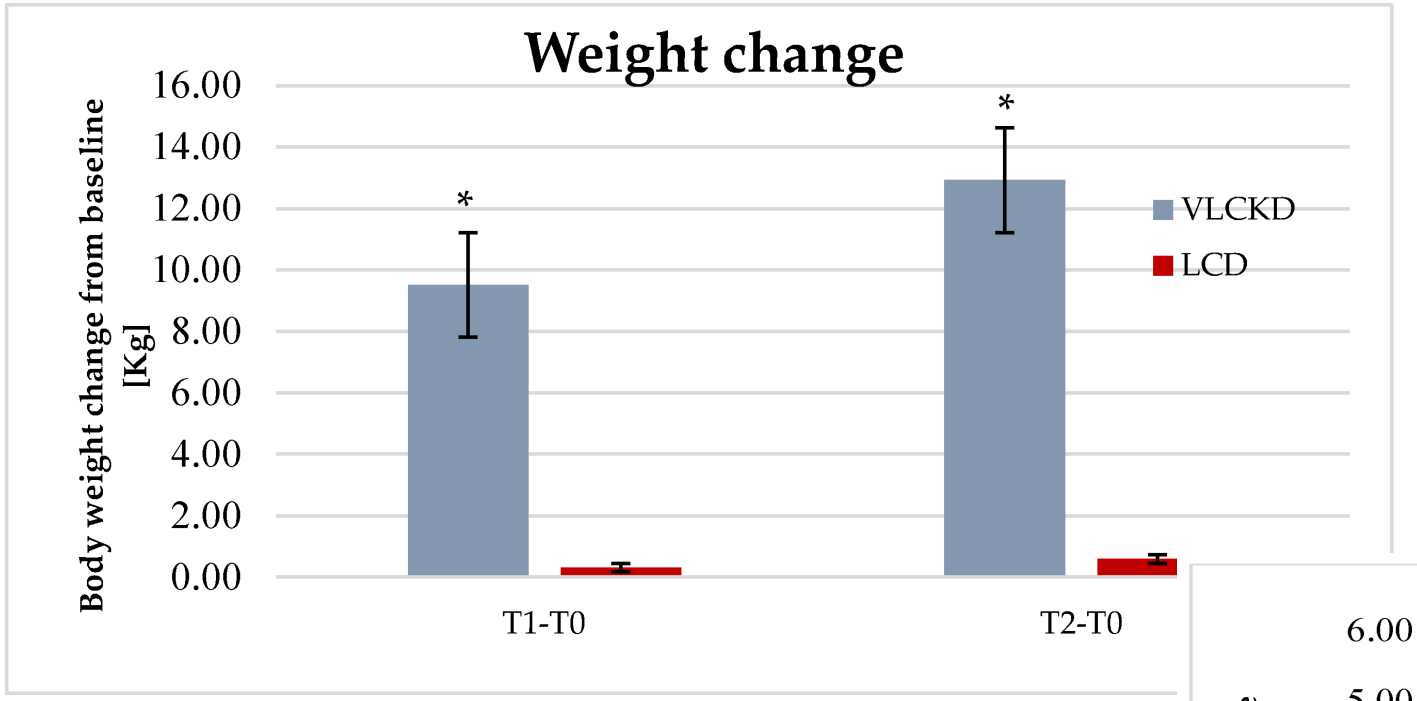


Figure 1. Mean weight loss (± SE) at T1 (3 months) and T2 (12 months) in VLCKD and LCD groups. * $p < 0.001$.

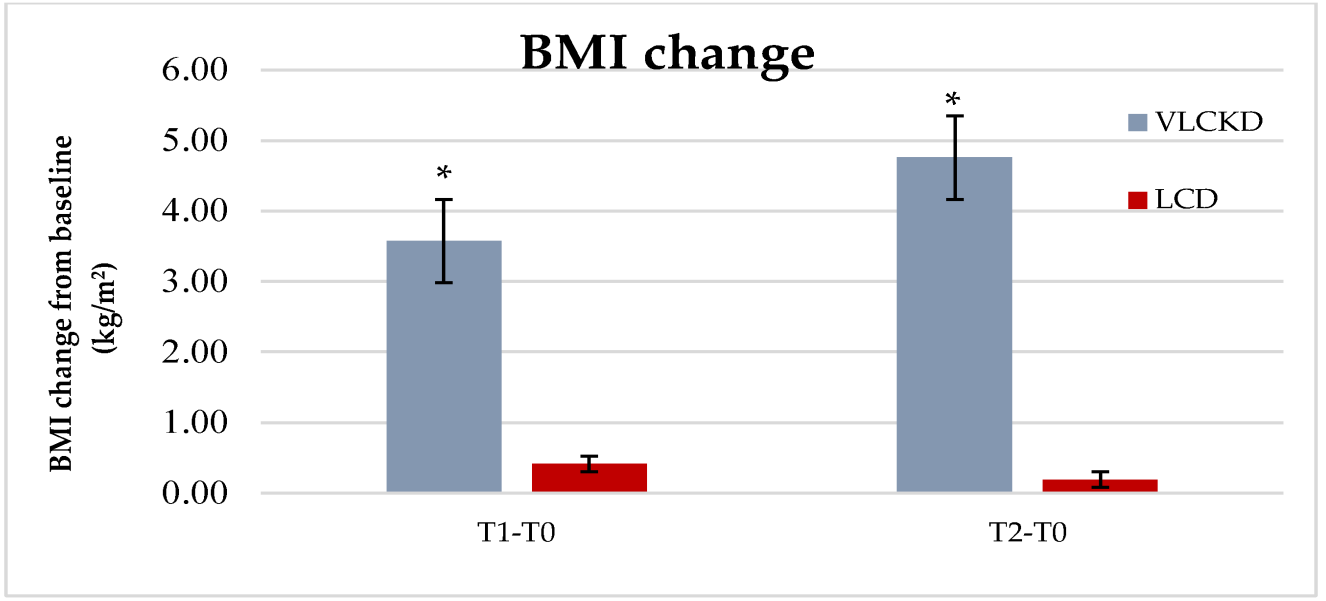
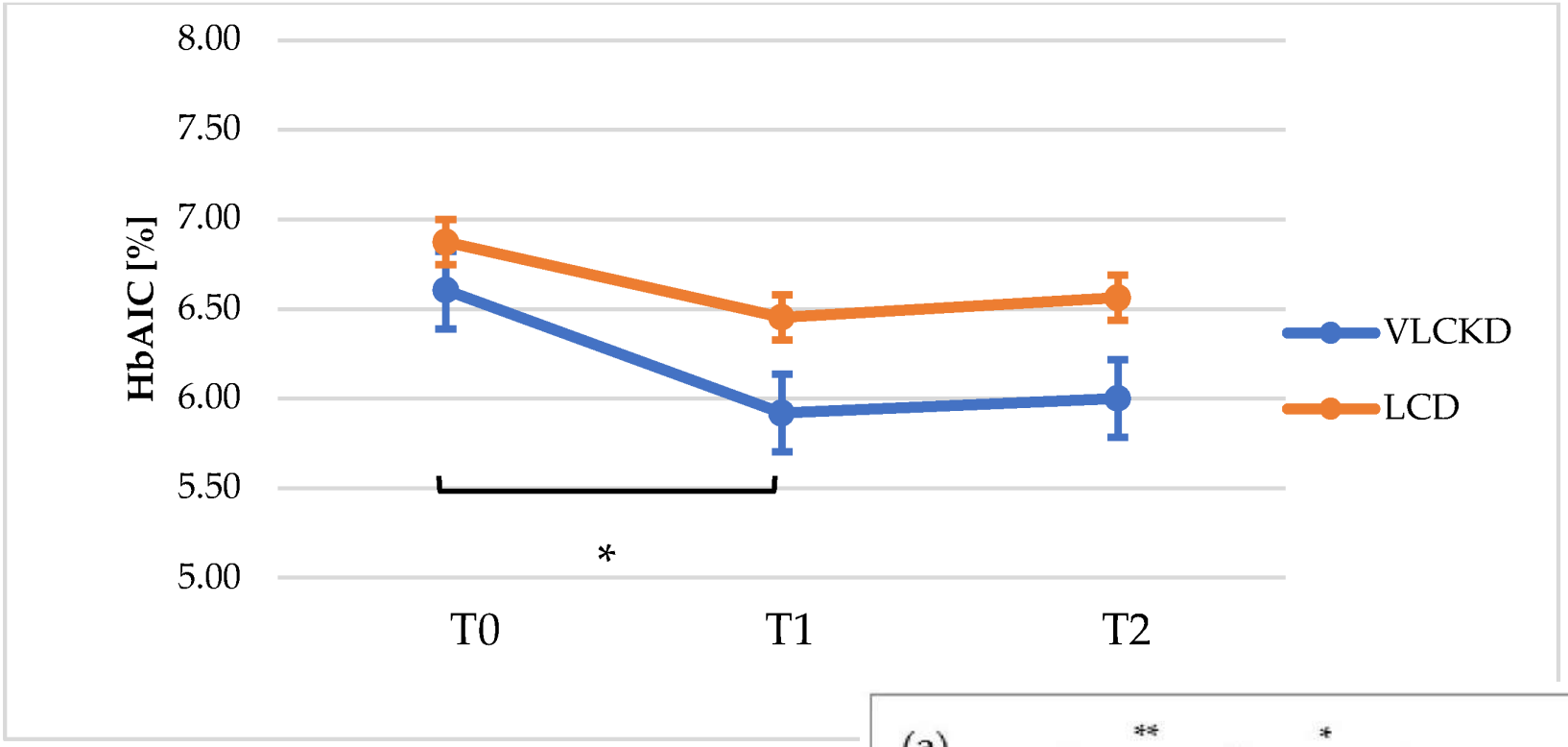
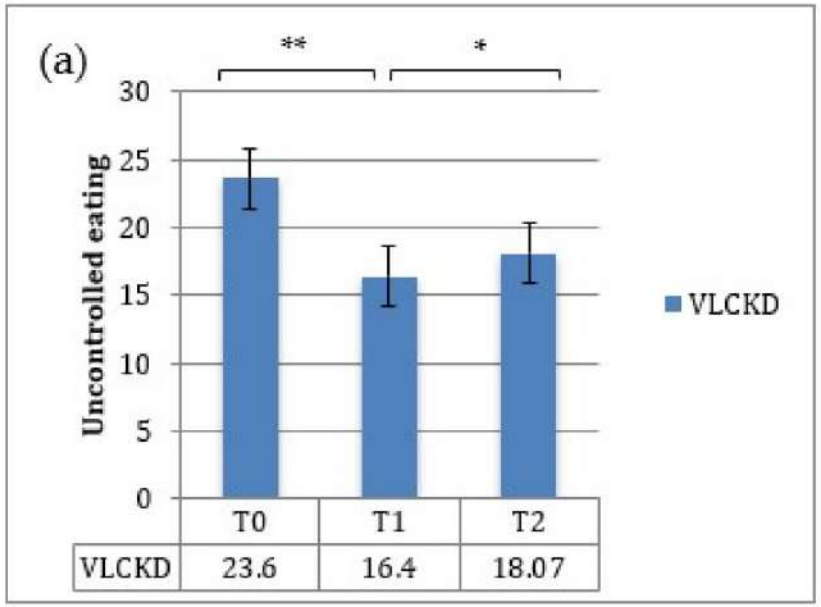


Figure 2. Mean BMI (±SE) reduction at T1 (3 months) and T2 (12 months) in VLCKD and LCD groups. * $p < 0.001$.





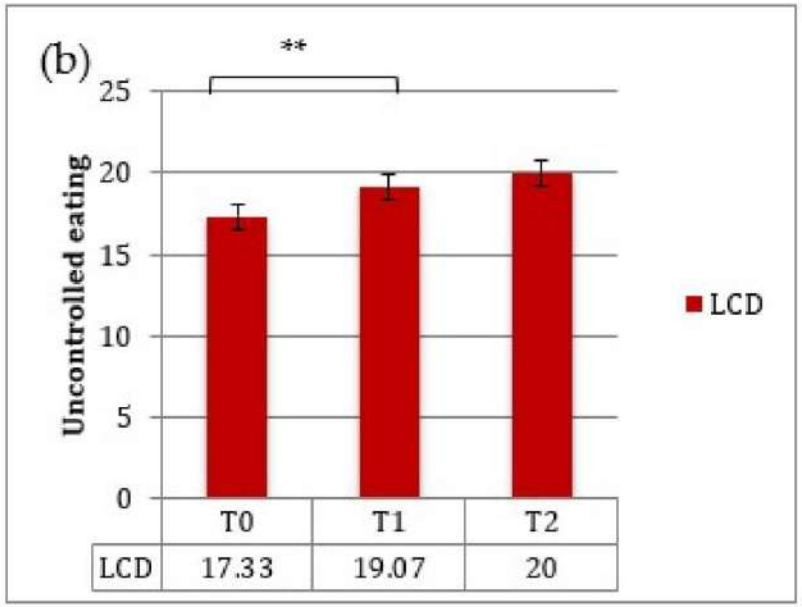


Figure 5. Mean scores (±SE) for uncontrolled eating at baseline, T1 and T2: (**a**) VLCKD group; (**b**) LCD group. * $p < 0.05$; ** $p < 0.001$.

Table 2. Characteristics and pharmacological treatment at baseline and after 12 months in VLCKD and LCD groups.

Characteristics	VLCKD		LCD	
	Baseline (T0)	After 12 Months (T2)	Baseline (T0)	After 12 months (T2)
Subjects	15		15	
Men	8		8	
Women	7		7	
Diabetes Duration (years)	2.53 ± 1.19		2.47 ± 1.36	
Pharmacological Treatment	**VLCKD**		**LCD**	
Diet	1	4	0	0
Metformin + Diet	5	11	15	8
Metformin + Sulphonylurea	2	0	0	0
Metformin + GLP-1 agonists	2	0	0	6
Metformin + SGLT2 inhibitors	3	0	0	1
Metformin + DPP4 inhibitors	2	0	0	0

Med Princ Pract. 2021;30(3):223-235.

Efficacy of Low-Carbohydrate Ketogenic Diet in the Treatment of Type 2 Diabetes

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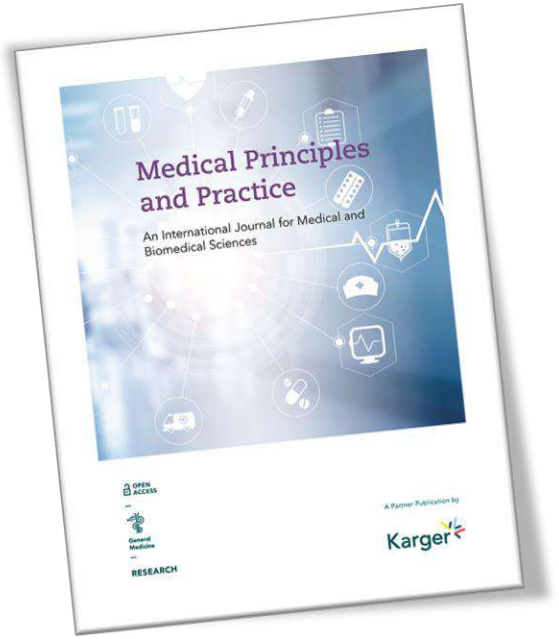


Conclusion

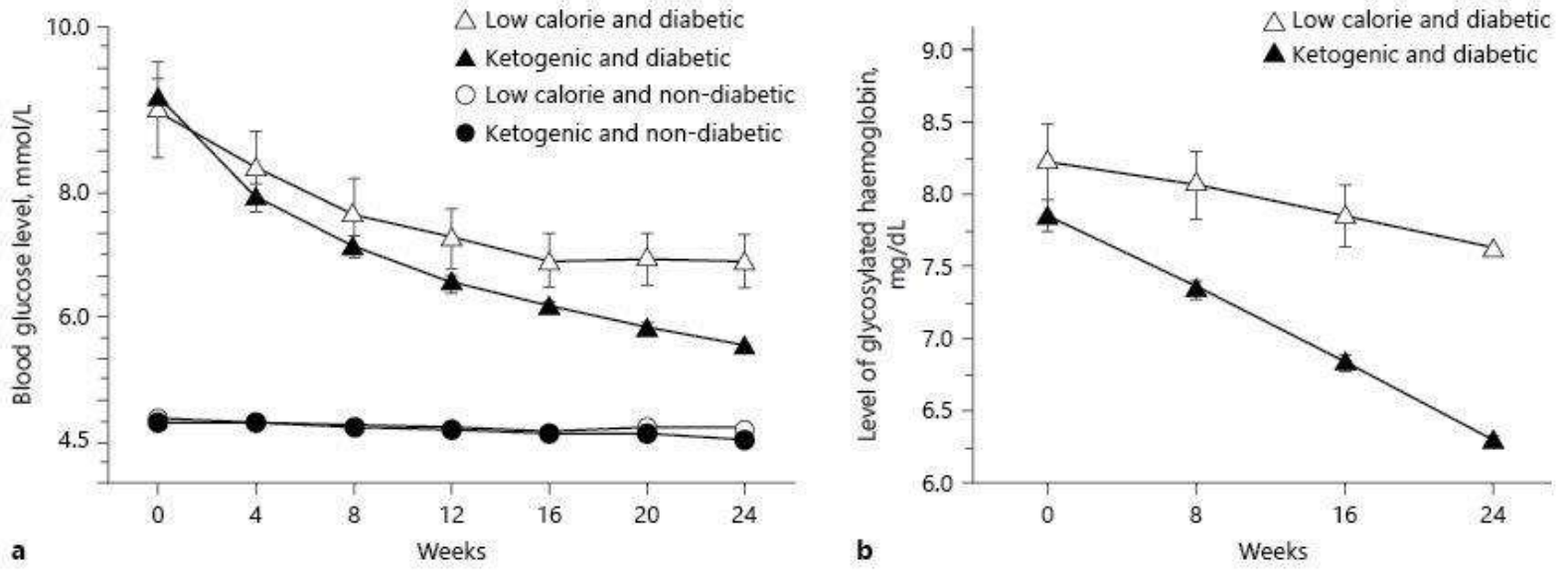
The information presented in this review shows efficacy of ketogenic diet in glycemic control in hyperlipidemic diabetic patients with type 2 diabetes. In addition to reduction in body weight and improving lipid profile, there was a significant improvement in HbA1c and reduction in the intake of insulin and oral antidiabetic drugs in patients with type 2 diabetes. Low carbohydrate shifts the body to an alternate metabolic pathway that stabilizes insulin resistance, normalizes blood glucose, glycosylated hemoglobin and hepatic, renal and plasma lipid profile in type 2 diabetic patients. Due to the significant effect of LCKD in lowering blood glucose level and contributing to the reduction of insulin and antidiabetic medication, the diabetic patients on LCKD diet should be routinely monitored to understand the optimal adjustments for insulin, antidiabetic, and diuretic medications in order to avoid hypoglycemia and dehydration complications.

Statistical significance between week 1 and week 56 observation of various parameters studied in diabetic subjects (*n* = 31)

	Week 1	Week 56	*p* value
Weight, kg	108.1+21.2	83.5+18.0	<0.0001
Glucose, mmol/L	10.5+3.0	4.9+0.6	<0.0001
Total cholesterol, mmol/L	6.8+1.1	4.9+0.5	<0.0001
Triglycerides, mmol/L	4.7+2.5	1.0+0.2	<0.0001
LDL, mmol/L	5.2+0.9	3.4+0.6	<0.0001
HDL, mmol/L	1.0+0.3	1.6+0.2	<0.0001
Urea, μmol/L	5.8+0.9	5.0+1.1	<0.0111

LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Changes in blood glucose (**a**) and glycosylated hemoglobin (**b**) level in diabetic and nondiabetic subjects after the administration of a low-calorie diet or a LCKD for 24 weeks. Black circles, ketogenic and nondiabetic; black triangles, ketogenic and diabetic; white circles, low calorie and nondiabetic; white triangles, low calorie and diabetic.
LCKD, low-carbohydrate ketogenic diet.



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Nutrients 2020, 12, 2005

Article

Impact of a Ketogenic Diet on Metabolic Parameters in Patients with Obesity or Overweight and with or without Type 2 Diabetes: A Meta-Analysis of Randomized Controlled Trials

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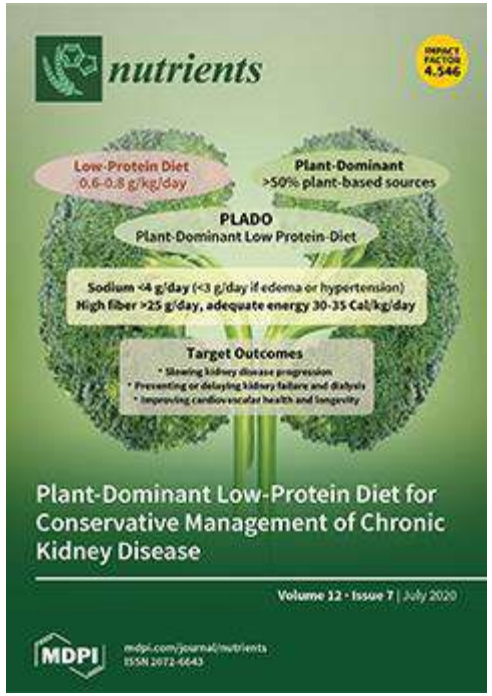


Abstract: The aim of this meta-analysis was to explore the efficacy of a ketogenic diet in metabolic control in patients with overweight or obesity and with or without type 2 diabetes. Embase, PubMed, and Cochrane Library were searched for randomized controlled trials that enrolled patients with overweight or obesity on a ketogenic diet for metabolic control. Fourteen studies were included in meta-analysis. The effects of ketogenic diets on glycemic control were greater for diabetic patients relative to those of low-fat diets, indicated by lower glycated hemoglobin (SMD, −0.62; $p < 0.001$) and homeostatic model assessment index (SMD, −0.29; $p = 0.02$), while comparable effects were observed for nondiabetic patients. Ketogenic diets led to substantial weight reduction (SMD, −0.46; $p = 0.04$) irrespective of patients' diabetes status at baseline and improved lipid profiles in terms of lower triglyceride (SMD, −0.45; $p = 0.01$) and greater high-density lipoprotein (SMD, 0.31; $p = 0.005$) for diabetic patients. Other risk markers showed no substantial between-group difference post intervention. Our study findings confirmed that ketogenic diets were more effective in improving metabolic parameters associated with glycemic, weight, and lipid controls in patients with overweight or obesity, especially those with preexisting diabetes, as compared to low-fat diets. This effect may contribute to improvements in metabolic dysfunction-related morbidity and mortality in these patient populations.

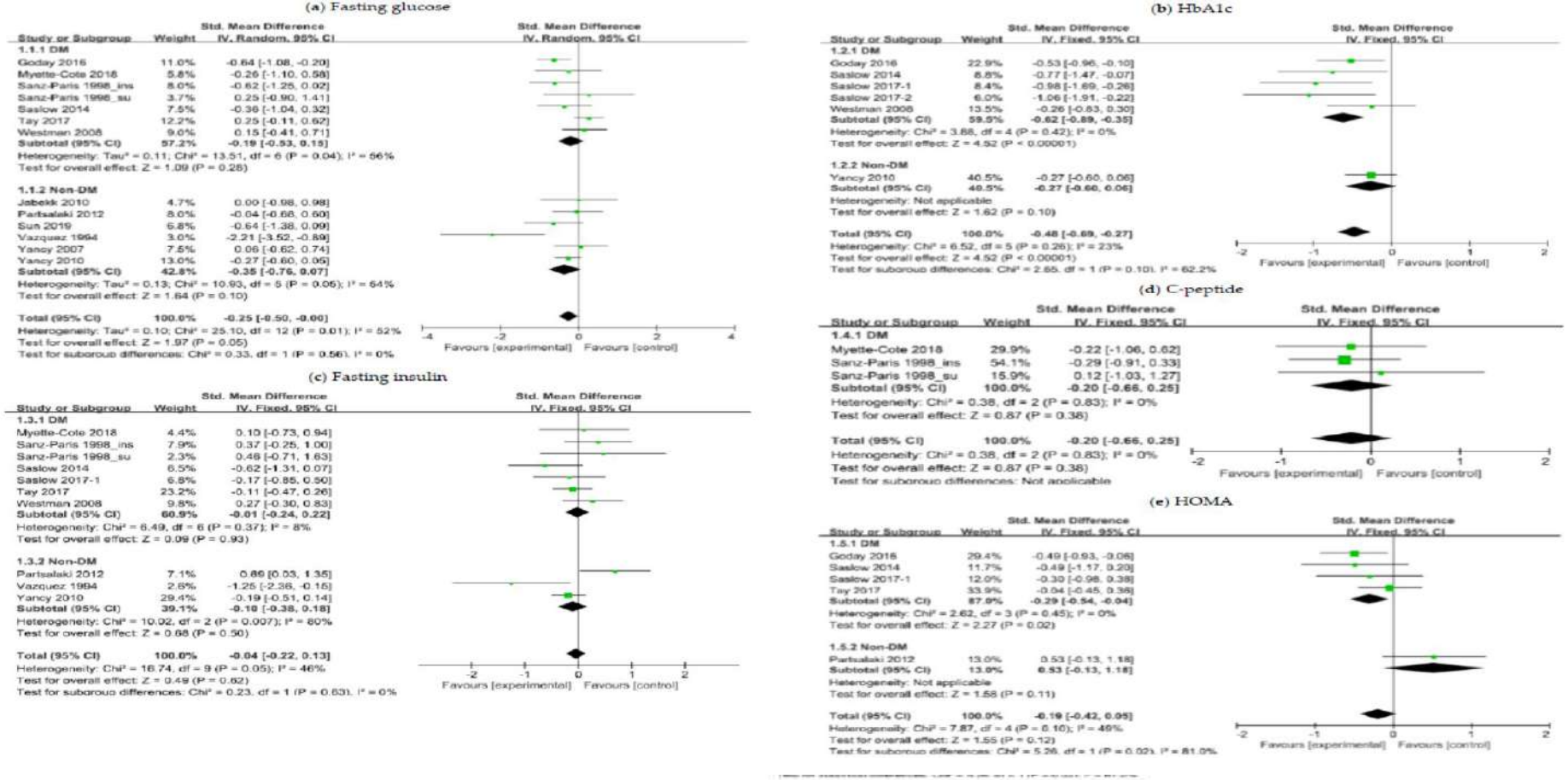
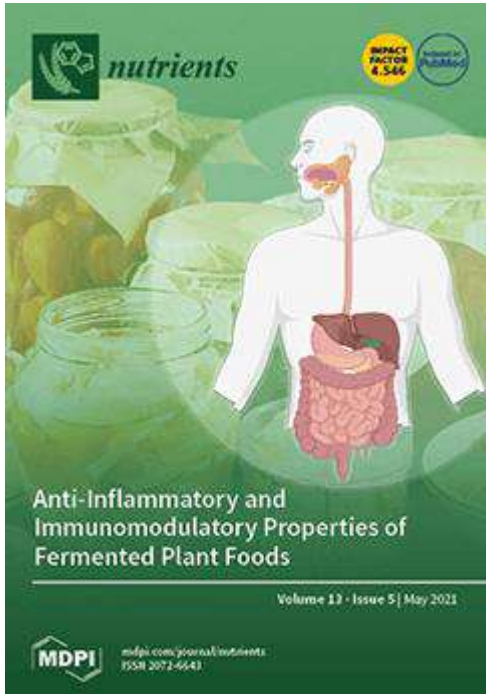


Figure 3. Forest plots for association between glycemic control and ketogenic diet in patients with overweight or obesity and with or without T2DM: (**a**) Changes in fasting glucose; (**b**) changes in HbA1c; (**c**) changes in fasting insulin; (**d**) changes in C-peptide; (**e**) changes in HOMA. Abbreviations: CI, confidence interval; DM, diabetes mellitus; Non-DM, non-diabetes mellitus; HbA1c, glycated hemoglobin; HOMA, homeostatic model assessment; T2DM, type 2 diabetes mellitus.

Conclusions

A ketogenic diet was more effective in improving weight control and metabolic parameters related to glycemic and lipid controls in patients with overweight or obesity, especially those with preexisting T2DM, as compared to low-fat based comparator diets. Its effects on other risk markers, such as blood pressure, CRP and SCr were comparable to those of low-fat diets. Further studies are warranted to determine the long-term sustainability of a ketogenic diet and its effects on the more clinically important endpoints such as obesity-related morbidity and mortality



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Article

Reduction of Cardio-Metabolic Risk and Body Weight through a Multiphasic Very-Low Calorie Ketogenic Diet Program in Women with Overweight/Obesity: A Study in a Real-World Setting

Elena Tragni [1], Luisella Vigna [2], Massimiliano Ruscica [1], Chiara Macchi [1], Manuela Casula [1,3], Alfonso Santelia [1], Alberico L. Catapano [1,3] and Paolo Magni [1,3,*]

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Abstract: Background: The prevention and treatment of obesity and its cardio-metabolic complications are relevant issues worldwide. Among lifestyle approaches, very low-calorie ketogenic diets (VLCKD) have been shown to lead to rapid initial weight loss, resulting in better long-term weight loss maintenance. As no information on VLCKD studies carried on in a real-world setting are available, we conducted this multi-centre study in a real-world setting, aiming at assessing the efficacy and the safety of a specific multiphasic VLCKD program in women with overweight or obesity. Methods: A multi-center, prospective, uncontrolled trial was conducted in 33 outpatient women (age range 27–60 y) with overweight or obesity (BMI: 30.9 ± 2.7 kg/m^2; waist circumference: 96.0 ± 9.4 cm) who started a VLCKD dietary program (duration: 24 weeks), divided into four phases. The efficacy of VLCKD was assessed by evaluating anthropometric measures and cardiometabolic markers; liver and kidney function biomarkers were assessed as safety parameters. Results: The VLCKD program resulted in a significant decrease of body weight and BMI (−14.6%) and waist circumference (−12.4%). At the end of the protocol, 33.3% of the participants reached a normal weight and the subjects in the obesity range were reduced from 70% to 16.7%. HOMA-IR was markedly reduced from 3.17 ± 2.67 to 1.73 ± 1.23 already after phase 2 and was unchanged thereafter. Systolic blood pressure decreased after phase 1 (−3.5 mmHg) and remained unchanged until the end of the program. Total and LDL cholesterol and triglycerides were significantly reduced by VLCKD along with a significant HDL cholesterol increase. Liver, kidney and thyroid function markers did not change and remained within the reference range. Conclusions: The findings of a multi-center VLCKD program conducted in a real-world setting in a cohort of overweight/obese women indicate that it is safe and effective, as it results in a major improvement of cardiometabolic parameters, thus leading to benefits that span well beyond the mere body weight/adiposity reduction.

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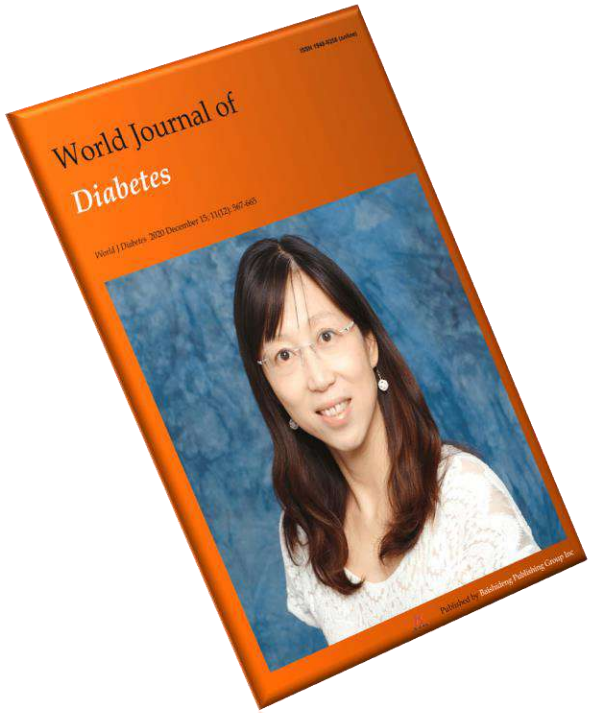
MINIREVIEWS

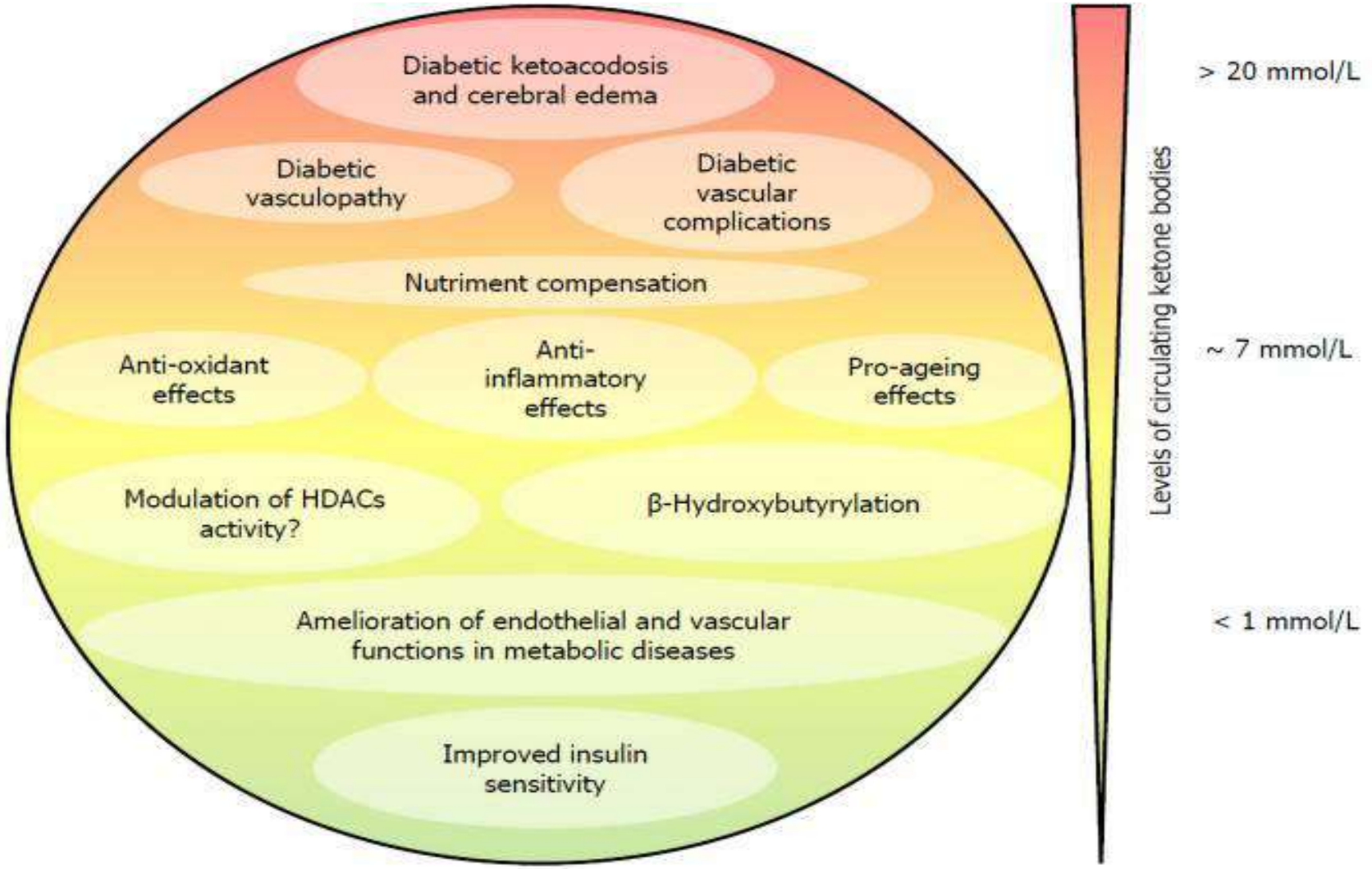
Effects of ketogenic diet and ketone bodies on the cardiovascular system: Concentration matters

Souad Nasser, Varvara Vialichka, Marta Biesiekierska, Aneta Balcerczyk, Luciano Pirola



Abstract

Ketone bodies have emerged as central mediators of metabolic health, and multiple beneficial effects of a ketogenic diet, impacting metabolism, neuronal pathologies and, to a certain extent, tumorigenesis, have been reported both in animal models and clinical research. Ketone bodies, endogenously produced by the liver, act pleiotropically as metabolic intermediates, signaling molecules, and epigenetic modifiers. The endothelium and the vascular system are central regulators of the organism's metabolic state and become dysfunctional in cardiovascular disease, atherosclerosis, and diabetic micro- and macrovascular complications. As physiological circulating ketone bodies can attain millimolar concentrations, the endothelium is the first-line cell lineage exposed to them. While in diabetic ketoacidosis high ketone body concentrations are detrimental to the vasculature, recent research revealed that ketone bodies in the low millimolar range may exert beneficial effects on endothelial cell (EC) functioning by modulating the EC inflammatory status, senescence, and metabolism. Here, we review the long-held evidence of detrimental cardiovascular effects of ketoacidosis as well as the more recent evidence for a positive impact of ketone bodies—at lower concentrations—on the ECs metabolism and vascular physiology and the subjacent cellular and molecular mechanisms. We also explore arising controversies in the field and discuss the importance of ketone body concentrations in relation to their effects. At low concentration, endogenously produced ketone bodies upon uptake of a ketogenic diet or supplemented ketone bodies (or their precursors) may prove beneficial to ameliorate endothelial function and, consequently, pathologies in which endothelial damage occurs.



Concentration dependency of the biochemical and physiological responses to ketone bodies. Low to medium concentrations of ketone bodies, attained through fasting, ketogenic diet, or physical effort, convey physiologically beneficial effects. Conversely, pathological ketone body concentrations, observed in diabetic ketoacidosis, contribute to the disease morbidity and can be life threatening. HDACs: Histone deacetylases.

Journal of Endocrinological Investigation
https://doi.org/10.1007/s40618-019-01061-2

CONSENSUS STATEMENT

Very-low-calorie ketogenic diet (VLCKD) in the management of metabolic diseases: systematic review and consensus statement from the Italian Society of Endocrinology (SIE)

M. Caprio[1,2] · M. Infante[3] · E. Moriconi[1,4] · A. Armani[1] · A. Fabbri[3] · G. Mantovani[5] · S. Mariani[4] · C. Lubrano[4] · E. Poggiogalle[4] · S. Migliaccio[6] · L. M. Donini[4] · S. Basciani[4] · A. Cignarelli[7] · E. Conte[7] · G. Ceccarini[8] · F. Bogazzi[9] · L. Cimino[10] · R. A. Condorelli[10] · S. La Vignera[10] · A. E. Calogero[10] · A. Gambineri[11] · L. Vignozzi[12] · F. Prodam[13] · G. Aimaretti[13] · G. Linsalata[14] · S. Buralli[14] · F. Monzani[14] · A. Aversa[15] · R. Vettor[16] · F. Santini[8] · P. Vitti[9] · L. Gnessi[4] · U. Pagotto[11] · F. Giorgino[7] · A. Colao[17] · A. Lenzi[4] on behalf of the Cardiovascular Endocrinology Club of the Italian Society of Endocrinology

2019 May 20

Table 1 Parameters that need to be monitored before, during and at the end of a VLCKD regimen

Parameters	Frequency of monitoring	Rationale of monitoring
Complete blood count	At baseline and at the end of the VLCKD program	To exclude patients with severe alterations of blood count
Creatinine, BUN, uric acid (serum)	At baseline and during the ketogenic phase	Monitoring of kidney function and potential increase in uric acid
Glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides (serum)	At baseline and at the end of the VLCKD program	Excluding patients with uncontrolled diabetes, monitoring of lipid profile
ALT, AST, γ-GT, total and direct bilirubin (serum)	At baseline, during the ketogenic phase and at the end of the VLCKD program	Monitoring of liver function and cholestatic parameters
Sodium, potassium, calcium, magnesium, inorganic phosphate (serum)	At baseline, during the ketogenic phase and at the end of the VLCKD program	Monitoring for potential dehydration and electrolyte abnormalities
β-Hydroxybutyrate (capillary blood or urine)	During the ketogenic phase	Monitoring of ketosis
TSH, FT4 (serum)	At baseline	To exclude thyroid function abnormalities
25-Hydroxyvitamin D (serum)	At baseline	To treat vitamin D deficiency, if present
Complete urinalysis and microalbuminuria (urine)	At baseline, during the ketogenic phase and at the end of the VLCKD program	To exclude any potential kidney damage
Body composition and hydration status (by bioelectrical impedance analysis)	At baseline, during the ketogenic phase and at the end of the VLCKD program	Monitoring of body composition (fat mass, fat-free mass, body cell mass, total body water, extracellular water)

ALT alanine aminotransferase, *AST* aspartate aminotransferase, *BUN* blood urea nitrogen, *FT4* free thyroxine, *γ-GT* gamma-glutamyl transferase, *HDL-cholesterol* high-density lipoprotein cholesterol, *LDL* cholesterol, low-density lipoprotein cholesterol, *TSH* thyroid-stimulating hormone, *VLCKD* very-low-calorie ketogenic diet

Table 2 Indications for the use of VLCKD in metabolic diseases

Strong recommendations	Strength of recommendations and quality of evidence according to GRADE system
Severe obesity	(1 ØØØO)
Management of severe obesity before bariatric surgery	(1 ØØØO)
Sarcopenic obesity	(1 ØØØO)
Obesity associated with type 2 diabetes (preserved beta cell function)	(1 ØØØO)
Obesity associated with hypertriglyceridemia	(1 ØØØO)
Obesity associated with hypertension	(1 ØØØO)
Pediatric obesity associated with epilepsy and/or with a high level of insulin resistance and/or comorbidities, not responsive to standardized diet	(1 ØØØO)
Weak recommendations	
Obesity associated with dysbiosis of the gut microbiota	(2 ØØØO)
Obesity associated with high levels of LDL-cholesterol and/or low levels of HDL-cholesterol	(2 ØØØO)
Obesity associated with non-alcoholic fatty liver disease (NAFLD)	(2 ØØØO)
Obesity associated with heart failure (NYHA I–II)	(2 ØOOO)
Obesity associated with atherosclerosis	(2 ØOOO)
Male obesity secondary hypogonadism	(2 ØØØO)
Obesity associated with polycystic ovary syndrome (PCOS)	(2 ØOOO)
Menopausal transition-related obesity	(2 ØOOO)
Neurodegenerative disorders associated with sarcopenic obesity	(2 ØOOO)

Table 3 Absolute contraindications to the use of VLCKD

Absolute contraindications
Type 1 diabetes mellitus, latent autoimmune diabetes in adults, β-cell failure in type 2 diabetes mellitus, use of sodium/glucose cotransporter 2 (SGLT2) inhibitors (risk for euglycemic diabetic ketoacidosis)
Pregnancy and breastfeeding
Kidney failure and moderate-to-severe chronic kidney disease, liver failure, hearth failure (NYHA III-IV), respiratory failure
Unstable angina, recent stroke or myocardial infarction (< 12 months), cardiac arrhythmias
Eating disorders and other severe mental illnesses, alcohol and substance abuse
Active/severe infections
Frail elderly patients
48 h prior to elective surgery or invasive procedures and perioperative period
Rare disorders: porphyria, carnitine deficiency, carnitine palmitoyltransferase deficiency, carnitine-acylcarnitine translocase deficiency, mitochondrial fatty acid β-oxidation disorders, pyruvate carboxylase deficiency

VLCKD, insulin resistance and type 2 diabetes

Recommendations

- VLCKD should be considered to obtain an early efficacy on glycemic control, particularly in obese patients with short duration of the disease (1 ØØØO).
- VLCKD should be considered to reduce the use of glucose-lowering agents, including insulin (1 ØØØO).

Evidence

In obese non-diabetic patients, the effect of VLCKD is powerful in reducing plasma insulin levels; consequently, HOMA-IR and HOMA-beta, which represent markers of insulin resistance and beta-cell function, respectively, display significant improvements after this type of dietetic intervention [97, 98]. Of relevance, an important benefit of VLCKD to improve insulin resistance is evident in youth obesity [99–102].

In obese patients with T2D, exposure to VLCKD for 1 week resulted in a significant improvement of beta-cell function not fully explained by the marginal weight loss achieved. The reduction in carbohydrate intake was associated with an early and significant decrease in hepatic triacylglycerol content; consequently, higher suppression of hepatic glucose production was observed as a consequence of improved hepatic insulin sensitivity [103]. Higher hepatic insulin sensitivity was also associated with lower fasting plasma glucose and plasma insulin levels. However, changes in peripheral insulin sensitivity only partly explain the effects of VLCKD in the short term [104]. On the other hand, a remarkable increase in skeletal muscle glucose uptake was observed only after a significant weight loss, which requires longer exposure to VLCKD regimen and follow-up [105]. An enhanced insulin response to arginine—an index of beta-cell function—has also been observed after a short period of VLCKD [103]. Specifically, after 1 week of VLCKD, obese patients with T2D in good glycemic control displayed a recovery of the acute insulin response assessed during hyperglycemic clamp, as well as of the second phase of insulin secretion [104]. VLCKD leads to recovery of the first phase of insulin secretion in 40% of participants at the end of a longer program (8 weeks) involving a heterogeneous group of patients with T2D [106]. Moreover, a higher disposition index was also observed [104]. Interestingly, VLCKD has been demonstrated to be as effective as the Roux-en-Y gastric bypass on insulin sensitivity and beta-cell function in patients with T2D in the short term [107].

Remarks

Current studies provide information mostly on short-term follow-up with VLCKD, albeit persistent lower fasting plasma glucose and HbA1c are observed even after 18 months of intervention [112]. Potential effects of VLCKD on long-lasting metabolic memory should also be adequately investigated. Finally, VLCKD promotes a metabolic improvement beyond the extent of weight loss; therefore, it should be considered in lifestyle intervention programs in patients with obesity and T2D.

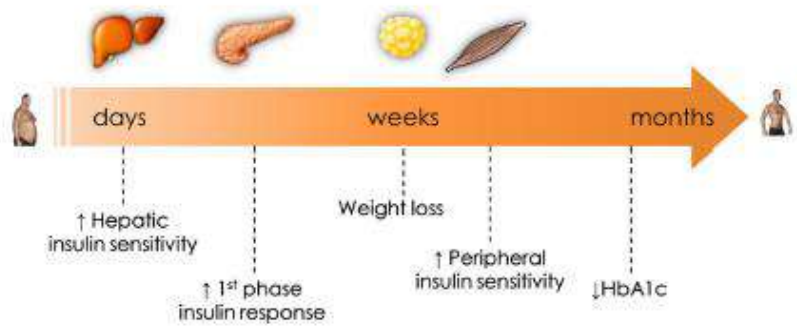


Fig. 2 Effects of VLCKD on glucose homeostasis and metabolic parameters in obese subjects with or without type 2 diabetes

Conclusions and perspectives

Despite the short- and middle-term benefits of VLCKD in terms of weight loss and reduction in cardiovascular risk factors are widely documented [18, 19, 23, 34], some concerns exist about its use in the long-term period due to the paucity of studies. Long-term studies are indeed needed to explore the potential benefit of VLCKD on specific endpoints such as cardiovascular and neurodegenerative diseases. A few studies have previously demonstrated that VLCKD is safe and effective in the long term [17, 20, 54, 55], although there is need for additional clinical trials. Major difficulties in planning such studies may depend on the poor adherence to a highly restrictive dietary regimen over a long-term period. However, VLCKD is a highly effective therapeutic tool in patients who need a rapid weight loss over a short-term period, such as individuals with moderate to severe obesity and cardiovascular risk factors. The potential of VLCKD in determining remission of T2D, particularly in obese patients with short disease duration [103], should be also taken into consideration. Once an ideal body weight is achieved, VLCKD should be necessarily followed by a long-term multifactorial strategy aimed at weight-loss maintenance, highlighting the importance of a comprehensive program of lifestyle modification which includes behavior therapy, nutritional counseling and physical activity [12, 14, 37], along with specific protocols for reintroduction of carbohydrates.

One of the open questions is related to the ideal duration and frequency of use of VLCKDs. In the past, the use of VLCKDs without proper medical supervision generated therapeutic failures and side effects that led to their default for many years. It should be emphasized that the use of VLCKD requires a clear clinical indication under strict medical supervision. If the results are unsatisfactory or a new cycle of VLCKD is needed, it is mandatory to investigate the causes of the previous failure. Furthermore, it is likely that specific protocols for VLCKD implementation will need to be defined according to the specific hols of nutritional therapy, characteristics of the patients, and clinical setting.

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The dark side of the spoon - glucose, ketones and COVID-19: a possible role for ketogenic diet?

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Abstract

The novel coronavirus disease (COVID-19) is posing a serious challenge to the health-care systems worldwide, with an enormous impact on health conditions and loss of lives. Notably, obesity and its related comorbidities are strictly related with worse clinical outcomes of COVID-19 disease. Recently, there is a growing interest in the clinical use of ketogenic diets (KDs), particularly in the context of severe obesity with related metabolic complications. KDs have been proven effective for a rapid reduction of fat mass, preserving lean mass and providing an adequate nutritional status. In particular, the physiological increase in plasma levels of ketone bodies exerts important anti-inflammatory and immunomodulating effects, which may reveal as precious tools to prevent infection and potential adverse outcomes of COVID-19 disease. We discuss here the importance of KDs for a rapid reduction of several critical risk factors for COVID-19, such as obesity, type 2 diabetes and hypertension, based on the known effects of ketone bodies on inflammation, immunity, metabolic profile and cardiovascular function. We do believe that a rapid reduction of all modifiable risk factors, especially obesity with its metabolic complications, should be a pillar of public health policies and interventions, in view of future waves of SARS-CoV-2 infection.

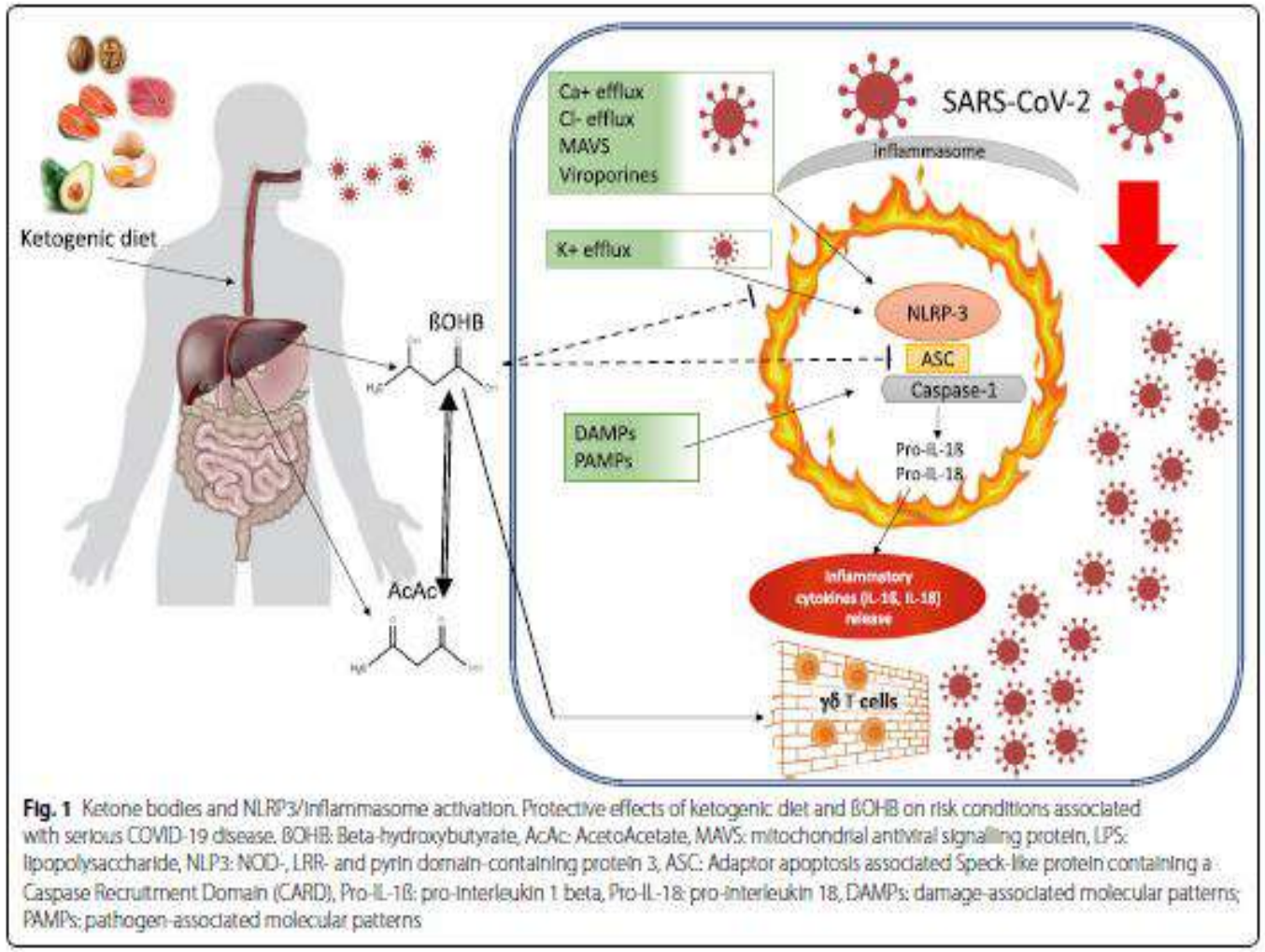


Fig. 1 Ketone bodies and NLRP3/inflammasome activation. Protective effects of ketogenic diet and ßOHB on risk conditions associated with serious COVID-19 disease. BOHB: Beta-hydroxybutyrate, AcAc: AcetoAcetate, MAVS: mitochondrial antiviral signalling protein, LPS: lipopolysaccharide, NLP3: NOD-, LRR- and pyrin domain-containing protein 3, ASC: Adaptor apoptosis associated Speck-like protein containing a Caspase Recruitment Domain (CARD), Pro-IL-1ß: pro-interleukin 1 beta, Pro-IL-18: pro-interleukin 18, DAMPs: damage-associated molecular patterns; PAMPs: pathogen-associated molecular patterns

Conclusions

There are multiple mechanisms through which ketone bodies might impact severe viral infections such as COVID-19 disease. A recent review article exhaustively summarizes this concept, proposing the administration of exogenous ketones to critical patients in order to target respiratory viruses complications as a possible therapy [74].

We believe that KD-induced increase in endogenous ketone bodies could represent a more valuable strategy to prevent Sars-Cov2 infection and adverse outcomes in obese patients, particularly in the current context of a prolonged pandemic emergency. Indeed, prevention and/or correction of all risk conditions associated with serious COVID-19 disease (obesity, hyperglycemia, high glycemic variability, insulin resistance, hypertension) is mandatory, in consideration of new waves of infections, in the absence of effective pharmacological therapies and vaccination. This could be obtained with a nutritional strategy aimed to induce fat mass loss, to reduce chronic inflammation, hepatic and systemic insulin resistance, and to improve nutritional status, cardiovascular health, immune response, glucose homeostasis and blood pressure control.

Finally, the adoption of a well-structured and personalized KD regimen could help a progressive nutritional education and rehabilitation in obese patients, providing an effective tool to modify lifestyle behavior, supporting a long-term control of body weight, and favoring a reduction in all associated risk factors for potentially severe complications related to Sars-Cov2 infection. Well-designed multicentric studies on the actual incidence of severe COVID-19 disease among obese patients who followed or not a structured protocol of KD, could be helpful to confirm such hypothesis.

During this difficult pandemic era, the adoption of lifestyle preventive measures is mandatory, and should be carefully implemented.

22° Congresso Nazionale AMD
27/30 Novembre 2019
PADOVA FIERE

Esperienze cliniche

EFFICACIA DELLA DIETA CHETOGENICA IN PAZIENTI AFFETTI DA OBESITA' ASSOCIATA A COMORBILITA': CASE REPORT

CRISTOFARO M. , MAZZOLA E.
SC ENDOCRINOLOGIA-DIABETOLOGIA
P .O. «A CARDARELLI» CAMPOBASSO

Tra tutti gli accessi del nostro ambulatorio per l'Obesità del mese di Giugno 2019, abbiamo selezionato 4 pazienti da trattare con VLCKD con le seguenti caratteristiche

Pz 1: *Maschio di 46 anni affetto da obesità di 2° grado associata a dislipidemia combinata,epastosteatosi e ipertensione arteriosa*

Pz 2: *Femmina di 54 anni affetta da Obesità di 3° associata a Diabete Mellito tipo 2, sindrome delle apnee notturne,dislipidemia e ipentensione arteriosa*

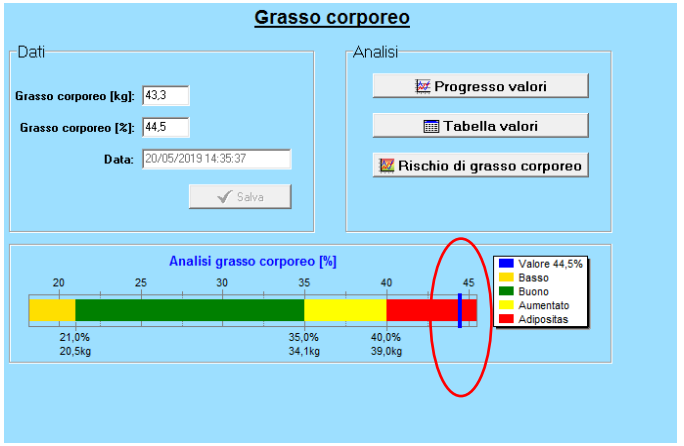
Pz 3: *Femmina di 38 anni con obesità di 2° grado , associata a diabete mellito tipo 2, dislipidemia, epatosteatosi e ipertensione arteriosa*

Pz 4: *femmina di 26 anni con sovrappeso, associato a policistosi ovarica ed insulino-resistenza*

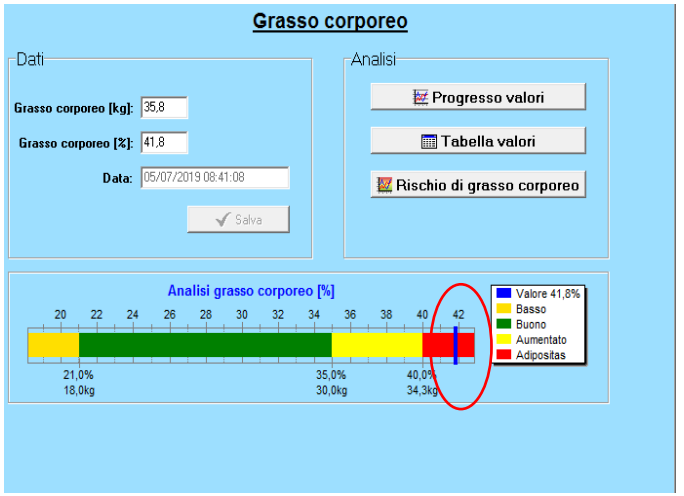
Alla visita iniziale tutti i pazienti hanno effettuato rilevazione misure antropometriche, esame della composizione corporea con apparecchio TANITA MC-180MA,
ed esami di laboratorio.
I parametri descritti sono stati poi rivalutati dopo
dopo 2 mesi (in corso di Dieta VLCKD)e dopo 3 mesi (a fine percorso)

In tutti i pazienti trattati con VLCKD abbiamo osservato una importante perdita di peso (15-20kg) con modificazioni significative della composizione corporea e una riduzione Dell'HOMA INDEX nella paziente con policistosi

Esempio modifiche della composizione corporea della Pz 3



44,5 %



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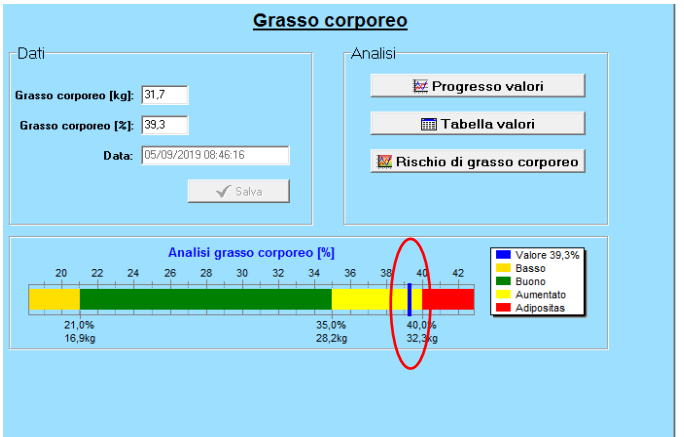

39,3 %

TAKE HOME MESSAGE

- La VLCKD può essere considerata una valida opzione terapeutica per il trattamento dell'obesità e delle comorbilità associate
- E' fondamentale che il paziente sia seguito durante la chetosi e nelle fasi successive da un team multidisciplinare
- Sono necessari ulteriori studi clinici a lungo termine per consolidare i benefici significativi che la VLCKD ha evidenziato in letteratura e nella real life

Grazie per l'attenzione !