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Rationale, Feasibility and Acceptability of Ketogenic Diet for Cancer Treatment

REVIEW

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Ketogenic diet has been used for more than 80 years as a successful dietary regimen for epilepsy. Recently, dietary modulation by carbohydrate depletion via ketogenic diet has been suggested as an important therapeutic strategy to selectively kill cancer cells and as adjuvant therapy for cancer treatment. However, some researchers insist ketogenic diet to be highly undesirable as ketogenic diet may trigger and/or exacerbate cachexia development and usually result in significant weight loss. This review revisits the meaning of physiological ketosis in the light of this evidence and considers possibility of the use of ketogenic diet for oncology patients. Article search was performed from 1985 through 2017 and finally 10 articles were analyzed. The review focused on the results of human trials for cancer patients and checked the feasibility of using ketogenic diet for cancer patients as adjuvant therapy. The main outcomes showed improvement of body weight changes, anthropometric changes, serum blood profiles, and reduction in novel marker for tumor progression, TKTL1, and increase of ketone body. Lactate concentration was reduced, and no significant changes were reported in the measurements of quality of life. Ketogenic diet may be efficacious in certain cancer subtypes whose outcomes appear to correlate with metabolic status, but the results are not yet supportive and inconsistent. Therefore, it warrants further studies.
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Key Words: Ketogenic diet, Neoplasms, High-fat diet, Ketosis

INTRODUCTION

Diet and exercise interventions in cancer patients may be of benefit for ameliorating adverse events during cancer treatment and may increase overall survival.[1-3] Metabolic processes in cancer are complex and highly regulated, and there is increasing evidence that dietary modulation can be efficacious in managing cancer, i.e., diet rich in fat and protein[4] or calorie restriction.[5,6] Calorie restriction has been shown to reduce the pro-growth signaling, partially achieved by temporarily reducing glucose and circulating insulin-like growth factor 1, which is highly associated with aging and cancer.[7] Also, manipulation of the molecular pathways using calorie restriction has been shown to render cancer cells susceptible to standard cytotoxic treatment with radiation and chemotherapy especially strong for breast cancer. However, considering the high drop-out rate (25%), this indicates that adherence to this low-calorie diet requires high commitment to the study participants.

Ketogenic diet is designed specifically to result in ketosis and is emerging as a metabolic therapy for treating cancer. The mechanism can be explained by inducing shortage of glucose and/or lactate for tumor cells to survive. Vander Heiden et al.[8] observed that tumors take up enormous amounts of glucose compared to the surrounding tissue and eventually produces lactate through aerobic glycolytic pathway. Therefore, limitation of glucose availability in cancer cell may reduce energy production of cancer cells, and thereby decreasing tumor proliferation.[9]

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The aim of this review is to assess the clinical evidence of ketogenic diet intervention in cancer patients by analyzing human trials.

STUDY SEARCH AND SELECTION

1. Literature search

The eligible literatures were retrieved by searching through databases (PubMed, MEDLINE, and Springer link) from 1985 until July, 2017. Searching keywords included "ketogenic diet" or "ketone", "cancer" or "tumor", and "oncology" with no language restriction and was limited to human clinical trials.

2. Inclusion and exclusion criteria

Articles were included under the following criteria: (1) randomized clinical trials with/without control, (2) prospective cohort study, (3) adult population, and (4) ketone diet composition mentioned. The exclusion criteria were as follows: (1) articles with incomplete data, (2) case studies, and (3) reviews. Letters or comments were irrespective.

3. Data extraction

After the completion of article screening, two investigators independently extracted the data from the eligible studies according to the predesigned protocol. The extracted information was summarized by the first author's name, journal name, publication year, geographical area of study population, mean age of the participants, sample size of the intervention and control groups, detailed dietary regimen and the length of the study, adherence rate, outcome measures, and results of each article, and finally reported side effects.

ELIGIBLE STUDIES

The process of search strategy is presented in Figure 1. The original search yielded a total of 468 citations (limited to clinical trials, human studies, and years from 1985-2017). First, there were 63 articles after removing the duplicates. Then, 47 articles were excluded because of obvious irrelevance after screening the title and abstract. Six among the remained 16 articles were removed after full-text review: 2 for case studies; 4 without available data. Finally, 10 articles were included in this review. The recommendation of the Cochrane Effective Practice and Organization of Care Review systematic review and meta-analyses, randomized controlled studies, and non-randomized controlled studies were included.[10]

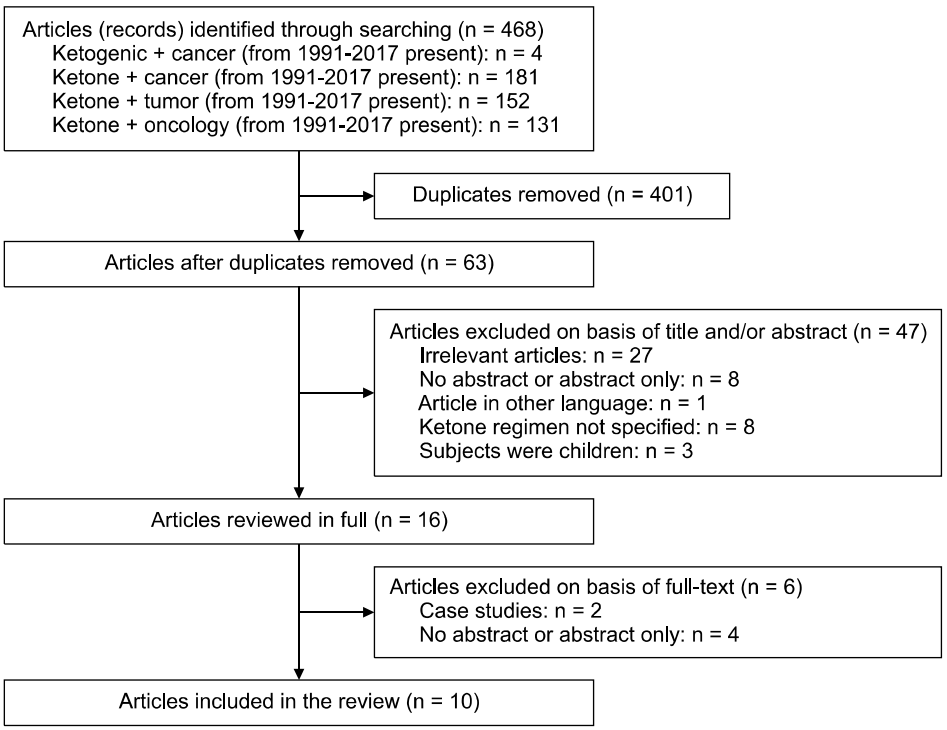

Figure 1. Flowchart of study search and selection.

Table 1. Clinical trials (including prospective cohort study) using KD in cancer patients

Author (journal and year)	No. of subjects and characteristics	Cancer type	KD intervention (duration and regimen)	Adherence	Outcome measures and results	Side effect
Fearon et al.[11] (Am J Clin Nutr 1988)	Total n = 5 Cachectic patients (mean age, 61 yr) Country: Italy	2 Gastric cancer 2 Lung cancer 1 Ovarian cancer	6 days balanced enteral formula (BD) → 7 days KD enteral formula (KD) BD: kcal: 44 kcal/kg/d prot: 1.5 g/kg/d (55% carbohydrate, 31% fat) KD: kcal: 44 kcal/kg/d prot: 1.5 g/kg/d (whey) 4.4 mmol argninine/kg/d (70% of calorie as MCT)	100%	BD No change of body weight No change of nitrogen balance No change of prot turnover KD Increased body weight No change of nitrogen balance No change of prot turnover	No GI upset
Rossi-Fanelli et al.[12] (Clin Nutr 1991)	Total n = 27 TNM staged Arm A: n = 9 (median age, 61 yr) Arm B: n = 9 (median age, 70 yr) Arm C: n = 9 (median age, 67 yr) Country: Italy	9 Oesophagus 9 Stomach 9 Colorectal	14 days intervention Iso-kaloric regimen Arm A: parenteral nutrition 100% dextrose 0.24 g/kg/d amino-acid Vitamin minerals Arm B: parenteral nutrition 80% as fat, 20% as dextrose 0.24 g/kg/d amino-acid Vitamin minerals Arm C: oral diet	100%	No group differences were found in S-phase fraction of cell cycle Total lymphocyte counts Blood glucose Triglycerides Body weight Mid-arm circumferences Serum albumin Pre-albumin Transferrin Retinol-binding prot	Not mentioned
Breitkreutz et al.[13] (Wien Klin Wochenschr 2005)	Total n = 23 Moderately malnourished cancer patients Group A: n = 11 (mean age, 60.6 yr) Group B: n = 12 (mean age, 58.8 yr) Country: Germany	12 Colorectal 11 Gastric All metastases	Group A 8 weeks of 35 kcal/kg/d, 1.1 g prot/kg/d (normal meals) Nutritional counseling every 14 days Group B 8 weeks of 20 kcal/kg/d, 1.1 g prot/kg/d (fat-enriched liquid diet + normal meals) Nutritional counseling every 14 days	100%	Group A Average intake 1,556 ± 497 kcal Progressive weight loss Progressive loss of FFM Decrease in serum albumin No change TLC No change of QOL Group B Average intake 1,865 ± 317 kcal Increased body weight Progressive increase of FFM No change in serum albumin Significant decrease of TLC No change of QOL	Not mentioned

Table 1. Continued

Author (journal and year)	No. of subjects and characteristics	Cancer type	KD intervention (duration and regimen)	Adherence	Outcome measures and results	Side effect
Schmidt et al.[14] (Nutr Metab (Lond) 2011)	Total n = 16 Metastatic tumors (mean age, 50.4 yr) Country: Germany	3 Ovarian cancer 1 Breast cancer 1 Osteosarcoma 5 Gastrointestinal cancer 2 Thyroid cancer 1 Endometrial 1 Lung cancer 1 Granulosa cell tumor 1 Parotis carcinoma	3 months of low CHO diet (KD) - CHO limitation to 70 g/d, 20 g/meal - 2 liquid meals (21 g fat, 5 g CHO, 14 g prot)/meal	31% (2 died, 9 dropped out)	KD 3 patients reached ketosis No change: Global health status Functional score Blood glucose, TG creatinine, Albumin Increase: appetite loss, constipation Diarrhea (at 4 wk) Increase: fatigue, pain Decrease: insomnia	No diet related adverse events
Fine et al.[15] (Nutrition 2012)	Total n = 109 Incurable, advanced cancer (mean age, 62.9 yr) Country: USA	2 Breast cancer 3 Colorectal 1 Ovary 1 Fallopian tube 2 Lung 1 Esophagus	26-28 days KD intervention - < 5% of kcal as CHO - Increase fat and prot encouraged	100%	KD Increased weight loss (−3.0 kg) Energy deficit (−35%) No change of serum glucose Increased dietary ketosis Inverse relationship of insulin vs. β-hydroxybutyrate	No unsafe adverse effects Except constipation, leg cramps, reversible fatigue
Schroeder et al.[16] (Nutr Cancer 2013)	Total n = 12 Head and neck cancer (mean age, 64 yr) Country: Germany	2 Larynx 3 Oral cavity 2 Hypopharynx 3 Oropharynx Unknown primary	5 days KD intervention Microdialysis	100%	KD Increase of urea in tumor tissues No change in plasma glucose Decrease in lactate concentration in tumor tissues Decrease in lactate/pyruvate ratio	Not mentioned
Rieger et al.[17] (Int J Oncol 2014)	Total n = 20 Patient from ERGO trial (mean age, 57 yr) Country: Germany	Recurrent malignant glioma	36 days intervention KD diet: ketogenic ratio, 3.41 : 1 - CHO limitation to less than 60 g/d - No calorie restriction - 500 mL yoghurt + plant oil	85%	KD Increased weight loss No change in blood glucose, HbA1c, lipid profiles Leukcytopenia in 2 patients Overall survival 32 weeks	Few reports on diarrhea, constipation but no major concern or toxicity
Jansen and Walach[18] (Oncol Lett 2016)	Total n = 78 Prospective cohort study (mean age, 68 yr) Country: Germany	18 Breast 16 Prostate 9 Colon 5 Lung 5 Otoharyngeal 25 Other	10 mo-2 yr 65 not ketogenic 6 partially ketogenic 7 fully ketogenic	Not mentioned	KD Reduction of TKTL1 (novel marker associated with tumor progression) 3 out of 7 patients had improvement 1 had full remission	Not mentioned

Table 1. Continued

Author (journal and year)	No. of subjects and characteristics	Cancer type	KD intervention (duration and regimen)	Adherence	Outcome measures and results	Side effect
Klement and Sweeney[19] (BMC Res Notes 2016)	Total n = 6 (mean age, 60.3 yr) Country: Germany	1 Breast 1 Prostate 3 Rectum 1 Lung during RT	32-73 d KD with weekly counseling - CHO limitation to 50 g/d - Encourage to consume olive oil, coconut oil, butter, fatty fish, cheese, meat	Not mentioned	KD - Decreased BW in 2 patients - Decreased fat mass in 2 patients - No change in hydration status - Decreased phase angle - Increased ketone body	Not mentioned
Tan-Shalaby et al.[20] (Nutr Metab (Lond) 2016)	Total n = 17 Advanced cancer pts not on hemotherapy (mean age, 65 yr) Country: USA	6 Gastrointestinal 2 Lung 3 Skin cancer 1 Prostate 1 Thyroid 2 Brain cancer 1 Head/neck 1 Renal	16 weeks (checked every 4 wk) KD - CHO limitation to 20-40 g/d (no restriction of cal, prot, fat)	64.7% (6 for 8 wk, 4 for 16 wk, 3 beyond 16 wk)	KD - 13% wt loss at week 16 No changes in glucose, creatinine, SBP/DBP, lipid profile, WBC count, uric acid, albumin, ALT Slight improvement of EORTC QLQ-30	8 Weight loss 7 Hyperuricemia 2 Hyperlipidemia 2 Pedal edema 2 Anemia 2 Halitosis 2 Pruritus 2 Hypoglycemia 2 Hyperkalemia 2 Hypokalemia 2 Hypomagnesemia 2 Flu-like symptom

KD, ketogenic diet; BD, balanced diet; MCT, medium chain triglyceride; prot, protein; GI, gastrointestinal; FFM, fat free mass; TLC, total lymphocyte count; QOL, quality of life; CHO, carbohydrate; TG, total cholesterol; RT, radiation therapy; BW, body weight; wt, weight; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; ALT, alanine aminotransferase; EORTC QLQ-30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30.

SUMMARY OF THE STUDY OUTCOMES OF ELIGIBLE ARTICLES

The detailed information of ketone diets from the selected articles are summarized in Table 1.[11-20]

A total of 214 subjects were included in the review. Most of the studies were intervention trials except for one prospective cohort study. The mean age of the studies was mostly from late fifties to early seventies. Eight out of ten articles were submitted from European countries (Germany and Italy) and only two were from USA. The duration of experimental intervention ranged from 5 days to 2 years and the outcome measures were mainly focused on the body weight and composition and blood profile. One article measured quality of life (QOL). The adherence rate in 5 studies were 100%, and the rest were from 31% to 85%. Reported side effects in the studies were relatively minor and included only few reported constipation, leg cramps, diarrhea, etc. Subjects maintained on ketogenic diet for a relatively short period (2 weeks in the study by Rossi-Fanelli et al.,[12]; 1 week in the study by Fearon et al.,[11]; 5 days in the study by Schroeder et al.[16]) did not show any significant changes of the markers, such as body weight or blood profile except for decrease in lactate concentration in the tumor tissues. Meanwhile, when subjects were maintained for a longer period, such as 8 weeks, ketogenic diet (normal meal + fat-enriched liquid diet) successfully showed increased energy intake and body weight of the subjects.[13] Ketogenic diet in this study was used for only malnourished gastro-intestinal cancer patient with metastases, suggesting the possibility of application in specific cancer patients. Evaluation on anticancer biomarkers was not measured in most of the articles except for study by Jansen and Walach[18] who found that TKTL1, a novel marker associated with tumor progression, was reduced by a 2-year ketogenic diet.

Notably, the results from Fine et al.,[15] Rieger et al.,[17] and Klement and Sweeney[19] showed that ketone diet increased significant weight loss. These results showed that unlike the consistent ketogenic effects on epilepsy patients, ketogenic effects on cancer patients were not consistent in this review.

KETOGENIC DIET AS A CANCER THERAPEUTIC STRATEGY

Recently, ketogenic diet has been newly emerged as a cancer therapy in both animal models and humans. Some of the preclinical studies have shown the effect of ketogenic diet to reduce tumor growth and improve survival in animal models of malignant glioma,[21-23] prostate cancer,[24-26] colon cancer,[27] and gastrointestinal cancer.[28] Low calorie diet, such as fasting inducing a state of ketosis, has been shown to enhance the responsiveness of cancer cells to chemotherapy in pre-clinical cancer therapy models and to ameliorate some of chemotherapy-induced side effects in normal tissues.[29]

More recently, numerous case reports were reported. First report was derived from confirmed glioblastoma multiforme treated with standard therapy together with a restricted ketogenic diet, and the response observed in the case suggested the possibility of calorie-restricted ketogenic diet.[30]

Ketogenic diet has been studied intensively in the European country including Germany. In these studies, the physical condition was successfully improved and tumor shrinkage was observed by ketogenic diet.[14] The studies here reviewed lack greatly in the homogeneity of type of cancer, location of cancer, the stages of cancer, and the treatment course of the cancer, and thus the results cannot be generalized. Because ketogenic diet normally results in an increased weight loss, there are continuous concerns to apply this diet for cancer patients. In this review, however, we found that ketogenic diet showed no significant adverse effects. It may be possibly because the subjects were adults, while in children long-term ketogenic diet induces renal damage such as kidney stones.[31] Any adverse effects reported in this review were constipation, diarrhea, fatigue, etc. In healthy obese adults with low-carbohydrate ketogenic diet for 6 months, the only adverse effects reported were an increase in the level of low-density lipoprotein cholesterol and some shakiness and uneasiness.[32]

Studies described in this review assessed the effects of a ketogenic diet in cancer patients. Only ten studies were analyzed and the characteristics and study design, the ketogenic diet regimen, the length of study, cancer type and stage, and site were heterogeneous, thereby contributing to a poor conclusion.

As for ongoing clinical trials, there are currently 62 trials assessing low carbohydrate diets as a potential therapy for a variety of diseases of which 13 trials are assessing ketogenic diet as an adjuvant cancer therapy. Three of the studies are not initiated, but, one study with pancreatic cancer patients was terminated because of the low participation and adherence (Table 2).

CONCLUSION

Our main aim in this review was to assess the feasibility and acceptability of ketogenic diet and to assess the changes of outcome variables, such as body composition, biochemical blood

Table 2. Ongoing clinical trials from clinicalTrials.gov (https://clinicaltrials.gov) (accessed on 08/04/2017)

	Title	Recruitment	Study Results	Conditions	Interventions
1	Ketogenic Diet for Recurrent Glioblastoma	Completed	Has results	Recurrent glioblastoma	Dietary supplement: TAVARLIN
2	Ketogenic Diet as Adjunctive Treatment in Refractory/End-stage Glioblastoma Multiforme: A Pilot Study	Recruiting	No results available	Glioblastoma multiforme	Other: ketogenic diet
3	Ketogenic Diet and Prostate Cancer Surveillance Pilot	Enrolling by invitation	No results available	Prostate cancer	Other: surveillance
4	Ketogenic Diet Adjunctive to Salvage Chemotherapy for Recurrent Glioblastoma: A Pilot Study	Recruiting	No results available	Glioblastoma multiforme	Dietary supplement: ketogenic diet Dietary supplement: standard diet
6	Impact of a Ketogenic Diet Intervention During Radiotherapy on Body Composition	Recruiting	No results available	Neoplasms	Dietary supplement: ketogenic breakfast Dietary supplement: ketogenic diet Radiation: radio(chemo)therapy
7	Ketogenic Diet Phase 1 for Head & Neck Cancer	Terminated	No results available	Head and neck neoplasms	Dietary supplement: Ketogenic diet
8	Ketogenic Diet With Concurrent Chemoradiation for Pancreatic Cancer	Terminated	No results available	Pancreatic neoplasms	Dietary supplement: ketogenic diet
9	Ketogenic Diet Treatment Adjunctive to Radiation and Chemotherapy in Glioblastoma Multiforme: A Pilot Study	Recruiting	No results available	Glioblastoma multiforme of brain	Other: ketogenic diet Other: standardized diet
10	Calorie-restricted, Ketogenic Diet and Transient Fasting During Radiation for Patients With Recurrent Glioblastoma	Recruiting	No results available	Recurrent glioblastoma	Dietary supplement: calorie-restricted ketogenic diet and transient fasting Dietary supplement: standard nutrition
11	Ketogenic Diets as an Adjuvant Therapy in Glioblastoma	Recruiting	No results available	Glioblastoma Glioblastoma multiforme	Other: MKD Other: MCT
12	Restricted Calorie Ketogenic Diet as a Treatment in Glioblastoma Multiforme	Recruiting	No results available	Glioblastoma multiforme	Other: ketogenic diet
13	Ketogenic Diet in Advanced Cancer	Completed	Has results	Cancer	Other: ketogenic diet

MKD, modified ketogenic diet; MCT, medium chain triglyceride ketogenic diet.

profiles, and QOL. From this review, we found further evidence that ketogenic diet in cancer patients is safe and feasible as an adjuvant therapy. As described above, we could conclude that in order to see any significant progression or improvement by ketogenic diet, at least 3 to 4 weeks of ketogenic diet is required. Additionally, we suggest that not only body composition but also biomarker or measures for tumor size or tumor metabolism assessment is essential. We also conclude that the acceptability for ketone diet may be better in some cancer type (better in glioblastoma than gastric cancer).

In conclusion, ketogenic diet can be safely used to cancer patients if carefully monitored. Most importantly, we have to establish standardized treatment protocol which include the length and regimen for ketogenic diet.

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CONFLICTS OF INTEREST

No potential conflicts of interest were disclosed.

REFERENCES

1. Demark-Wahnefried W, Morey MC, Sloane R, Snyder DC, Cohen HJ. Promoting healthy lifestyles in older cancer survivors to im-

prove health and preserve function. J Am Geriatr Soc 2009;57 Suppl 2:S262-4.
2. Kushi LH, Kwan ML, Lee MM, Ambrosone CB. Lifestyle factors and survival in women with breast cancer. J Nutr 2007;137: 236S-42S.
3. Patterson RE, Cadmus LA, Emond JA, Pierce JP. Physical activity, diet, adiposity and female breast cancer prognosis: a review of the epidemiologic literature. Maturitas 2010;66:5-15.
4. Imoberdorf R, Rühlin M, Ballmer PE. Cancer and nutrition: a paradigma shift. Laryngorhinootologie 2017;96:514-8.
5. Wei M, Brandhorst S, Shelehchi M, Mirzaei H, Cheng CW, Budniak J, et al. Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. Sci Transl Med 2017;9:eaai8700.
6. Champ CE, Baserga R, Mishra MV, Jin L, Sotgia F, Lisanti MP, et al. Nutrient restriction and radiation therapy for cancer treatment: when less is more. Oncologist 2013;18:97-103.
7. Bonkowski MS, Dominici FP, Arum O, Rocha JS, Al Regaiey KA, Westbrook R, et al. Disruption of growth hormone receptor prevents calorie restriction from improving insulin action and longevity. PLoS One 2009;4:e4567.
8. Vander Heiden MG, Cantley LC, Thompson CB. Understanding the Warburg effect: the metabolic requirements of cell proliferation. Science 2009;324:1029-33.
9. Huebner J, Marienfeld S, Abbenhardt C, Ulrich C, Muenstedt K, Micke O, et al. Counseling patients on cancer diets: a review of the literature and recommendations for clinical practice. Anticancer Res 2014;34:39-48.
10. Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions version 5.1.0. http://handbook.cochrane.org. [updated March 2011].
11. Fearon KC, Borland W, Preston T, Tisdale MJ, Shenkin A, Calman KC. Cancer cachexia: influence of systemic ketosis on substrate levels and nitrogen metabolism. Am J Clin Nutr 1988;47:42-8.
12. Rossi-Fanelli F, Franchi F, Mulieri M, Cangiano C, Cascino A, Ceci F, et al. Effect of energy substrate manipulation on tumour cell proliferation in parenterally fed cancer patients. Clin Nutr 1991;10:228-32.
13. Breitkreutz R, Tesdal K, Jentschura D, Haas O, Leweling H, Holm E. Effects of a high-fat diet on body composition in cancer patients receiving chemotherapy: a randomized controlled study. Wien Klin Wochenschr 2005;117:685-92.
14. Schmidt M, Pfetzer N, Schwab M, Strauss I, Kämmerer U. Effects of a ketogenic diet on the quality of life in 16 patients with advanced cancer: a pilot trial. Nutr Metab (Lond) 2011;8:54.
15. Fine EJ, Segal-Isaacson CJ, Feinman RD, Herszkopf S, Romano MC, Tomuta N, et al. Targeting insulin inhibition as a metabolic therapy in advanced cancer: a pilot safety and feasibility dietary trial in 10 patients. Nutrition 2012;28:1028-35.
16. Schroeder U, Himpe B, Pries R, Vonthein R, Nitsch S, Wollenberg B. Decline of lactate in tumor tissue after ketogenic diet: in vivo microdialysis study in patients with head and neck cancer. Nutr Cancer 2013;65:843-9.
17. Rieger J, Bähr O, Maurer GD, Hattingen E, Franz K, Brucker D, et al. ERGO: a pilot study of ketogenic diet in recurrent glioblastoma. Int J Oncol 2014;44:1843-52.
18. Jansen N, Walach H. The development of tumours under a ketogenic diet in association with the novel tumour marker TKTL1: a case series in general practice. Oncol Lett 2016;11:584-92.
19. Klement RJ, Sweeney RA. Impact of a ketogenic diet intervention during radiotherapy on body composition: I. Initial clinical experience with six prospectively studied patients. BMC Res Notes 2016;9:143.
20. Tan-Shalaby JL, Carrick J, Edinger K, Genovese D, Liman AD, Passero VA, et al. Modified Atkins diet in advanced malignancies - final results of a safety and feasibility trial within the Veterans Affairs Pittsburgh Healthcare System. Nutr Metab (Lond) 2016;13:52.
21. Maurer GD, Brucker DP, Bähr O, Harter PN, Hattingen E, Walenta S, et al. Differential utilization of ketone bodies by neurons and glioma cell lines: a rationale for ketogenic diet as experimental glioma therapy. BMC Cancer 2011;11:315.
22. Seyfried TN, Sanderson TM, El-Abbadi MM, McGowan R, Mukherjee P. Role of glucose and ketone bodies in the metabolic control of experimental brain cancer. Br J Cancer 2003;89: 1375-82.
23. Stafford P, Abdelwahab MG, Kim DY, Preul MC, Rho JM, Scheck AC. The ketogenic diet reverses gene expression patterns and reduces reactive oxygen species levels when used as an adjuvant therapy for glioma. Nutr Metab (Lond) 2010;7:74.
24. Freedland SJ, Mavropoulos J, Wang A, Darshan M, Demark-Wahnefried W, Aronson WJ, et al. Carbohydrate restriction, prostate cancer growth, and the insulin-like growth factor axis. Prostate 2008;68:11-9.
25. Masko EM, Thomas JA 2nd, Antonelli JA, Lloyd JC, Phillips TE, Poulton SH, et al. Low-carbohydrate diets and prostate cancer: how low is "low enough"? Cancer Prev Res (Phila) 2010;3:1124-31.
26. Mavropoulos JC, Buschemeyer WC 3rd, Tewari AK, Rokhfeld D, Pollak M, Zhao Y, et al. The effects of varying dietary carbohydrate and fat content on survival in a murine LNCaP prostate cancer xenograft model. Cancer Prev Res (Phila) 2009;2:557-65.
27. Beck SA, Tisdale MJ. Nitrogen excretion in cancer cachexia and its modification by a high fat diet in mice. Cancer Res 1989;49:3800-4.
28. Otto C, Kaemmerer U, Illert B, Muehling B, Pfetzer N, Wittig R, et al. Growth of human gastric cancer cells in nude mice is delayed by a ketogenic diet supplemented with omega-3 fatty acids and medium-chain triglycerides. BMC Cancer 2008;8:122.
29. Lee C, Raffaghello L, Brandhorst S, Safdie FM, Bianchi G, Martin-Montalvo A, et al. Fasting cycles retard growth of tumors and sensitize a range of cancer cell types to chemotherapy. Sci Transl Med 2012;4:124ra27.
30. Zuccoli G, Marcello N, Pisanello A, Servadei F, Vaccaro S, Mukherjee P, et al. Metabolic management of glioblastoma multiforme using standard therapy together with a restricted ketogenic diet: case report. Nutr Metab (Lond) 2010;7:33.
31. McNally MA, Pyzik PL, Rubenstein JE, Hamdy RF, Kossoff EH. Empiric use of potassium citrate reduces kidney-stone incidence with the ketogenic diet. Pediatrics 2009;124:e300-4.
32. Yancy WS Jr, Olsen MK, Guyton JR, Bakst RP, Westman EC. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial. Ann Intern Med 2004;140:769-77.