

Citation:

Johnstone AM, Horgan GW, Murison SD, Bremner DM, Lobley GE. Effects of a high-protein ketogenic diet on hunger, appetite, and weight loss in obese men feeding ad libitum. *Am J Clin Nutr.* 2008 Jan;87(1):44-55.

PubMed ID: [18175736](#)

Study Design:

Randomized Crossover Trial

Class:

A - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare the hunger, appetite, and weight loss responses to a high-protein, low-carbohydrate (LC) ketogenic diet and a high-protein, medium-carbohydrate (MC) non-ketogenic diet in a group of obese men fed ad libitum.

Inclusion Criteria:

- Subjects were not on a specialized diet
- Were not receiving medications
- Baseline biochemical and hematologic laboratory tests were within normal limits
- BMI >30
- Males 20-65 years old

Exclusion Criteria:

None specifically stated.

Description of Study Protocol:

Recruitment: Subjects recruited through newspaper advertisement

Design: Randomized crossover trial

Blinding used (if applicable) implied for measurements

Intervention (if applicable)

- Subjects were exposed to a 3 day diet maintenance period followed by random assignment to either a ketogenic diet (LC) (30% protein, 4% CHO, 66% fat) or a medium-carbohydrate

non-ketogenic diet (MC) (30% protein, 35% CHO, 35% fat).

- Diets were prescribed for 4 weeks followed by another 3 day maintenance period,
- Subjects then were assigned the alternate diet for another 4 week period in a cross over design.

Statistical Analysis:

- Data were analyzed by hierarchical ANOVA with subject, period (order) within subject, and day within period as blocking factors (random effects) and diet, order and day as treatment terms (fixed effects)

Data Collection Summary:

Timing of Measurements:

- Beginning of study: weight, height
- Other anthropometrics and resting metabolic rate: beginning and end of each diet intervention
- Appetite and hunger: hourly during waking periods
- Measures of compliance and metabolic profile: daily weights, weekly urine and blood analysis at 4 timepoints (before and after treatment period)

Dependent Variables:

- Hunger and appetite (measured by visual analog scales and a motivation questionnaire)
- Weight loss
- Metabolic profile (urinary ketone body, urine and plasma 3-hydroxybutyrate, plasma glucose and insulin and lipid profile).
- Body composition was calculated using dual x-ray absorptiometry, air displacement, and deuterium dilution.

Independent Variables:

- Subjects were exposed to a 3 day diet maintenance period followed by random assignment to either a ketogenic diet (LC) (30% protein, 4% CHO, 66% fat) or a medium-carbohydrate non-ketogenic diet (MC) (30% protein, 35% CHO, 35% fat).

Control Variables

Description of Actual Data Sample:

Initial N: 20 males

Attrition (final N): 17 males

Age: 20-65 years (mean 38 ± 10 years)

Ethnicity: not reported

Other relevant demographics: none reported

Anthropometrics

Summary of Results:

Key Findings

- Ad libitum energy intakes were lower with the LC diet than with the MC diet [P = 0.02, SE of the difference (SED): 0.27] at 7.25 and 7.95 MJ/day, respectively
- Over the 4-week period, hunger was significantly lower (P = 0.014, SED = 1.76) and weight loss was significantly greater (P = 0.006, SED = 0.62) with the LC diet (6.34 kg) than with the MC diet (4.35 kg)
- The LC diet induced ketosis with mean 3-hydroxybutyrate concentrations of 1.52 mmol/L in plasma (P = 0.036 from baseline, SED = 0.62) and 2.99 mmol/L in urine (P < 0.001 from baseline, SED = 0.36).

Variable	LC Diet Group	MC Group	Difference between 2 groups (p value)
Hunger	16.8	21.4	1.76 (0.014)
Weight Loss	-6.34 kg	-4.35 kg	p=.006
Energy Intake	7.25 MJ	7.95 MJ	0.27 (0.02)
Fasting Blood sugar (mmol/L)	-0.62	-0.35	<0.001
3-OH butyrate (mmol/L)	1.32	0	0.007
Insulin (IU/ml)	-3.98	-1.41	<0.001
Insulin resistance	-1.22	-0.52	<0.001
Total (mmol/L)Cholesterol	-0.39	-0.92	0.002
LDL	-0.18	-0.67	0.004
Triacylglycerol(mmol/L)	-0.69	-0.61	0.05

Other Findings:

- In addition to finding differences in hunger, energy intake, metabolic profiles and weight loss, the authors found the weight loss differences could be accounted for by differences in body composition.
- The LC diet induced greater loss of body water, fat mass, and fat free mass.

Author Conclusion:

In the short term, high-protein, low-carbohydrate ketogenic diets reduce hunger and lower food intake significantly more than high-protein, medium-carbohydrate non-ketogenic diets.

Reviewer Comments:

- Only 17 subjects, all male
- Each diet period duration of only 4 weeks, washout period only 3 days

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	Was the research question clearly stated?	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	Was the selection of study subjects/patients free from bias?	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	N/A
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes

2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	Were study groups comparable?	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blinding used to prevent introduction of bias?	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A

5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	N/A
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes

8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes

Copyright American Dietetic Association (ADA).