

Citation:

Buonacorso V, Nakandakare ER, Nunes VS, Passarelli M, Quintão EC, Lottenberg AM. Macrophage cholesterol efflux elicited by human total plasma and by HDL subfractions is not affected by different types of dietary fatty acids. *Am J Clin Nutr.* 2007 Nov; 86(5): 1,270-1,277.

PubMed ID: [17991635](#)

Study Design:

Randomized controlled trial.

Class:

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

Research Design and Implementation Rating:

 NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To clarify the effects on lipoprotein composition and rates of cell cholesterol efflux for whole plasma and High Density Lipoprotein (HDL) subfractions during trans Fatty Acid (TFA), Saturated Fatty Acid (SFA) and Polyunsaturated Fatty Acid (PUFA) enriched diets in healthy persons during fasting and post-prandial conditions.

Inclusion Criteria:

Employees of the University of Sao Paulo Medical School were recruited for the study. Acceptable participants also had:

- Body Mass Index less than 30
- Fasting blood glucose less than 100mg per dL
- Two-hour glucose tolerance test less than 140mg per dL
- Plasma Low Density Lipoprotein (LDL) less than 200mg per dL
- Plasma triacylglycerol less than 150mg per dL.

Exclusion Criteria:

Subjects with chronic disease or who were taking medication that could interfere with lipid metabolism.

Description of Study Protocol:**Recruitment**

30 healthy employees of the medical school were recruited.

Design

Randomized clinical trial. 30 subjects were randomly distributed among three groups (10 per group). Subjects were paired by sex, age and BMI before random distribution to diet groups. There was a two-week run-in period (30% energy from fat, less than 10% energy as SFA, less than 300mg cholesterol per day) followed by a four-week experimental diet period (fat free ad lib breakfast plus prepared frozen lunch and dinner). Blood samples were drawn after an overnight fast and four hours after a standard meal.

Intervention

Experimental diets were described as shown in the table:

Fatty Acids	Basal	TFA	PUFA	SFA
Trans Fat (g per 100g total fatty acid)	0	36	0	1
PUFA (g per 100g total fatty acid)	60	0	51	10
SFA (g per 100g total fatty acids)	17	27	8	45
Monounsaturated (g per 100g total fatty acids)	22	36	41	43
PUFA/SFA	3.52	N/A	6.37	0.22
Sources	Sunflower oil	Hydrogenated soybean oil	46% rapeseed oil, 54% sunflower oil	12% olive oil, 88% palm oil

Statistical Analysis

- NCSS 2004 statistical software (version 2004; NCSS Kaysville, UT)
- Results were treated by analyses of repeated measures, with diet as a between-subject factor and time (final compared with basal) and post-prandial status as within-subject factors.

Data Collection Summary:

Timing of Measurements

- Basal: Not specified if beginning of two-week run-in period or beginning of four-week experimental period
- Final: End of experimental period
- Fasting: Morning after an overnight fast
- Post-prandial: Four hours after ingestion of meal.

Dependent Variables

- Total cholesterol
- Triacylglycerol
- Phospholipid
- Apolipoprotein (Apo A-I)

- Apolipoprotein (Apo A-II)
- High Density Lipoprotein (HDL, HDL₂, HDL₃).

Independent Variables

- Experimental diet assignment (TFA, SFA, PUFA)
- Time (basal vs. final and fasting vs. post-prandial).

Description of Actual Data Sample:

- Initial N: 30 (nine males, 21 females)
- Attrition (final N): No attrition, 10 per group, three males and seven females in each group
- Age: Mean 34 to 37 years
- Anthropometrics: Subjects were paired by sex, age and BMI before random distribution among the groups. There were no significant differences between groups at baseline.
- Location: Brazil.

Summary of Results:

Key Findings

- Plasma total cholesterol and triacylglycerol were not affected by the diets, by time (basal vs. final), or by period (fasting vs. post-prandial)
- Triacylglycerol was significantly ($P=0.012$) higher in the post-prandial period, independent of diets and time
- TFA diet increased concentrations of HDL₂, total cholesterol, phospholipid and apo A-I and apo A-II and decreased the ratio of lipids to apo A over time
- SFA diet decreased the concentrations of total cholesterol, phospholipid and apo A-I and apo A-II and increased lipids:apo A over time
- PUFA diet decreased only lipids:apo A over time.

Other Findings

- TFA, PUFA and SFA diets did not influence the ability of HDL₂ or HDL₃ to remove macrophage cholesterol either during fasting or post-prandially
- HDL₃ displayed greater efficiency in removing cellular cholesterol than did HDL₂.

Author Conclusion:

There was no major differences over time in plasma total cholesterol and triacylglycerol concentrations. Although epidemiologic trials have shown a strong association between cardiovascular disease and the consumption of TFA, our data show that the proatherogenic effect of TFAs is not related to a faulty efficiency of macrophage cholesterol efflux. A lack of significant lipoprotein composition differences in HDL cholesterol efflux rates by cells is likely attributed to our limiting the total fat intake to 30% of total energy and simultaneously controlling the proportions of fatty acids in the experimental diets.

Reviewer Comments:

Detailed descriptions of diets, related research and procedures. Small numbers of subjects in groups. Potential bias and lack of generalizability, as recruited subjects were medical school employees.

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? | No |
| 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? | Yes |
| 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? | No |
| 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?	No
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?	N/A
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?	N/A
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?	Yes
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?	Yes
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)?	Yes
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?	No
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?	???

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