American Dietetic Association

RESEARCH

Review

Green Tea Catechins Decrease Total and Low-Density Lipoprotein Cholesterol: A Systematic Review and Meta-Analysis

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ABSTRACT

Green tea catechins (GTCs) have been studied in randomized control trials for their lipid-lowering effects. Studies, however, have been small and demonstrated conflicting results. The objective of this study was to perform a systematic review and meta-analysis of randomized controlled trials evaluating the relationship between GTCs and serum lipid levels, including total, low-density lipoprotein (LDL), high-density lipoprotein (HDL) cholesterol, and triglycerides. A systematic literature search of MEDLINE, EMBASE, Cochrane CENTRAL, and the Natural Medicines Comprehensive Database was conducted through March 2010. Randomized controlled trials evaluating GTCs vs control in human beings and reporting efficacy data on at least one of the aforementioned serum lipid endpoints were included. Weighted mean differences for changes from baseline (with 95% confidence intervals [CIs]) for lipid endpoints were calculated using random-effects models. Twenty trials (N=1,415) met all inclusion criteria. Upon meta-analysis, GTCs at doses ranging from 145 to 3,000 mg/day taken for 3 to 24 weeks reduced total (−5.46 mg/dL [−0.14 mmol/L]; 95% CI −9.59 to −1.32) and LDL cholesterol (−5.30 mg/dL [−0.14 mmol/L]; 95% CI −9.99 to −0.62) compared to control. GTCs did not significantly alter HDL cholesterol (−0.27 mg/dL [−0.007 mmol/L]; 95% CI −1.62 to 1.09) or triglyceride (3.00 mg/dL [−0.034 mmol/L]; 95% CI −2.73 to 8.73) levels. The consumption of GTCs is associated with a statistically significant reduction in total and LDL cholesterol levels; however, there was no significant effect on HDL cholesterol or triglyceride levels.

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Lipid level modification remains an important target for cardiovascular disease prevention. Both the American Heart Association (1) and the National Cholesterol Education Program (2) acknowledge the association between high levels total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, and low levels of high-density lipoprotein (HDL) cholesterol and cardiovascular morbidity and mortality. Strategies to modify lipid parameters may include medication, lifestyle modification, or the use of herbal supplements.

Green tea has sparked growing interest in its potential health benefits, such as the ability to modify serum lipid parameters. It has been suggested that the effects of green tea can be attributed to polyphenols; high levels of these antioxidants can be found in green tea (3). Catechins comprise 80% to 90% of the polyphenols found in green tea, most abundantly including epigallocatechin, believed to be the most potent (3). The remaining catechins include epicatechin, epicatechin gallate, epigallocatechin, gallocatechin, catechin gallate, gallocatechin gallate, and catechin (3). Animal studies have suggested that green tea catechins (GTCs) reduce lipid absorption in the intestines (4), promote fecal excretion of cholesterols (5), and inhibit enzymes involved in hepatic cholesterol synthesis (6).

In human beings, large epidemiologic studies suggest efficacy of GTCs in reducing lipid levels (7,8). Several randomized controlled trials (RCTs) also exist to answer the clinical question of GTCs' efficacy; however, there are conflicting results among them and modest sample sizes (9-28). To summarize the available evidence and to increase statistical ability to detect effects, a systematic review and meta-analysis of RCTs to determine the effect of GTCs on serum lipid parameters was conducted.

METHODS

Study Selection

A systematic literature search was conducted through March 2010 in the following databases: MEDLINE (beginning 1950), EMBASE (beginning 1990), Cochrane Central Register of Controlled Trials (Indexed January 2010), and the Natural Medicines Comprehensive Data-

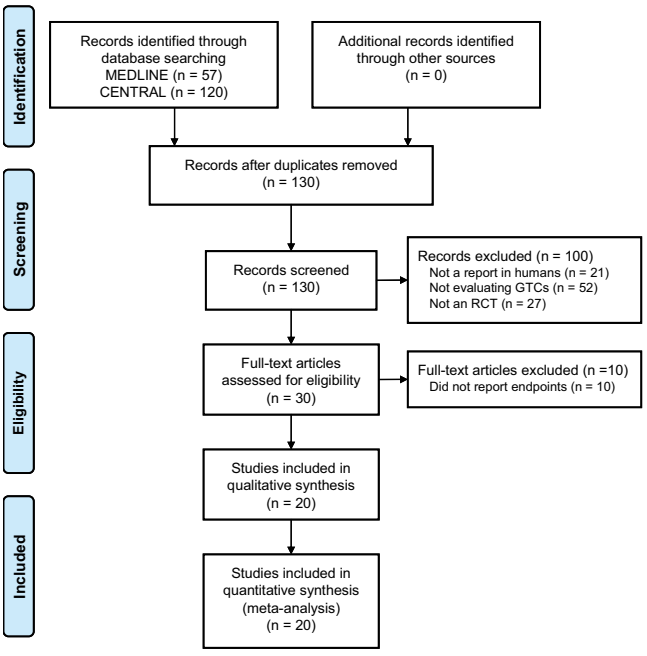

Figure 1. Preferred reporting items in systematic reviews and meta-analyses flow diagram of study selection, inclusion, and exclusion of randomized controlled trials (RCTs) evaluating green tea catechins on serum lipid levels.

base. A search strategy was performed combining the Medical Subject Headings and text keywords "tea," "green tea," "green tea extract," "catechin," "EGCG," "tea polyphenols," "theaflavin," or "*Camelia sinesis*," with "total cholesterol," "LDL cholesterol," "HDL cholesterol," "triglycerides," or "metabolic syndrome." No language restrictions were imposed and duplicate citations were removed. In addition, a manual search of references from primary or review articles was performed to identify additional relevant trials.

Trials were included in the analysis if they were randomized trials evaluating the use of GTCs (in any dose or form, including extract tablets/capsules, powders, or beverages) and reported data on at least one of the following endpoints: total cholesterol, LDL cholesterol, HDL cholesterol, or triglycerides. Both parallel and crossover trials were eligible for inclusion. Crossover trials that reported data separately among different treatment periods were analyzed and recorded as a parallel trial using data from the first period. Two investigators reviewed potentially relevant articles independently with differences resolved through discussion (O.J.P., C.I.C.). Institutional review board approval was not necessary for this systematic review.

Data Abstraction and Validity Assessment

Through the use of a standardized data abstraction tool, two reviewers of the research team independently abstracted data from each trial (A.K., A.C., M.K.B.), with disagreement resolved through discussion or by a third investigator (O.J.P.). The following information was obtained from each trial: author identification, year of publication, study design, source of study funding, study population (including study inclusion and exclusion criteria and baseline lipid values), sample size, duration of participant follow-up, catechin dose and formulation used, caffeine use, concurrent diet, and effect on lipid parameters (ie, total, LDL, and HDL cholesterol and triglyceride). In cases where data insufficient for meta-analysis were provided, authors were contacted with requests to provide additional data.

Validity assessment was performed by two investigators (A.C., M.K.B.) using the American Dietetic Association Research Design and Implementation Checklist for primary research (29). This checklist includes 10 validity questions covering the following domains: a clear statement of research question, bias-free subject selection, comparable groups, description of withdrawal handling, blinding, detailed description of protocol, clear definition of outcomes, appropriate statistical analysis, conclusions supported by data, and unlikely bias due to sponsorship or funding. Each of the 10 questions has a series of subquestions that aid in answering the overall question as either yes, no, or unclear. The four questions pertaining to bias-free subject selection, comparable groups, detailed description of protocol, and clear definition of outcomes received the most consideration, whereas evaluating the overall study quality. The study was rated as positive if the four major criteria were met along with at least one other "yes," neutral if the four major criteria were not all "yes," and minus if most ($\geq$6) questions were answered as "no."

Statistical Analysis

The mean changes in total, LDL, and HDL cholesterol and triglyceride levels from baseline were treated as continuous variables, and the weighted mean differences were calculated as the differences between the mean change from baseline in the GTCs and control groups. A DerSimonian and Laird random-effects model (a variation on the inverse variance method that incorporated an assumption that the different studies were estimating different, yet related, treatment effects) was used in calculating the weighted mean differences with accompanying 95% confidence intervals (CIs) (30). Changes from baseline in outcomes were extracted from trials; in instances where changes were not reported directly, they were calculated from end-of-study and baseline results. When necessary, variances for the changes from baseline were calculated using a correlation coefficient of .5, as suggested by Follman and colleagues (31).

The statistical analysis was performed by using StatsDirect software (version 2.4.6, 2008, StatsDirect Ltd, Cheshire, UK). A P value <0.05 was considered statistically significant for all analyses. Statistical heterogeneity was be assessed using the I^2 statistic, where values of 25%, 50%, and 75% represent low, medium, and high degrees of heterogeneity, respectively, where low levels of heterogeneity are desired. To assess for the presence of publication bias, visual inspection of funnel plots were used to investigate the relationship between effect size and sample size, and Egger's weight regression statistics tested for asymmetry.

Subgroup and sensitivity analyses were performed in an attempt to assess the effect of potential clinical or methodologic heterogeneity on our meta-analysis' results.