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SYSTEMATIC REVIEW

The effect of green tea on blood pressure and lipid profile: A systematic review and meta-analysis of randomized clinical trials

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Abstract *Introduction:* Many different dietary supplements are currently marketed for the management of hypertension, but the evidence for effectiveness is mixed. The aim of this systematic review was to evaluate the evidence for or against the effectiveness of green tea (*Camellia sinensis*) on blood pressure and lipid parameters.
Methods and results: Electronic searches were conducted in Medline, Embase, Amed, Cinahl and the Cochrane Library to identify relevant human randomized clinical trials (RCTs). Hand searches of bibliographies were also conducted. The reporting quality of included studies was assessed using a checklist adapted from the CONSORT Statement. Two reviewers independently determined eligibility, assessed the reporting quality of the included studies, and extracted the data. As many as 474 citations were identified and 20 RCTs comprising 1536 participants were included. There were variations in the designs of the RCTs. A meta-analysis revealed a significant reduction in systolic blood pressure favouring green tea (MD: −1.94 mmHg; 95% CI: −2.95 to −0.93; $I^2 = 8\%$; $p = 0.0002$). Similar results were also observed for total cholesterol (MD: −0.13 mmol/l; 95% CI: −0.2 to −0.07; $I^2 = 8\%$; $p < 0.0001$) and LDL cholesterol (MD: −0.19 mmol/l; 95% CI: −0.3 to −0.09; $I^2 = 70\%$; $p = 0.0004$). Adverse events included rash, elevated blood pressure, and abdominal discomfort.
Conclusion: Green tea intake results in significant reductions in systolic blood pressure, total cholesterol, and LDL cholesterol. The effect size on systolic blood pressure is small, but the effects on total and LDL cholesterol appear moderate. Longer-term independent clinical trials evaluating the effects of green tea are warranted.

Introduction

Hypertension is a leading cause of death, and a major risk factor for cardiovascular disease [1]. Its global prevalence varies worldwide from as low as 3.4% to as high as 72.5% [2]. Although over 90% of hypertensive cases are idiopathic [3], dietary and lifestyle factors are major risk factors associated with its increasing incidence [4,5]. Many different dietary supplements are currently marketed for the management of hypertension, but the evidence for effectiveness is mixed [6]. One such supplement thought to have an antihypertensive effect is the extract of *Camellia sinensis*, green tea.

Green tea is one of the most commonly consumed beverages worldwide [7]. The leaves of the plant contain a variety of phytochemicals including phenols and catechins [8]. The polyphenolic compounds in green tea are thought to possess antioxidant properties by virtue of their ability to scavenge for free oxygen and nitrogen radicals [9]. The

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catechins in green tea comprise epigallocatechin-3-gallate (EGCG), epigallocatechin, epicatechin-3-gallate, and epicatechin. EGCG is reported as the most abundant catechin in green tea, comprising over half of the total catechin content, as well as being the most bioactive component [10,11].

Green tea catechins have been postulated to stimulate thermogenesis, modify appetite and downregulate the enzymes involved in lipid metabolism [12]; consequently this group of flavonoids are commonly marketed as slimming aids. *Invitro* studies have shown that the epigallocatechins in green tea have angiotensin converting enzyme inhibitor properties [13,14], and findings from several animal studies have suggested that green tea lowers blood pressure by suppressing the NADPH oxidase activity and reducing the numbers of reactive oxygen species in the vascular system [15,16]. Molecular studies have demonstrated that green tea catechins enhance cholesterol 7alpha-hydroxylase gene expression in HepG2 cells [17,18], a process which is thought to stimulate bile acid production and decrease cholesterol concentration in the hepatocytes. Animal studies have also shown that green tea extracts inhibit intestinal absorption of lipids and also upregulate low-density lipoprotein receptors in the liver [19–21]; mechanisms which lead to improvements in the blood lipid profile.

Case-control and epidemiologic studies have suggested that green tea intake has a cardioprotective effect [22,23], but a previous meta-analysis of five studies concluded that green tea had no beneficial effect on blood pressure [24]. However, a recent meta-analysis reported beneficial effects of green tea on blood vessel dilatation [25], and two meta-analyses (both including open-label and blinded trials) reported beneficial effects on lipid profile [26,27]. Therefore, the purpose of this systematic review was to evaluate the evidence for or against the efficacy of green tea extracts on blood pressure and lipid profile, using published data from blinded-only clinical trials.

Methods

We conducted electronic searches in the following databases: Medline, Embase, Amed, Cinahl, and The Cochrane Library. Each database was searched from inception to May, 2013. The search terms used included green tea, *Camellia sinensis*, catechins, blood pressure, hypertension, lipids, and derivatives of these (comprehensive search strategy included as a Supplement Fig. 1S). We also searched the internet for relevant conference proceedings and hand searched relevant medical journals. The bibliographies of all located articles were also searched. No age, gender, or language restrictions were imposed.

Only double-blinded, randomized clinical trials (RCTs) were included in this review. To be considered for inclusion, RCTs had to test the effectiveness of orally administered green tea supplement against placebos or identical controls for blood pressure reduction in normotensive or hypertensive human volunteers. Studies had to report blood pressure and lipid profile as outcome measures, and must have had at least two weeks of intervention. Studies were included irrespective of lifestyle modification.

Two reviewers [IO and ES] independently assessed the eligibility of studies. Data extracted by two reviewers [IO and ES] included patient characteristics, interventions and results. The reporting quality of all included studies was assessed by the use of a quality assessment checklist adapted from the Consolidated Standard of Reporting Trials (CONSORT) Statement [28]. Disagreements were resolved through discussion.

The data were presented as means with standard deviations. Mean changes in systolic blood pressure, diastolic blood pressure, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides were used as primary endpoints to assess the differences between the intervention (green tea) and comparison (placebo or identical control) groups. Using standard meta-analysis software (RevMan 5.0) [29], we computed mean differences (MD) and 95% confidence intervals (CI) for studies with sufficient data for statistical pooling. The random-effects model was used for meta-analyses [30]. Sensitivity analyses (by analyzing trials based on reporting quality, duration of intervention, green tea formulation or lifestyle modification) were used to test the robustness of overall analyses. Subgroup analyses (by assessing the difference between groups in trials with similar participant characteristics, and by funding source) were used to investigate heterogeneity, using the I^2 statistic; values of 25%, 50%, and 75% indicated low, medium, and high statistical heterogeneity respectively. Heterogeneity was further explored by using dose-effect correlations (scatter plots of mean differences against daily dose) to examine the relationship between the dosage of EGCG and changes in blood pressure and lipid profile for studies $\geq$12 weeks in duration. Funnel plots with cumulative forest plots were used to test for publication bias.

Results

Our electronic searches returned 474 non-duplicate citations (Fig. 1), out of which 34 eligible trials were identified. Five RCTs were excluded because they did not report blood pressure as an outcome measure [31–35], and four because they were not double-blinded [36–39]. Two RCTs were excluded because they lasted less than two weeks in duration [40,41], and another two because green tea was combined with other supplements [42,43]. A total of 21 articles comprising 20 RCTs [44–64], and including a total of 1536 participants were included in the review. Key details of the RCTs are summarized in Tables 1 and 2.

All the RCTs were parallel design except three which were cross-over (Table 1). Nine RCTs reported adequate randomization techniques, four reported adequate allocation concealment, and three did not report adequate blinding procedures. Nine RCTs reported performing sample size calculations, and three reported intention-to-treat analyses. Participants in all RCTs had similar baseline demographics, except in one RCT where the green tea group had higher systolic and diastolic blood pressures compared with controls [64]. Only in one RCT were all participants described as hypertensive [45].