



SYSTEMATIC REVIEWS AND META-ANALYSES

Effect of vitamin D3 supplementation on blood pressure in adults: An updated meta-analysis



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Abstract *Background and aims:* Previous randomized clinical trials (RCTs) of the effects of vitamin D3 supplementation (VD3S) on blood pressure have generated inconsistent results. We evaluated the effect of VD3S on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in a meta-analysis.

Data synthesis: Literature searches of PubMed, Scopus, Ovid, and Google scholar for publications in English were conducted up to April 2015. RCTs that assessed the effect of VD3S on SBP and DBP were selected.

Conclusions: A total of 30 RCTs with 41 arms including 4744 participants were included. The mean duration of the studies was 5.6 ± 4.0 months, and doses of VD3S varied between 200 and 12,000 IU/day. VD3S had no effect on SBP (-0.68 mmHg, 95%CI: -2.19 to 0.84), and DBP (-0.57 mmHg, 95%CI: -1.36 to 0.22). Subgroup analysis revealed that daily vitamin D3 therapy at a dose of >800 IU/day for <6 months in subjects ≥ 50 years old reduced both SBP and DBP ($p < 0.001$). In addition, VD3S showed hypotensive effects in healthy subjects and hypertensive patients, but a hypertensive effect in overweight and obese subjects. However, after excluding overweight and obese subjects, VD3S significantly reduced SBP and DBP. VD3S in combination with calcium supplementation significantly elevated SBP (3.64 mmHg, 95%CI: 3.15 – 4.13) and DBP (1.71 mmHg, 95%CI: 1.25 – 2.18). No evidence of publication bias was found. The effects of VD3S on blood pressure depend on dose of supplementation, treatment regimens, trial duration, and population subgroup. Supplementation may be beneficial at daily doses >800 IU/day for <6 months in subjects ≥ 50 years old.

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Introduction

Hypertension (HTN) is a chronic condition that can lead to renal disease, cardiovascular disease (CVD), stroke, and mortality. The prevalence of HTN in 2000 was 24.6% worldwide, and it is estimated to reach 29.2% by 2025 [1]. According to the National Health and Nutrition Examination Survey (NHANES) report in 2011–2012, the burden of HTN was estimated to be 29.1% among the American adult population [2]. Previous studies have shown that outcomes of HTN can be reduced by lowering blood pressure levels [3,4]. A meta-analysis revealed that a 10-mmHg decrease in systolic blood pressure (SBP) and a 5-mmHg decrease in diastolic blood pressure (DBP) reduced the risks of coronary heart disease (CHD) and stroke by 20% and 32%, respectively [5].

Vitamin D plays a key role in the regulation of calcium and bone homeostasis. Studies have indicated that vitamin D status is associated with mortality, type 2 diabetes, metabolic syndrome, CVD, and renal disease [6–8]. Moreover, previous cross-sectional and cohort studies have shown an inverse association between 25-hydroxyvitamin D (25(OH)D) concentration and blood pressure [9–12]. A previous meta-analysis including eight prospective studies reported that the level of 25(OH)D was inversely associated with the incidence of HTN (RR: 0.70; 95% CI: 0.58–0.86) [13]. In addition, a per-10 ng/mL increase in 25(OH)D levels was associated with 12% (95% CI: 0.81–0.97) lower risk of HTN. Previous randomized clinical trials (RCTs) have assessed the effect of vitamin D3 supplementation (VD3S) on blood pressure; however, their results are inconsistent [14,15]. A meta-analysis including four RCTs published in 2010, including normotensive and hypertensive subjects, indicated that VD3S significantly decreased SBP (–2.44 mmHg; 95%CI: –4.86 to –0.02), although it produced no significant change in DBP (–0.02 mmHg; 95%CI: –4.04 to 4.01) [16]. Since then, several other RCTs assessing the effect of VD3S on blood pressure have been conducted. Consequently, an updated meta-analysis is required. This study aimed to update the evidence from RCTs on the effect of VD3S on SBP and DBP.

Methods

Data source and strategy of search

We conducted a systematic review and meta-analysis of studies based on the PRISMA guidelines [17]. PubMed, Scopus, Ovid, and Google scholar databases were searched for RCTs that assessed the effect of VD3S on blood pressure with an inclusion period until the end of April 2015. The following keywords were used for studies pertinent to the study objectives: ((“Cholecalciferol”[Mesh] OR Vitamin D3 supplementation [title/abstract]) OR (vitamin d3[title/abstract] AND supplementation[title/abstract])) AND ((“Hypertension”[Mesh] OR “blood pressure”[Mesh]) OR (hypertens*[title/abstract])). The search was limited to studies published in English. There was no restriction for

publication date. We also checked the reference lists of published papers for relevant studies.

Study selection

The PICOS (patients, intervention, comparator, outcome, study design) criteria used to establish study eligibility are provided in [Supplementary Table 1](#). Studies were eligible for inclusion if they fulfilled the following criteria: a) the study design was an RCT, b) the intervention was oral VD3S, c) the outcomes of interest were SBP and DBP, and d) the population of interest was adults (aged >18 years). Trials that compared VD3S versus placebo, or used VD3S in combination with calcium versus calcium, were included. Interventions were included independent of the duration and dose. Studies were excluded if they were animal studies or observational studies, uncontrolled RCTs, studies without a placebo group, and trials that involved vitamin D in forms other than cholecalciferol, such as vitamin D3-fortified products, or that used variable doses of vitamin D3. Studies were also excluded if they involved children and adolescents, pregnant and lactating women, and patients with renal disease, hypercalcemia, hyperparathyroidism, malabsorption, and hyperthyroidism. Studies that did not report SBP and DBP at baseline, or the changes after intervention from baseline, were also excluded.

Definitions

The outcome was defined as the change in SBP and DBP from baseline. The intervention was VD3S (cholecalciferol).

Extraction of data and assessment of quality

Data were extracted independently by two investigators (MG and GK) using a predefined data collection form. Any disagreement was resolved by consensus. The following information was extracted: sample size of each group, details of the population under study (age, sex, and ethnicity), geographic location, year of publication, dose of VD3S, duration of study, mean and standard deviation of SBP and DBP in both the intervention and placebo groups at baseline and at the end of study, and their changes from baseline. Authors were contacted if extra data were required. If studies used different doses of vitamin D3 versus placebo, each dose of vitamin D3 was included separately in the analysis. When studies had measured blood pressure at different intervals during the study, we only included the final SBP and DBP in the analysis.

The quality of studies was assessed using the Jadad scale for reporting randomized controlled trials [18]. The Jadad score is based on a description of randomization, blinding, and dropouts. The studies were considered to be of low quality if their Jadad score was <3, and the rest were considered as high-quality studies.

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