Complementary and alternative medicine approaches to blood pressure reduction

An evidence-based review

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ABSTRACT

Objective. *To review the evidence supporting complementary and alternative medicine approaches used in the treatment of hypertension.*

Quality of evidence. *MEDLINE and EMBASE were searched from January 1966 to May 2008 combining the key words* hypertension *or* blood pressure *with* acupuncture, chocolate, cocoa, coenzyme Q10, ubiquinone, melatonin, vitamin D, meditation, *and* stress reduction. *Clinical trials, prospective studies, and relevant references were included.*

Main message. *Evidence from systematic reviews supports the blood pressure–lowering effects of coenzyme Q10, polyphenol-rich dark chocolate, Qigong, slow breathing, and transcendental meditation. Vitamin D deficiency is associated with hypertension and cardiovascular risk; supplementation lowered blood pressure in 2 trials. Acupuncture reduced blood pressure in 3 trials; in 1 of these it was no better than an invasive placebo. Melatonin was effective in 2 small trials, but caution is warranted in patients taking pharmacotherapy.*

Conclusion. *Several complementary and alternative medicine therapies can be considered as part of an evidence-based approach to the treatment of hypertension. The potential benefit of these interventions warrants further research using cardiovascular outcomes.*

EDITOR'S KEY POINTS

- Complementary and alternative (CAM) therapies are becoming increasingly popular among patients. Do CAM therapies have any place in the treatment of common health conditions, such as hypertension?
- Level I evidence for use in hypertension exists for dark chocolate, coenzyme Q10, Qigong, slow breathing techniques, and meditation. The author concludes that these interventions can be considered for use in patients with hypertension, particularly in those with an interest in CAM therapies.
- It should be noted, however, that the studies looked mainly at the effects of these therapies on intermediate end points, such as blood pressure lowering, rather than on cardiovascular outcomes, such as cardiac events or death.

High blood pressure (BP) is one of the most important cardiovascular risk factors worldwide. (1) Only about one-third of patients achieve optimal BP control using drug therapy. (2) Because a reduction of 5 mm Hg in systolic BP has been associated with a 7%

reduction in all-cause mortality, (3) it is important to consider other interventions that reduce BP.

The Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure recommends 5 lifestyle changes for all patients with hypertension: reducing sodium intake, increasing exercise, moderating alcohol consumption, losing weight, and following the Dietary Approaches to Stop Hypertension (DASH) eating plan. (2)

Less widely prescribed – but increasingly popular among patients – are complementary and alternative medicine (CAM) antihypertensive therapies. *Complementary and alternative medicine* describes the field of inquiry into therapies that are not widely taught in medical schools nor generally available in hospitals. (4) Canadian use of CAM therapies is similar to that in the United States, (5) where 36% of people regularly use CAM. (6) This article reviews some CAM approaches to BP reduction and the clinical evidence supporting their use. ❑

QUALITY OF EVIDENCE

MEDLINE and EMBASE were searched from January 1966 to May 2008 combining the key words *hypertension* or *blood pressure* with *acupuncture, chocolate, cocoa, coenzyme Q10, ubiquinone, melatonin, vitamin D, meditation,* and *stress reduction*. Human clinical trials and prospective studies were selected, along with relevant references. The interventions were selected by the author based on a familiarity with the CAM literature and popular use by patients and CAM practitioners.

Level I evidence was available for most of the interventions (Table 1), although some studies had methodologic limitations inherent to nondrug clinical trials. This was most relevant to acupuncture and mind-body trials. ❑

Table 1. Evidence supporting CAM approaches to BP reduction

INTERVENTION	EVIDENCE
Dark chocolate	Meta-analysis of 5 RCTs
Coenzyme Q10	Meta-analysis of 12 RCTs
Melatonin	2 RCTs
Vitamin D	2 RCTs, 2 case-control studies
Qigong	4 of 5 trials including 2 RCTs
Slow breathing	Systematic review
Meditation	Meta-analysis of 9 RCTs
Acupuncture	2 of 3 RCTs

BP – blood pressure, CAM – complementary and alternative medicine, RCT – randomized controlled trial.

CHOCOLATE

Dark chocolate and other foods derived from the cacao bean (*Theobroma cacao*) are rich in flavonoid polyphenols such as procyanidins.7 The Olmec and Aztec Mesoamericans used cacao to treat pain and inflammation.

An impressive relationship between cacao intake, BP, cardiovascular outcomes, and mortality was first demonstrated in the Dutch Zutphen Elderly Study. When 470 elderly men were followed prospectively for 15 years, those with the highest cocoa consumption had lower BP – and an adjusted 50% relative reduction in risk of cardiovascular and all-cause mortality. (8)

This is confirmed by several small trials. A recent metaanalysis of 5 randomized controlled trials (N = 173) measured BP before and after daily consumption of chocolate. Patients consumed an average of 100 g daily (500 mg of polyphenols) for approximately 2 weeks. There was a reduction in systolic BP of 4.7 + 2.9 mm Hg ($P < .002$) and in diastolic BP of 2.8 + 2.0 mm Hg ($P < .006$). (9)

The meta-analysis was statistically rigorous; 2 authors reviewed each of the studies and their methodologic quality (Jadad scale score of 8 to 10 out of 13). A funnel plot showed no publication bias, sensitivity analysis identified 1 study with undue influence, and Cochran Q testing uncovered some interstudy heterogeneity. The authors did not report concurrent methods of BP measurement or medication use. Blood pressure reduction was seen in 2 trials of hypertensive patients and in 2 of 3 trials of normotensive subjects.

The authors subsequently found long-term BP reduction from regular consumption of smaller amounts of chocolate. (10) They randomized 44 hypertensive patients to receive a 6.3 g square of dark chocolate or white chocolate daily for 18 weeks; those who ate dark chocolate had a reduction in systolic BP of 2.9 ± 1.6 mm Hg ($P < .001$) and in diastolic BP of 1.9 ± 1.0 mm Hg ($P < .001$).

This study was also important because the authors found a substantial rise in serum levels of S-nitrosoglutathione, which reflects levels of nitric oxide. This supports other evidence that suggests flavonoids in cacao upregulate nitric oxide synthase in endothelial cells (11) and that chocolate improves endothelial function. (12)

It seems reasonable to recommend that people with hypertension eat 10 to 30 g of dark chocolate daily. Recent data suggesting that dark chocolate also improves vascular function in diabetic patients should alleviate concern in this

population. (13) Because most commercial chocolate bars are processed under conditions that destroy flavonoids, so-called *gourmet* chocolate containing at least 70% cacao is a better choice. One potential risk is the triggering of migraine headaches in some patients. ❑

COENZYME Q10

Coenzyme Q10 (CoQ10) is known as *ubiquinone* because of its ubiquitous distribution in nature. First isolated in beef mitochondria in 1957, it is an integral component of the mitochondrial electron transport chain in humans. (14) Supplemental CoQ10 is known to reduce lipid peroxidation. (15) Good evidence supports its use in congestive heart failure, and small trials have found benefits for patients with type 2 diabetes, atherosclerosis, migraine, and Parkinson disease. (16) Coenzyme Q10 levels are reduced by statin therapy because it shares the hepatic mevalonate synthetic pathway with cholesterol. (17) Patients with hypertension have reduced serum levels of CoQ10. (18) A meta-analysis of 12 clinical trials of 352 patients concluded that CoQ10 lowers BP. (19) Blood pressure decreased by 16.6/8.2 mm Hg ($P < .001$) in 3 randomized, double-blind controlled trials (n = 120), and by 13.5/10.3 mm Hg ($P < .001$) in the other studies, which were open-label, uncontrolled trials. Patients were treated at doses of 60 to 120 mg daily for 6 to 12 weeks. While the meta-analysis was limited by heterogeneity of the study populations, in many studies patients were able to discontinue medication.

Evidence from a large, prospective, multicentre trial with conventional end points of death and major cardiac events is much needed; however, the study's authors stated that "until the results of such trials are available, it would seem acceptable to add CoQ10 to conventional antihypertensive therapy." (19)

Coenzyme Q10 is available over-the-counter in doses ranging from 30 to 150 mg. The usual dose of 60 to 120 mg once to 3 times daily is not associated with any serious risks; mild gastrointestinal upset is the only side effect reported in a long-term trial of 3500 patients with congestive heart failure. (20) It might be wise to ask patients to monitor their BP for the first 2 to 3 weeks of therapy in the event of symptomatic BP reduction. ❑

MELATONIN

In the absence of light, retinal stimulation triggers adrenergic input to pineal production of melatonin. (21) René Descartes called the pineal gland "the seat of the soul," but melatonin (*N*-acetyl-5-methoxytryptamine) was not characterized until 1950. It is available over-the-counter, and its use as a sleep aid is based on a systematic review establishing its efficacy in treating jet lag. (22)

Several findings support a link between melatonin and BP. Decreases in BP at night (23) are consistent with diurnal variation in cardiac events. (24) Nighttime BP is more predictive of cardiovascular outcomes than daytime BP. (25) People with coronary artery disease have reduced serum melatonin levels, (26) and diurnal variation in endotheliumdependent vasodilation is impaired in these patients. (27)

Some preliminary evidence supports the potential use of melatonin in hypertension. A randomized, double-blind crossover study examined 18 women; 9 had hypertension and were treated with angiotensin-converting enzyme inhibitors. (28) They were each given 3 mg of melatonin or placebo nightly for 3 weeks, and 24-hour ambulatory BP readings were taken at the end of each study period. Melatonin use modestly lowered mean BP by 3.77/3.63 mm Hg ($P = .013$). The number of patients demonstrating a nocturnal BP-drop rose from 39% to 84%.

In another double-blind crossover study, 16 men with untreated hypertension each received 2.5 mg of melatonin or placebo for 3 weeks; 24-hour ambulatory BP readings were similarly used. Patients experienced a significant 6/4 mm Hg drop in BP after 3 weeks of melatonin use (systolic, $P = .046$; diastolic, $P = .020$). (29) There was also a nonsignificant trend to greater diurnal BP variation.

While there have been no reported adverse events associated with use of melatonin, caution is warranted in patients taking antihypertensive medication. Melatonin raised BP in 1 study of 47 patients taking nifedipine. (30) Conversely, 10 weeks of b-blocker therapy reduced melatonin levels in 42 patients. (31) ❑

VITAMIN D

Although vitamin D is traditionally known for its effects on calcium homeostasis, a growing body of evidence points to its widespread effects on cancer, immunity, and cardiovascular disease. (32) A link between vitamin D status and BP is suggested by evidence that 1,25-dihydroxyvitamin D inhibits renin production (33) and blocks proliferation of vascular smooth muscle

cells. (34) Such a link could explain why BP rises with increasing distance from the equator, is higher in the winter than the summer, and is higher in patients of African origin. (35)

Vitamin D deficiency has been associated with increased risk of hypertension in 2 large prospective cohort studies. In a pooled analysis of more than 1700 normotensive patients, those with serum 25-hydroxyvitamin D (25-[OH]D) levels less than 40 nmol/L had a relative risk of 3.18 for developing hypertension over a 4-year period (95% confidence interval [CI] 1.39 to 7.29). (36) The importance of this finding is increased by a recent case-control study of 1354 patients in the Health Professionals Followup Study in which those with serum 25(OH)D levels less than 75 nmol/L had a relative risk of myocardial infarction of 2.42 (95% CI 1.53 to 3.84, $P < .001$). (37)

Short-term treatment of vitamin D deficiency appears to lower BP. In a randomized controlled trial (RCT), 148 elderly women with baseline 25(OH)D levels of less than 50 nmol/L were given either 1200 mg calcium plus 800 IU of vitamin D3 or 1200 mg calcium alone. At the end of 8 weeks, systolic BP decreased by 13.1 mm Hg in the calcium and vitamin D3 group compared to 5.7 mm Hg in the calcium-only group ($P < .02$). (38)

Ultraviolet (UV) B light waves trigger endogenous vitamin D production. A small RCT randomized 18 vitamin D–deficient hypertensive adults to undergo 18 tanning bed sessions over 6 weeks providing either UVA and UVB light or UVA light alone. Ambulatory 24-hour BP decreased by 6/6 mm Hg in the UVB group but did not decrease in the UVA group ($P < .001$).

Patients with deficiency should be treated and retested monthly until serum levels are greater than 75 nmol/L. While some patients might require high doses, experts agree that the risk of toxicity is low; up to 50000 units of vitamin D3 have been used daily for up to 5 months without side-effects. (39) ❑

MIND-BODY APPROACHES

Emotional and psychological stress is an acknowledged mediator of hypertension; several mind-body interventions have been evaluated for BP-lowering potential.

Qigong is a part of traditional Chinese medicine (TCM) that incorporates movement, breathing, and meditation. Two systematic reviews have examined its role in hypertension. The first examined 12 RCTs involving 1218 patients. Overall outcomes were positive, but control groups were very different among the trials. Metaanalysis of 2 suitable trials demonstrated significant decrease in systolic BP of 12.1 ± 5.0 mm Hg (95% CI 7.0 to 17.1 mm Hg) and diastolic BP of 8.5 ± 4.1 mm Hg (95% CI 4.4 to 12.6 mm Hg). (40) The second meta-analysis examined 9 RCTs involving 908 patients and concluded that Qigong was superior to inactive control (decrease in systolic BP 17.0 ± 5.5 mm Hg, diastolic BP 10.0 ± 7.5 mm Hg) but not to drug or exercise control. (41)

Slow, controlled breathing can increase parasympathetic and decrease sympathetic nervous system activity, (42) which are important factors controlling BP. (43) A systematic review found 5 prospective studies, 2 of which were RCTs, involving a total of 356 patients, investigating the role of slow, controlled breathing in hypertension. Four out of 5 trials demonstrated benefit, with the only negative trial involving 30 diabetic patients for whom autonomic dysfunction was deemed a confounding factor. (44)

Transcendental meditation is a form of meditation in which the practitioner sits twice daily with eyes closed and repeats a mantra in a prescribed manner. While it has been called into question owing to the controversial nature of the transcendental meditation organization, 45 a meta-analysis of 9 RCTs found a reduction of 4.7 mm Hg (95% CI 7.4 to 1.9 mm Hg) in systolic BP and 3.2 mm Hg (95% CI 5.4 to 1.3 mm Hg) in diastolic BP. (46) ❑

ACUPUNCTURE

Acupuncture is a therapeutic modality anchored in TCM. The nature of the intervention creates unique methodologic challenges and controversies, including the choice of placebo and the different forms of treatment based on a non-Western system of diagnosis. Nonetheless, standards have evolved to address these issues. (47)

Acupuncture has been evaluated in 3 RCTs with mixed results. In one, 160 Germans with mild to moderate hypertension were randomized to receive real or sham acupuncture. Patients were treated by Chinese TCM physicians who did not speak German. Points were selected based on 1 of 4 types of hypertension according to TCM criteria. After 6 weeks (22 treatments), real acupuncture led to a 6.4 + 2.9 mm Hg and 3.7 +2.1 mm Hg greater reduction in systolic and diastolic BP, respectively ($P < .001$), than the sham treatment.

Similar findings were reported in a trial of 30 patients, with declines of 14.8/6.9 mm Hg in the

real acupuncture group versus 4.0/1.1 mm Hg in the sham group. (48) One large negative trial, the Boston SHARP study, found no significant difference between active and sham treatments in 188 patients. Blood pressure declined significantly in both groups, and the authors suggested that their results might have been different had they used a noninvasive control. (49) ❑

CONCLUSION

These interventions can be considered for all hypertensive patients, particularly those with an interest CAM. In most cases, level I evidence supports their use.

While the evidenc1e supporting these CAM interventions is not as robust as that for pharmacotherapy, this should be considered in the context of the limitations of evidence-based medicine. Large, multinational RCTs provide the best clinical evidence, but their massive cost limits their viability largely to patented pharmaceutical drugs. Governments and insurers should direct more funding to these and other rational CAM interventions. Until then, our review concludes the following:

- The best evidence exists for dark chocolate, coenzyme Q10, Qigong, slow breathing techniques, and meditation. All are supported by systematic reviews. The largest BP reduction was seen with use of coenzyme Q10.
- Two RCTs support BP reduction by treating vitamin D deficiency using UVB light or supplementation. Serum vitamin D levels have also been associated with risk of cardiovascular events in large prospective cohort studies and short-term supplementation reduced BP in 1 randomized trial.
- Two small trials support the use of melatonin, but other studies suggest caution when combining it with calcium-channel blockers or β-blockers.
- The evidence from 3 acupuncture trials is mixed, but this might be related to some therapeutic effect of the placebo chosen in the 1 negative trial.
- Dark chocolate was effective in a meta-analysis of 5 RCTs. Increased consumption was associated with significantly reduced risk of cardiovascular events and all-cause mortality in 1 prospective cohort study. ❑

Dr Nahas is the founder and Medical Director of Seekers Centre for Integrative Medicine in Ottawa, Ont.

Competing interests

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