

Review Article

Integrated review of management of hypertension by lifestyle changes, yoga, exercise, acupressure, plant/herbal and allopathic medications and newer interventions

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ABSTRACT

Hypertension is a global epidemic with prevalence almost similar in urban and rural populations and it is a significant modifiable risk factor for cardiovascular disease, stroke, and renal diseases. Although many modalities of treatment are available, a large percentage of patients don't have their blood pressure (BP) under control, hence, the management of hypertension has become a vital issue. We do find very few integrative reviews considering all feasible modalities of treatment for hypertension like lifestyle changes (low sodium intake, diet, reduction of bodyweight, limitations of alcohol consumption and cessation of smoking), yoga, exercise, acupressure, plant/herbal and allopathic medications and newer interventions, therefore, we performed a Medline search to review relevant articles in English literature. Data were constructed and issues were reviewed and we found that all the above modalities of treatment have reasonable scientific evidence and suggest to be used judiciously as monotherapy or in compatible adjunct combinations for better control of hypertension. We recommend more integrated treatment approaches and reviews in future.

Keywords: Hypertension, Lifestyle Changes, Yoga, Acupressure, Herbal Medicine.

Hypertension is one of the leading causes of morbidity and mortality worldwide and a primary risk factor for cardiovascular and cerebrovascular diseases, chronic kidney disease, and dementia [1,2]. Population is very diverse across the globe with people of different regions like developed countries, developing countries, under developed- poor/ tribal communities, have varied levels of educational awareness, affordability and accessibility towards health care. As per the WHO, there were 1.13 billion people with hypertension (BP >140/90mmHg) in 2015 and among them, nearly half of the World's adults with hypertension were living in Asia (approximately 226 million in China and around 210 million in India).

Prevalence of hypertension has been increasing steadily over the last decade [2-4]. In a particular geographic area, patients tend to use the modality of treatment for hypertension, based on their affordability and accessibility. Uncertainties remain about the optimal therapy for hypertension even though there are many well established national/international guidelines for management of hypertension. Due to paucity of articles integrating all feasible modalities of treatment of hypertension like lifestyle changes - low sodium intake, diet, reduction of bodyweight, limitation of alcohol consumption and cessation of smoking, yoga, exercise, acupressure, plant, herbal and allopathic medications and newer interventions, we performed a Medline search to review relevant articles in English literature. Data were collated and various issues were reviewed from there.

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Lifestyle changes

JNC-7 (Joint national committee) have endorsed lifestyle changes for all patients with prehypertension or hypertension [1].

A. Sodium intake and hypertension

Increased sodium consumption (>2 grams/day, equivalent to 5 grams salt per day) and inadequate potassium intake (less than 3.5 grams per day) can contribute to high blood pressure and increase the risk of cardiovascular diseases, stroke and renal diseases. The main sources of sodium in our diet are salt and condiments. The increased sodium intake and the raise in blood pressure levels are related to water retention, increased systemic arterial resistance, alterations in the endothelial function, changes in the structure and function of large elastic arteries, modifications in sympathetic activity, and also due to excess sodium induced autonomic neuro hormonal modulation of the cardiovascular system [5-7]. Up to date numerous epidemiologic, clinical, and experimental studies, have found significant link between dietary sodium intake and blood pressure, and a reduction in dietary salt intake (less than 5 grams per day) has been documented to lower blood pressure and also reduce the risk of cardiovascular disease [8,9].

Many people consume excess salt, on an average 9 to 12 grams per day, or around twice the recommended maximum level of intake. A meta-analysis of longer-term trials, conducted by Feng and Graham to check at the dose response between salt reduction and fall in blood pressure and compared this with two well-controlled studies of three different salt intakes, they found all the 3 studies demonstrated a consistent dose response to salt reduction within the range of 12 to 3 g/d. A reduction of 3 g/d, could reduce blood pressure of 3.6 to 5.6/1.9 to 3.2 mm Hg (systolic/diastolic) in hypertensives and 1.8 to 3.5/0.8 to 1.8 mm Hg in normotensives and the effect would be doubled with a 6 g/d reduction and tripled with a 9 g/d reduction [10-12].

B. Other Dietary elements and hypertension

Vegetarian diets are usually associated with lower blood pressure levels compared to meat eaters and people adopting dietary reductions of calories and sodium, consuming more dietary fiber, polyunsaturated fat, potassium and significantly low saturated fat, have significantly lower mean blood pressures [4, 13-15]. Appel L J et al, involving 459 adults (133 hypertensive adults and 326 normotensive adults) in the Dietary Approaches to

Stop Hypertension Trial demonstrated, that, a combination diet high in fruits, vegetables, and low-fat dairy servings and with reduced saturated and total fat could, reduce blood pressure by 5.3 and 3.0 mm Hg systolic and diastolic blood pressure, respectively among hypertensive adults, in the absence of either sodium restriction or weight loss [16]. A meta-analysis of randomized controlled trials by Tommaso F, found adequate potassium intake is desirable, but excessive potassium supplementation should be avoided particularly in specific subgroups like chronic kidney disease, can also improve blood pressure control [17].

Dietary intakes of potassium, calcium, and magnesium each have been reciprocally associated with hypertension. Frank M Sacks et al, tested a hypothesis among 300 normotensive persons who had low habitual intake of these minerals would be particularly responsive to supplementation and found that, potassium, but not calcium or magnesium supplements, exhibited blood pressure lowering effect in normotensive persons with low dietary intake [18].

C. Body weight and hypertension

Many studies have found weight loss can independently reduce blood pressure. Reisen et al conducted a study involving three groups of overweight patients with uncomplicated essential hypertension, 24 subjects not receiving antihypertensive-drug therapy (Group I) and 83 subjects on regular but inadequate antihypertensive-drug therapy (Group II) and all patients in Group I and 57 randomly selected patients from group II (IIa) were subjected to a weight-reduction program, with remaining 26 from Group II (IIb) did not receive a dietary program. All patients on the dietary program including normal salt intake, lost at least 3 kg (mean, 10.5 kg), and showed significant reduction in blood pressure; 75 per cent of Group I and 61 per cent of Group IIa [19,20].

Tuck et al, investigated the relation between changes in the renin-aldosterone axis and reduction in blood pressure in 25 obese patients placed on a 12-week weight reducing diet; sodium intake was either 120 mmol or 40 mmol and found that weight loss was associated with reductions in PRA (plasma renin activity) and aldosterone; PRA reductions, irrespective of sodium intake, could contribute to the decrease in blood pressure [21]. Maxwell et al, conducted a controlled prospective comparative study involving two groups of obese hypertensive subjects subjected to 12 weeks of a hypocaloric protein-supplemented fast containing 40 mEq of sodium daily in which one group received additional sodium chloride

sufficient to maintain baseline sodium intake measured prior to the fast (210 mEq/day). Sodium restriction resulted in greater weight loss and marked BP reduction only during the initial week of fasting but, in spite of sodium equilibrium, further substantial weight loss and BP reduction were similar in both groups [22].

D. Smoking and hypertension

Smoking tobacco can cause an acute increase in blood pressure (BP) and heart rate. The chemical components of smoke like nicotine, act as sympathetic agonist, mediating local and systemic catecholamine release and possibly the release of vasopressin, which in turn increases the blood pressure. As smoking and BP have been shown to have a synergistic adverse effect on the risk of cardiovascular diseases, it is very important that, people with raised BP are advised to stop smoking and many studies have depicted the benefits of cessation of smoking on blood pressure [23-26]. Szu-Ying sai et al, in a cohort study found that smoking cessation program significantly reduced both systolic and diastolic blood pressure and the results were more significant in the hypertensive group compared to the non-hypertensive group [27].

E. Alcohol and hypertension

Alcohol consumption should be restricted to - no more than 2 drinks per day (24 oz beer, 10 oz wine, 3 oz of 80 proof whiskey) for most men and no more than one drink per day for women. Excess alcohol levels in blood, induces an increased sympathetic outflow, most probably linked to secretion of corticotropin releasing hormone and diminishes the baro (presso) reflex by interacting with receptors in the brain stem centers like, nucleus tractus solitarius and rostral ventrolateral medulla. One more possible mechanism of alcohol induced hypertension could be due to shift in baroreceptor reflex curves, which indicate the gain in baroreceptor reflex sensitivity, and reduced slope in ethanol fed rats when challenged with vasoconstrictors (phenylephrine and angiotensin II) compared with controls, indicating impairment of baroreceptor control and sympathetic system.

Additionally, an imbalance of specific endogenous vasoconstrictor such as angiotensin II, endothelin-1 and nor-epinephrine and vasodilator nitric oxide (NO) may also play an important role in alcohol-induced elevation of blood pressure. Skliros E A et al, involving 637 elderly Greek population, found that hypertension was positively associated with heavy alcohol consumption. Study conducted by Ueshima et al, has shown that a reduction in alcohol intake is effective in lowering the blood pressure both in hypertensives and normotensives

and also may help prevent the development of hypertension [28-31].

Yoga and hypertension

Yoga is a unique psycho-somatic-spiritual discipline for achieving harmony between our mind, body, and soul and the ultimate union of our individual consciousness with the universal consciousness. When people practice yoga, with yogic attitude (attitude of patience, persistent practice, overcoming obstacles within self, that is, trouncing laziness, anger, delusion, and desire for being different or better than others), several physiological changes can occur. Worldwide, yoga practices have been shown to reduce blood pressure in many research studies. In a study conducted at Bengaluru, India, there was statistically significant decrease in both systolic as well as diastolic blood pressure with $p < 0.5$, with six months of yoga practice [32,33].

Concordantly McCaffrey R conducted a study among hypertensive patients in Thailand and found that yoga significantly decreased both systolic and diastolic blood pressures [34]. Damodaran A et al found that yoga practices among middle aged men and women significantly helped in modifying cardiovascular risk factors by decreasing heart rate and systolic and diastolic blood pressures [35]. Another study conducted by Deepa T involving 30 hypertensive patients, found significant fall of mean blood pressure after 3 months of Yoganidra and suggested that yoga can be used as adjunctive therapy with drug therapy on mild and moderate essential hypertensives [36].

Similarly, a study conducted by Thiyagarajan R et al, also showed mean SBP reduction by 4 and 6 mmHg with lifestyle changes alone and lifestyle changes plus yoga therapy respectively. Yoga also resulted in reduction of heart rate, waist circumference and lipid levels, which in turn reduce CVD prevalence and mortality [37]. Selvamurthy W et al performed a study on 20 male patients of Essential Hypertension (EH) in order to explore the possible role of baroreflex mechanism in the etiology of Essential hypertension and also to find out whether by restoration of baroreflex sensitivity to normal level by yogic postural exercise (Yogic asanas), and they found that yogic asanas significantly reduced blood pressure [38].

Exercise and hypertension

Numerous studies have consistently demonstrated beneficial effects of exercise on hypertension with decrease in both systolic and diastolic blood pressure as

much as 5–7 mmHg. Regular exercise could result in more sustained decrease and control of high blood pressure [39,40]. Ebrahim et al, conducted a study involving eight clinical trials, in which exercise was a primary component in blood pressure reduction and found significant impacts on blood pressure reduction of 0.8 to 3.7 mm Hg resulting from exercise [41].

A meta-analysis of the effects of exercise on blood pressure conducted by Kelley et al, depicted a decline in systolic blood pressure of 3 to 5 mm Hg associated with moderate exercise [42]. The decrease in blood pressure with exercise is possibly due to reduction in peripheral vascular resistance, which could be due to neurohormonal and structural responses with decrease in sympathetic nerve activity and an increase in arterial lumen diameters. Other possible mechanisms for blood pressure reduction could include changes in oxidative stress levels, inflammatory changes, endothelial function, and arterial compliance, body mass, renin-angiotensin system activity, parasympathetic activity and renal function [43,45].

Acupressure and hypertension

Acupressure is one of the methods used in traditional medicine and it is a simple, non-invasive technique, for treatment as well as prevention of many diseases including hypertension. Li-Wei Zheng et al, conducted a study to evaluate the effect of acupressure on blood pressure and sleep quality in middle-aged and elderly patients with hypertension, out of 75 elderly hypertensive patients involving an experimental group (n = 38) or a control group (n = 37), the experimental group received acupressure treatment along with conventional treatment. The score of PSQI (Pittsburgh Sleep Quality Index) and blood pressure were measured and recorded before and after the treatment and they found that after the intervention, the systolic (SBP) and diastolic blood pressure of the experimental group decreased significantly ($p < 0.01$). After four weeks of intervention, the total PSQI score in the experimental group was significantly lower compared to the control group ($p < 0.01$), and they concluded that acupressure can lower BP and effectively improve the sleep quality in middle-aged and elderly patients with hypertension [46].

Bicer S et al, conducted a randomized controlled study involving a total of 91 people, 47 in the intervention group and 44 in the placebo group and found that acupressure, applied to the Neiguan (PC 6) acupuncture point in individuals with essential hypertension, helps in blood pressure regulation and is effective for management of numerous hypertension-related symptoms [47].

Paskalis et al, conducted research with 42 respondents with the provision of complementary interventions gymnastics prolans and acupressure extremities 3 times a week, for 4 weeks, and found decrease of systolic blood pressure and diastolic blood pressure and suggested gymnastics and acupressure limb extremities for patients with grade II hypertension as an alternative treatment [48].

Sulton W, et al have suggested that, the suppression effect of acupressure points Taixi (KI3) and Sanyinjiao (SP6) were effective to decrease blood pressure in the elderly with hypertension [49]. Zubaidha conducted an observational study involving 15 patients, subjected them to acupressure therapy and found that acupressure can reduce systolic and diastolic blood pressure among hypertensive patients [50].

Plant/Herbal medicines and hypertension

The rich Indian Ayurveda, siddha, Unani and homeopathy systems, the Pun-tiao records of the Chinese, the Hippocratic Corpus of the Greek, the Roman De Materia Medica and the Egyptian papyrus, have documented thousands of plants and herbal sources for treating ailments over many years. Herbal medicine usage has increased over the last decade probably due to cheaper alternative with fewer undesired side effects. However, the increased desire to use herbal treatment does not reflect the economic status of an individual from a certain region or a country. About 70% and more of the population in developed nations have developed inclination towards Complementary and Alternative Medicine (CAM) for treatment purposes, and herbal medicine forms a large percentage of its application and the usage of CAM in developing countries has increased exponentially [51-56].

Chinese Herbal Medicine (CHM) and Traditional Chinese Medicine (TCM): TCM like Danshen injection, astragalus injection, Shengmai injection, and Danhong injection, 12 oral CPM (Chinese proprietary medicines) such as the Niu Huang Jiangya pill, Liuwei Dihuang pill, and Songling Xuemaikang capsule and 13 types of oral CHM decoctions such as Xuefu Zhuyu decoction, Banxia Bbaizhu Tianma decoction, and Lingjiao Gouteng decoction have shown advantages as adjunctive therapy for improving hypertension. Similarly, the development trend of CHM and non-drug therapy for the prevention and treatment of hypertension, reflects the diverse TCM effectiveness for hypertension [57]. Xinxing et al found that SXC (Songling xuemaikang capsule) was well tolerated and demonstrated noninferior to losartan in BP lowering in patients with mild hypertension. SXC might be an alternative for mild hypertension, particularly for patients with a preference for natural medicine [58].

A survey conducted by H. De wet in rural community in northern Maputaland, South Africa, to document the plants used by 100 lay persons for the treatment of hypertension, found that a total of 28 medicinal species were used and played a vital role in the treatment of not just communicable diseases but also in the treatment of chronic ailments. The species most used were: *Momordicabalsamina*, *Aloe marlothii*, *Hypoxishemerocallidea*, *Musa acuminata*, *Strychnosmadagascariensis*, and *Senecioserratuloides* [59]. Reserpine (which depletes adrenergic neurotransmitters) is still used for treatment for hypertension in some parts of the globe [60].

A review conducted by Sara, to study the pharmacological actions of herbs or herbal isolates *Allium sativa*, *Coriandrum sativum*, *Crocus sativa*, *Panax*, *Andrographis paniculata*, *Bidens pilosa* L., *Solanum sisymbriifolium*, *Solanum paludosum*, root extract of wild tomatoes basil, parsley, celery seeds, *Bacopamoni*, garlic, thyme, cinnamon, ginger, and cardamom, appeared to favorably modulate several parameters implicated in the pathogenesis of blood pressure, including but not limited to ROS (reactive oxygen species) production, endothelial function, platelet activation, pro-inflammatory signaling, and gene expression [61].

Another review by T Verma, analyzed the traditional utilization, phytochemical constituents and pharmacological values of medicinal herbs used to normalize hypertension. *Hibiscus sabdariffa*, *Allium sativum*, *Andrographis paniculata*, *Apium graveolens*, *Bidens pilosa*, *Camellia sinensis*, *Coptis chinensis*, *Coriandrum sativum*, *Crataegus* species, *Crocus sativus*, *Cymbopogon citrates*, *Nigella sativa*, *Panax ginseng*, *Salvia miltiorrhiza*, *Zingiber officinale*, *Tribulus terrestris*, *Rauwolfia serpentina*, *Terminalia arjuna* etc., affected the pathogenesis of hypertension by modulating parameters like endothelial function, ROS production, pro-inflammatory signaling, platelet activation, opening and closing of different ion channels, ACE inhibition, gene expression [62].

Raha Kamyab et al, depicted that Herbal Medicines used for hypertension in different regions of Iran. In Mobarakeh of Isfahan, curly dock (*Rumex crispus* L.), jujube (*Ziziphus jujuba* L.), and olive (*Olea europaea* L.) were used, whereas in Sistan and Baluchestan province, *Nigella* (*Nigella sativa* L.) was used, and Milk thistle (*Silybum marianum* L.), yarrow (*Achillea tenuifolia*), chicory (*Cichorium intybus*), barberry (*Berberis vulgaris*), shepherd's purse (*Capsella bursa-pastoris*), field horsetail

(*Equisetum arvense*), Persian walnut (*Juglans regia*), and annual yellow sweetclover (*Melilotus indicus*) were utilised in Kazerun for high blood pressure [63]. Amla (Indian gooseberry), Gotukola (Indian pennywort), Ashwagandha (Indian ginseng), *Parthadyarishta*, Brahmi have significant beneficial effects in hypertensive patients. Natural plants and herbs like black cumin, Chinese sage, coriander, garlic, ginger, ginseng, and tea can be our source of drugs, with fewer side effects and better bioavailability for treatment of hypertension in future [64].

Allopathic medicines and hypertension

The trials like ACCOMPLISH, ACCORD, ACCELERATE, ALLHAT, HOPE, CAPP, SPRINT, VALUE, ADVANCE, have elucidated the importance of starting antihypertensive treatment to achieve target BP control and prevent morbidity and mortality. The first line drugs used in treatment for stage 1–2 hypertension include: (1) Angiotensin converting enzyme inhibitors (ACEi), (2) Angiotensin receptor blockers (ARBs), (3) Calcium channel blockers, (4) Diuretics and (5) β -blockers. Other classes of antihypertensive drugs include Mineralocorticoid receptor antagonist, α blockers, central α 2 agonists, arterial vasodilators. The selection of an antihypertensive agent is dependent on age, concomitant risk factors, presence of HMOD (Hypertension mediated organ damage), other co-existing diseases, and socioeconomic considerations, availability of the drug and experience of the treating doctor. Combination therapy is often required, when target BP control is not achieved, with different classes of drugs with different mechanism of actions, with minimal side effects [1,4, 65].

Treatment for stage 2 hypertension, can be started either with two drugs or as a fixed dose combination. The ACCOMPLISH trial showed that combination of Angiotensin converting enzyme inhibitors with Calcium channel blockers was better than a combination of ACEi with diuretic. Usually, younger hypertensive patients have high renin levels; hence ACEi/ARBs or newer β -blockers could be preferred; while older hypertensives have low renin levels and hence diuretics or CCBs could be preferred as first line agents. While combining antihypertensives, one out of the two groups A [ACE inhibitor/ARB] or B [β - blocker] can be combined with C [calcium channel blocker] or D [thiazide diuretic] (step 2) and among refractory hypertensive patients, when three agents are to be used, A + C + D could be preferred (step 3). Stepped care approach with certain drug combinations have synergistic effect and increase the effectiveness of the other agent. However, some combinations are not effective and hence not be combined [1, 4,65,66].

In a recent study, Marc A Succhard et al, generated 22,000 calibrated, propensity-score adjusted hazard ratios (HRs) comparing all classes and outcomes across databases by involving 4.9 million patients, and revealed no effectiveness differences between classes. Thiazide (THZ), however, demonstrated better primary effectiveness than ACEi: acute myocardial infarction (HR 0.84; 95% CI 0.75–0.95), hospitalization for heart failure (0.83; 0.74–0.95) and stroke (0.83; 0.74–0.95) risk while on initial treatment. They also put forth that equivalence between drug classes for initiating monotherapy for hypertension in keeping with current guidelines with the exception of THZ superiority to ACEi and the inferiority of non-dihydropyridine calcium channel blockers (ndCCB) [67].

Newer approaches for hypertension

In this section, we would like to highlight the newer approaches/interventions for management of hypertension. A substantial portion of the hypertensive population have uncontrolled blood pressure despite taking treatment, hence few researchers have been developing new drugs and devices/procedures to treat hypertension and its comorbidities. New drug classes are:

1. Inhibitors of vaso peptidases, aldosterone synthase and soluble epoxide hydrolase.
2. Agonists of natriuretic peptide A and vasoactive intestinal peptide receptor 2.
3. A novel mineralocorticoid receptor antagonist which is in phase II/III of development.
4. Inhibitors of aminopeptidase A, dopamine β -hydroxylase, and the intestinal Na(+)/H(+) exchanger 3.
5. Agonists of components of the angiotensin-converting enzyme 2/angiotensin (1-7)/Mas receptor axis.
6. Vaccines directed toward angiotensin II and its type 1 receptor are in phase I or preclinical development.

Even though the SIMPLICITY III trial had not shown any effect on BP reduction with renal denervation compared to sham-controlled placebo therapy, the interventional approaches -transcatheter renal denervation and baroreflex activation therapy, are used in clinical practice with some technical modifications, for severe resistant hypertension in some countries. Renal denervation is also being evaluated for treatment of various comorbidities, like chronic heart failure, cardiac arrhythmias and chronic renal failure. Few more novel interventional approaches for treatment of hypertension, like carotid body ablation and arteriovenous fistula placement are in early developmental stages [4, 68-70].

Limitations of current review

We did not highlight many other modalities of management of hypertension like Tai chi, qigong, Chiropractic, aromatherapy, biofeedback, Reiki, Mindfulness therapy, spiritual therapy etc. Furthermore, under herbal medicine section of our review, we addressed herbs/plants in general, instead of categorizing them into Unani, Ayurvedic, Homeopathic, Siddha etc.

CONCLUSION

This present review found many therapeutic modalities with reasonable scientific evidence with regard to control of BP. Although lifestyle changes are often neglected, they should be started as early as possible and continued to get the beneficial effects. If adequate blood pressure control is not achieved despite of adopting life style changes, exercise, yoga, acupressure, then, either allopathic or herbal/plant medicines in compatible adjunct combinations in an integrated approach, can to be initiated to achieve target BP values. Constant communication between public health policy makers, physicians, other healthcare professionals, and patient education regarding risks of high blood pressure, benefits of lifestyle changes need for long term monitoring and adherence to treatment is also equally important in the successful management of hypertension. We recommend more integrated therapy approaches, research and reviews in future, for hypertension management.

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