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Herbal preparation for the treatment of Hypertension; A review

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ABSTRACT

Hypertension is a major risk factor for coronary heart disease, stroke, and premature deathand a leading risk factor for global disease burden. Prevalence for those 18 years and older in the United States has remained around 29% since 1999 with little improvement. Further, approximately one-third of U.S. adults have prehypertension, which is also associated with a graded, increased risk of cardiovascular disease and progression to hypertension. The overall evidence that diet modification can prevent and treat hypertension is strong. The current national guideline of lifestyle modification for blood pressure control includes the DASH eating pattern, sodium reduction, weight loss, increased physical activity, and moderate consumption of alcohol. Concurrent adherence to several recommendations is likely to hold the greatest promise for preventing and treating hypertension and has been shown to be feasible. In addition to addressing unresolved nutritional hypotheses, future research should focus on strategies to motivate and maintain lifestyle changes long term for blood pressure control. At both the population and individual levels, success in dietary and lifestyle intervention relies on multiple levels of support ranging from clinicians to government agencies to private institutes and industries. In particular, partnering with industry to improve the nutritional quality of the food supply, such as reducing sodium, sugar, and saturated and trans fat content of processed foods, and promoting foods and nutrients consistent with the DASH dietary pattern will play a critical role in implementing dietary and lifestyle modifications. Consistent efforts to educate and promote adherence to dietary and lifestyle guidelines by dietetic and other health care professionals are also instrumental to the prevention and management of hypertension. Many of the medications on hypertension causes various side effects that's why need of herbal medication is more nowadays. In this review we have gathered information about herbal medications on hypertension(1).

I. INTRODUCTION

Hypertension is defined as an abnormally high blood pressure (BP) and is one of the most important risk factors for cardiovascular disease and death. The limits that define hypertension are chosen to reflect the risk for disease related to the elevated BP although risk increases even within the 'normal' BP range. Hypertension is a risk factor for stroke, myocardial infarction (MI), left ventricular hypertrophy (LVH) and failure, renal disease, retinopathy, and peripheral arterial disease. Therefore, effective evaluation and treatment of hypertension remains an important medical goal, and understanding the pathogenesis of hypertension through animal models and clinical studies is a critical component.

Hypertension can be due to unknown causes, primary hypertension (previously called essential hypertension), or known causes, secondary hypertension. Primary hypertension accounts for about 85–90% of the cases of hypertension, which is lower than often quoted in most textbooks. The lower percentage is due to the recent appreciation of the role of primary aldosterone, which was once thought to be rare (< 1%) but is now known to constitute between 10% and 15% of hypertensive cases. Primary hypertension clusters in families and shows concordance in genetically related individuals illustrating the importance of genetic predisposition. The known inheritable syndromes regulating BP are caused by mutations regulating renal sodium handling.

Genetic factors interact with environmental factors to produce hypertension. Diet is an important determinant both in its salt content and in the increasing public health problem of obesity. Dietary salt may have chronic effects and relate to the observed increases in BP in Western societies with age. Obesity is now known to be a chronic inflammatory disease that increases the risk of hypertension and likely relates to the interaction of hypertension in increasing the risk of cardiovascular disease.

Abnormalities in a number of systems are seen in primary hypertension, yet the originating

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causes have remained elusive. Neural systems show an increased sympathetic flow with elevations of catecholamines. Central nervous system (CNS) interventions in a number of experimental systems can alter BP and prevent hypertension. The sympathetic system interacts with the hormonal systems that involve adrenal catecholamines and the important action of the renin–angiotensin–aldosterone system (RAAS). The RAAS involves multiple organs with the primary role of the kidney and adrenal cortex (glomerulosa layer producing aldosterone).

It is the major hormonal regulator of sodium and volume homeostasis and hence a major regulator of BP. Many of the pharmacological interventions used clinically to treat hypertension target this system. Defects in the vascular endothelial and smooth muscle cell function have been described(2).

TYPES OF HYPERTENSION

1 . Primary Hypertension

Primary hypertension is also known as essential hypertension. Most adults with hypertension are in this category.

Despite years of research on hypertension, a specific cause isn't known. It's thought to be a combination of genetics,

diet, lifestyle, and age. Lifestyle factors include smoking, drinking too much alcohol, stress, being overweight,

eating too much salt, and not getting enough exercise. Changes in your diet and lifestyle can lower your blood

pressure and risk of complications from hypertension.

2. Secondary hypertension

Secondary hypertension is when there's an identifiable— and potentially reversible— cause of your hypertension.

Only about 5 to 10% of hypertension is the secondary .It's more prevalent in younger people. An estimated30

percent of those ages 18 to 40 with hypertension have secondary hypertension.

Plants used in treatment of hypertension.

Uncariatomentosa

Uncariatomentosa (Willd. ex Schult.) DC. (Family: Rubiaceae), commonly known as cat's claw, is a tropical medicinal vine originating at the Amazon rainforest and other areas of South and Central America. It has been traditionally used to treat asthma, abscesses, fever, urinary tract infections, viral infections, and wounds and found to be effective as an immune system rejuvenator, antioxidant, antimicrobial, and anti-inflammatory agent. U. tomentosa is rich in many phytoconstituents such as oxindole and indole alkaloids, glycosides, organic acids, proanthocyanidins, sterols, and triterpenes. Biological activities of U. tomentosa have been examined against various microorganisms and parasites, including pathogenic bacteria, viruses, and Plasmodium, Babesia and Theileria parasites. Several formulations of cat's claw (e.g., tinctures, decoctions, capsules, extracts, and teas) are recently available in the market. The current review covers the chemical constituents, biological activities, pharmacokinetics, and toxic properties of U. tomentosa extracts(3).

Centellaasiatica

The cardiovascular effects of Centellaasiatica (CA) leave juice were studied using hypertensive animal model.Single oral administration of lyophilized powder of CA leave juice at doses 16, 24 and 32 g of fresh leaves/kg (equivalent to 0.26, 0.38 and 0.52 g of lyophilized powder/kg) on blood pressure, heart rate and regional cerebral blood flow (rCBF) were investigated in deoxycorticosterone acetate (DOCA)-salt hypertensive rats. CA lyophilized juice powder contained asiaticoside 0.42% w/w. The results showed that CA leave juice had blood pressure lowering and slight negative chronotropic effect in DOCA-salt hypertensive group, but not in normal. CA leave juice at the doses of 24 and 32 g/kg BW significantly decreased blood pressure from 30 to 90 and from 45 to 60 min with the maximal reduction of 11% and 12%, respectively, at 45 min in DOCA-salt hypertensive group. In addition, these two doses of CA leave juice significantly decreased HR at 60 and 45 min, respectively. Captopril at dose 25 mg/kg BW significantly reduced blood pressure at 30 to 120 min with a maximal reduction of 20% at 60 min and 19% at 90 min. in normal and DOCA-salt hypertensive groups, respectively. The significant effect on heart rate were not observed after captopril administration in both groups. Prior administration of CA leave juice, the rCBF level of DOCA-salt hypertensive group was significantly low, compared to that of the normal. After CA leave juice administration at the dose of 32 g/Kg BW, rCBF increased significantly at 5-90 and 5-120 min in normal and DOCA-salt hypertensive groups, respectively. The increased rCBF was greater in DOCA-salt hypertensive than normal group (maximum increased rCBF: 52.27% vs 37.37

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%). The increased rCBF was accompanied with significant decreased blood pressure at 15 to 120 min only in DOCA-salt hypertensive group. The maximum decrease of SBP and DBP were 13.86and 14.10 % at 60 minutes. These results demonstrates that CA leave juice possesses the actions as antihypertensive and regional cerebral blood flow enhancement in both normal and hypertensive rats. The present study suggested the beneficial use of CA in elderly especially in hypertensive condition(4).

EcliptaalbaHassk

Bhringarajais recently reported to have diuretic & antihypertensive activity in an ayurvedic study. This creates renewed interest for scientific evaluation of the claimed activity.Hypertension was induced in male wistar albino rats by providing fructose (66%) in their diet for 15 days. Ethanolic extract of Eclipta alba (EEEA) leaves was administered in 100,200&400 mg/kg doses P.O.to different groups of rats for 7days starting from day 16th of fructose administration.

The systolic, diastolic & mean arterial pressure (SBP, DBP, MAP) & heart rate(HR) were measured on day 7th,14th,21st & 28th day of administration standard & test drugs by non invasive BP system for rodents.

A rise in blood pressure was found on day 16th of fructose diet. EEEA decreased the rise in B.P significantly in a dose dependent manner comparable to Quinapril. Conclusion-EcliptaalbaHassk was found to possess significant antihypertensive activity in rat model. Further study in this line is necessary to pass its beneficial effects to clinical use(5).

Viscum album

Viscum album, an infrequently used antihypertensive in homeopathy, is evaluated by 1-group pretest–posttest model in primary hypertension. The drug was administered for 12 weeks at a dosage of 10 drops 3 times a day. Using paired t test, a significant drop in blood pressure ($P < .0001$) and serum triglyceride ($P < .0001$) was observed in the treatment group. This dual effect of Viscum album shows promise in optimizing therapy for primary hypertension(6).

Asparagus racemosus

Evaluate the anti-hypertensive activity of Asparagus racemosus rhizomes. In vitro study of Angiotensin Converting Enzyme (ACE) inhibitor activity of Asparagus racemosus had positive correlation with samples concentration (100 to 500µg/ml) and % ACE inhibition value. Increase in the sample concentration will increase the % ACE Inhibition value. This result suggested that the presence of phytochemical compounds in the Asparagus racemosus might be responsible for the inhibition of the ACE inhibition activity(7).

Ecliptaalba (EA) and Boerhaaviadiffusa (BD)

Ecliptaalba (EA) and Boerhaaviadiffusa (BD) are two herbaceous plants. EA is used to treat hepatic-dysfunction, hair diseases and anemia since ancient time. Similarly, BD is a great treatment-option for renal and urinary disorders. They have also been found quite effective in the safe treatment of hypertension. But studies in this respect are very scanty and confirmatory role of these herbs in hypertension is yet to be established. In the present study, effects of EA and BD on normal blood pressure (NBP) and hypertension were studied. Their antihypertensive activities were also compared with those of Amlodipine (Amlo). Adult Wistar rats of both sexes, weighing 140-150 g were randomized equally to make 9 groups (6 rats/ group). First 6 groups were given high fat diet for 49 days to produce hypertension. Then drugs were given for next 45 days without stopping high fat diet. 7th , 8th & 9th groups were meant to see the effects of EA and BD on NBP; they were kept on normal diet and were given EA-200 mg/kg, BD-200 mg/kg, EA+BD (200 mg/kg of each) respectively for first 45 days. SBP (systolic blood pressure) was measured by 'Tail-cuff method' with the help of NIBP (non-invasive blood pressure measurement)-controller machine(8).

Ashwagandha (Withaniasomnifera)

Ashwagandha (Withaniasomnifera) is widely used in Ayurvedic medicine, and it is one of the ingredients in many formulations to increase energy, improve overall health and longevity, and prevent disease. The main objective of the study was to analyze the efficacy of Ashwagandha root powder with water and with milk in treatment of hypertension. The experiment was conducted on 51 stress-oriented hypertensive subjects in the age group of 40 to 70 years, selected by purposive sampling. Subjects were divided into group I and group II. Supplementation of 2gm of Ashwagandha root powder was given to group I and group II with milk and water respectively in morning. Blood pressure was also recorded over a period of three months. Overall decrease in systolic blood pressure was found though it was non- significant. Further, decrease in systolic blood pressure was significant in group I, whereas decrease in diastolic blood

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pressure was significant in both the groups. Hence, supplementation of Ashwagandha with milk is recommended in treatment of stress- oriented hypertension(9).

Ginkgo biloba

Ginkgo bilobaextract (GBE), a traditional natural herbal product, is often used in the treatment of essential hypertension (EH) as complementary therapy in China and European countries. Aim: To critically assess the current clinical evidence of efficacy and safety of GBE for EH. Methods: 7 electronic databases (Cochrane Library, PubMed, EMBASE, VIP, CBM, Wanfang data, and CNKI) were searched to identify randomized controlled trials (RCTs) of GBE for EH. Methodological quality was assessed independently using the Cochrane Handbook for Systematic Reviews of Interventions. Results: A total of 9 RCTs with 1012 hypertensive patients were identified and reviewed. Most RCTs were of high risk of bias with flawed study design and poor methodological quality. 6 trials demonstrated potential positive effect of GBE as complementary therapy on BP reduction when compared with antihypertensive drug therapy; however, it was not associated with a statistically significant effect on both SBP and DBP reduction in 3 other trials. Despite the positive findings, there were so many methodological limitations and significant clinical heterogeneity. Most of the trials did not report adverse effects, and the safety of GBE is still uncertain(10).

Garlic

Effects of garlic on blood pressure in patients with essential hypertension were studied. Patients (n=210) with stage 1 essential hypertension were divided into 7 groups named as A, B, C, D, E, F and G. Each group comprised of 30 patients. Each patient in group A, B, C, D and E has received garlic tablets at the dose of 300/mg. 600/mg, 900/mg, 1200/mg and 1500/mg in divided doses per day respectively for 24 weeks while Group F & group G were given tablet atenolol and placebo respectively. Blood pressure readings were recorded at weeks 0, 12 and 24. Present study showed significant decrease in both Systolic and Diastolic blood pressure in both dose and duration dependent manner. In each garlic treated group, significant reduction in SBP and DBP(11).

paniculate

Evaluated the antihypertensive activity of the ethanolic extract of A. paniculata herbs (EEAP) in Wistar rats with a non-invasive method. In the study, the herb was extracted by 90% ethanol, and identified for its andrographolide, flavonoids and phenolics contents. Antihypertensive activity was evaluated using CODA "Non Invasive Blood Pressure (NIBP) system with Volume Pressure Recording method". High blood pressure was induced with an alpha adrenergic receptor agonist, phenylephrine (0.9 mg/kgBW). EEAP at doses of 45, 90 and 180 mg/kgBW was evaluated for its antihypertension in comparison to nifedipine (10.8 mg/kgBW). Blood pressure measurements were performed 3 times i.e. before induced (baseline), 15 and 45 minutes after phenylephrine administration. Based on TLC-densitometric data, andrographolide, total flavonoids and total phenolics contents in EEAP were 12.85 ± 0.46%, 0.72 ± 0.01% and 1.66 ± 0.01%, respectively. EEAP exhibited a potent antihypertensive activity in phenylephrine-induced hypertensive rats. EEAP could decrease systolic and diastolic blood pressures up to 120% and 150%, respectively. EEAP fractions are potential to develop as a hypotensive agent in hypertension therapy(12).

Gossypiumbarbadense L

Gossypiumbarbadense L. is used against hypertension. Looking for a scientific basis for this use, the blood-pressure-lowering effect of the decoction of the leaves was confirmed. Fraction II (frII) of the crude extract of G. barbadense showed a dose-dependent hypotensive effect in anaesthetized rats. In hexamethonium-treated rats, the blood-pressure-lowering effect of frII was almost abolished. A small decrease of the blood-pressure-lowering effect was followed by an increase in the blood pressure. Phentolamine antagonized the increase in blood pressure in hexamethoniumtreated rats. High doses of atropine (4mg/rat) suppressed both depressor and heart effects. In-vitro experiments revealed that atropine did not antagonize the contraction of the ileum of the rat. Tripelennamine in a concentration of 100·g could not influence the contraction either, whereas 300·g did. In the guinea-pig ileum 10·g tripelennamine did not reduce the contraction significantly. In the mechanism of action of frII, acetylcholine receptors could be involved, but not histaminergic or adrenergic receptors. Although it is still not known which compound(s) in G. barbadense is (are) the active substance(s), the results obtained may explain the use of this plant in traditional medicine in Suriname(13).

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Ocimumbasilicum

Ocimumbasilicum L. (OBL), sweet basil, is a medicinal herb used in traditional Chinese medicine to treat cardiovascular diseases including hypertension. The objective of the study was to investigate the possible antihypertensive effects of OBL extract in renovascular hypertensive rats. The two-kidney one-clip (2K1C) Goldblatt model of renovascular hypertension was used in Wistar rats. Rats were randomized into sham, untreated 2K1C, captopril- (30 mg kg1 per day orally) and OBL- (100, 200, 400 mg kg1 per day orally) (low (L)-, medium (M)-, high (H)-OBL) treated 2K1C groups (n¼10–12 per group), followed up for 4 weeks. Blood pressure, heart weight/body weight, plasma angiotensin-II and endothelin (ET)-1 were studied. OBL reduced systolic and diastolic blood pressure by about 20 and 15 mm Hg, respectively, compared with 35 and 22 mm Hg for captopril, from the lowest dose tested with no dose dependency. Cardiac hypertrophy was reduced from 3.6±0.7 mg g1 for untreated 2K1C to 3.0±0.6, 2.9±0.6 and 2.4±0.4 mg g1 for L-, M- and H-OBL, respectively, compared with 2.6±0.5 for sham and 3.1±0.4 mg g1 for captopril (Po0.05). Renal function was improved with captopril. Angiotensin was reduced to a lesser extent than with captopril. ET was reduced to lower concentrations (78±15, 80±22, 82±15 pg ml1 for L-, M-, H-OBL, respectively) than in sham (116±31 pg ml1), untreated 2K1C (174±72 pg ml1) or captopril (117±72 pg ml1) groups. The effects of OBL on blood pressure, cardiac hypertrophy and ET, are consistent with an effect on ET-converting enzyme, and warrant further exploration(14).

II. CONCLUSION

Hypertension continues to be an important public health challenge worldwide. Given that most of the major risk factors for hypertension are modifiable, and strong evidence that hypertension can be prevented altogether, the importance of primary prevention strategies in reducing the global burden of hypertension and cardiovascular diseases cannot be overstated. Relatively small blood pressure reduction around 5 mmHg may prevent one-third of strokes and one-fifth of coronary events in Western societies (Chobanian et al., 2003). Therefore, public health strategies to shift population blood pressure to a lower level are of utmost importance in reducing the burden of hypertension and cardiovascular disease worldwide.

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