

A Randomised Controlled Trial to Evaluate the Effectiveness of Simillimum as an Adjuvant to Standard Care on Anger, and Hypertension against Standard Care for Hypertension Alone

Leena S. Bagadia

Visiting Professor Forensic Medicine & Toxicology at Smt.C. M. P. Hom. Medical College, Mumbai

Abstract

Background: Hypertension constitutes an important public health issue affecting more than 30% of the world's population. 76% of adult patients diagnosed with hypertension have sub-optimally regulated Blood Pressure (BP) despite appropriate medication and lifestyle changes. Essential Hypertension (EHT) is a psychosomatic and polyetiological disease which may positively correlate with anger variables. Also, it has been studied that a positive family history of hypertension is commonly found in hypertensive patients, with heritability varying between 35% and 50%. Homeopathy helps holistically correcting all these factors. Even homeopathic case-taking seems to have a therapeutic influence on patients' mental states.

Methods: 1187 individuals were screened, from that 295 people were found to have essential HTN, confirmed by basic laboratory investigations, and 172 eligible subjects, 108 men & 64 women (86 cases and 86 controls), were enrolled after taking voluntary, informed consent. They were divided into 2 groups by simple randomisation. More than 50% of patients in both arms were already on Anti-Hypertensive Treatment (AHT) before enrolment. In the remaining subjects, AHT was prescribed to participants having stage 2 HTN. A thorough homeopathic case history was taken, and the STAXI-2 scale was applied at the beginning of the study and after six months to measure the change in anger.

Results: In the intervention arm, the BP of the patients who were not on AHT remained under control while on a simillimum. However, 16% of patients in the control arm had to be prescribed standard antihypertensive treatment AHT as their BP escalated.

Of the patients in the control arm, who were already on standard AHT, 98% continued with the same dose of AHT. However, in the intervention group, standard AHT was stopped in 33% of the patients, and the dose was reduced by 28%. Reduction in blood pressure and anger variables in both arms at the end of the study period were statistically significant ($p=0.001$) with a 95% confidence interval but was greater in the treatment arm.

In the treatment group, 39.5% of participants with a positive family history of HTN, there were statistically significant higher values in the trait anger variables [Females: mean difference of 6.11 units ($p=0.01$, 95% confidence interval); Males: mean difference of 4.63 units ($p=0.01$, 95% confidence interval)]. Along with anger expression variable [Females: mean difference of 5.2 units ($p=0.03$, 95% confidence interval) Males: mean difference of 5.31 units ($p=0.02$, 95% confidence interval)].

Conclusion: It was observed that the EHT patients with a family history of HTN had higher angry dispositions and tended to suppress their anger & hostile impulses. A statistically significant reduction in anger and blood pressure variables was found in the participants of both groups. But the reduction in anger and BP variables was significantly higher in the treatment group, suggesting that adjuvant individualised homeopathy might be useful in reducing anger and, thereby, hypertension.

Keywords: Anger • State • Trait • Simillimum • Essential Hypertension • Individualized homeopathic treatment

Introduction

Hypertension (HTN) is highly prevalent in the adult population, especially among those aged >60 years, and is likely to affect approximat-

**Address for Correspondence:* Leena S. Bagadia, Visiting Professor Forensic Medicine & Toxicology at Smt. C. M. P. Hom. Medical College, Mumbai, India. E-mail: leenabagadia@gmail.com

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-ely one billion adults worldwide [1]. It is the largest, singular contributor to global mortality. In untreated cases, life expectancy reduces to 50-60 years, compared to 71 years in the population at large. Framingham Heart Study denotes normotensive persons aged 65 years had a 90% lifetime risk of developing hypertension (predominantly of the systolic subtype) if they lived a further 20 to 25 years [2].

According to modern ideas, the aetiology of HTN cannot completely be explained by physiological, genetic, and lifestyle factors. Instead, a substantial body of evidence supports the role of psychosocial factors as a primary risk for HTN [3]. Hence, psychosocial interventions to prevent or delay the onset of HTN are included in the national HTN treatment guidelines [4].

His/her psychological status influences the physical state of an individual. Hypertension is considered one of the seven psychosomatic diseases caused by a mental crisis, as was proposed in the 1950 [5]. Anger elevates BP directly through psychophysiological activation and indirectly by facilitating the emergence of a coping style that contributes to maintaining elevated BP [6-8].

Also, anger and hostility are associated with adverse lifestyle behaviour, such as excess alcohol consumption and smoking, higher BMI values, and increased total energy intake, recognised as critical behavioural risk factors for HTN and cardiovascular diseases [9].

In most studies, positive family history is generally found in hypertensive patients, with the transmissibility varying between 35% and 50% [10-14].

A family history of hypertension doubles the risk of developing hypertension¹⁴, independent of other risk factors, such as weight, age, and smoking status. Most frequently, maternal medical history of hypertension seems to have a more significant influence than the paternal counterpart after adjustment for sex, age, smoking, BMI, physical activity, and alcohol consumption [15-17]. Furthermore, evidence suggests that maternal and paternal hypertension coexistence is strongly associated with incident hypertension [18,19]. However, parental hypertension must be diagnosed early (before parents reach 60) to affect hypertension [18]. The explanation for the association between parental medical history and hypertension is based on genetic susceptibilities and shared lifestyle influences: eating habits, physical activity, and smoking [15]. Pickering and Gerin (1990) observed that, though not universal, most studies reported in the literature found heightened reactivity in hypertensives than normotensive individuals [20]. The 'reactivity hypothesis' states that enhanced cardiovascular responsiveness to stress plays some role in developing arterial hypertension, either as a causal factor or a predictive marker [21]. Approximately one-third of the published studies showed more significant systolic blood pressure or heart rate reactivity in participants with a positive family history participant [22]. Moreover, people with a family history of HTN were more likely to suppress their anger [23].

Rutledge and Hogan have charted the pathways linking psychological factors to an increased risk of incident Essential Hypertension (EHT) [24]. Anger as a factor for hypertension and its modification leading to control of blood pressure readings was researched.

Anger can be explained as

It is the most basic emotion varying from mild irritation to intense fury in response to feeling threatened or hurt.

It has 3 components:

1. Physical – fight or flight response
2. Cognitive – angry thoughts.
3. Behavioural – anger expressed verbally, physically, or just withdrawal.

Unfortunately, anger is poorly understood in current diagnostic practices compared to anxiety and depression. For example, in DSM V, no Axis I disorders directly address the emotion of anger, unlike anxiety & mood disorders. Anger is an innate emotion, but if it escalates, it can cause disastrous effects on the body and, most conspicuously, upon the heart [25]. It is observed that healthy persons occasionally have an apparent boost in their blood pressure when angry explains that anger is a rousing state with emotions varying from slight irritation to intense fury or rage [26, 27]. It is reported that anger-arousing situations also contribute to increased blood pressure [28]. Franz Alexander, in 1939, first found the inhibition of anger as a leading cause of HTN and further examined its detrimental effects on the human body. Individuals prone to HTN react to environmental stress with intense anger, as explained by the reactivity hypothesis [29]. An earlier study on people with HTN reports that blood pressure rises considerably during anger states [30]. Many researchers have confirmed the association of anger with HTN, a well-established risk factor for Chronic Heart Diseases (CHD) further stressing the association between HTN and cardiovascular diseases [24, 30-33].

Anger is a crucial variable in Essential Hypertension. Unresolvable anger causes prolonged Sympathetic Nervous System over-activity [34]. Anxiety & guilt as a result of expressing anger leads to the suppression of anger [35]. In susceptible persons, neural mediation of frequent high blood pressure incidents causes structural adjustments in arterioles resulting in Sustained Hypertension. Anger could be conducive to the elevation of BP directly through psychophysiological activation and indirectly by promoting the development of a coping style that helps in the maintenance of elevated BP.

Psychologists have developed different types of scales that measure anger and its components that give a fair idea of a person's state of mind and coping mechanisms that initiate the hyper-response of the cardiovascular system in

terms of raised blood pressure. STAXI-2, i.e., State-Trait Anger Expression Inventory – 2, is one such scale.

STAXI-2

Spielberger's (1999) State-Trait Anger Expression Inventory-2 (STAXI-2) measures anger experience and the expressions used to assess aggression and violence, given the close association between anger dysregulation and aggressive and violent behaviour. The STAXI-2 is one of the most widely used measures in clinical and research settings [36].

It calculates the experience and expression of anger and is a 57-item self-report questionnaire. It consists of six scales and an anger expression index. It is a widely used scale for assessment with the following dimensions:

1. State Anger (S-Ang): the intensity of angry feelings at the time of completion.
2. Trait anger (T-Ang)- a disposition to experience anger.
3. Anger Expression-Out (Ax-O) - the expression of angry feelings out.
4. Anger Expression-In (AX-I) - the suppression of angry feelings.

Anger Control-Out (AC-O): the prevention of anger expression toward other people or objects.

Anger Control-In (AC-I) - the control of suppressed anger and The Anger Expression Index (AX-index) is an overall index of the frequency of anger expression, regardless of direction.

The homeopathic perspective

Homeopathy focuses on the patient with hypertension rather than on hypertension itself. It considers the mind and body as one phenomenon. Health is considered a state indicating the harmonious functioning of the life force. The disease is a deviation from health which develops when the life force cannot overcome obstructions to its smooth functioning. It can be seen as the organism's total response to adverse environmental factors, internal or external, conditioned by constitutional factors, inherited or acquired, which is true for all diseases, including essential hypertension.

Aim

To evaluate the effectiveness of homeopathic simillimum to modify the underlying anger state, trait, and expressions in patients of mild to moderate EHT, thereby reducing hypertension.

Objectives

Identifying the anger state-trait and expressions with the help of State-Trait Anger Expression Inventory – 2 (STAXI- 2) in patients with EHT.

Correlating anger state-trait and expressions with systolic and diastolic blood pressure levels.

To explore the effectiveness of individualised homeopathic treatment in patients with mild to moderate EHT in modifying the underlying anger state trait and expression.

Hypotheses

Anger is an emotion that can be measured, and STAXI-2 can be successfully used for this purpose in our study population.

There is a positive relationship between the components of anger and hypertension.

Patients with a family history of hypertension are more prone to hyper-react to stressors and, thereby, more susceptible to hypertension.

Methods

Study setting and design

This trial was randomised, placebo-controlled, comparative, open-label and conducted at an urban and a rural charitable homeopathic hospital and a plastic factory between January 2016 to July 2018 as per the Reporting Data on Homeopathy Treatments (ReDHoT) guidelines where participants were masked [37]. The trial registration no. is ISRCTN26742330. The study protocol was as

per the latest revision of the Helsinki declaration on human experimentation and Good Clinical Practices in India [38, 39]. An independent statistician used statistical software to generate a random allocation sequence before recruiting subjects. Participant allocation to the groups (1:1) was done after initial case taking. Approval was received from the Institutional Ethics Committee. Each participant was clearly explained about the research, with the help of the Patient Information Sheet, and thereafter, written consent was obtained from them. They were explained that, if they wished, they could withdraw from the study at any point in time [40].

Study population and enrolment

1187 adults were screened for hypertension. They were asked about their history of hypertension as well. During the screening, 303 patients with either history of hypertension or were detected with hypertension. The screening was carried out at a rural and an urban charitable hospital and a plastic factory. Secondary hypertension was ruled out by checking routine blood biochemistry, USG, ECG, and x-ray chest. 8 patients were found to have secondary causes like renal artery stenosis, Conn's syndrome, and coarctation of the aorta; these patients were excluded.

Inclusion criteria

1. Adults of age 18 to 65 years
2. Suffering from mild and moderate essential hypertension as per JNC7

Exclusion criteria

1. Patients with secondary hypertension.
2. Patients with uncontrolled Diabetes Mellitus or any uncontrolled endocrine disorders.
3. Patients diagnosed with psychiatric disorders like schizophrenia or endogenous depression.
4. Pregnant or breastfeeding mothers having HTN

Study design

172 patients among the 295 detected hypertensive gave their informed, voluntary consent and were included in the study as per the ethical clearance. 108 (62.8%) were males, and 64 (37.2%) were females. At first, thorough homoeopathic case-taking was done for all, along with an evaluation with STAXI 2 for anger variables. Later, they were randomised into two groups, i.e., placebo and intervention groups.

53% of patients in the intervention group and 56% in the control group were on Antihypertensive (AHT) which included ARBs, ACEIs, and Beta-blockers as prescribed by the physician before the enrolment in the study.

All the patients were given necessary lifestyle management advice and suggested a DASH41 diet and regular exercise.

Patients in the placebo group were continued with standard management (if prescribed prior) and the identical-looking placebo. In the intervention, arm patients were given individualised homoeopathic treatment with standard management (if prescribed prior). The homoeopathic medicines were procured from Good Manufacturing Practices-certified pharmacies. These patients were followed up every two weeks for subjective criteria like anger, anger episodes, fights, and moods. Also, objective criteria like BP, Pulse rate, and physical complaints were assessed.

At the end of six months' study period, the STAXI-2 scale was applied again to evaluate the change in anger variables in all the patients.

Outcome measures

The primary outcome measure was a reduction in anger variables compared to baseline as per the STAXI-2 scale at the exit of a six-month treatment period. The secondary outcome was a reduction in systolic blood pressure >10 mm of Hg and diastolic blood pressure >5mm of Hg. Also, relief in the symptom severity of these subjects' associated illnesses observed during follow-ups was considered.

Sample size

The effect size calculated from the study on HTN conducted by CCRH

was 0.6 (SBP: 157.65+/-13.05 versus 143.41+/-12.41, Cohen's d =1.13, effect size =0.5; DBP: 100.77+/-4.04 versus 89.13+/-7.75, Cohen's d =1.88, effect size =0.7; overall effect size =0.6; calculated at UCCS Effect Size Calculators. Dr Lee A. Becker, University of Colorado, Colorado Springs). The effect size (standardised difference) of 0.6, power of 90%, and significance level (α) of 5% were considered, and the required sample size was determined to be 118 using Altman's nomogram. The targeted sample size came to 150 after providing dropouts of approximately 27% [42].

Statistical analysis

Data was collected with variables' values entered in MS Excel and then transferred to SPSS SW V.21 for analysis. The quantitative data were represented as mean +/- SD & compared using a student's t-test. In addition, a Pearson correlation test was performed to find correlations between variables.

The primary endpoint was a change in anger variables during the six months of the study period in the intention-to-treat population. Secondary efficacy endpoints included changes in systolic and diastolic blood pressure.

Results

The mean age of the participants was 41 years, with 18 years old as the youngest and 65 years old as the eldest participant. We had a maximum number of participants, 78 (46%) from the middle age group defined for the research as between 36 to 50 years of age. Among them, 108 (63%) were males, and the rest were females.

Other variables like income and education were collected to classify patients into socioeconomic status. Most participants, 70 (41%), earned between 5 to 15 thousand per month, while 30 (18%) participants earned more than 50 thousand a month. In addition, 89 (52%) were educated up to SSC or below, and 83 (48%) were educated above SSC (Table 1).

The baseline Mean BP among all participants was 149+/-9 mm of Hg systolic and 96+/-6 diastolic mm of Hg. The intervention group was 150+/-9 systolic and 97+/-8 diastolic; in the control group, it was 148+/-9mm of Hg of systolic BP and 95+/-5 mm of Hg diastolic. Further patients were divided into Stage I (mild) and Stage II (moderate) hypertension.

At the beginning of the study, 94 (55 %) patients were already on antihypertensive treatment. Rest 45% were newly detected hypertensive who were not on any medications. Sixty-four participants (28 females and 36 males) out of 171 (37.4%) had a positive family history of hypertension. Trait anger was found to be more in the treatment group. P-value=0.002, along with Trait anger/R, was found to be more in the treatment group. P-value=0.006

There was no statistically significant difference between the groups comparing all other variables (Table 2).

State anger & its subgroups, all other anger variables & Systolic and diastolic BP have a statistically significant reduction with a p-value<0.001 with a 95% confidence interval.

After six months of intervention, changes in various anger components, except state anger and its variables, showed a statistically significant trend favouring homoeopathy.

There was no significant correlation between anger variables and systolic and diastolic blood pressure.

The higher values in the trait anger variables and anger expression variable (red) in females were observed in the treatment group with a positive family history of HT (Table 3).

There appears to be a significant difference in the Trait Anger (T-Ang) variable in females' two groups, with a mean difference of 6.11 units (p=0.01, 95% confidence interval).

Also, a significant difference in the Angry Temperament (T-Ang/T) variable with a mean difference of 6.11 units (p=0.01, 95% confidence interval).

There is a significant difference in the Anger Expression- In (AX-I) variable with a mean difference of 5.2 units (p=0.03, 95% confidence interval).

There is a significant difference in the Anger Control-Out (AC-O) variable with a mean difference of 7.94 units (p=0.003 with a 95% confidence interval).

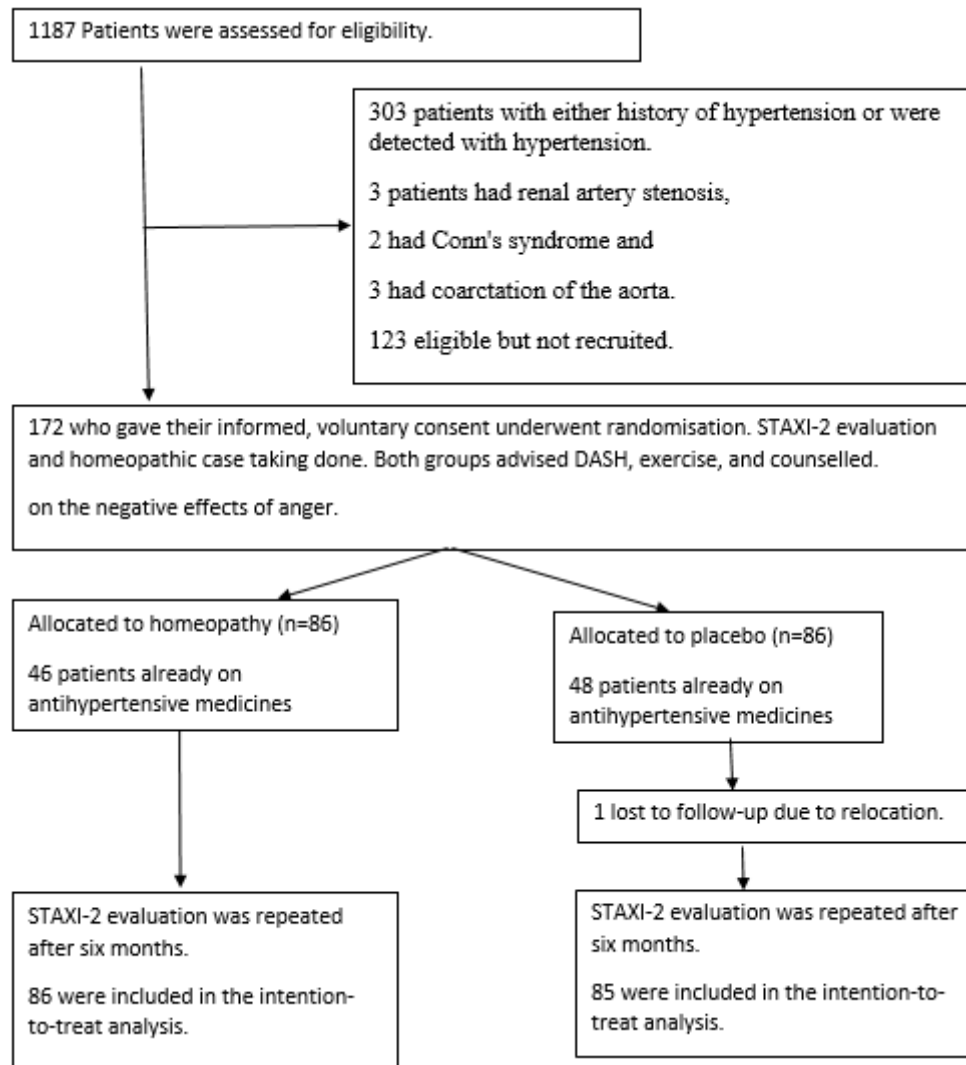


Figure 1. Consort study flow diagram (evaluate the change in anger variables in all the patients)

Table 1. Baseline demographic data and clinical indices

Socio-demographic characteristics	Intervention group	Control
	(n = 86)	(n = 85)
	41.4 +/- 10	41.04 +/- 10
Age; M +/- SD; n (%)		
18-35 years	30 (34.8)	24 (28.2)
36-50 years	36 (41.8)	42 (49.4)
51-65 years	19 (22)	20 (23.5)
Gender; (n%)		
Male	54 (62.7)	54 (62.7)
Female	34 (39.5)	30 (35.2)
The income per month in INR		
Below 5000	4 (4.6)	5 (5.8)
5000-15000	34 (39.5)	36 (42.35)
15001-50000	32 (37.2)	30 (35.2)
Above 50001	14 (16.2)	16 (18.8)
HABIT DETAILS		
Alcohol consumption n (%)		
Consumption	24 (28)	22 (25.8)
Smoking/ Tobacco n (%)		
Consumption	19 (22.3)	11 (12)
F/H of hypertension n (%)		
	HOMOEOPATHY	PLACEBO

F/H present	34 (39.5) – 19males 15females	30 (35.2) 17males 13 females
F/H absent	52 (60.4)	55 (64.7)
Clinical indices	Intervention (n = 86)	Placebo (n = 85)
Respiratory rate; M+/- SD	19.7+/- 1.6	19.9 +/- 1.4
Heart rate; M+/-SD	82.7+/-11.8	84.5+/- 10.9
Hypertension stages n (%)		
Stage – 1	25 (29)	22 (25.8)
Stage – 2	61 (70.9)	63 (74)
Systolic blood pressure; M+/- SD	150.13+/- 8.73	148.21 +/- 8.61
Stage – 1	145.5+/- 5.4	142.5+/- 5.4
Stage -2	156.5+/-8.7	154.5+/-9.6
Diastolic blood pressure M +/-	97.09 +/- 7.96	95.41 +/- 5.33
Stage -1	97.6+/-6.3	95.6+/-5.0
Stage -2	101.1+/-5.2	100.2+/-5.4

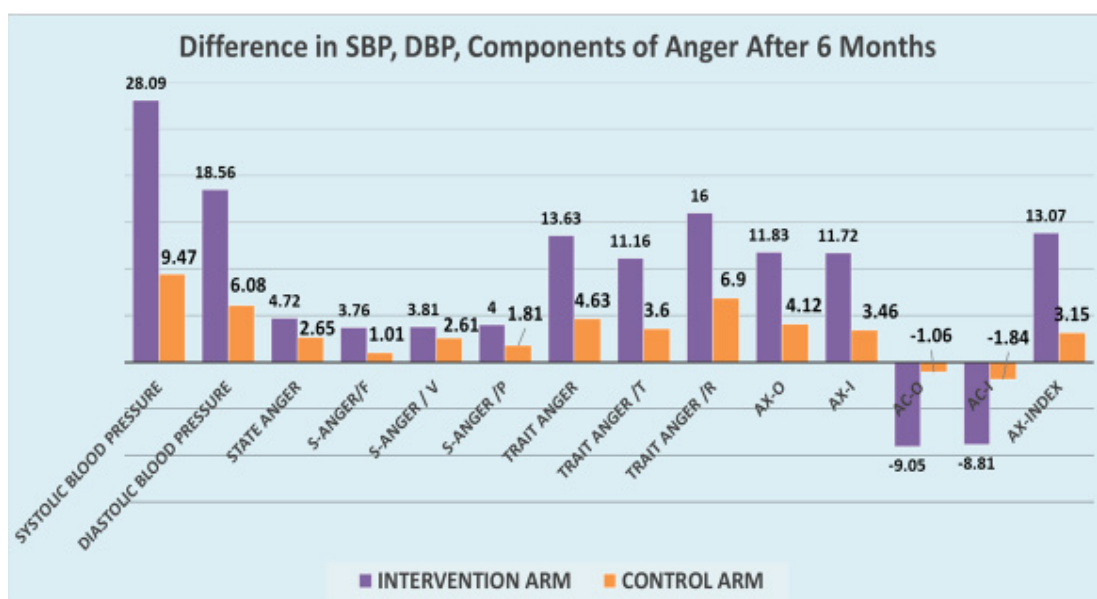


Figure 2. Final values of the variables in both arms

There is a significant difference in the Anger Control-In (AC-I) variable with a mean difference of 8.42 units (p=0.003 with confidence interval).

There appears to be a significant difference in the Anger Expression Index (AX-I) variable, with a mean difference of 8.42 units (p=0.003 with a 95% confidence interval).

The higher values in the trait anger variables and anger expression variable in males were observed in the treatment group with a positive family history of HT.

There appears to be a significant difference in the Trait Anger (T-Ang) variable in the two groups in males, with a mean difference of 4.63 units (p=0.01, 95% confidence interval). Also, a significant difference in the Trait anger – trait (T-Ang_T) variable with a mean difference of 4.67 units (p=0.01, 95% confidence interval).

There is a significant difference in the Anger Expression – Index (AX-Index) variable with a mean difference of 5.31 units (p=0.02, 95% confidence interval).

The higher values in the trait anger variables along with anger expression variable in both male and female participants in the treatment group (39.5% participants) with a positive family history of HT may have resulted in a statistically significant difference in trait anger variables in the pre-treatment assessment of homogeneity between both groups. At the end of the study period, in the control arm, of the patients who were not on standard AHT, 16% had to be prescribed standard AHT, whereas, in the intervention arm, the BP of all patients were maintained on simillimum (Table 4).

For patients on standard AHT, 98% of patients in the control arm continued with the same doses of their medicines at the end of the study period. In

comparison, standard AHT was stopped in the intervention group in 33% of patients. In 28% of patients, the dose of AHT was reduced (Table 5).

During the study period, while prescribing the remedies to the study participants of the intervention group, as expected, some of the remedies where high anger has been documented in our Materia Medica like Nux vomica (10 patients 11.6%), Natrum group (10 patients: 11.6%), Ferrum group (8 patients: 9.3%), Anacardium (2 patients: 2.3%), Arsenic alb (2 patients-2.3%), Aurum Met (2 patients: 2.3%), Causticum (3 patients: 2.3%), Lachesis (3 patients:3.4%), Lycopodium (7 patients: 8.1%), Medorrhinum (single male patient- 1.1%), Mercurius (single patient1.1%), Sepia (all six female patients -6.9%), Staphisagria (3 patients: 3.4%) Nitric acid (single male patient 1.1%), Kali carb (single female patient 1.1%) and Veratrum alb (single male patient 1.1%) came up.

However, there were surprising entries in the Calcarea group (five patients: 5.8%), Bryonia (single male patient 1.1%), Petroleum (single female patient with skin complaints predominantly with HT 1.1%), Pulsatilla (4 patients: 4.6%), Silicea (single female patient 1.1%) Graphites (single female patient with skin complaints 1.1%), and phosphorus (single male patient 1.1%). From this, the highest score for suppressed anger was four for Pulsatilla. Although Petroleum and Graphites may have dominated the repertorial chart for the skin symptoms, they also carried higher marks in anger rubrics, especially Petroleum (12) [26]. Another surprise was Bryonia, which carried 16 and was one of the four remedies charted under suppressed anger rubric with one mark in the complete repertory [39]. It proved to be similar as it brought the epileptic attacks of the patient to negligible along with marked improvement in his volatile temperament. Silicea patients' common impressions are malleable, pleasant, and stubborn

	S_ang_PostHomRx	S_Ang_F_Post	S_Ang_V_Post	S_Ang_P_Post	T_AngPost	T_Ang_T_Post	T_Ang_R_Post	AX_O_Post	AX_I_Post	AC_O_Post	AC_I_PostHomRx	AX_Index_Post	Post_sys_BP	Post_dia_BP
S_ang_PostHomRx	1													
S_Ang_F_Post	Pearson Correlation Sig. (2-tailed)	0.951**	1											
S_Ang_V_Post	Pearson Correlation Sig. (2-tailed)	0.613**	0.526**	1										
S_Ang_P_Post	Pearson Correlation Sig. (2-tailed)	0.594**	0.506**	0.969**	1									
T_AngPost	Pearson Correlation Sig. (2-tailed)	0.289*	0.311**	0.115	0.071	1								
T_Ang_T_Post	Pearson Correlation Sig. (2-tailed)	0.236*	0.276*	0.107	0.072	0.922**	1							
T_Ang_R_Post	Pearson Correlation Sig. (2-tailed)	0.279*	0.341**	0.102	0.036	0.848**	0.636**	1						
AX_O_Post	Pearson Correlation Sig. (2-tailed)	-0.006	-0.014	-0.171	-0.211	0.516**	0.515**	0.294**	1					
AX_I_Post	Pearson Correlation Sig. (2-tailed)	0.302**	0.354**	0.033	0.019	0.461**	0.383**	0.474**	0.135	1				
AC_O_Post	Pearson Correlation Sig. (2-tailed)	0.11	0.136	0.153	0.151	-0.278*	0.017	-0.577**	0.131	0.229	1			
AC_I_PostHomRx	Pearson Correlation Sig. (2-tailed)	0.087	0.066	0.164	0.134	0.063	0.024	0.215*	-0.213*	0.083	0.757**	1		
AX_Index_Post	Pearson Correlation Sig. (2-tailed)	0.016	0.034	-0.178	-0.183	0.352**	0.379**	0.155	0.675**	0.282*	-0.881**	-0.781**	1	
Post_sys_BP	Pearson Correlation Sig. (2-tailed)	-0.112	-0.12	-0.003	0.024	0.033	0.049	0.017	0.135	-0.040	-0.178	-0.163	0.172	1
Post_dia_BP	Pearson Correlation Sig. (2-tailed)	-0.047	-0.067	0.178	0.184	0.044	0.012	0.072	0.166	-0.049	-0.046	0.012	0.042	0.738**

Figure 3. Pearson correlation test to check the correlation between the variables

Table 2. Comparison of positive and negative F/H of HT in control and treatment groups: Females

F/H of HT	Mean	Standard Deviation	Standard Error Mean	t	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference		
							Lower	Upper	
S_ang_diff	0	4.91	9.053	1.53	-0.193	0.848	-0.493	-5.604	4.617
	1	5.41	11.064	2.129					
S_ang_F_diff	0	1.03	17.049	2.882	-1.282	0.205	-4.749	-12.157	2.658
	1	5.78	10.112	1.946					
S_Ang_V_diff	0	4.23	10.138	1.714	0.058	0.954	0.154	-5.171	5.48
	1	4.07	10.72	2.063					
S_ang_P_diff	0	2.91	8.936	1.51	-0.927	0.358	-2.715	-8.576	3.146
	1	5.63	14.055	2.705					
T_Ang_diff	0	7.14	7.945	1.343	-2.514	0.015	-6.116	-10.982	-1.251
	1	13.26	11.206	2.157					
T_Ang_T_diff	0	5.89	7.955	1.345	-2.572	0.013	-6.114	-10.869	-1.359
	1	12	10.77	2.073					
diff_T_Ang_R	0	9.6	7.997	1.352	-1.938	0.057	-4.993	-10.146	0.16
	1	14.59	12.239	2.355					
Diff_AX_O	0	5.31	10.22	1.728	-1.711	0.092	-4.315	-9.36	0.729
	1	9.63	9.332	1.796					
Diff_AX_I	0	4.57	7.77	1.313	-2.143	0.036	-5.206	-10.067	-0.346
	1	9.78	11.345	2.183					
Diff_AC_O	0	-1.83	9.79	1.655	3.044	0.003	7.949	2.725	13.173
	1	-9.78	10.703	2.06					
Diff_AC_I	0	4.69	11.029	1.864	-3.07	0.003	-8.425	-13.916	-2.935
	1	13.11	10.293	1.981					
Diff_AX_Index	0	4.69	11.029	1.864	-3.07	0.003	-8.425	-13.916	-2.935
	1	13.11	10.293	1.981					

but vulnerable and not high on anger. However, we found it higher in our chart, with 7 [15].

Discussion

The maximum number of patients in the study was 36-50 years. 78 out of 171 (46%) patients belonged to this age group.

Sixty-four participants (28 females and 36 males) out of 171 (37.4%) had a positive family history of hypertension. Furthermore, it was observed that participants with a family history of hypertension were more likely to suppress their anger.

Correlation between anger and family history of HTN

The result in Table 2 suggests that women with a positive family history of

hypertension scored higher on trait anger and angry temperament. Still, they tended to suppress their outward expression of anger more than participants with a negative family history (F/H) of HTN. This also correlated with higher blood pressure values. In expressing anger, cultural standards define what is appropriate and appear to determine such physiological consequences of angry expressions. In the group analysis of male participants in the study, as shown in Table 3, the results suggest that even men with a positive family history of hypertension had higher values of variables like trait anger and angry temperament. Still, they tend to suppress their outward expression of anger compared to participants with negative F/H of HTN. Besides, they try to resolve their anger by controlling themselves.

Although a family history of hypertension was a meaningful predictor of change in BP status on its own, high trait anger greatly potentiated this increased risk of developing elevated blood pressure. It suggests that high-stress responsivity itself may have a genetic basis. Further, this effect will be more significant if the individual's daily life environment involves sufficiently

Table 3. Comparison of positive and negative F/H of HT in control and treatment groups: (Males)

	fam_hist	Mean	Standard Deviation	Standard Error Mean	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% confidence interval of the difference	
								Lower	Upper
S_ang_diff	0	2.03	5.99	0.737	0.11	-2.262	1.405	-5.048	0.523
	1	4.29	8.527	1.332					
S_ang_F_diff	0	1.06	7.51	0.924	0.262	-2.305	2.043	-6.356	1.746
	1	3.37	13.619	2.127					
S_Ang/V_diff	0	2.03	6.762	0.832	0.233	-1.823	1.52	-4.837	1.191
	1	3.85	8.893	1.389					
S_ang_P_diff	0	1.67	6.587	0.811	0.287	-1.602	1.495	-4.567	1.364
	1	3.27	8.829	1.379					
T_Ang_diff	0	7.03	9.628	1.185	0.012	-4.628	1.806	-8.208	-1.048
	1	11.66	8.111	1.267					
T_Ang_T_diff	0	4.94	8.891	1.094	0.012	-4.67	1.818	-8.276	-1.065
	1	9.61	9.542	1.49					
diff_T_Ang/R	0	9.88	10.864	1.337	0.081	-3.536	2.006	-7.513	0.441
	1	13.41	8.675	1.355					
Diff_AX_O	0	6.82	13.07	1.609	0.093	-4.06	2.395	-8.809	0.689
	1	10.88	10.159	1.587					
Diff_AX_I	0	6.85	10.366	1.276	0.13	-2.956	1.935	-6.793	0.88
	1	9.8	8.6	1.343					
Diff_AC_O	0	-3.27	10.885	1.34	0.055	4.337	2.234	-0.093	8.767
	1	-7.61	11.783	1.84					
Diff_AC_I	0	6.55	11.707	1.441	0.022	-5.308	2.286	-9.84	-0.776
	1	11.85	11.139	1.74					

Table 4. Change in the BP in participants of both groups at the end of the study period.

At the beginning of the study-the Control Group		After six months of the study period		
		No change in AHT	Stopped AHT	Reduced AHT
Patients not on AHT	37 (43.5%)	NA	NA	NA
Patients on AHT	48 (56.4%)	47 (98%)	1 (2%)	0

Table 5. List of Homoeopathic remedies used for patients in the intervention arm.

Sr. No.	Name of homoeopathic remedy	Potency	Used in No. of patients	Outcome		
				Reduction in BP	No reduction in BP	Increase in BP
1	Anacardium Orientale	200, 1M	2	1	1	0
2	Arsenicum Album	200, 1M	2	1	1	0
3	Aurum Met.	200	2	2	0	0
4	Bryonia Alba	200, 1M	1	1	0	0
5	Calcarea Arsenicum	200, 1M	1	1	0	0
6	Calcarea Iodatum	200	1	0	1	0
7	Calcarea Phosporicum	200	2	1	1	0
8	Calcarea Carbonicum	200	2	1	1	0
9	Carcinocin	200	2	2	0	0
10	Causticum	200, 1M	3	2	1	0
11	Ferrum Iodatum	200, 1M	1	1	0	0
12	Ferrum Metallicum	200, 1M	6	4	1	1
13	Ferrum Phosphoricum	200	1	0	0	1
14	Graphites	200	1	1	0	0
15	Hyoscyamus Niger	200, 1M	2	1	1	0
16	Kalium Carbonicum	200, 1M	3	2	1	0
17	Lachesis	200, 1M	3	3	0	0
18	Lycopodium Clavatum	200, 1M	7	5	1	1
19	Medorrhinum	200	1	0	1	0
20	Mercurius Corrosivus	200	1	0	1	0
21	Natrum Muriaticum	200, 1M	9	7	2	0
22	Natrum Sulphuricum	200	2	2	0	0
23	Nitric Acidum	200	3	2	1	0
24	Nux Vomica	200, 1M, 10M	10	8	2	0

25	Petroleum	200	1	1	0	0
26	Phosphorus	200, 1M	1	1	0	0
27	Pulsatilla	200, 1M	4	3	1	0
28	Sepia	200, 1M	6	4	2	0
29	Silicea	200	1	1	0	0
30	Staphysagria	200, 1M	3	2	1	0
31	Veratrum Album	200	1	1	0	1
Total		-	85	61 – 70.9%	21- 24%	4 – 4.6%

high exposure to stressors and/or a lack of stress buffers. The present study must consider only a preliminary test of this updated hypothesis. There is also concern about the possible lack of generalizability to older persons and minorities because the sample was restricted to 18-65 years.

Socioeconomic status, perceived stress and behavioural risk factors for HTN

In this study, the participants were pooled from charitable hospitals and a plastics factory, where most participants belonged to the low-income group. Hence, only 18% of patients had middle or high Socioeconomic Status (SES) [41,42]. Although employment itself does not seem to be a risk factor, there is some evidence that the combination of jobs and a family may increase women's hypertension and Chronic Heart Disease (CHD) incidence. In two studies, the Framingham study and the Minnesota Heart Survey, working women reported greater stress levels than working men or homemakers [43-45]. A similar observation was found in the female participants in the present study.

Many study participants were rotational factory shift workers, including working days, afternoon, and night shifts. However, this work arrangement frequently disrupts the sleep-wake cycle and circadian rhythms, which in turn affects cardiovascular function, including BP [46].

Blood pressure elevation effects appear to be mainly mediated by maladaptive or unhealthy coping behaviours such as excessive consumption (food, cigarettes or bidis, tobacco, and alcohol) and physical inactivity. We found many male participants resorting to alcohol and tobacco addiction. However, a detailed analysis of the same was not performed.

There were lifestyle differences in the study populations and different perceptions of overwork and stress. It was found that psychological stress, which was released in the form of anger, was associated with age, sex, and socioeconomic status.

Correlation between anger and HTN

A correlation between anger and hypertension was examined (Figure 1-3). The finding that none of the anger measures was associated with resting BP in this study is consistent with literature reviews on anger and hypertension [47-49]. In addition, previous reviews have found only low and inconsistent associations between trait anger and HTN [50-52].

Homeopathic perspective of the treatment of HTN

All homeopathic medicines change the state of mind and disposition in their distinctive fashion (Organon of Medicine§212) [53]. Therefore, the alterations in the patient's state of mind and disposition must be examined and paired with the particular homeopathic remedy that can bring about a similar state in a healthy individual. As a result, the disease is annihilated. As Dr Catherine Coulter penned: "The homeopath does not treat the disease entity but rather the symptom complex of the person who has a disease with any name and of any system of the body [54]. Furthermore, this ability to make distinguish the patients and superficially similar disease processes – that is, to "individualise" each case – is due to the concern for the person as a whole, which lies at the helm of the homeopathic treatment."

Therapeutic effects of homeopathic case-taking

The results also depicted a statistically significant reduction in anger in the control group, though which was not to the level of the reduction in the treatment group. This implies that empathy, forthright agenda-setting, and affirming social and emotional matters, as done during homeopathic case-taking, may aid in enhancing the quality of care and efficiency. There are curative prerequisites of the consultation process on health outcomes in conventional medicine and Complementary and Alternative Medicine (CAM) [55, 56]. These contextual end results are not the treatment's active components but inherent within the

complete therapy package [57-60]. Exploration into homeopathic consultation has recognised contextual elements such as empathy and empowerment placating the homeopathic process. Homeopathic consultation considers a thorough investigation of the patient's emotional, spiritual, and physical well-being to allow the treatment of the person as a whole and not just the disease [61].

To standardise the consultation procedure, specific topics were covered (e.g., detailed clinical history, current symptoms and medication, assessment of emotional and mental states, etc.) to identify the relevant information to prescribe. The contents of the consultation varied between patients and between consultations; homeopathic intervention was individualised and patient-centred and guided by the narratives of the patients.

The results affirm preceding studies demonstrating that therapeutic effects arise from explorations within the homeopathic consultation that include communication skills, empathy, hopefulness, enablement, and narrative competence [59-61]. In addition, homeopathic consultation requires a deep understanding of the patient and is a unique and personalised approach. Therefore, the placebo effects of the homeopathic consultation may be distinct to this therapy, possibly reliant on the process of the collaborative and highly individualised consultation vital to find a fitting remedy and the analogous illustrative meaning response for that patient.

During regular follow-ups every two weeks, we did not find any adverse reaction to homeopathic medicine in any study participants in the intervention group, proving the safety of the individualised medicine prescribed to the patients.

Conclusion

The anger measurement scale STAXI-2 was successfully utilised to measure the various anger variables in the study.

All the variables in both the groups were statistically not significantly different except the Trait Anger (T-Ang), Angry Temperament (T-Ang/T), and Angry Reaction (T-Ang/R), which were higher in the treatment group in comparison with the control group at the beginning of the study.

Convincing evidence did not emerge for strong linear relationships between anger and blood pressure in the study.

There was a statistically significant direction of effect favouring homeopathy against placebo as an adjuvant treatment of anger and hypertension.

No adverse reaction to the homeopathic medicine was observed in any intervention group study participants during regular follow-ups every 2 weeks demonstrating the safety of the individualised remedy prescribed to the patients.

There was a statistically significant correlation found between high blood pressure and suppressed anger in patients with a positive family history of HTN.

A reduction of anger in the control group, which was statistically significant but not as much as the reduction of the anger variables in the treatment group, was observed, implying rapport building, up-front collaborative agenda-setting, and acknowledging social and emotional concerns as done during homeopathic case taking might help improve quality of care and efficiency.

Limitation and Future direction

The study needs replication with a larger sample size over a longer duration, accommodating the older age group.

Presence of "Social desirability bias" – cannot be denied in a self-reporting scale-like STAXI-2.

Ambulatory BP monitoring was not used, so there could have been misdiagnosed cases of white-coat hypertension or missed cases of masked HTN.

A Double-blind, randomised, controlled trial without conventional antihypertensives is highly recommended.

Highlights

Psychological status of an individual greatly affects his/her physical condition.

Hypertension is considered one of the seven psychosomatic diseases caused by mental aetiologies.

A family history of hypertension doubles the risk of developing hypertension.

Anger is an important variable in Essential Hypertension.

Simillimum can have a positive effect on the management of anger and EHT in the population.

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