THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 10, Supplement 1, 2004, pp. S-245–S-250

Recommendations and Guidelines Regarding the Preferred Research Protocol for Investigating the Impact of an Optimal Healing Environment on Patients with Hypertension

KATHLEEN M. WESA, M.D.,[1] and RICHARD H. GRIMM, Jr., M.D., Ph.D.[2]

ABSTRACT

Cardiovascular disease is the leading cause of death in the United States. Hypertension is the most common single reason for visits to primary care physicians accounting for more than 35 million visits annually. Pharmacotherapy can achieve adequate control of blood pressure. Multiple interventions compares to single therapies are more efficacious in treating hypertension, and this fact supports using the holistic approach to hypertension treatment. Implementing an optimal healing environment (OHE) in a hypertension treatment regimen has the potential to impact not only health care costs, but also to optimize blood pressure control, and thus decrease the total cardiovascular disease burden. The research questions for the study of OHE in hypertension may differ between the individual patient perspective and the public health perspective. The use of a 2×2 factorial design would allow analysis of both perspectives simultaneously. Using an OHE setting with multiple interventions in formulating an individualized approach to hypertension management merits further exploration and research.

INTRODUCTION

Cardiovascular disease is the leading cause of death in the United States.[1] The control of blood pressure is one of the most effective methods of reducing mortality from cardiovascular disease. Hypertension is the most common single reason for visits to primary care physicians with more than 35 million visits annually.[1] Approximately 43 million adults, or nearly one quarter of the population in the United States are diagnosed with hypertension or are taking antihypertensive medications.[2]

The Joint National Committee (JNC) 2003 states the evaluation of hypertension has three objectives: (1) to assess lifestyle and identify other cardiovascular risk factors; (2) reveal identifiable causes of hypertension; and (3) assess the presence or absence of target organ damage and cardiovascular disease. Despite widespread use of medications for hypertension, appropriate control of hypertension is achieved in only approximately 31% of the population.[3]

Hypertension is a multifactorial condition. Risk factors for the development of hypertension include obesity, family history or genetic basis, diabetes, inactivity, and excess dietary sodium and alcohol intake. Interventions targeted to these areas that are amenable to behavior modification have been thoroughly studied. Medications are usually used to adequately control blood pressure. However, lifestyle intervention may supplant or enhance the lowering of blood pressure. If there is failure to provide lifestyle modifications, adequate antihypertensive drug doses or appropriate drug combinations may result in inadequate blood pressure control.[1]

BLOOD PRESSURE MEASUREMENT

Optimal healing and care cannot occur in the treatment of hypertension without high quality blood pressure measurements. Critical treatment decisions are based primarily

[1]Department of Medicine, University of Minnesota, Minneapolis, MN.
[2]Berman Center for Outcomes and Clinical Research, Department of Medicine and Epidemiology, University of Minnesota, Minneapolis, MN.

on levels of pressure. The JNC has reclassified blood pressure levels into four main categories in an effort to increase the efficacy of blood pressure management for treating and preventing hypertension (Table 1).

Similar to all biologic variables, blood pressure varies considerably as it is constantly changing minute to minute. And this pattern of blood pressure variability has been well described. Both systolic and diastolic have large within-individual variability. Diastolic blood pressure standard deviation ranges from 4–8 mm Hg, and systolic from 7–14 mm Hg. This large variation makes accurate blood pressure measurement difficult. The fact that the temporal variation of blood pressure can be larger than the treatment effect hampers assessment of progress in lowering pressure from visit to visit to a clinic.

Thus, high-quality measurements are essential in any research study designed to assess the impact of an OHE. This can be accomplished by addressing the following:

1. Perform standardized measurements according to the American Heart Association guidelines.[4]
2. Perform multiple measures, at least two, and use the average of all pressures to reduce the variability of the measure.
3. Perform measurements using an automatic device, which has been certified by the British Hypertension Society, for example, Omron Sphygmomanometer (Omron Healthcare, Vernon Hills, IL).[5,6]

LIFESTYLE MODIFICATIONS

Exercise has been proven to be beneficial in lowering blood pressure, especially when associated with weight loss. Weight loss of as little as 10 pounds reduces blood pressure and/or prevents hypertension in a large proportion of overweight persons.[1]

Intensive diet alterations, such as the Kempner Rice Diet or the Pritikin program, have been successful in a controlled setting. However, they are very costly, extremely restrictive, and have been tested under a structured living setting. The Kempner Rice Diet was delivered in a residential setting in which the daily sodium intake was restricted to 20 m/mol over several weeks.[7] Following discharge from the Duke program, the patients quickly reverted back to their normal diet. The weight loss and diet were not maintained, and baseline levels were returned to rapidly.

Comprehensive lifestyle modification programs such as the Ornish program or the TOMHS study[8] have shown beneficial results in obtaining hypertension control and in reversing cardiovascular disease. Maintaining the diet and lifestyle changes on a long-term basis has been difficult. The Dietary Approaches to Stop Hypertension (DASH) diet, which is rich in fruits, vegetables, low-fat dairy products combined with reduced dietary cholesterol, saturated fat as well as total fat and lower sodium intake, is an entire dietary modification program. Although the DASH diet is highly effective in lowering blood pressure in feeding studies, it remains to be seen how effective this diet is in a free-living group. The TOMHS diet was successful in lowering blood pressure in a free-living group and could be maintained, but it is not cost effective because of the intense focus on individualized counseling requiring frequent interaction with a skilled nutritionist.

Table 1. Joint National Committee's Reclassification of Hypertension

	Systolic (mm Hg)	*Diastolic (mm Hg)*
Normal	< 120	< 80
Prehypertensive	120–139	80–89
Stage l	140–159	90–99
Stage ll	≥ 160	≥ 100

STRESS AND HYPERTENSION

There are only a few well-designed longitudinal studies that have associated stress with hypertension. Work related stress over time has been related to hypertension.[9] Increased job-related stress with a decreased level of job satisfaction effort coupled with low decision autonomy have been shown as predictors of hypertension and heart disease in multiple studies.[10–12] One recent well-designed study, however, did not find heart rate variability and high job strain a major risk factor for future hypertension.[13]

Many of the studies on the role of stress contributing to hypertension have suffered from methodological problems including not accounting for regression to the mean in their analysis. The definitions of what constitutes stress or the measures of stress are not standardized or validated. The stress-inducing stimulus studied has varied, including handgrip measurements, working mathematical tasks or being in harassing environments. Interventions labeled as "stress management" have included a variety of techniques, such as meditation, imagery, progressive muscle relaxation, mindfulness practice, and relaxation response.

Psychosocial stressors have also been implicated in an increased risk for developing future hypertension.[14,15] Matthews et al.[15] correlated the ongoing trajectory of socioeconomic status and not having enough money for basics as an independent risk factor for hypertension. Difficulties paying for basic living expenses at study entry and continued difficulties during the 2- to 10-year follow-up were independently associated with increased incidence of hypertension after adjusting for race–gender group, body–mass index, site, age, and initial systolic blood pressure. This study did not, however, control for physical activity and smoking status.

STRESS MANAGEMENT INTERVENTIONS

Various stress management interventions in treating hypertension have been examined. Transcendental Meditation™, yoga postures/yogic lifestyle as well as mindfulness-based stress reduction (MBSR) interventions show some promise in hypertension treatment. It has been much easier to demonstrate physiologic changes such as a decrease in heart rate and acutely decreased blood pressure while performing the practice, but long-term sustained reductions in blood pressure have been inconsistent. Acupuncture has been used in China for centuries, and is currently being studied as a treatment for hypertension. The long-term efficacy of these interventions is not known.

The phase l Trials of Hypertension Prevention (TOHP-l) used stress management as one of seven nonpharmacologic approaches to lowering diastolic blood pressure in healthy adults with diastolic blood pressure 80–89 mm Hg.[16] There were 242 and 320 participants randomized to the stress management or an assessment only control group. The stress program lasted for 18 months, and included training in four relaxation methods, techniques to reduce stress reactions, cognitive approaches, communication skills, time management, and anger management within a problem-solving format. A significant reduction in diastolic blood pressure was seen in both groups. However, the two groups were indistinguishable when using intention-to-treat analysis. In subgroup analysis, there was a significant reduction in diastolic blood pressure relative to controls in the participants who attended more than 61% of the intervention sessions. It is not known if this isolated finding is chance or will be replicated in other studies.

Meta-analysis regarding any potential benefit from stress management interventions has not been helpful. In the 1993 meta-analysis by Eisenberg et al.,[17] many of the studies used for the "cognitive behavioral technique" intervention, were in fact very different intervention methods, including biofeedback, meditation, the relaxation response, progressive relaxation techniques and stress management, which included cognitive restructuring, adaptive emotional learning strategies, imagery, and physical or mental relaxation. In this meta-analysis, no single intervention method was superior compared to the others or to various different control interventions.

RATIONALE FOR MULTICOMPONENT INTERVENTIONS IN HYPERTENSION TREATMENT

In response to methodological difficulties in other stress management studies, Linden et al.[18] tried a different strategy in their 2001 study design. Linden and colleagues showed that individualized stress management intervention resulted in a clinically significant decrease (of at least 5 mm Hg) blood pressure in 55% of the participants. This study included individual flexibility in the delivery of specific interventions rather than one standard intervention for all participants. Patients received an average of 3.8 interventions. The most frequent interventions used were anger/hostility management training, autogenic training and discussion of relationship or existential issues. The least frequent were biofeedback, cognitive behavioral therapy (CBT) for anxiety or depression. CBT is a standard psychiatric approach, as discussed by DeRubeis et al.[19] It was not used in previous studies.

The evidence for multiple interventions being more efficacious in treating hypertension when compared to single therapies supports using the holistic approach to hypertension treatment. Thus, using an OHE setting with multiple interventions as options in formulating an individualized approach to hypertension management merits further exploration and research.

STUDY DESIGN

In designing a study evaluating the outcomes of OHE it is important that the primary study questions be stated clearly. Thought must also be given to the issue of which perspective is of interest, the individual patient or the public health perspective. For example, with high blood pressure, a 2–3 mm Hg lower systolic blood pressure would be considered clinically trivial in an individual patient. In fact, it would be difficult to detect given the large within individual variability in blood pressure. However, a 2–3 mm Hg lower systolic blood pressure in the population perspective would be very effective in preventing cardiovascular disease. This is because even though the absolute risk is highest in the upper distribution of blood pressure, most of the disease actually occurs in the middle to upper third of the blood pressure distribution because many more people are in this part of the distribution.

One way to learn the contributions of both the patient and population is through the use of a 2×2 factorial design in a clinical trial incorporating the assessment of OHE environment alone, patient interventions alone, and the combination of the two. Such an approach would involve both clinics and patients in the analysis (Table 2).

Another approach would be an observational cohort study with obtaining baseline and subsequent intermittent measurements of multiple variables at multiple clinic sites. This design might consist of a cohort of clinics with smaller studies on various subsets of OHE implementation success. The unit of measurement is the clinic. The quantity and quality of OHE attributes present in the facility setting, and the variety of interventions offered should serve as a marker for the support of the patient in their healing process.

Each clinic would be given a score rating their level of OHE achievement at baseline, and then a ranking of all of

Table 2. Factorial 2 × 2 Design for Clinical Trial

	Environment	
	OHE	*Usual care*
Special intervention Patient focus	OHE (clinic) Special intervention (patient)	Usual care (clinic) Special intervention (patient)
Usual care	OHE (clinic) Usual care (patient)	Usual care (clinic) Usual care (patient)

OHE, optimal healing environment.

the study clinics according to their OHE score from highest to lowest. The clinics could be grouped by category, with the use of multivariate analysis on single and combinations of various OHE components to explain the variance observed. The primary dependent variable is the individual clinic's blood pressure control rates using the patient's blood pressure measurements as the basic measurements. Different blood pressure subgroups would be examined in the secondary analysis (i.e., newly diagnosed, chronic hypertension, uncontrolled and controlled).

BASIC ELEMENTS FOR AN OHE

Not all of the prerequisites for an OHE have been documented in research studies. However, they most likely are those attributes that exist in a research clinic that has an outstanding reputation for participant satisfaction and study completion. Instruments such as the Press-Ganey questionnaire[20] measure patient satisfaction, and the Texas Christian University organizational readiness for change (ORC) questionnaire can be used to measure an institution's readiness for change. Incorporating these two instruments together plus determining a clinic total score for their OHE qualities could be verified and validated in preparation for the OHE intervention study.

Variables that are important for OHE assessing include:

- An awareness of the importance of a healing environment in patient care by at least one high ranking administrator/supervisor
- An awareness of the importance of a healing environment in patient care by the facility staff, including the receptionist/front desk personnel
- Willingness to facilitate change and support of personal growth and mastery
- The presence of a cohesive staff
- Availability of alternative therapies such as yoga, *qigong*, meditation, MBSR, acupuncture
- Physical environment that supports healing: physical sense of safety while present in the facility, clean, quiet/low-decibel level, pleasing décor and cheerfulness, sense of nurturing while in the facility, fresh air free of strong odors.
- Patient-centered relationships
- Respectful manner of treating patients
- Access for privacy in patient–health care provider interactions
- Continuity of care between the provider and patient
- Methods of following patients sequentially over an extended period of time
- Adequate interpreter services, if needed
- Ability of the system to be flexible in accommodating treatment assessments and requirements for patients with varied needs
- Minimal waiting time to see practitioner
- Behavioral interventions or referrals to community organizations with resources for diet, smoking cessation, exercise, and environmental alterations
- Educational materials with menu of options such as motivational, educational, maintenance interventions
- Personal counseling for high-risk groups
- Wellness counselor/educator
- Individual goal setting and awards for goal achievement
- Support groups available
- Cognitive behavioral therapy/dialectical behavioral therapy available
- Nutritionist available for referrals.

VARIABLES IN THE PATIENT'S LIFE

All of the following elements in the patient's life need to be examined and assessed for an OHE intervention. Each aspect can serve as a support or hindrance in the patient's quest for health and healing. The supportive life aspects should be enhanced and the barriers overcome or minimized.

- Family interaction/support
- Friends

- Community network
- Religious affiliation
- Spirituality
- Work environment
- Lifestyle—diet, exercise, quality of life
- Home, house/apartment/transient, environment
- Thought process and mood/outlook on life/psychologic scales
- Emotional health and well-being
- Financial status
- Treatment engagement/treatment subgroups: medication adherence, dietary compliance, dietary fat intake, sodium intake, exercise level and frequency, high-risk patients, early intervention versus late intervention, number of interventions used, dubgroups by ethnicity, gender and certain disease states
- Medical condition: quality of blood pressure measurements, weight (BMI), smoking status, alcohol/drug use, serum cholesterol, urinary sodium excretion, health attitudes, aerobic capacity, risk stratification, classification of blood pressure, cccurrence of any major or secondary cardiovascular event, co-morbidities.

POTENTIAL MEASUREMENT INSTRUMENTS FOR OUTCOME MEASUREMENTS

Measurement instruments may include:

- Texas Christian University (TCU) readiness for change instruments for organizations, personnel and participants
- Press-Ganey Satisfaction Measurement Questionnaire
- Quality of Life questionnaire combined from Medical Outcomes Study,[21] and from the Rand Health Insurance Experiment,[22] used in the TOMHS study[23]
- Global Hypertension Health statistic calculated from the Quality of Life questionnaire[22]
- Short-Form-36
- Spielberger State-Trait Anxiety Questionnaire
- Framingham Tension Scale
- Spielberger Trait Anger Scale (intensity and frequency of anger)
- Urinary sodium excretion
- Twenty-four–hour ambulatory blood pressure, automatic blood pressure measurements
- Dietary records
- Weight measurement.

INVESTIGATOR TEAM

Each facility would need a research coordinator for the OHE recommendations and for administering the instruments.

- Administrators: support the implementation of procedure changes, and to approve expenses associated with initiation/ implementation of the OHE
- Physicians: open to the holistic approach to treatment and supportive of OHE implementations
- Nurses: bridge between the administration and the patient in effective implementation of OHE
- Allied health practitioners/CAM practitioners: early involvement in the study design process to obtain the best and most generalizable information
- Statisticians: create the best design for obtaining interpretable data to answer the study question.

SUMMARY

Achieving optimal management of hypertension for the American population can significantly reduce both the morbidity and the mortality from cardiovascular disease. Pharmacotherapy can result in adequate control of blood pressure, however, behavioral interventions can provide an important adjunct for controlling blood pressure. Using an OHE in hypertension intervention has the potential to impact not only health care costs, but also to optimize blood pressure control and thus decrease the total cardiovascular disease burden. The research question may differ in studying OHE in hypertension from the individual patient versus the public health perspective. One approach is to utilize a 2×2 factorial design. This would allow analysis of both perspectives simultaneously. We have recommended issues to consider when studying the effect of an OHE on hypertension. If implemented, these approaches can yield important information guiding future treatment of cardiovascular disease and holistic management of lifestyles for the purpose of obtaining and maintaining optimum health.

ACKNOWLEDGMENTS

The authors acknowledge the Berman Center for Outcomes in Clinical Research, the Minneapolis Medical Research Foundation and NIH Fellowship # 1-T32-AT00487 for their support in preparing this manuscript.

REFERENCES

1. Chobanian AV, Bakris GL, Black HR, et al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and treatment of High Blood Pressure [JNC 7: Complete Version]. Hypertension 1993;42:1206–1252.
2. Burt VL, Whelton P, Rocella EJ, et al. Prevalence of hyper-

tension in the U.S. adult population: Results from the Third National Health and Nutrition Examination Survey, 1988–1991. Hypertension 1995;25:305–313.
3. Hajjar I, Kotchen TA. Trends in prevalence, awarness, treatment, and control of hypertension in the United States, 1988–2000. JAMA 2003;290:199–206.
4. Perloff D, Grim C, Flack J, et al. Human blood pressure determination by sphygmomanometry. Circulation 1993;88: 2460–2470.
5. O'Brien E, Petrie J, Littler W, deSwiet M, Padfield PL, O'Malley K, Jamieson M, Altman D, Bland M, Atkins N. The British Hypertension Society protocol for the evaluation of automated and semi-automated blood pressure measuring devices with special reference to ambulatory systems. J Hypertens 1990;8:607–619.
6. O'Brien E. Modification of blood-pressure-measuring devices and the protocol of the British Hypertension Society. Blood Pressure Monitoring 1999;4:53–54.
7. Kempner W. Treatment of hypertensive vascular disease with rice diet. Arch Int Med 1974;133:758–790.
8. Neaton JD, Grimm RH Jr, Prineas RJ, et al. Treatment of mild hypertension study: Final results. JAMA 1993;270:713–724.
9. Schnall PL, Schwartz JE, Landsbergis PA, et al. A longitudinal study of job strain and ambulatory blood pressure: Results from a three-year follow up. Psychosom Med 1988;60:697–706.
10. Krantz DS, Contrada RJ, Hill DR, Freidler E. Environmental stress and biobehavioral antecedents of coronary heart disease. J Counsel Clin Psychol 1988;56:333–341.
11. Siegrist J, Peter R, Junge A, Cremer P, Seidel D. Low status of control, high effort at work and ischemic heart disease: Prospective evidence from blue-collar men. Soc Sci Med 1990; 31:1127–1134.
12. Haynes SG, Feinleib M, Kannel WB. The relationship of psychosocial factors to coronary heart disease in the Framingham Study. Am J Epidemiol 1980;111:37–58.
13. Fauvel JP, M'Pio I, Quelin P, Rigaud JP, Laville M, Ducher M. Neither perceived job stress nor individual cardiovascular reactivity predict high blood pressure. Hypertension 2003;42: 1112–1116.
14. Raikkonen K, Matthews KA, Kuller LH. Trajectory of psychological risk and incident hypertension in middle-aged women. Hypertension 2001;38:798–802.
15. Matthews KA, Kiefe CI, Lewis CE, Liu K, Sidney S, Yunis C. Socioeconomic trajectories and incident hypertension in a biracial cohort of young adults. Hypertension 2002;39:772–776.
16. Batey DM, Kaufnmann PG, Raczynski JM, Hollis JF, Murphy JK, Rosner B, Corrigan SA, Rappaport NB, Danielson EM, Lasser NL, Kuhn CM. Stress management intervention for primary prevention of hypertension: Detailed results from Phase l Trials of Hypertension Prevention (TOHP-l). Ann Epidemiol 2000;10:45–58.
17. Eisenberg DM, Delbanco TL, Berkley CS, Kaptchuk TJ, Kupelnick B, Kuhl J, Chalmers TC. Cognitive behavioral techniques for hypertension: Are they effective? Ann Intern Med 1993;118:964–972.
18. Linden W, Lenz JW, Con AH. Individualized stress management for primary hypertension: A randomized trial. Arch Intl Med 2001;161:1071–1080.
19. DeRubeis RJ, Tang TZ, Beck AT. Cognitive therapy. In: Dobson KS, ed. Handbook of Cognitive–Behavioral Therapies, 2nd ed. New York: Guilford, 2001:349–392.
20. Press-Ganey Satisfaction Measurement. Online document at: www.pressganey.com
21. Tarlov AR, Ware JE, Greenfield S, et al. The Medical Outcomes Study: An application of methods for monitoring the results of medical care. JAMA 1989;262:925–930.
22. Donald CA, Ware JE. The Quantification of Social Contacts and Resources. Santa Monica, CA. RAND Publication R-2937-HHS.
23. Grimm RH Jr, Grandits GA, Cutler JA, et al. Relationships of quality-of-life measures to long-term lifestyle and drug treatment of mild hypertension study. Arch Intern Med 1997;157: 638–648.

Address correspondence to:
Kathleen M. Wesa, M.D.
Department of Medicine
University of Minnesota
701 Park Avenue South, Adabee 865B
Minneapolis, MN 55415

E-mail: Kathleen.wesa@co.hennepin.mn.us