Clinical Research

Influence of psychosocial factors on treatment of elderly Chinese patients with hypertension

Guolong Yu, Tianlun Yang, Cesar V. Borlongan, Christine E. Stahl, Xiumei Xie, Jin He, Biefei Li, Ke Xia

1Department of Cardiology, Xiangya Hospital, Southern Central University, Changsha 410008, China
2Department of Neurology, Medical College of Georgia, Augusta, GA 30912, USA
3Department of Internal Medicine, Dwight D. Eisenhower Army Medical Center, Fort Gordon, GA 30909, USA

Objective
The aim of the study is to investigate the effects of psychosocial factors on the treatment of elderly patients with hypertension.

Methods
A total of 260 elderly Chinese patients with hypertension were treated with benazepril alone or benazepril combined with amlopidine for 8 weeks. The target blood pressure (BP) (both <140 mmHg systolic, SBP, and <90 mmHg diastolic, DBP) was achieved in 180 patients, who were then assigned to the well-controlled BP group; the rest were placed in the modestly controlled BP group. The psychosocial factors present in both groups were assessed by the Hamilton depression scale, Hamilton anxiety scale, life event scale and social support evaluation list before and after anti-hypertensive treatment.

Results
There were no significant differences in gender, mean age, history of hypertension, education and smoking habit, or in SBP and DBP between the groups before treatment. Significant differences were also not found in all psychosocial factors before and after treatment in the patients. However, significant differences were found between the groups with respect to post-treatment SBP and marital status. The patients with modestly controlled BP had significantly higher scores, as well as incidences, on the depressive, anxiety, and stressful life event scales than those with well-controlled BP. The patients with well-controlled BP had significantly higher scores in tangible support, subjective support, and social support compared to the patients with modestly controlled BP. Logistic regression analysis showed the independent contribution of psychosocial factors in reaching the goal of lowering BP at treatment endpoint in these hypertensive patients.

Conclusions
The results suggest that psychosocial factors stand as a main barrier to achieving the BP-lowering target in the management of elderly Chinese patients with hypertension.

Key Words: hypertension; psychosocial factor; elderly; treatment outcome

Introduction
Hypertension is one of the most important modifiable risk factors for cardiovascular disease (CVD), peripheral vascular disease, and renal disease. The prevalence and absolute numbers of hypertension have increased dramatically in China during recent decades. For example, the estimated number of hypertension cases among Chinese adults has increased from 30 million in 1960 to 94 million in 1990, and to 149 million in 2002. Hypertension generally affects people in later life. Approximately two-thirds (62%) of the Chinese population with hypertension are aged 55 or older.

According to recent studies, only 45% of patients with hypertension are being treated for the disorder, and 8.1% of them have their hypertension adequately controlled. There is now substantial evidence from randomized control trials of the benefits of pharmacological treatment for patients with hypertension. A recent meta-analysis of eight clinical trials of hypertensive treatment found risk reductions of 13% for all-cause mortality, 30% for stroke, and 23% for coronary events after BP was controlled.

The results from one randomized controlled clinical trial by Gueyffier and associates showed that substantial BP differences between the study groups might largely be responsible for different incidences of CVD in the patients. It was also confirmed that greater CVD risk reductions were produced in hypertensive patients when lower blood pressure goals were targeted in the value randomized trial (i.e., regimens based on valsartan or amlopidine). Determining whether anti-hypertensive medication will be effective for a particular patient is very complicated. Many genetic variations in pathways involved in drug absorption, transport, activation, metabolism, and excretion as well as some demographic factors such as age, race, and gender are known to influence the treatment outcome with anti-hypertensive medication.
Accumulating evidence suggests that psychosocial factors including depression, anxiety, stress, lack of social support/social integration, low socio-economic status, and occupational stress be associated with hypertension, and that psychosocial factors might independently predict subsequent cardiovascular events or complications and co-morbidity. An increasing number of studies have implied that psychosocial factors play an important role in the pathogenesis of hypertension. However, until recently little attention has been given to evaluation of the influence of psychosocial factors on the therapeutic effects of anti-hypertensive medication in the management of hypertension. The aim of this study is to test the hypothesis that higher levels of psychosocial stress would be associated with decreased likelihood of achieving the targeted lower BP goals during anti-hypertensive treatment in elderly Chinese patients with hypertension. The objective of this study is to provide vital information that could help doctors and health administrators in recognizing the importance of psychosocial factors in the treatment of patients with hypertension.

Methods

Subjects and treatment

The study design included a placebo wash-out period of 2 weeks and an active treatment period of 8 weeks. This clinical trial was approved by the institutional review boards of the Biomedical Institute at Xiangya Medical School of Central Southern University, China. Written informed consent was obtained from each subject who agreed to participate. Eligible patients had to be between 60 and 79 years old, retired white-collar workers, and with sitting systolic blood pressure (SBP) of 140 to 180 mmHg and/or diastolic blood pressure (DBP) of 90 to 115 mmHg before the active treatment period. Exclusion criteria included secondary or more severe hypertension (sitting DBP over 115 mmHg or SBP over 180 mmHg during the wash-out period), renal or hepatic disease, poorly controlled diabetes, severe heart failure, myocardial infarction, unstable angina, and percutaneous transluminal coronary angioplasty or coronary bypass graft and clinically relevant valvular or cerebrovascular diseases in the past three months. The patients were also excluded if the value of any of the psychosocial factors before and after anti-hypertensive treatment was different significantly by 20% because of family or personal events, accompanying other diseases or medical education. At last 260 elderly patients with hypertension from the outpatient clinic of geriatric cardiology department from the university hospital completed this study from January to December, 2005. All patients received 10mg benazepril every morning for 4 weeks. Amlodipine 5 mg was added every morning for the next 4 weeks if BP did not reached the BP-lowering target, which was defined as a sitting SBP <140 mmHg and/or DBP <90 mmHg, after the first 4 weeks of treatment. The total duration of the treatment lasted for 8 weeks.

Blood pressure measurements

All subjects were asked to visit the clinics around 9 AM daily during the treatment. A standard mercury sphygmomanometer was used for all BP measurements taken by the same nurse. The BP was recorded after 15 minutes of rest in a sitting position. Two sitting measurements were performed subsequently, separated by a 5-minute interval. The mean of the two measurements was used as the reference value.

Questionnaire

The patients were administered a standardized questionnaire when the duration of treatment was completed. A clinic assistant collected the self-administered questionnaires. The following information was included: 1) demographic and clinical data for gender, mean age, marital status, education, current smoking habit, and history of hypertension; 2) psychosocial characteristics were assessed by a Chinese version of the Hamilton depression scale,11 Hamilton anxiety scale,12 life event scale,13 and social support evaluation list.14 The psychometric properties of all of these four instruments have been vigorously examined.

The Hamilton depression scale has been used in our study and other previous studies and consists of 24 statements referring to depressive behavior in everyday life situations. The subject responds to each statement on a five-point scale (0-4). The scale ranges between 0 and 96 points, with higher scores indicating more depressive reaction; a patient who scores greater than 20 points is defined as a depressive subject.

Anxiety was measured by the Hamilton anxiety scale, which has been used in our study and other previous studies. The subject responds to each of 14 statements referring to anxiety and a patient who scores higher than 14 points is considered an anxiety patient.

The questionnaire on stressful life events was a modified Chinese version of an extensive life event scale by Dohrenwend and colleagues. The present version, which comprises 10 statements, has been used in a previous clinical study. The subject responds to each statement on a three-point scale (0-2). The stressful life events within 1 year before the investigation were recorded in the present study. Thus, the possible score ranges from 0 to 20 points and higher scores are indicative of significant stressful events.

The social support evaluation list, which was modified from the interpersonal support evaluation list by Xiao, was used to assess social support of the patients. The questionnaire has been used in many different medical settings in published studies and consists of 10 items designed to assess perceived availability of three types of
support; namely, tangible support or the perceived availability of practical aid, subjective support or the availability of people to talk to and provide advice, and objective support or the perceived availability of social contacts with whom one can do things. Response to the 10 items on a five-point scale (0-4) were completed in order to generate composite scores for tangible support, subjective support, objective support and total social support respectively, with higher values reflecting positive social support.

Statistical analysis

We used the statistical package SPSS V.11.0 (SPSS Inc., Chicago, Illinois, USA) for data management and analysis. Descriptive statistics are presented as percentages for categorical data and means and standard deviations for continuous variables. Bivariate comparisons were tested by χ² or t-test. In addition, logistic regression analyses were performed to assess the relative contribution of the several domains of psychosocial factors in reaching the goal of lowering BP at endpoint. A P value less than 0.05 was pre-set to indicate statistical significance.

Results

Clinical and demographic characteristics

The subjects were classified into two groups: well-controlled BP and modestly controlled BP according to whether patients reached a target BP of sitting SBP <140 mmHg and/or DBP <90 mmHg at the end of treatment. The target BP (both <140 mmHg systolic and <90 mmHg diastolic) was achieved in 180 patients, who were then assigned to the well-controlled BP group; those who did not reach this criterion were assigned to the modestly controlled BP group. The clinical and demographic characteristics of the patient in the two groups were shown in Table 1. Direct comparisons between the groups revealed no significant differences in gender, mean age, history of hypertension, level of education, current smoking habit or in SBP and DBP before treatment. The only difference between the two groups at baseline was marital status, as patients with modestly controlled BP had significantly lower percentages of either having spouses or being divorced/widowed compared to those with well-controlled BP. Significant differences were found between the groups with respect to SBP at endpoint in which the well-controlled BP patients had significantly lower SBP than those patients with modestly controlled BP. Although SBP was also significantly decreased after treatment in the modestly controlled BP group, the SBP in this group did not reach the pre-set criterion of <140 mmHg systolic.

Significant differences were also not found in all psychosocial factors before and after treatment in all patients.

Comparison of depressive and anxiety status between groups

As shown in Fig. 1, the patients with modestly controlled BP had significantly higher scores on the depressive or anxiety scale than those with well-controlled BP before treatment. Compared with the group with well-controlled BP, the amount of depression or anxiety was also increased significantly in the group with modestly controlled BP before treatment.

Comparison of life events and social support between groups

In a univariate comparison (Fig.2), the patients with modestly controlled BP had a significantly higher stressful score and number of stressful life events than those with well-controlled BP before treatment. Conversely, the group with well-controlled BP had significantly higher scores in tangible support, subjective support, and social support than those with modestly controlled BP before treatment.

Logistic regression analysis

Table 1  Clinical and demographic characteristics of subjects

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group with well-controlled BP(n=180)</th>
<th>Group with modestly controlled BP(n=80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>68.24±8.12</td>
<td>67.87±9.18</td>
</tr>
<tr>
<td>Male, %</td>
<td>62.50%</td>
<td>62.5%</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married, %</td>
<td>82.22%</td>
<td>72.50%</td>
</tr>
<tr>
<td>Divorced/widowed</td>
<td>17.78%</td>
<td>27.50%</td>
</tr>
<tr>
<td>Level of education, yr</td>
<td>9.23±2.3</td>
<td>78.66±2.06</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>30%</td>
<td>27.50%</td>
</tr>
<tr>
<td>Years since diagnosis</td>
<td>15.55±4.35</td>
<td>14.67±5.66</td>
</tr>
<tr>
<td>Blood pressure, mmHg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP/DBP at baseline</td>
<td>165±19/81±12</td>
<td>168±20/79±14</td>
</tr>
<tr>
<td>SBP/DBP after treatment</td>
<td>130±17** /75±10</td>
<td>151±19* /77±13</td>
</tr>
</tbody>
</table>

Values are mean±SD or %; †P<0.05 between the groups; ‡P<0.05, ∗P<0.01 between baseline and after treatment in the same group.
Logistic regression analyses were performed to study the independent contribution of the domains of psychosocial factors in reaching the goal of lowering BP at endpoint. Table 2 shows significant effects of depression, anxiety, stressful life event, tangible support, subjective support and total social support, but not a number of stressful events and objective support, in hypertensive patients who achieved the BP lowering target criterion.

### Table 2 Logistic regression analysis of several domains of psychosocial factors on patients reaching the goal of lowering BP

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>Word test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressive score</td>
<td>-0.566</td>
<td>5.127</td>
<td>0.011</td>
</tr>
<tr>
<td>Anxiety score</td>
<td>-0.360</td>
<td>4.004</td>
<td>0.040</td>
</tr>
<tr>
<td>Number of stressful events</td>
<td>-0.111</td>
<td>1.965</td>
<td>0.234</td>
</tr>
<tr>
<td>Stressful score</td>
<td>-0.499</td>
<td>4.969</td>
<td>0.024</td>
</tr>
<tr>
<td>Tangible support score</td>
<td>0.512</td>
<td>5.658</td>
<td>0.013</td>
</tr>
<tr>
<td>Subjective support score</td>
<td>0.437</td>
<td>4.444</td>
<td>0.028</td>
</tr>
<tr>
<td>Objective support score</td>
<td>0.276</td>
<td>2.987</td>
<td>0.154</td>
</tr>
<tr>
<td>Total social support score</td>
<td>0.495</td>
<td>5.465</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Note: Values are mean±SD or %. Compared with Group with well-controlled BP, * p<0.05; ** p<0.01. DS:Depressive score, PD(%):Patients with depression, AS: Anxiety score, PA(%): Patients with anxiety.

Discussion

In the present study, psychosocial factors were shown to influence anti-hypertensive drug treatment in lowering BP in elderly Chinese patients with hypertension. In particular, the results showed that, compared with the well-controlled BP patients, significantly higher depressive or anxiety scores and incidence of depression or anxiety were found in those with modestly controlled BP. Significantly higher stressful scores and number of stressful life events were also recognized in the patients with modestly controlled BP. Moreover, the well-controlled BP patients had significantly higher scores in social support. Our data demonstrated that there were no significant differences in gender, mean age, history of hypertension, level of education, current smoking habit or in SBP and DBP at baseline between the two groups, with exception of marital status, thereby making the analyses more reliable. In multivariate analysis, high depression, high anxiety and low social support were strongly significant contributors to reaching the BP-lowering goal in these hypertensive patients. The psychosocial differences between subjects in the two groups might explain the differences in therapeutic response to the anti-hypertensive. These results provide support to the hypothesis that psychosocial distress would be associated with decreased likelihood of achieving the goal of BP lowering during anti-hypertensive treatment in elderly Chinese patients with hypertension.

A major finding of this study was the observation of significant lower percentages of having spouses in the patients with modestly controlled BP, which suggested that support of spouse or children be beneficial to controlling BP. Marital status was not a part of the social support evaluation list in this study. However, it can still be considered a separate dimension of social support. Married patients who
received encouragement or care from spouse and children may be more likely to have a better quality of life and a higher adherence to physician recommendations. The recent report by Steptoe found that social support has a buffering effect which reduces the impact of stress on cardiovascular activity.

Previous studies were focused mainly on the relationship or association between psychosocial characteristics and hypertension. For example, Waldstein and colleagues demonstrated that hypertensive individuals had a lower psychological function than normotensive individuals. Other recent studies showed the prevalence rates of depression and anxiety as high as 36.4%, and 39.4% in female and 32.2%, and 27.4% in male hypertensive patients respectively. Compared to younger adults, psychological distress was found to have a more significant association for the elderly patients with hypertension. Other reports indicated that considerable stress or stress life events, lack of social support/social integration, and low-economic status were likely to accompany the hypertensive patients.

The mechanisms responsible for the impact of psychosocial distress on the therapeutic effect of anti-hypertensive treatment are complex and not fully understood. Findings from previous studies, however, provided evidence that increased and persistent sympathetic activity, increased BP reactivity and stimulation of hypothalamic-pituitary-adrenal axis were associated with increased BP in individuals with hypertension and psychosocial distress, which might explain the reduced positive outcome for anti-hypertensive medication in patients with modestly controlled BP. In addition, the higher levels of psychosocial distress in the elderly were likely to result in a decreased adherence to physician recommendations on medications and lifestyle.

Psychosocial problems that were documented during the present treatment might be side effects of anti-hypertensive medications. For example, β-blockers in the elderly might have an adverse effect on psychosocial characteristics including cognition, mood, depression and social function. In the present study, however, all patients received the same anti-hypertensive medications, thus eliminating the possibility that differences in psychosocial factors between the two groups are due to the drugs. Moreover, a variety of previous reports indicated that the angiotensin-converting enzyme inhibitor, benazepril, and calcium antagonist, amlodipine, did not affect psychological, cognitive, and social functions.

This study was aimed to evaluate the impact of psychosocial distress on hypertensive treatment in elderly Chinese patients and to extend our previous study. Additional psychosocial factors (e.g., depressive or anxiety scores as well as incidence of depression or anxiety) were recognized in this study. These results are consistent with one earlier report that found psychosocial factors, such as anxiety and lower family and social support, might affect the pharmacological therapeutic effect in the adult Chinese patients with hypertension.

The Chinese Hypertension League issued its guidelines for the prevention, detection, and treatment of hypertension in 1999. Overall, the therapeutic outcome targeted by Chinese physicians is in concert with their European and American colleagues in that the BP-lowering goal is SBP <140 mmHg and/or DBP <90 mmHg. A bulk of clinical studies have clearly demonstrated the benefits of treating hypertensive patients aged between 60 and 79 in reducing morbidity and mortality of CVD by regimens that targeted lower BP. Furthermore, BP reduction has been linked to differences in risks of CVD. Therefore, BP-lowering as one of the main objectives of the present study, is directly relevant to the treatment of hypertensive patients. However, conventional strategies for hypertensive management give emphasis to pharmacological therapies and lifestyle modification. The physicians usually focus on observing and examining the contribution of drug treatment to reach the BP-lowering target and neglect the important influences of psychosocial factors on hypertensive control.

This study has limitations. First, subjects were obtained from the outpatient clinic of the geriatric department of a university hospital. All patients enrolled in this study were between 60 and 79 years old, retired white-collar workers from urban areas with relatively better economic status, and with sitting BP of 140 to 180 mmHg and/or DBP of 90 to 115 mmHg. The patients in this study may not be entirely representative of all individuals with hypertension. Second, psychosocial factors are probably subject to fluctuations over time. Therefore, the relationship between the domains and BP-lowering level is not stable and may also change over time. In the present study, patients were also excluded if the values of psychosocial factors before and after anti-hypertensive treatment were different significantly. The psychosocial factors of the patients enrolled in this study were relatively stable during anti-hypertension. Thus, this study had diminished greatly the influence of psychosocial factors fluctuations on the results. Finally, the power of the statistical comparison of psychosocial dimensions between the two groups was limited as a consequence of the relatively short study period and small sample size. Thus, it is interesting to explore the relationship between psychosocial factors and anti-hypertensive effects for a longer time or for the larger sample including those of different backgrounds and regions, or younger adults in China.

In conclusion, we have identified that psychosocial distress is an important factor for managing BP of elderly Chinese patients with hypertension. Psychosocial distress is likely not only a principal risk factor for hypertension, but also a key element that affects anti-hypertensive therapeutic outcome. Accordingly, adequate management of psychosocial distress in patients with hypertension should be
considered in the clinic.

Acknowledgment

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References