Original Article

Effects of Guideline-based Hypertension Management in Rural Areas of Guangdong Province

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Abstract

Background: Despite the improvement in the health care industry, the rates of undetected, untreated, and uncontrolled hypertension (HTN) are still very high, especially in rural areas of China. The aim of this study was to investigate the efficacy and efficiency of a guideline-based HTN management (novel therapy) in population of rural areas of Guangdong Province.

Methods: Totally, 3113 patients with essential HTN in a rural area of Guangdong Province were enrolled and assigned to two groups, named traditional ($n = 372$) and novel therapeutic ($n = 2741$) groups, respectively. Patients in the traditional group were treated routinely, and patients in the novel group were treated in a novel model characterized by regular educational programs for hypertensive populations, close monitoring of blood pressure in combination with finely tuned antihypertensive medications, strict implementation of lifestyle modification and improving medical knowledge and skill of local medical staff efficiently. After 2 years of follow-up, primary endpoints including magnitude of systolic and diastolic blood pressures (SBP and DBP) decrease, treated and controlled rates, as well as secondary endpoints, were evaluated in both groups.

Results: Initially, the treated rate was significantly higher in traditional group than that of novel group (71.15% vs. 64.99%, $P < 0.05$), while the controlled rates were comparable and insignificant difference between baseline BP in both groups (31.07% vs. 26.88%, $P > 0.05$). Four variables were significantly different, namely smoking rate, daily vegetable consumption (VC), and serum levels of low-density lipoprotein-cholesterol and fasting blood glucose between these two groups. After 2 years of follow-up, decreases in SBP and DBP were more prominent in the novel group ($P < 0.001$). Treated and controlled rates in both groups were both increased. Nevertheless, in comparison to the traditional group, controlled rate increased more significantly in the novel group (64.31% vs. 37.85%, $P < 0.001$). Variables indicating lifestyle modification such as high sodium consumption, percentages of alcohol abuse, daily VC were profoundly improved in the novel group.

Conclusions: The guideline-based HTN management implemented in the current study was beneficial for HTN control in rural areas of Guangdong Province.

Key words: Hypertension Management; Population; Rural Areas

Introduction

It is well-known that hypertension (HTN) imposes great burdens on individuals and the whole country due to its direct contributions to atherosclerotic cardiovascular diseases, congestive heart failure, ischemic or hemorrhagic stroke and renal diseases.[1,2] As estimated, the prevalence of HTN is approaching 40% globally,[3] and in China, from the year of 2002 to 2010, the prevalence of HTN increased from nearly 20% to 40%.[4] Unfortunately, only 35.7% of Chinese hypertensive patients are aware of their condition and <18% of these individuals have their blood pressure well-controlled.[4] Worse than what is mentioned, a substantial portion of these hypertensive populations are located in rural areas of China where health resources are less accessible and less available. Therefore, seeking highly efficient and effective approaches, particularly highly cost-effective and easily performed ones, so as to improve the treated and controlled rate of HTN and reducing the incidence of HTN-induced cardiovascular diseases is of particular importance.

Previously, guidelines have strongly recommended that lifestyle interventions such as quitting smoking, getting regular aerobic exercises, losing weight in overweight or obese individuals, digesting more vegetables and fruits, and reducing sodium intake should all be integrated into

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the comprehensive management of HTN.[5,6] However, based on our previous on-site observations, it is infeasible for the rural hypertensive population to accept and/or adhere to guideline-recommended lifestyle interventions, and the main reasons are largely due to lack of effective monitoring and educational program. Notably, results from a study conducted by Nguyen *et al*.[7] showed that delivering knowledge of HTN to community population, implementing lifestyle modification, and improving clinical skill of local medical staff were beneficial for comprehensive management of HTN in a low resource context of Vietnam rural commune.

Unfortunately, in China, despite improved health system in terms of broadening medical insurance coverage and strengthening the significance of blood pressure management nationwide, the rates of undetected, untreated, and uncontrolled HTN are still up to 40%, 50%, and 80%, respectively, as recently reported by Feng *et al*.[4] Taken together, in light of our previous observations and the reports of Nguyen *et al*.,[7] our research group conducted a pilot study in Liaobu Town (a rural area of Guangdong province) for the purpose of seeking whether guideline-based HTN management (novel therapy) could effectively and efficiently treat hypertensive population with a relatively less health resources requirement.

Methods

Patient enrolment and therapeutic strategies

All participants were from Liaobu Town and provided informed consents before enrollment. All the patients were older than 18 years and were definitely diagnosed as essential HTN in accordance with the diagnostic criteria.[8] Secondary HTN, acute coronary syndrome or cerebrovascular events within 3 months, incapable of finishing questionnaire because of intellectual impairment and other conditions, complicated by other severe diseases with <1-year life expectancy and their unwillingness to take part in the current study were the ruled-out criteria. Totally, 372 patients with essential HTN were assigned to the traditional therapeutic group, and 2741 in the novel therapeutic group (named the guideline-based HTN management). Specifically, strategy for the traditional therapeutic group was the same as it was routinely performed. For example, patients were informed of the definition, potential detrimental effects and risk factors of HTN by local medical staff at an out-patient visit. Medical and nonmedical managements (in terms of lifestyle intervention) of HTN were also clearly explained to patients and their family members in the initial stages. In the novel therapeutic group, in addition to the aforementioned projects,[8] patients were also given educational programs quarterly by specialists of HTN from our cardiovascular center for the very first time and by local medical staff thereafter. Implementation of lifestyle modification was also concomitantly evaluated. Specifically, daily vegetable consumption (VC) was assessed by asking the subjects how many kilograms of vegetables he or she had approximately consumed every day, and the daily sodium consumption was also assessed by the same method. Blood pressure was monitored regularly, and medication was timely adjusted. Finally, all involved local medical staffs were further educated in medical knowledge and skill by specialists of HTN from our cardiovascular center. Specific therapeutic strategies for traditional and novel groups were presented in Table 1.

Study endpoints

After 2 years of follow-up, primary study endpoints including decrease in the magnitude of systolic and diastolic blood pressures (SBP and DBP), as well as the treated and controlled rates of initial and follow-up were all assessed in both groups. Body mass index (BMI), waist circumference, daily VC, daily sodium intake, the percentages of smoking and alcohol abuse, as well as laboratory parameters such as lipid profile and fasting blood glucose (FBG) served as the secondary endpoints, were also evaluated in both groups.

Statistical analysis

Continuous variable was presented as mean ± standard deviation (SD) or median appropriately, and compared using the Student's *t*-test when data were normally distributed, otherwise compared using Wilcoxon rank-sum test. Categorical data were presented as a percentage and compared using χ^2 test. Statistical analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). A value of $P < 0.05$ was considered statistically significant.

Results

Comparison of baseline characteristics between the traditional and novel therapeutic groups

As shown in Table 2, five parameters at baseline showed significant difference between these two groups, namely smoking rate, daily VC, serum levels of low density lipoprotein-cholesterol (LDL-C) and FBG, and treated rate. Specifically, smoking rate was higher, and daily VC, serum levels of LDL-C and FBG, and treated rate were lower in the novel therapeutic group ($P < 0.05$). Other parameters were also compared between these two groups. Most of the participants in both groups graduated from elementary

Table 1: Specific therapeutic strategies for traditional and novel therapeutic groups

Strategies	Traditional group	Novel group
Definition of HTN (informed)	Yes	Yes
Potential detrimental effects of HTN (informed)	Yes	Yes
Risk factors of HTN (informed)	Yes	Yes
Lifestyle intervention recommendation	Yes	Yes
Educational program	No	Yes
Lifestyle modification monitoring	No	Yes
Regular blood pressure monitoring	No	Yes
Timely adjustment of medication	No	Yes
CME of local medical staffs	No	Yes

HTN: Hypertension; CME: Continuous medical education.

Table 2: Baseline characteristic of the traditional and novel therapeutic groups

Variables	Traditional group (n = 372)	Novel group (n = 2741)
Age (mean ± SD, years)	63.33 ± 13.57	63.06 ± 12.67
Degree of elementary education, n (%)	251 (67.47)	1958 (71.43)
Male, n (%)	157 (44.35)	1117 (42.23)
Duration of HTN (mean ± SD, years)	4.86 ± 4.89	3.80 ± 4.04
Smoking, n (%)	48 (13.56)	544 (20.57)*
HSC, n (%)	61 (17.28)	474 (17.92)
VC (mean ± SD, g)	303.54 ± 195.46	276.05 ± 125.82*
Alcohol abuse, n (%)	14 (3.95)	144 (5.44)
Waist (mean ± SD, cm)	88.07 ± 9.52	88.04 ± 9.83
BMI (mean ± SD, kg/m^2)	25.38 ± 3.63	25.39 ± 3.91
SBP (mean ± SD, mmHg)	142.74 ± 18.76	144.75 ± 16.69
DBP (mean ± SD, mmHg)	85.34 ± 11.35	86.37 ± 11.48
Treated rate, n (%)	254 (71.75)	1719 (64.99)*
Controlled rate, n (%)	110 (31.07)	711 (26.88)
TC (mean ± SD, g/L)	1.99 ± 0.47	1.94 ± 0.46
TG (mean ± SD, g/L)	1.90 ± 1.38	1.89 ± 1.54
LDL-C (mean ± SD, g/L)	1.17 ± 0.35	1.11 ± 0.30*
HDL-C (mean ± SD, g/L)	0.52 ± 0.13	0.51 ± 0.13
FBG (mean ± SD, mmol/L)	5.69 ± 1.90	5.42 ± 1.70*

*P < 0.05 versus traditional group. VC: Daily vegetable consumption; HSC: High sodium consumption, specifically, HSC means daily sodium consumption higher than 5 g; HTN: Hypertension; SD: Standard deviation; BMI: Body mass index; TC: Total cholesterol; TG: Triglyceride; LDL-C: Low density lipoprotein-cholesterol; HDL-C: High density lipoprotein-cholesterol; FBG: Fasting blood glucose; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

school (67.47% vs. 71.43%), and females were predominant in our current study (55.65% vs. 57.77%). Nearly, 17% of the participants in both groups consumed sodium exceeding 5 g/d. Notably, the controlled rates were only 31.07% and 26.88% in both groups in the initial stages, indicating that despite treatment of more than 60% of the participants in both groups with antihypertensive medications, the controlled rates were far from satisfactory. Notably, there was no significant difference between these two groups with regards to baseline blood pressure.

Comparison of primary endpoints between the traditional and novel therapeutic groups

As shown in Table 3, after 2 years of follow-up, the magnitude of SBP and DBP decreased significantly in the novel therapeutic group when compared to the traditional group (P < 0.001). Notably, treated rate and controlled rate in both groups were increased. Nevertheless, in comparison with the traditional therapeutic group, a controlled rate increased significantly in the novel therapeutic group (37.85% vs. 64.31%, P < 0.001). Specifically, approximately 52.50% and 80.20% of patients in the traditional and novel groups had improved their lifestyle, respectively (P < 0.05), and 30.60% and 33.70% were treated with single antihypertensive agent and 62.70% and 61.40% were with dual antihypertensive agent in the traditional and novel groups, respectively, and

Table 3: Comparison of primary endpoints after 2 years of follow-up

Variables	Traditional group (n = 372)	Novel group (n = 2741)
SBP (mean ± SD, mmHg)		
Initially	142.74 ± 18.76	144.75 ± 16.69
Follow-up	138.74 ± 18.79	132.86 ± 13.91*
DBP (mean ± SD, mmHg)		
Initially	85.34 ± 11.35	86.37 ± 11.15
Follow-up	83.40 ± 13.36	79.44 ± 9.08*
Treated rate, n (%)		
Initially	254 (71.75)	1719 (64.99)†
Follow-up	290 (81.92)	2128 (80.45)
Controlled rate, n (%)		
Initially	110 (31.07)	711 (26.88)
Follow-up	134 (37.85)	1701 (64.31)*

*P < 0.001 and †P < 0.05, versus traditional group. SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

there were no significant differences between these two groups (P > 0.05).

Comparison of secondary endpoints between the traditional and novel therapeutic groups

As shown in Table 4, with either traditional or novel therapeutic strategy, some secondary endpoints in both groups were improved after 2 years of follow-up. Notably, when compared to the initial data, the percentages of participants with high sodium consumption (HSC) in both groups were reduced to 12.71% and 11.46%, respectively, and serum levels of LDL-C and the percentages of alcohol abuse in both groups were also notably reduced. Waist circumferences in both groups were decreased, and BMI was reduced only in the novel therapeutic group but there was no significant difference between these two groups. Daily VC in the traditional therapeutic group was decreased, whereas there was no prominent change in the novel therapeutic group when compared to the initial data, indicating that strictly implementing lifestyle modification might be helpful to maintain a healthy lifestyle. Disappointedly, smoking rates in both groups were similar to the initial data, indicating that how to effectively and efficiently persuade patients to stop smoking needed further consideration.

Discussion

Importantly, our current study showed that in comparison with the traditional model of HTN management in rural areas of Guangdong, the novel therapeutic strategy in terms of guideline-based HTN management including regularly giving educational programs to hypertensive populations, closely monitoring blood pressure combined with finely tuned antihypertensive medications, strictly implementing lifestyle modification and efficiently improving medical knowledge and skill of local medical staff all have better outcomes of HTN management, as well as higher controlled rate and improved lifestyle.

Table 4: Comparison of secondary endpoints after 2 years of follow-up

Variables	Traditional group (n = 372)	Novel group (n = 2741)
BMI (mean ± SD, kg/m^2)		
Initially	25.38 ± 3.63	25.39 ± 3.91
Follow-up	25.78 ± 4.11	25.23 ± 4.05
Waist (mean ± SD, cm)		
Initially	88.07 ± 9.52	88.04 ± 9.83
Follow-up	85.96 ± 9.73	87.19 ± 9.97*
VC (mean ± SD, g)		
Initially	303.54 ± 195.46	276.05 ± 125.82*
Follow-up	267.00 ± 123.89	273.21 ± 128.52
HSC, n (%)		
Initially	61 (17.28)	474 (17.92)
Follow-up	45 (12.71)	303 (11.46)
Smoking, n (%)		
Initially	48 (13.56)	544 (20.57)
Follow-up	53 (14.97)	534 (20.19)*
Alcohol abuse, n (%)		
Initially	14 (3.95)	144 (5.44)
Follow-up	7 (1.98)	108 (4.08)
TC (mean ± SD, g/L)		
Initially	1.99 ± 0.47	1.94 ± 0.46
Follow-up	2.04 ± 0.48	2.02 ± 0.43
TG (mean ± SD, g/L)		
Initially	1.90 ± 1.38	1.89 ± 1.54
Follow-up	1.52 ± 0.94	1.52 ± 1.19
LDL-C (mean ± SD, g/L)		
Initially	1.17 ± 0.35	1.11 ± 0.30*
Follow-up	0.97 ± 0.26	0.97 ± 0.29
HDL-C (mean ± SD, g/L)		
Initially	0.52 ± 0.13	0.51 ± 0.13
Follow-up	0.49 ± 0.13	0.50 ± 0.14
FBG (mean ± SD, mmol/L)		
Initially	5.69 ± 1.90	5.42 ± 1.70*
Follow-up	5.27 ± 1.94	5.02 ± 1.67*

*P < 0.05, versus traditional group. VC: Vegetable consumption; HSC: High sodium consumption; BMI: Body mass index; SD: Standard deviation; TC: Total cholesterol; TG: Triglyceride; LDL-C: Low density lipoprotein-cholesterol; HDL-C: High density lipoprotein-cholesterol; FBG: Fasting blood glucose.

Accordingly, the rates of undetected, untreated, and uncontrolled HTN are still very high in China, particularly in the rural areas where health resources are less accessible and less available.[9-11] In addition, compared to the urban areas, the mortality and morbidity rates of HTN-induced cardiovascular diseases are also much higher in China's rural areas.[9-11] Therefore, it is of particular importance to seek a feasible and highly-efficient approach to improve treated and controlled rates of HTN so as to decrease the incidence of coronary artery diseases and strokes in rural areas of China. With regard to our previous observations and results from other epidemiological studies,[7,12-14] the main reasons underpinned the fact that high undetected, untreated, and uncontrolled rates of HTN were mainly due to the following reasons: Individuals lack knowledge of HTN and its associated diseases, insufficient blood pressure monitoring, without timely adjustment of medications, and noncompliance to lifestyle modification. Previously, some researchers have done pilot studies to investigate the efficacy and efficiency of different models of HTN management in rural areas and communities.[7,12-14] For example, Nguyen *et al*.[7] implemented top-down and bottom-up approaches to assess the HTN management in rural areas of Vietnam. Results from their study suggested that both local authorities and a cardiac care network led by an outstanding cardiac referral center could play important roles in implementing comprehensive program for the management of HTN at primary healthcare level and also could be of benefit to severe hypertensive population.[7] Our current study also showed that educational programs presented by an HTN specialist played critical roles in many aspects. On one hand, for example, after education, the patients had more knowledge about the importance of HTN management, which we believed partially contributed to their willingness to adhere to lifestyle modification. On the other hand, the medical knowledge and skill of local medical staffs were also improved by educational programs, which ultimately enhanced their capacity in handling hypertensive patients, and this might be one of the reasons why the treated and controlled rates of HTN in the traditional therapeutic strategy group were also increased when compared to the initial. Nevertheless, after 2 years of follow-up, despite the treated rate increasing to 81.92% in the traditional therapeutic group, a controlled rate was still too low to satisfy (37.85%). Our current study showed that with a novel therapeutic strategy, which we adopted and modified from previous studies,[7] the treated and controlled rates of the hypertensive population were profoundly increased. The novel strategy we applied herein was characterized by four key features which we believed played an important role in improving HTN management in rural areas of our province. First of all, in light of our previous observations, we found out that rural medical staffs medical knowledge and skills in the effective management of HTN were relatively inadequate when compared to the physicians from urban areas. Therefore, we invited experienced physicians of HTN management to give HTN -related educational programs to local medical staffs so as to improve their skills and knowledge of managing HTN efficiently and effectively, and our on-site assessment during out-patient visits revealed that the capacity of local medical staffs had significantly improved compared to the initial observation, which we believe contributed to the increased treated and controlled rates. Second, not only did we educate local medical staffs but also gave regular educational courses to hypertensive population which we believe were critical to improving their lifestyle and enhance their adherence to lifestyle modification as reflected in secondary endpoints assessment, which showed that when compared to the initial, the rates of alcohol abuse and HSC, waist circumference and BMI had all decreased, and daily vegetable intake had increased in the novel therapeutic group. Third, unlike the traditional therapeutic strategy, patients in the novel therapeutic group deliberately underwent blood pressure

monitoring which must be helpful in closely evaluating the efficacy of HTN management and timely adjustment of antihypertensive therapy. Last but not the least, local medical staffs and physicians of our cardiovascular center rigorously implemented lifestyle modification in the novel therapeutic group must be also crucial for the improvement of treated and controlled rates. Since lifestyle modification is recognized as one of the most cost-effective strategies, we believe that strengthening the importance of healthy lifestyle and rigorously implementing lifestyle modification might be one the most promising and affordable approaches to increase the treated and controlled rates of HTN in rural areas. Finally, since it was reasonable to believe that strictly following guideline recommendations would undoubtedly result in a better outcome of HTN management, therefore, we included more participants in the novel therapeutic group. In addition, since this was the first time, we conducted such study to investigate the efficacy and efficiency of the novel therapeutic strategy, it was therefore logical to set a control group so as to better evaluate the difference between the traditional and novel therapeutic strategies.

In conclusion, the study showed that after 2 years of follow-up, the guideline-based HTN management, which is characterized by regularly delivering educational programs to local population, efficiently improving clinical knowledge and skill of local medical staffs, finely tuned antihypertensive medications and strictly implementing lifestyle modification, was a feasible, applicable, and useful approach to improve treated and controlled rates of hypertensive individuals in a rural area of Guangdong Province, and had substantial favorable effects on increasing treated and controlled rates of HTN.

References

1. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, *et al.* 2013 ACC/AHA guideline on the assessment of cardiovascular risk: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;129:S49-73.
2. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R, Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002;360:1903-13.
3. Gwatkin DR, Guillot M, Heuveline P. The burden of disease among the global poor. Lancet 1999;354:586-9.
4. Feng XL, Pang M, Beard J. Health system strengthening and hypertension awareness, treatment and control: Data from the China Health and Retirement Longitudinal Study. Bull World Health Organ 2014;92:29-41.
5. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, *et al.* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 report. JAMA 2003;289:2560-72.
6. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, *et al.* 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2013;34:2159-219.
7. Nguyen QN, Pham ST, Nguyen VL, Wall S, Weinehall L, Bonita R, *et al.* Implementing a hypertension management programme in a rural area: Local approaches and experiences from Ba-Vi district, Vietnam. BMC Public Health 2011;11:325.
8. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, *et al.* 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2013;34:2159-219.
9. Wu Y, Huxley R, Li L, Anna V, Xie G, Yao C, *et al.* Prevalence, awareness, treatment, and control of hypertension in China: Data from the China National Nutrition and Health Survey 2002. Circulation 2008;118:2679-86.
10. Gu D, Reynolds K, Wu X, Chen J, Duan X, Muntner P, *et al.* Prevalence, awareness, treatment, and control of hypertension in china. Hypertension 2002;40:920-7.
11. Feng XL, Zhu J, Zhang L, Song L, Hipgrave D, Guo S, *et al.* Socio-economic disparities in maternal mortality in China between 1996 and 2006. BJOG 2010;117:1527-36.
12. Farzadfar F, Murray CJ, Gakidou E, Bossert T, Namdaritabar H, Alikhani S, *et al.* Effectiveness of diabetes and hypertension management by rural primary health-care workers (Behvarz workers) in Iran: A nationally representative observational study. Lancet 2012;379:47-54.
13. Twagirumukiza M, Van Bortel LM. Management of hypertension at the community level in sub-Saharan Africa (SSA): Towards a rational use of available resources. J Hum Hypertens 2011;25:47-56.
14. Lloyd-Jones DM, Evans JC, Larson MG, Levy D. Treatment and control of hypertension in the community: A prospective analysis. Hypertension 2002;40:640-6.

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