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Full Length Research Paper

Effect of clinical pharmacist's pharmaceutical care intervention to control hypertensive outpatients in China

Pei-Xi Zhao[1], Chao Wang[1], Li Qin[2], Ming Yuan[3], Qian Xiao[4], Ying-Hua Guo[5] and Ai-Dong Wen[1]*

[1]Department of Pharmacy, Xijing Hospital, Fourth Military Medical University, 710032 Xi'an, Shaanxi, China.
[2]Department of Pharmacy, the 302 Military Hospital of PLA, 100039 Beijing, China.
[3]Department of Cardiology, Xijing Hospital, Fourth Military Medical University, 710032 Xi'an, Shaanxi, China.
[4]Department of Dermatology, Xijing Hospital, Fourth Military Medical University, 710032 Xi'an, Shaanxi, China.
[5]Department of Immunology, Xijing Hospital, Fourth Military Medical University, 710032 Xi'an, Shaanxi, China.

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Hypertension is an increasingly common health problem that affects more than 1 billion people throughout the world. Antihypertensive drugs are the current pharmacotherapy of choice, however uncontrolled blood pressure (BP) accounts for 7.1 million deaths worldwide each year. Little is known about the efficacy of clinical pharmacist's pharmaceutical care on BP control and medication adherence. The aim of this study was to describe if pharmaceutical care could improve antihypertensive medication adherence and BP control, especially by clinical pharmacists recommendations. This report evaluates the clinical pharmacist interventions during a prospective randomized controlled trial. Out patients with essential hypertension were enrolled in a bimestrial follow-up during 6-month period study; patients were randomly allocated either intervention group (IG) or to control group (CG). Pharmacist interventions involved recommendations to physicians, educational and counseling directly to the patient. The main outcome measure for this analysis was the measure of systolic blood pressure (SBP), diastolic blood pressure (DBP), BP control and medication adherence using a validated questionnaire assessed at the baseline visit and the end of pharmaceutical care. Data from 278 patients were included and analyzed (139 in CG and 139 in IG). There were no significant differences (P < 0.05) in both groups at the baseline. Changes in drug therapy were recommended 192 times for IG patients, the majority of these, involved adding a new antihypertensive drug (42.7%); the largest numbers of pharmacist recommendations (39.6%) were made at the baseline visit. At the end, BP was controlled among significant patients more in IG (76.4%) than in CG (50.6%) (P = 0.0000). Significant lower SBP (-8.5 mmHg, P = 0.0001) and DBP (-4.7 mmHg, P = 0.0013) levels were observed in IG. Low medication adherence, there was also significantly difference between two groups at the end (24.8% versus 41.7%, P = 0.0014). Clinical pharmacist recommendations for alterations in pharmacotherapy intervention can significantly improve medication adherence and BP control in patients with hypertension. Clinical pharmacist recommendations can complement physicians in the management of hypertensive patients. Pharmacist interventions are effective in improving anti-hypertensive medication adherence and reducing systolic and diastolic blood pressure. Pharmacists can effectively participate in health education and promotion to improve blood pressure control.

Key words: Blood pressure, clinical pharmacist, hypertension, clinical pharmacy, medication adherence, pharmaceutical care.

INTRODUCION

Hypertension is one of the most common chronic disease and an important public health problem worldwide, which

doubles the risk of cardiovascular diseases, including coronary heart disease (CHD), congestive heart failure (CHF), stroke, renal failure and peripheral arterial disease (PAD) (European Society of Hypertension-European Society of Cardiology Guidelines Committee, 2003; Brundtland, 2002). According to a published survey in 2002, the Chinese prevalence of hypertension among adults over the age of 18 was 18.8% (Li et al., 2005; Cui et al., 2011), which meant that 200 million hypertensive patients at least, and approximately 1 in 5 of the world's patients were in China. In recent decades, the awareness, treatment and control rates of hypertension improved progressively, but still less than 50, 40 and 10%. More so, in China which has already stepped into an aged society, it was observed that the hypertension patients are mainly old people that are physically weak and they suffered from many complications. It is common that the hypertension patients take in different medicines for different illnesses together during the disease course; thus, interaction among those different medicines may easily occur, from which many high-risk diseases such as malfunctions of the heart and liver, cerebral haemorrhage and other complications result in most cases. Therefore, hypertension has already become a formidable enemy of people's health.

At home and abroad, it was proved that high blood pressure can be prevented and controlled by comprehend-sive interventions (Levey et al., 2003). The importance of improving adherence to antihypertensive medication had been addressed by "2010 Chinese Guidelines for the Management of Hhypertension (CGMH)" (Liu, 2011) and emphasis had been put on the role of all health care professionals to improve adherence to treatment. Now, therapy is recommended for individuals with a stable blood pressures of 140/90 mmHg or over. Although, antihypertensive therapy clearly reduces the risks of cardiovascular disease and extends the patients' life; large portions of the hypertensive population are either untreated or inadequately treated as lack of adherence to blood pressure (BP)-lowering medication being a major factor. Patients with hypertension may fail to follow their medication, because of a symptomless nature of their condition, long duration of therapy, side effects of medication, complicated drug regimens, lack of under-standing about hypertension management and risks, problem of economic status and individual differences among medications. Therefore, with more comprehensive knowledge of drugs, clinical pharmacists could offer their ability to participate in clinical drug treatment by giving advice on therapy and pharmaceutical care to hypertensive patients, which may improved the adherence to treatment and the results of the clinical therapy eventually. Green et al. (2008) and Weber et al. (2010) studies showed that pharmacist- physician co-management team can improve control blood pressures and 24 h ambulatory blood pressures.

How to improve the medication compliance of the patients decides whether the patients can get a systematical and long-period treatment, and whether the blood pressure can be maintained at a controllable level; thereby, the probability of complications can be reduced. Besides, during the treatment process, both the side effects caused by the medicines and the short and long term efficacy should be taken into consideration. Our study shows that clinical pharmacist can take advantage for hypertensive patients, make a comprehensive analysis on the drugs prescribed to the patients and prevent irrational medication so as to improve medication safety and efficiency significantly.

Aim of the study

The objectives of the study were to evaluate the clinical pharmacist's interventions effect during a randomized controlled clinical trials (RCT), aimed to improve antihypertensive medication adherence and BP control and reduce adverse drug reaction of hypertensive patients in the clinic service and community.

METHODOLOGY

This prospective, randomized, controlled study was carried out from September, 2010 to April, 2011 in a cardiology clinic in the Xijing Hospital, the Fourth Military Medical University, People's Republic of China, located in the Central Region of China. The study was approved by the institutional Ethics Committee for the use of humans in research, and written informed consent was obtained from all participants before their enrollment in the study. In this randomized controlled trials, participants were individually randomized allocated in two parallel groups (allocation ratio 1:1). Patients included in the main study were recruited from the current patient population showed at the clinics, patient inclusion and exclusion criteria were provided in Table 1, eligible participants were all adults of age 21 to 85 and with an established medical diagnosis of hypertension, whether their BP was controlled or not. According to CGMH (Liu, 2011) guidelines, BP control was defined as BP measurements in the clinic of systolic BP (SBP) < 140 mmHg and diastolic BP (DBP) < 90 mmHg for patients without diabetes, coronary heart disease (CHD) or chronic nephrosis and of SBP < 130 mmHg and DBP < 80 mmHg for patients with diabetes, CHD or chronic nephrosis. Furthermore, all included patients had been on established antihypertensive drug treatment for at least 6 months. Exclusion criteria were dementia or cognitive impairment, stage 3 hypertension, serious kidney or liver disease (serious liver disease is Child-Pugh classification scoring C and serious kidney disease is creatinine (Cr) ≥ 445 μmol//L or blood urea nitrogen (BUN) ≥ 20mmol/L), recent myocardial infarction or stroke, pregnancy and breastfeeding.

Outpatients attending the medical clinic for routine follow-up were randomly allocated either to a control group (CG, usual care, where no pharmaceutical care is provided) or to an intervention group n(IG,

*Corresponding author. E-mail: adwen@fmmu.edu.cn. Tel: +86-29-84773636. Fax: +86-29-84773636.

Table 1. Eligibility criteria.

Inclusion criteria
1. Males or females, 21–85 years of age
2. Patients with an established medical diagnosis of hypertension, whether their BP was controlled or not
3. all included patients had been on established antihypertensive drug treatment for at least 6 months
Exclusion criteria
1. Stage 3 hypertension (≥180/110) or any evidence of hypertensive urgency or emergency
2. Recent myocardial infarction or stroke (within past 6 months prior to enrollment)
3. breastfeeding
4. Serious renal or hepatic disease
5. Pregnancy
6. Dementia or cognitive impairment
7.Tumor

pharmaceutical care, consisting of bimestrial follow-up by a hospital clinical pharmacist during a 6-month period). Participants were allocated following simple randomization procedures (equal allocation and without restrictions) using a computer-generated list of random numbers. The allocation sequence was concealed from the clinical pharmacist enrolling and assessing participants in sequentially numbered, opaque, sealed envelopes. The computer generated the allocation sequence and the envelopes were prepared by an investigator with no clinical involvement in the trial.
The pharmaceutical care provided to the IG by clinical pharmacists at the baseline visit and the follow-up visits, including hypertension staging, risk stratification, determination of a goal BP and treatment recommendations to the patient's physician, the physicians could also schedule additional optional visits between scheduled visits at his discretion.

Inclusion of the intervention group's pharmaceutical care

(1) Spread the knowledge of hypertension to patients and their family members.
(2) Educated patients need long-term antihypertensive medication to maintain stable blood pressure and other announcements.
(3) Supervise patients with adverse drug reactions. While in the process of taking medication, get in touch with a clinical pharmacist and physician in time to find a solution.
(4) Follow-up survey: Make telephone calls and get messages from patients in order to understand their medication compliance and note the registration table monthly. Intervention patients were encouraged to bring all empty blisters and boxes of antihypertensive medication to clinic visits in order to verify their compliance to therapy.
(5) Basic medication treatment principles (Liu, 2011): (a) small dose starts from the smallest effective dose; (b) increase the smallest dosage if the small dose failed to reach the adequate blood pressure; (c) applying for durative action preparations as a priority can improve patients' medication compliance, lower blood pressure stably and reduce target organ damage; (d) drug combination. If the current anti-hypertensive drugs do not have an obvious effect or adverse reactions on the patients, we should combine different kinds of drugs rather than increasing the dosage. However, there should be appropriate and reasonable combination in the use of antihypertensive drugs to achieve maximum antihypertensive effect, while reducing adverse reactions.
(6) Individualization.

Control group

The control group had no clinical pharmacist involvement and patients received traditional service provided by the hospital clinic.

Adherence investigation

Patients with hypertension were investigated in the form of a standard questionnaire recommended (Morisky et al., 1986, 1983), with four questions to evaluate the adherence to medication: (1) whether there were forgotten medication experience; (2) whether sometimes do not pay attention to the medication; (3) when the symptoms improve, the medication had been discontinued or not; (4) when the symptoms got worse after taking the drug, the medication was withdrawn or not.

Four answers are "no", adherence was good; 1 or 2 of the answers are "yes", relatively poor; 3 or 4 of the answers are "yes", very poor.

Reasons for poor medication adherence investigation

Before intervention, a self-designed questionnaire was provided to invest the reasons for medication poor-adherence individually. Then, targeted to the reasons, interventions, such as individual medication, strengthen guidance and scientific and rational drug regimens were presented to the individuals.

Blood pressure measurement and standards

With a qualified desk-top mercury sphygmomanometer, the BP clinic measurement was performed by the same trained nurse blind to the study, according to the published guidelines in China on proper BP measurement. The BP values of general hypertensive individuals < 140/90 mmHg, and patients with diabetes and renal disease < 130/80 mmHg, were considered reaching the standards.

All data was expressed as the Mean ± standard deviation (SD), frequency and percentages. Student's test was used to compare continuous variables and groups were compared using chi-square test. All statistical analyses were done with Statistical Package for

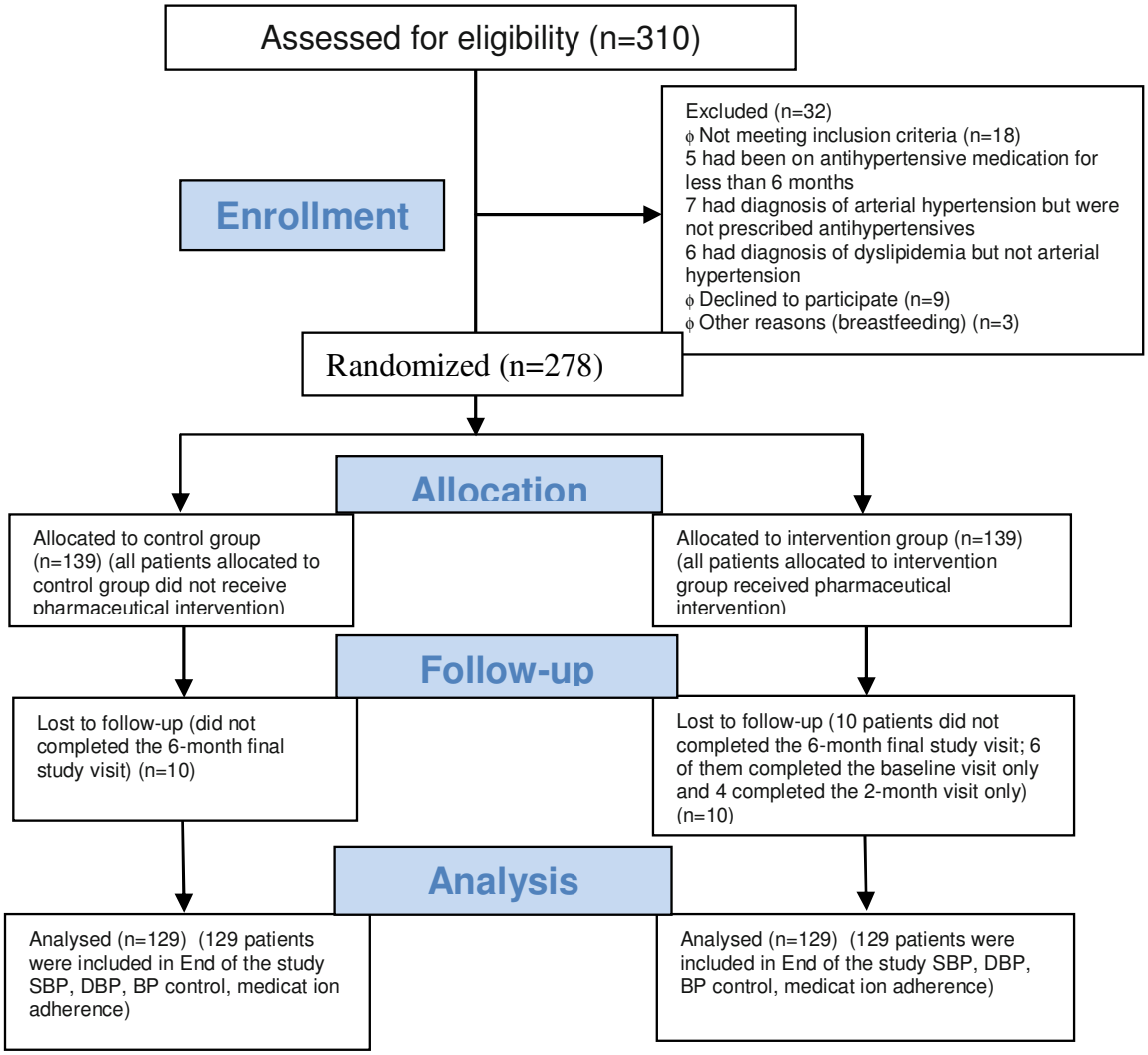

Figure 1. Flow diagram of patients through the study protocol BP blood pressure, DBP diastolic blood pressure and SBP systolic blood pressure.

Social Sciences (SPSS), version 17.0 and a P value < 0.05 was considered statistically significant.

RESULTS

A total of 310 patients attended the medical clinic during the recruitment period (from September 2010 to April 2011) and all were assessed for eligibility. Of these, 18 were excluded from the study because they did not meet the inclusion criteria, 3 was excluded because of breastfeeding and 11 were excluded because they declined to participate. Out of the remaining 278 hypertensive patients meeting the inclusion criteria and consenting to participate, 139 were allocated to the control group with usual care and 139 were allocated to pharmaceutical care in intervention group (Figure 1).

The intervention group and control group were comparable with respect to age, gender, education, marital status, body mass index, smoking status, prevalence of chronic illness, number of antihypertensive drugs per patient and number of years in antihypertensive treatment (Table 2). The percentage of antihypertensive medication was no significant difference between the two groups at baseline (Table 3). Baseline SBP and DBP, BP control, hypertension and medication adherence did not significantly differ in both groups either (Table 4).

As seen in Figure 1, a total of 20 subjects (7.2%) withdrew from the study following allocation, in which 10 (3.6%) from the intervention group and 10 (3.6%) from the control group. In the intervention group, 133 completed the 2-month visit, and 129 completed the 6-month as well

Table 2. Patients demographics and clinical characteristics at baseline (n = 278).

Demographic/clinical	Control group (n = 139)	Intervention group (n = 139)	P value
Gender, n (%)			
Male	80	82	0.9032
Female	59	57	0.9032
Age, mean (SD)[a]	65.6 ± 18.8	62.4 ± 19.1	0.8527
Body mass index (kg/m^2), mean (SD)	23.1 ± 3.6	22.8 ± 4.1	0.5168
Married, n (%)	128 (99.2)	120 (93.0)	0.1760
Education, n (%)			
Illiterate	79	85	0.5421
Elementary schooling	32	30	08854
High schooling	24	19	0.5070
University education	4	5	1.0000
Current smoker, n (%)	83	74	0.3332
Comorbid conditions, n (%)			
Cerebrovascular disease	24	19	0.5070
Chronic kidney disease	11	16	0.4179
Diabetes	27	34	0.3846
Heart failure	39	49	0.2458
Ischemic heart disease	31	39	0.3334
Myocardial infarction	27	29	0.8811
Left ventricular hypertrophy	39	27	0.1210
Dyslipidemia	53	49	0.7089
Metabolic syndrome	55	64	0.3322
Obesity (body mass index ≥30)	50	46	0.7051
Advanced age (≥65 years), n (%)	83	86	0.8059
Number of antihypertensive drugs per patient, mean (SD)	2.7 ± 0.7	2.5 ± 0.8	0.1179
Number of years in antihypertensive drug treatment, mean (SD)	5.1 ± 3.4	5.0 ± 3.1	0.2791

[a]SD standard deviation.

Table 3. Antihypertensive medication prescribed to hypertensive patients at baseline and at the end of the study.

Antihypertensive drug class	Control group (n = 139)	Intervention group (n = 139)	P value
Thiazide diuretics (%)	39	45	0.5137
Beta blockers (%)	39	33	0.4936
ACE inhibitors (%)	67	71	0.7189
Angiotensin II receptor antagonists (%)	14	11	0.6750
Calcium channel blockers (%)	36	38	0.8921
α blockers (%)	6	8	0.7839
Chinese drugs pharmaceutics (%)	36	44	0.3537

Bold means that there is a statistically significant difference (P value < 0.05). [a], Includes last medication prescribed before the final study visit (including to dropouts).

Table 4. Clinic BP figures, BP control, antihypertensive medication adherence and knowledge about hypertension (baseline and end of the study).

Variable	Control group	Intervention group	P value
Baseline	**(n = 139)**	**(n = 139)**	
Baseline SBP, mean (SD), mmHg	143.9 (17.2)	142.5 (16.6)	0.4905
Baseline DBP, mean (SD), mmHg	86.4(11.7)	85.2 (10.2)	0.3628
Baseline BP control, n (%)	45 (32.8)	44 (31.7)	0.8977
Baseline low medication adherence, n (%)	74 (53.2)	73 (52.5)	1.0000
Knowledge of target BP values, n (%)	81 (58.6)	84(60.4)	0.8071
Knowledge of hypertension risks, n (%)	70 (50.4)	72 (51.8)	0.9045
End of the study	**(n = 129)**	**(n = 129)**	
End SBP, mean (SD), mmHg	142.1 (16.2)	134.0 (16.3)	0.0001
End DBP, mean (SD), mmHg	84.6 (10.9)	80.5 (9.3)	0.0013
End BP control, n (%)	65 (50.6)	98 (76.4)	0.0000
End low medication adherence, n (%)	58 (41.7)	32 (24.8)	0.0014
Knowledge of target BP values, n (%)	86 (66.5)	109 (84.6)	0.0014
Knowledge of hypertension risks, n (%)	97 (75.6)	119 (92.3)	0.0004

Bold means that there is a statistically significant difference (P value < 0.05).

as the final study visit.

At the beginning of the study, only 44 of 139 (31.7%) patients in the intervention group had both SBP and DBP controlled. This was not significantly different from the number in the control group, where 45 of 139 (32.8%) patients had their BP controlled (P = 0.480). At the end of the study, BP was controlled among significantly more patients in the intervention group (76.4%) than in the control group (50.6%) (P = 0.0000). And SBP was reduced by 1.8 mmHg in the control group and 8.5 mmHg in the intervention group (P = 0.0001 for between-group SBP comparison). The DBP was reduced by 1.8 mmHg in the control group and 4.7 mmHg in the intervention group (P = 0.0013 for between group DBP comparison) (Table 3).

Similarly, baseline patient knowledge of target BP values and of the potential complications of high BP to their health did not significantly differ in both groups (Table 4). However, at the end of the study, there was a significant difference in the percentage of patients reporting correctly both target BP figures and hypertension risks (Table 4).

Clinical pharmacists made a total of 192 recommendations to change drug therapy, of which 171 were implemented, yielding a 89.1% cardiology physician acceptance rate (Table 5). Majority of these recommendations for a change in treatment involved adding a new antihypertensive drug (42.7%) or increasing a dose (26.6%). The largest numbers of pharmacist recommendations (39.6%) were made at the baseline visit, and 80.2% of all recommendations were made by the 2-month visit. The average number (±SD) of recommendations for a change in drug therapy was 1.38 ± 1.05 per patient.

Baseline low medication adherence did not significantly differ in both groups (53.2% in the intervention group and 52.5% in the control group, P = 1.0000). However, at the end of the study, there was a significant difference (P = 0.0014) in the percentage of patients with low medication adherence between the intervention group (24.8%) and the control group (41.7%). We investigate the reason for low medication adherence of hypertension patient before intervention, the most important reason is patient consider they do not require treatment (18.4%) and discontinued hypertension medication when they consider has been cured (14.3%) (Table 6).

DISCUSSION

This study showed significant reduction of SBP and DBP and in an increase in the proportion of patients with controlled BP according to CGMH guidelines. Majority of the pharmacists' recommendations occurred within the first 2 months. This finding suggests that the pharmacists were making recommendations early in order to quickly achieve BP control. Early BP control is important because studies have found that controlling BP within the first 6 months can significantly reduce cardiovascular events (Julius et al., 2004).

The medication compliance of patients was poor previously due to some reasons, such as the complicated and hard-to-control disease course, the life-time dosing period, the economic condition of the patients as well as

Table 5. Pharmacist recommendations to modify therapy in intervention group.

Recommendation	n	Frequency by visit				
		0 Mo	Opt[a]	2 Mo	4 Mo	6 Mo
Added a new antihypertensive drug	82	48	13	18	3	0
Increased dose	51	19	9	13	5	5
Changed dose frequency(time)	19	4	2	8	3	2
Switch within class	11	2	0	5	3	1
Decreased dose	13	2	3	3	4	1
Drug discontinued	16	1	3	7	4	1
Total	192	76	30	54	22	10

[a]Opt = Optional visit; Mo = month. Most optional visits occurred within the first 2 months of the study.

Table 6. Reasons for low medication adherence of hypertension patient before intervention.

Serial	Reason for low medication adherence	Number (n)	Percentage (%)
1	Patient consider they do not require treatment	27	18.4
2	Oral medication therapy is too complex	18	12.2
3	Discontinued hypertension medication when they consider has been cured	21	14.3
4	Withdrawal medication because of irregular life style	11	7.5
5	Unauthorized withdrawal because of poor efficacy	9	6.2
6	Discontinuation medication of long course of medical treatment	19	12.9
7	Change dosage and time or missed medication without permission	14	9.5
8	Patient withdrawal medication because of adverse drug reactions	10	6.8
9	Patient withdrawal medication because of economic burden is too heavy	18	12.2
Total		147	100

the irrational and complex drug use; thereby, most of the patients cannot be healed thoroughly (Jokisalo et al., 2003). This research on medication compliance of hypertensive patients was mainly conducted by pharmacist in the perspective of clinical medicine and clinical nursing. Nowadays, few hospitals have fully played the advantages of clinical pharmacist and have done some research on the intervention conducted by clinical pharmacist in the management of patient. And more traditional dispensing pharmacists began changing to clinical pharmacist which could provide more comprehensive services to patients (Carter and Elliott, 2000).

Before our study, there were no significant differences in all items between the intervention group and control group, after clinical pharmacist' interventions mentioned in the “methodology” for 6 months, a significantly change was clearly shown (Table 4). The statistical data indicated that the rates of hypertension education, medication adherence and blood pressure control were directly correlated, which improved by pharmacist in our program. Previously reported reduction of SBP and DBP levels in patients receiving pharmaceutical care varied between 6.0 to 31.0 mmHg and 3.0 to 14.2 mmHg, respectively (Carter et al., 2009; Machado et al., 2007). However, in most of these studies only uncontrolled hypertensive patients were recruited, contrary to our study, all hypertensive patients that experienced antihypertensive medication for at least 6 months were included (whether their BP was controlled or not). With a low mean SBP and DBP level of the study population at baseline (142.5/85.2 mmHg), a 8.5/4.7 mmHg reduction was gained in the IG at the end of our study, which was 4.7 times more than the CG reduction (1.8/1.8 mmHg) in SBP control ($P = 0.0001$) and 2.6 times in DBP control ($P = 0.0013$). The results were so exciting and full of clinical significance, because all the cases have been treated for at least 6 months especially for those whose BP was not controlled, and the Asian population with hypertension was more prone to stroke and coronary heart disease events. According to a report of Asia (Lewington et al., 2002), each 10 mmHg increase in SBP, stroke in Asian populations and the risk of fatal myocardial infarction increased by 53 and 31%, while Australia and New Zealand population increased by only 24 and 21%. With a meta-analysis of hypertensive patients of age 60 to 69 years, the additional 6.8 mmHg reduction in SBP control observed in intervention arm would be expected to yield a 22% reduction in stroke mortality and a 17% reduction of mortality in ischemic heart disease. These studies also suggested that the BP control is the key to reduce the risk of stroke for Chinese people with hypertension and more

effective control strategies are badly needed than that in western countries. Fortunately, this situation is improving by the pharmacist participation with their unique way, and in IG the reduction of mean blood pressure meant average mortality risks of the two complications decrease by 45 and 26%, while in IG just without pharmacist the risk decrease of those diseases was sharply down only by 9.5 and 5.6%. According to the data in Table 4, all items in CG were improved when compared with themselves six months ago, although, very obviously less than that in IG. Since, the two groups benefited from the same status quo of our social progress, respectively, an additional improvement in IG should be mainly attributed to the interventions of pharmacist with expertise and experience in drug therapy and participation in our outpatient clinic (Vivian, 2002). In our study, pharmacist conducted a total number of 192 medicative recommendations for drug therapy in IG, in which "Added a new antihypertensive drug" and "Increased dose" were the most frequent practice, accounting for 82 (42.7%) and 51 (26.6%). Most of the interventions (83.3%) were completed within the first follow-up and the largest part of pharmacist recommendations (39.6%) were made at the baseline visit. These results suggested that early interventions of drug treatment were very important and directly affect the final outcomes in the study. Furthermore, the importance of early intervention also might be used for other chronic diseases, such as diabetes, liver diseases and blood disorders (Kirwin et al., 2010). Foreign study also found that early use of antihypertensive treatment can prevent complications, prolong life, and especially reduce the actual costs when compared with the late use patients with antihypertensive drugs (McCombs et al., 1994; Sokol et al., 2005).

In the low medication compliance survey, we found that patients "consider they do not require treatment" was the top 1 in the list, which may be associated with the low national awareness situation in China. Many patients do not consider themselves sick, especially those asymptomatic patients with hypertension and the ones in the vicinity of pre-hypertension with normal value. The other two main reasons, "Discontinued hypertension medication when they consider has been cured" and "Discontinuation medication of long course of medical treatment", were also common causes for poor adherence investigation, often not only in hypertension. However, according to qualitative analysis studies, it was shown that poor compliance was mainly for lack of communication, which resulted in misunderstanding and a lot of subjective factors for low adherence (Roumie et al., 2006; Tsiantou et al., 2010). The top three main reasons were subjective factors and all situations could be improved by our pharmacist in the form of the practice mentioned in the methodology part. The proportion of "Patient withdrawal medication because of economic burden" was too heavy, which is a typical objective reason associated with the national status of china, especially in underdeveloped regions and rural areas. Although, this problem cannot be completely solved, there will be a cost-effective solution provided by clinical pharmacist to those patients according to their existing conditions. Some reports also indicated that pharmacist interventions were not likely to gain a statistically significant improvement in this outcome when medication adherence at baseline is already high (about 75%) (Chabot et al., 2003; Jokisalo et al., 2003), and in our study, low baseline medication adherence (47.5%) made it feasible for pharmaceutical intervention to get an obvious positive effect in this outcome and hence in treatment outcomes. And in the end, our percentage of low medication adherence accounted for 24.8%, which perfectly matched that in other studies. In summary, our clinical pharmacist could improve the low medication compliance comprehensively and efficiently.

There were several limitations in our study. Firstly, the Chinese pharmacists' lack of experience and education may have prevented the detection of more interventions, and the BP value may have a white-coat effect on the study, although there was just one well-trained blind nurse to measure. Therefore, a longer training period for the researcher might have produced better results. Secondly, the evaluation of BP control was based on the measurements performed in two single clinic appointments (baseline and after a 6-month follow up period). These BP measurements may or may not be representative of the adequacy of BP control in hypertensive patients. Thirdly, medication adherence was measured by the research (not blinded) pharmacist, who was potentially biased in situations where the patients did not respond with determination to the questionnaire. Finally, the higher average medication adherence in this study for the ordinary Chinese patients was mainly attributed to the fact that all our patients from an urban population based in Xi'an area (the most economically developed city in the northwest of China) had received at least six months of treatment. So, there may be a lack of statistical power to represent more significant differences for patients in other areas. Thus, to generalize the results, larger sample sizes and wider areas would be needed. Subjects were all recruited from a cardiovascular clinic of Xijing hospital, so extrapolating our results to other clinical settings may also be limited. Furthermore, recruitment and participation of patients was voluntary. Hence, it was systematically possible to differentiate patients who did not participate from those that participated.

Conclusion

Based on the outcome of our prospective randomized controlled trial that ranged 6-month, medication adherence and achieved BP control rates of patients treated with

antihypertensive drugs were significantly improved by clinical pharmacist intervention including varied measures, such as education, supervision, follow up etc. Moreover, our study suggests one effective pharmaceutical care process to widespread improvement in BP control provided by clinical pharmacist, steps of which are comprised of recognizing inadequate drug therapy, analyzing the reason of BP uncontrolled individuals, taking an appropriate series of measures and giving specific recommendations to patients needing medication changes or meeting adverse drug reactions. Furthermore, this report also addresses the pharmacists' role on effective participation in the management of hypertensive patients as an essential supplement to traditional physician-only mode. Finally, this study may provide a practice framework for the future development of other antihypertensive studies in pharmaceutical care to patients.

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