





## A clinical trial on the effect of a multifaceted intervention on blood pressure control and medication adherence in patients with uncontrolled hypertension

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### Original Article

#### Abstract

**BACKGROUND:** Hypertension (HTN) is the key risk factor for cardiovascular diseases (CVDs). The purpose of this study was to determine the effect of a multifaceted intervention on blood pressure (BP) control and medication adherence (MA) among patients with uncontrolled HTN.

**METHODS:** A randomized controlled clinical trial study was conducted on 72 patients in the emergency ward who were selected through convenience sampling method. They were randomly divided into intervention and control groups. The studied multifaceted intervention includes motivational interviews and 90 minutes of training sessions, use of a drug reminder box, family support, and 4 phone call follow-ups. The 8-Item Morisky Medication Adherence Scale (MMAS-8) was used before and after the intervention. BP was measured in both groups before and after the intervention and compared between them.

**RESULTS:** No significant difference existed between the two groups in terms of MA and systolic and diastolic BP before the study. The differences between the mean changes in post-intervention systolic ( $-25.75 \pm 19.39$  vs.  $-2.88 \pm 11.92$  mmHG;  $P < 0.001$ ) and diastolic ( $-6.18 \pm 8.87$  vs.  $-1.06 \pm 8.70$  mmHG;  $P = 0.010$ ) BP in the intervention and control groups were statistically significant. The mean changes in post-intervention MA in the intervention and control group was  $2.91 \pm 1.64$  and  $-0.36 \pm 1.15$ , respectively; this difference was statistically significant ( $P < 0.001$ ).

**CONCLUSION:** The studied multifaceted intervention promoted MA and reduced systolic and diastolic BP. Thus, the use of this method as a supplementary treatment is recommended after patient discharge.

**Keywords:** Blood Pressure, Hypertension, Medication Adherence, Nursing, Iran

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#### Introduction

Cardiovascular diseases (CVD) are the first cause of death due to non-communicable diseases worldwide.<sup>1</sup> More than 22% of the urban and rural population in Isfahan, Iran, had hypertension (HTN) in 2014.<sup>2</sup> HTN is a key risk factor for increased mortality and morbidity of CVD. Hence, its management and treatment can significantly reduce the prevalence of CVD in societies.<sup>3,4</sup>

Managing and controlling HTN through lifestyle modification and adherence to drug therapy throughout life is feasible.<sup>5</sup> However, the lack of

appropriate medication adherence (MA) is an obstacle for the healthcare team and also a major challenge of controlling this disease.<sup>6</sup>

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The role of drug therapy in controlling or non-controlling blood pressure (BP) is very important.<sup>7</sup> HTN-drugs not only control the disease, but also reduce mortality, side effects, and delayed complication of diseases in societies.<sup>8</sup> Despite the efforts of the healthcare team, many patients still refuse to treat HTN or have uncontrolled HTN, which may be due to side effects of medications. Nearly 85% of patients have experienced at least 1 medication side effect.<sup>9</sup> Moreover, some patients have no symptoms despite their lack of medication use. However, they may experience side effects after taking medications; therefore, they do not take their medications.<sup>5,10</sup> Regardless of the differences in the quality of medication adherence in different cultures and nationalities, about a quarter of hypertensive patients do not follow a suitable medical treatment.<sup>11</sup>

According to a study in Isfahan, over 40% of patients under medical treatment, especially men, have uncontrolled HTN.<sup>12</sup> Another study has shown that 60 out of 100 hypertensive patients under medical treatment suffered from the lack of disease control.<sup>13</sup> Accurate controlling of HTN cannot only improve the quality of life (QOL), but also reduce or eliminate acute and chronic complications.<sup>14</sup>

Various factors negatively affect medication adherence (MA) such as culture, educational facilities, and long-term use of medication and its resulting complications. Therefore, intervention and greater attention of the healthcare team is recommended in these areas so that better results can be achieved from the treatment and management of HTN.<sup>15</sup> Since the training of patients by the healthcare team has a great and constructive role in promoting and improving MA, and also because suitable MA requires high personal awareness, trust in treatment, and trust in the healthcare team, training should be considered as the main key to increasing patients' desire to use prescribed medication.<sup>16,17</sup>

In addition, medication training of patients by the healthcare team can provide satisfaction with medical therapy.<sup>18</sup> Negative consequences of BP control caused by discontentment with HTN treatment could lead to increased frequency of hospitalization.<sup>19</sup> Training provided for patients with HTN should be related to explaining the disease and treatment status, resolving any misunderstandings for patients, and encouraging patients to discuss their medication and schedule.<sup>20,21</sup>

According to a review study in 2012 by Noohi et al., utilizing patient capacities in training and

creating satisfaction in using medication along with support from the healthcare team are some of the most manageable factors of this disease.<sup>22</sup>

However, the lack of HTN control in the patients cannot be solved only by training and assurance of promoting medical information. Another problem that causes patients to reduce MA is untimely medication intake, which is more pronounced due to the long-term medication intake, and therefore, using a reminder is the best way of solving this problem.<sup>7,23</sup> In addition, using a multi-part medication box embedded for daily medication can be beneficial.<sup>23</sup> Moreover, in order to improve treatment adherence in patients, we can use encouragements and persuasion through family support<sup>24,25</sup> and remote tracking of the patient by the healthcare team to improve MA and HTN control. Social support between the healthcare team, patient, and families not only result in patients' satisfaction, but also leads to elimination of negative factors such as untimely medication intake.<sup>6,26</sup>

Medical therapy alone cannot be successful in controlling HTN and one-dimensional interventions like training cannot be beneficial for promoting MA. Therefore, our aim is to determine the effects of new multifaceted strategies for improvement of MA by using encouragement interviews and training sessions and its positive feedback on adherence to the treatment by the patients and their families, and the healthcare team support.

## Materials and Methods

This randomized clinical trial (RCT) was conducted from April to June 2018 in the emergency ward of Al-Zahra Hospital of Isfahan, Iran. This study was conducted with two groups of intervention and control. First, the study was explained to 72 patients referring to the emergency ward who had the inclusion criteria; those who were willing to take part in the study were asked to provide a written consent form. The participants were chosen based on the inclusion criteria and through convenience sampling. Next, each participant received a numbered card and based on the number, whether it was odd or even, they were randomly assigned to the control and experimental groups. Sample allocation continued until the sample size reached the predetermined number.

The inclusion criteria consisted of at least a 1-year history of HTN approved by the physician and undergoing HTN medical therapy, lack of a history of Alzheimer's disease, BP of higher than 140/90 mmHg at the time of reception in the

emergency ward, and accompaniment of 1 family member. The exclusion criteria consisted of death, any serious or life-threatening problems and any disability during the study, discontentedness or withdrawal from the study. The data were collected through reviewing of medical records and completion of the questionnaire by the researcher. Prior to the beginning of the study and 1 week after the last training session, the BP of the right hand in the intervention group was measured and recorded at 2 times with a 5-minute interval. Moreover, the same measurement was implemented in the control group at the beginning of the study and 1 month after. In addition, MA of both groups was measured and recorded at the beginning of the study and 1 month after the intervention. In order to collect data, a multi-section questionnaire containing questions on demographic information (age, gender, education, marital status, job, duration of the disease, and drug abuse), the type and number of daily medication, systolic and diastolic BP, and pulse. The second section of the questionnaire consisted of the 8-Item Morisky Medication Adherence Scale (MMAS-8), with yes (1)/no (0) answers for questions 1 to 7 and a 5-item Likert scale ranging from always (0) to sometimes (1) for question 8. A score of 8, 6-8, and 6 was considered as high MA, average MA, and low MA, respectively. The MMAS-8 was approved in 2008 by Morisky et al. with a Cronbach's alpha of 0.83 and a high validity in chronic diseases studies.<sup>27</sup> The Persian version was approved in 2015 by Moharamzad et al. for patients suffering from HTN.<sup>28</sup>

To determine the desired sample size, the following formula was used:

$$n = \frac{2(z_1+z_2)^2s^2}{d^2}$$

where  $z_1$  is the safety factor (95%),  $z_2$  is the test power (80%), and  $d$  is the average of a minimum difference of BP score that is 0.7 S. N was equal to 32 which was increased to 36 individuals in each group with the consideration of a 10% dropout rate.

The intervention groups, 4 groups consisting of 10 patients each with a family member, participated in an encouragement interview and received a medication reminder box consisting of 7 parts used for 1 week of medication. Subsequently, in a class located at the entry of Al-Zahra Hospital, 3 training sessions (90 minutes) were held in 3 weeks and emphasis was placed on family support for taking medications. Moreover, a 10-minute phone call was made with the participants and their family member

at the end of each week for 4 weeks. The content of the training sessions consisted of the nature and side effects of the disease, the consequences of not taking HTN medication, methods of controlling the disease via appropriate lifestyle changes, and etcetera (Table 1). The information was presented through lectures, PowerPoint, discussions between participants, and a training booklet. The content of the phone calls included question and answer sessions regarding the reinforcement of the content of the training sessions, techniques of strengthening family support, utilization of the medication reminder box, and answers to possible problems of the participants. However, only data collection was performed for the control group before and 1 month after the study. At the end of the study, in order to follow ethical codes, the subjects in the control group were given a medication reminder box and a training booklet with regard to discussions of the training sessions.

This study was implemented with the ethics license number IR.MUI.REC 1396.3.841 from Isfahan University of Medical Sciences, Isfahan, and a code from the Iranian Registry of Clinical Trials (IRCT20110821007391N6).

The numerical variables are reported as mean  $\pm$  standard deviation (SD), and categorical variables are presented as frequencies and percentages. Using the Kolmogorov-Smirnov normality test, variables were normally distributed. For intra-group comparisons, the paired t-test was used, and for between-group comparisons, the independent t-test was used. The non-numerical values were compared between the two groups using the chi-squared test. For data analysis, chi-squared test, and paired and independent sample t-tests were applied in SPSS software (version 18; SPSS Inc., Chicago, IL, USA).

## Results

No significant difference was observed between the two groups regarding age ( $P = 0.800$ ), years of education ( $P = 0.170$ ), and duration of the disease ( $P = 0.240$ ). The average age of the participants in the intervention and control group was  $59.17 \pm 12.63$  and  $58.44 \pm 12.59$ , respectively. The mean  $\pm$  SD of the years of education was  $8.78 \pm 5.8$  years in the intervention group and  $7.8 \pm 5.40$  years in the control group. Moreover, the duration of HTN in the intervention and control group was  $10.49 \pm 8.91$  and  $8.42 \pm 5.88$  years, respectively. There was no significant difference between the two groups in terms of gender ( $P = 0.810$ ), marital

**Table 1.** The content of the training sessions

Row	Content	The goal and expectation of the researcher	Training method	Time
<b>First session</b>				
1	Introduction of the researcher and explanation of the purpose of the research and its implementation to the participants	Building trust	Lecture +PowerPoint	10 min
2	Motivation for participation in the research and attention to disease	Encouraging knowledge and understanding about HTN and motivation for research participation	Question and answer	20 min
3	Distribution of drug reminder boxes among patients	Removing or reducing untimely medication intake	Personal	
4	Training of families to remind the patient of drug use	Reminding the patient of the timely intake of medicine by the family	Lecture	
<b>Second session</b>				
1	Explanation of the definition of HTN and its risk factors and risks of not controlling HTN	Increasing their understanding and correcting their perspective toward the conditions of their disease	Lecture +PowerPoint	15 min
2	Questions about the drug problems of patients	Motivating the recognition of a drug problem and trying to solve the problem	Question and answer	5 min
3	Explanation of how to control HTN and maintain a healthy lifestyle	Encouraging increased self-care in controlling HTN	Lecture +PowerPoint	10 min
<b>Third session</b>				
1	A review of the contents of the previous session	Removing or reducing forgetfulness among patients	Lecture	5 min
2	Questions about the complications of uncontrolled BP and explaining the causes of not controlling the disease	Increasing their awareness and encouraging them to learn more about helping themselves to better control their illness and identify their own problems	Question and answer	5 min
3	Evaluation of non-drug intake factors	Informing patients about their condition in drug therapy	Lecture +PowerPoint	10 min
4	Questions and answers about medications	Increasing their knowledge of medicine	Question and answer	5 min
5	A brief explanation of the use of antihypertensive drugs	Increased patient satisfaction with treatment	Lecture +PowerPoint	5 min
<b>Fourth session</b>				
1	A review of the contents of the previous session	Removing or reducing forgetfulness among patients	Lecture	5 min
2	Questions about the complications of not controlling HTN	Increasing their awareness and encouraging them to learn more about helping themselves to better control their illness and identify their own problems	Question and answer	5 min
3	Study of the factors causing non-controlled HTN	Helping the patients to have an understanding about their treatment condition	Lecture +PowerPoint	10 min
4	Questions and answers about medications	Increasing their knowledge of medicine	Question and answer	5 min
5	An explanation of the use of antihypertensive drugs	Increasing patient satisfaction with medication therapy	Lecture +PowerPoint	5 min

HTN: Hypertension; BP: Blood pressure

status ( $P = 0.520$ ), employment status ( $P = 0.280$ ), cigarette, pipe, and hookah smoking ( $P = 0.120$ ), diabetes ( $P = 0.200$ ), and hyperlipidemia ( $P = 0.380$ ). Of the intervention and control group participants, 19 (52.8%) and 18 (50%) were women. Most of the

subjects in the intervention ( $n = 29$ ; 80.6%) and control groups ( $n = 31$ ; 86.1%) were married. In the intervention group, 13 (36.2%), 7 (19.4%), and 16 (44.4%) individuals were, respectively, employed, retired or unemployed, and housewives.

**Table 2.** Comparison of demographic and clinical characteristics between the intervention and control groups

Group	Intervention group (n = 36)		Control group (n = 36)		P*	P**	
	Mean ± SD		Mean ± SD				
Age (year)	59.17 ± 12.63		58.44 ± 12.59		0.800	-	
Years of education	8.78 ± 5.08		7.08 ± 5.40		0.170	-	
Duration of the disease (year)	10.49 ± 8.91		8.42 ± 5.88		0.240	-	
		n (%)		n (%)			
Sex	Female	19 (52.8)		18 (50.0)		-	0.810
	Male	17 (47.2)		18 (50.0)			
Marital status	Married	29 (80.6)		31 (86.1)		-	0.520
	Divorced or widowed	7 (19.4)		5 (13.9)			
Job	Employed	13 (36.2)		8 (22.2)		-	0.280
	Retired/unemployed	7 (19.4)		12 (33.3)			
	Housewife	16 (44.4)		16 (44.5)			
Smoking, pipe, and hookah	Yes	8 (22.2)		14 (38.9)		-	0.120
Diabetes	Yes	4 (11.1)		8 (22.2)		-	0.200
Hyperlipidemia	Yes	6 (16.7)		9 (25.0)		-	0.380

Values are presented as mean ± standard deviation (SD) or number (%).

\* values of the independent t-test; \*\* values of the chi-square test

In the control group, 8 (22.2%), 12 (33.3%), and 16 (44.5%) individuals were, respectively, employed, retired or unemployed, and housewives. In the intervention and control group, respectively, 8 (22.2%) and 14 (38.9%) individuals used tobacco. The prevalence of diabetes and hyperlipidemia was 11.1% (n = 4) and 16.7% (n = 6) in the intervention group, and 22.2% (n = 8) and 25% (n = 9) in the control group, respectively (Table 2).

The mean ± SD of systolic and diastolic BP in the intervention group was, respectively, 162.79 ± 14.21 and 84.08 ± 10.79 before the intervention, and 137.04 ± 14.21 and 77.90 ± 8.74 1 month after the intervention, thus representing a significant decrease (P < 0.001). In the control group, the mean ± SD of systolic and diastolic BP was, respectively, 166.69 ± 15.29 and 81.84 ± 13.17 before the intervention, and 163.80 ± 14.90 and 80.77 ± 11.57 after the

intervention, representing no significant difference. There was a significant difference in terms of average changes in systolic BP between the intervention group (-25.75 ± 19.39) and the control group (-2.88 ± 11.92) (P < 0.001). The average of variation in diastolic BP in the intervention and control group was -6.18 ± 8.87 and -1.06 ± 8.70, respectively; there was a statistically significant difference between the two groups (P = 0.010). The reduction of diastolic BP in the intervention group was greater than that in the control group (Table 3).

Before the intervention, no significant difference was observed between the two groups regarding MA score (P = 0.770). However, after the study, this difference was significant (P < 0.001). The pre-intervention and post-intervention mean ± SD of MA score in the intervention group was 3.86 ± 1.75 and 6.77 ± 1.39, respectively, which were significantly different (P < 0.001).

**Table 3.** The average of pre-intervention and post-intervention blood pressure in the intervention and control groups

BP	Intervention group		Control group		P*	
	Mean ± SD		Mean ± SD			
Systolic BP	Before the intervention	162.79 ± 14.21		166.69 ± 15.29		0.260
	After the intervention	137.04 ± 14.21		163.80 ± 14.90		< 0.001
P**	< 0.001		0.150			
Mean changes in systolic BP	-25.75 ± 19.39		-2.88 ± 11.92		< 0.001	
Diastolic BP	Before the intervention	84.08 ± 10.79		81.84 ± 13.17		0.430
	After the intervention	77.90 ± 8.74		80.77 ± 11.57		0.230
P**	< 0.001		0.460			
Mean changes in diastolic BP	-6.18 ± 8.87		-1.06 ± 8.70		0.010	

Values are presented as mean ± SD.

\* values of the independent t-test; \*\* values of the paired t-test

SD: Standard deviation; BP: Blood pressure

**Table 4.** Pre-intervention and post-intervention medication adherence score in the intervention and control groups

Medication adherence score	Intervention group	Control group	P*
	Mean ± SD	Mean ± SD	
Before the intervention	3.86 ± 1.75	3.75 ± 1.46	0.770
After the intervention	6.77 ± 1.39	3.38 ± 0.99	< 0.001
P**	< 0.001	0.060	P**
Mean changes of medication adherence score	2.91 ± 1.64	-0.36 ± 1.15	< 0.001

Values are presented as mean ± standard deviation (SD).

\* values of the independent t-test; \*\* values of the paired t-test

Nevertheless, this difference was not significant in the control group ( $P = 0.060$ ). Based on independent t-test, the mean changes in MA score between the pre-intervention and post-intervention in the intervention and control group was  $2.91 \pm 1.64$  and  $-0.36 \pm 1.15$ , respectively, and the difference was statistically significant ( $P < 0.001$ ) (Table 4).

### Discussion

Adherence to the drug regimen is important in controlling HTN. The purpose of this study was to determine the effect of a multifaceted intervention on MA and BP scores among 72 participants. Based on the results of various researches, factors such as gender, age, education, duration of HTN, and diseases such as diabetes and hyperlipidemia are effective factors impact BP management.<sup>29</sup> Thus, the two groups were compared in this regard and no significant difference existed, showing that they were similar in terms of these factors. Furthermore, the two groups were similar in terms of marital status, employment status, and smoking, with no statistically significant difference. In the intervention group, there was a significantly lower average of systolic and diastolic BP after the intervention compared to before the intervention. However, there was no significant difference in the post-intervention systolic and diastolic BP in the control group compared to pre-intervention. The systolic and diastolic BP of the two groups did not have a significant difference before the intervention. After the intervention, only the difference in systolic BP between the two groups was significant.

Leiva et al. reported a reduction in systolic and diastolic BP in the intervention group through a multifaceted intervention including self-control of BP, physician's visit, encouragement interview, drug reminder box, and family support during the first, third, and ninth months of intervention.<sup>23</sup> Their findings were in agreement to those of the present study. Moreover, Fakhri et al. performed 3 sessions of weekly training accompanied with stimulation interviews for 3 weeks, which led to a greater

reduction in the systolic and diastolic BP of the intervention group than the control group.<sup>30</sup>

Changes in average systolic and diastolic BP from pre-intervention to post-intervention in the intervention group was  $-25.75 \pm 19.39$  and  $-6.18 \pm 8.87$ , respectively. In a study by Williams et al., systolic BP in the intervention group decreased to 6.9 mm Hg and their diastolic BP to 2.25 mm Hg after the intervention.<sup>31</sup> Furthermore, MA in the intervention group was improved compared to the beginning of the study,<sup>31</sup> which is consistent with the results of the present study. Moreover, after performing 5 sessions of lifestyle education during 5 weeks, Babaei-Sis et al. reported an 8.3 mmHg decrease in the systolic BP and a 2.5-mmHg decrease in the diastolic BP of the intervention group. There was a significant difference between the two intervention and control groups after the intervention, although there was no statistical difference before the intervention.<sup>32</sup> The results of another study indicated that every 10 mmHg reduction in systolic BP significantly reduced the risk of major CVD events, coronary heart disease, stroke, and heart failure.<sup>33</sup> It also significantly decreased all-cause mortality by 13%.<sup>33</sup>

Furthermore, the results of this study showed that although there was no significant difference between the two groups before the intervention in terms of the MA score, there was a significant difference between the two groups after the study. The MA score of the intervention group had increased, while the MA score of the control group had decreased. In fact, this multifaceted intervention has been able to notably enhance this substantial element in controlling and treating HTN.

According to the results of this study, the average score of MA before the study in the intervention and control group was about 4, which is indicative of a poor MA in all subjects. This outcome was in line with the cross-sectional study by Al-Ramahi in which over 54% of the participants had poor adherence.<sup>34</sup>

Based on the findings, the mean changes in MA score in the intervention and control group were

2.91 ± 1.64 and -0.36 ± 1.15, respectively, and the two groups had a significant difference meaning a greater increase in the score of the intervention group than the control group. Fakhri et al. performed a study with the purpose of determining the effect of a theory-based education on improving the compliance with the drug regimen with 3 sessions of training for 1 month. Before the intervention, 8.6% of the participants in the intervention group and 7.1% in the control group had a good MA that reached 50% in the intervention group after the intervention, while the control group had an unchanged percentage.<sup>30</sup>

### Conclusion

The results of this study indicated that family support of the patient along with healthcare team phone call follow-ups have complemented the effects of training and the use of a drug reminder box. It has also contributed to the stabilization of trained behaviors, thus positively affecting the management of systolic and diastolic BP and MA.

According to the findings of the research, it can be concluded that a multifaceted intervention focusing on healthy lifestyle education, strengthening patient support for drug use by its most important supporter, the family, and using a drug reminder box to eliminate untimely medication intake can significantly affect the reduction of BP and its control, and therefore, reduce systolic and diastolic BP by more than 25 and 6 mmHg, respectively. Research findings also suggested that this multifaceted intervention not only reduces BP, but also improves patient MA, which is one of the most important challenges the healthcare team are faced with. Therefore, it can decline the concern for disease control and improper use of drugs for patients, their families, and the healthcare team in the society.

It can be concluded that the increase of the 3 MA scores in the intervention group in comparison with the control group shows that this type of intervention has had an undeniable contribution to medication use and adherence to HTN medication in hypertensive patients.

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### Conflict of Interests

Authors have no conflict of interests.

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