The impact of a community trial on the pharmacological treatment in the individuals with the metabolic syndrome: findings from the Isfahan Healthy Heart Program, 2001-2007

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Abstract

Introduction: Pharmacological therapy is a crucial step in the management of individuals with the metabolic syndrome, when lifestyle modifications alone cannot achieve the therapeutic goals. The present study aimed to evaluate the efficacy of comprehensive interventions with the pharmacological treatment in individuals with the metabolic syndrome.

Material and methods: A cross-sectional population-based survey examined a sample of adults before and after conducting a community trial. Physical examination and blood sampling, data regarding the demographic characteristics, medical status and history of medication use were obtained. Pharmacologic treatment related to metabolic syndrome's components was also determined.

Results: The most common pharmacologic agents consumed by individuals with metabolic syndrome were β-blockers (26.1% and 30.4% in 2001 and 2007, respectively), followed by lipid-lowering agents (5.4% and 14% in 2001 and 2007, respectively), with significant differences before and after intervention. The prevalence of metabolic syndrome was higher in women than in men both before (36.4% vs. 14%) and after the community trial (26.1% vs. 16%, respectively) in the intervention areas ($p < 0.001$).

Conclusions: We found a significant increase in medication use to control blood pressure and dyslipidemia among the individuals with the metabolic syndrome, notably in the intervention areas. In addition to the population approach, the high-risk approach should be considered in community trials for prevention and control of non-communicable diseases.

Key words: metabolic syndrome, pharmacological treatment, community trial, Iran.

Introduction

The metabolic syndrome is a great public health concern, and patients with this cluster of risk factors are at significantly increased risk of developing diabetes and cardiovascular disease (CVD) [1]. This condition is highly prevalent in both developed and developing countries and carries a risk of diabetes, cardiovascular morbidity and mortality [2]. The metabolic syndrome has recently aroused universal attention from the scientific societies and healthcare managers [3]. The main goal of treatment for the metabolic

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disease is to reduce cardiovascular risk [4]. Components of the metabolic syndrome that need control are atherogenic dyslipidemia, elevated blood pressure, elevated fasting glucose, prothrombotic factors, and proinflammatory state [4]. Pharmacological therapy is a critical step in the management of subjects with the metabolic syndrome when lifestyle modifications fail to achieve the therapeutic goals [5].

In addition to weight loss, there is no single best therapy, and the treatment should consist of treatment of the individual components of the metabolic syndrome [6]. Although lifestyle change is the first line of therapy, medical treatment is usually needed for the optimal control [7].

A recent community-based interventional program, named the Isfahan Healthy Heart Program (IHHP), is a community-based interventional program for CVD and control of related risk factors. The goal of the IHHP study was to make a strategic shift towards prevention and control of non-communicable diseases (NCDs) and their risk factors and promote healthy lifestyles by using comprehensive population and high-risk approaches to prevention [8]. Several interventional trials have reported the effects of lifestyle intervention programs among the high-risk populations [9]. However, the pooled effects suggest that multiple risk factor intervention has no effect on mortality. In spite of recent meta-analyses there is doubt about whether lifestyle interventions actually help to reduce the cardiovascular disease risk factors [10].

The present study aimed to evaluate the efficacy of IHHP on drug compliance in the individuals with the metabolic syndrome after comprehensive intervention in both sexes in an intervention area compared with a reference area. The hypothesis for intervention was that participants in the intervention area would achieve greater compliance in the management of the metabolic syndrome components than found in the reference area.

Material and methods

The Isfahan Healthy Heart Program, a comprehensive integrated community-based action-oriented study with a reference community, has been conducted by the Isfahan Cardiovascular Research Centre since 2001 to 2007 [11]. Two intervention counties (Isfahan and Najafabad) and a reference area (Arak), all located in the central part of Iran, were included in the study. According to the 2000 National Census, the population was 1,895,856 in Isfahan and 275,084 in Najafabad – a county neighboring Isfahan. Arak, located 375 km North-West of Isfahan, with a population of 668,531, was selected as a reference area because of socioeconomic, demographic and health profile similarities to the intervention areas. In each community, a random inde-

pendent sample of adults was selected by multi-stage cluster sampling. Clusters were chosen from three counties in the central part of Iran, based on their demographic and socioeconomic characters. The effect of confounding has been addressed by using random, stratified household sampling, based on age and sex groups. The IHHP was conducted as three phases: the situational analysis or baseline phase, the second or implement interventional activities in the interventional area, and the last phase or outcome evaluation phase. During the second phase, we carried out an organized approach to program evaluation including each activity (i.e. process evaluation) and program annual monitoring (i.e. impact evaluation).

The participants were more than 19 years old. The samples underwent a 30-minute interview to complete validated questionnaires containing questions on demography, socioeconomic status, smoking behavior, physical activity, nutritional habits and other behavior regarding CVD [12].

Written informed consent was obtained from subjects after full explanation of the procedure. The study was approved by the Ethics Committee of the Isfahan Cardiovascular Research Center. IHHP was covered under IRB protocol FW A00008578 and was performed at the Isfahan Cardiovascular Research Center with the collaboration of Arak University. The details of the program, inclusion and exclusion criteria, have previously been reported elsewhere [11-13].

Anthropometric measurements

Waist circumference (WC) was measured at the level of the umbilicus and recorded in centimeters using standard WHO methods [13].

Biochemical measurements

Blood lipids were measured enzymatically with the commercially available reagents (Cholesterol/HP, cat. no. 816302, and Triglycerides/GPO, cat. no. 816370, both from the Boehringer Mannheim). HDL cholesterol was measured in the clear supernatant after precipitating the other lipoproteins with heparin and $MnCl_2$ (1.3 g/l and 0.046 mol/l, respectively) and removing excess Mn^{2+} by precipitation with $NaHCO_3$. Fasting glucose was measured using the Glucose Standard Assay (Sigma chemical, St Louis) [14].

Metabolic syndrome definition

The updated ATP-III definition of the metabolic syndrome was met when three or more of the following criteria were present: waist circumference ≥ 102 cm (40 inches) in men and 88 cm (35 inches) in women; HDL > 1.03 mmol/l (40 mg/dl) in men and 1.30 mol/l (50 mg/dl) in women or specific treatment for this lipid abnormality; triglycerides

≥ 1.7 mmol/l (150 mg/dl) in men and women or specific treatment for this lipid abnormality; systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg in men and women or treatment of previously diagnosed hypertension; and fasting glucose ≥ 5.6 mmol/l (100 mg/dl) in men and women [15].

Pharmacological treatment

The pattern of medication use was defined by the drugs used to control and treat each component of metabolic syndrome, including chemical and herbal drugs, determined by validated questionnaire. Anti-hypertension drugs (e.g. calcium channel blocker, β-blocker and angiotensin-converting enzyme (ACE) inhibitors) were considered relevant. Insulin resistance treatment drugs such as, thiazolidinediones, and statins for dyslipidaemia were taken into account. Aspirin was recommended by physicians for primary prevention of prothrombotic factors and the proinflammatory state in patients with the metabolic syndrome. We asked the participants about the herbal drugs, since the Iranian subjects are interested in using the herbal drugs for different health disorders including dyslipidemia, hypertension and hyperglycemia.

Statistical analysis

Results are reported as mean ± standard deviation (SD). An independent t-test was used to examine the difference between the quantitative variables, and a χ^2 test was used to examine the difference between the qualitative variables in individuals with or without the metabolic syndrome according to sex. P of 0.05 or less was considered statistically significant. Logistic regression was conducted to assess the determinants of the pharmacological treatment among subjects with the metabolic syndrome before and after interventions. Antihypertensive, diabetes drugs and lipid-lowering agents were entered in the model to estimate their independent effects in each area and study phase. P of < 0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS (SPSS Inc., Chicago, IL, USA) version 15.

Results

Total participants of IHHP in the intervention areas were 6175 in 2001, and 4719 in 2007 (the corresponding figures in the reference area were 6339 and 4853, respectively). The number of the individuals with the metabolic syndrome in 2001 and 2007 was 1570 and 982 in the intervention areas, and 1245 and 973 in the reference areas. The prevalence of the metabolic syndrome was 25.5% in 2001 and 21.1% in 2007 in the intervention areas and 19.9% in 2001 and 20.2% in 2007 in the reference area

($p < 0.05$). The prevalence of the metabolic syndrome was higher in women than in men both before (36.4% vs. 14%) and after the community trial (26.1% vs. 16%, respectively) in the intervention areas ($p < 0.001$). The average age of individuals with the metabolic syndrome was 47.67 ±14.59 years in women, and 49.75 ±15.25 years in men ($p < 0.001$). In 2001 the mean age of women in the intervention and reference areas was 45.99 ±14.28 and 47.95 ±14.4, and in men 50.16 ±14.31 and 49.98 ±14.58, respectively ($p < 0.001$), while in 2007, in women the mean age was 49.45 ±14.78 and 48.48 ±14.92 and in men 49.83 ±15.66 and 48.88 ±16.56 in the intervention and reference areas, respectively. The minimum and maximum age was 19 and 89 years ($p < 0.001$).

Demographic data of participants are shown in Table I. The prevalence of abdominal obesity, hyper-triglyceridemia and high blood pressure decreased significantly after intervention in both sexes and study areas, whereas the frequency of low HDL cholesterol increased significantly from 2001 to 2007 in both sexes and in both areas. Table II presents the number of patients for each category of recommended medications for the different components of the metabolic syndrome according to sex. Medications were categorized in five groups as anti-hypertensive, lipid-lowering, antidiabetic, aspirin and herbal. The most common single medication for control of hypertension was a β-blocker (26% in 2001 and 34% in 2007), without significant differences before and after intervention. The most common drug to control diabetes taken by the subjects in the intervention areas was glibenclamide, without a significant difference after interventions (females: 47.5% in 2001 and 49.1% in 2007; males: 43.6% in 2001 and 46.2% in 2007). Among lipid-lowering agents statins were the least frequent medication used in males and females before intervention (2.9% and 1.1%, respectively), whereas after intervention the total number of statin users was increased from 2.4% to 14% ($p < 0.001$). The total number of aspirin users was 8% in 2001 and 18.0% in 2007 ($p < 0.001$). There was a significant difference in the use of herbal medicine before and after interventions; 8.3% of the participants used herbal medicine in 2001 and 18.0% in 2007 ($p < 0.001$). After the IHHP interventions hypertension was managed more frequently by β-blockers (34%) ($p < 0.004$) and diabetes with glibenclamide (47.8%) ($p < 0.699$) than before the intervention. No significant difference was observed between males and females regarding the type of medications used. Table III shows the number of patients for each category of drugs for the different components of the metabolic syndrome according to sex in the references area. Our results showed that the rate of using β-blockers, ACE inhibitors, statins, metformin, and aspirin increased in the interven-

Table I. Characteristics of participants by sex and living area

	Intervention area					Reference area				
	Female (n = 1767)		Male (n = 785)		Value of p	Female (n = 1632)		Male (n = 586)		Value of p
	2001, n (%)	2007, n (%)	2001, n (%)	2007, n (%)		2001, n (%)	2007, n (%)	2001, n (%)	2007, n (%)	
	1150 (65.1)	617 (34.9)	420 (53.5)	365 (46.5)		963 (59)	669 (41)	282 (48.1)	304 (51.9)	
Age [years]	45.99 ±14.28	50.16 ±14.32	50.16 ±14.32	49.84 ±15.66	< 0.0001	47.95 ±14.44	48.48 ±14.92	49.98 ±14.58	48.88 ±16.57	0.94
Central obesity	1116 (97.5)	575 (93.8)	280 (67.1)	190 (52.9)	< 0.0001	148 (52.7)	138 (53.9)	1026 (82.6)	696 (81.3)	< 0.0001
Raised FBS or known case of type 2 diabetes	205 (17.9)	166 (26.9)	125 (28.9)	117 (32.1)	< 0.0001	86 (30.6)	79 (26.0)	261 (21.1)	221 (22.7)	0.485
Low HDL cholesterol	897 (78.9)	543 (88.6)	254 (60.0)	308 (84.4)	< 0.0001	200 (72.2)	253 (83.2)	974 (79.1)	850 (87.4)	< 0.0001
Hypertriglyceridemia	1026 (89.8)	468 (76.1)	397 (94.5)	323 (89.0)	< 0.0001	265 (94.3)	285 (93.8)	1106 (89.0)	854 (87.8)	0.004
High systolic blood pressure	539 (46.9)	256 (41.8)	278 (66.3)	219 (60.2)	0.041	180 (63.8)	181 (59.5)	660 (53)	492 (50.6)	0.073
High diastolic blood pressure	422 (36.7)	217 (35.5)	221 (52.7)	196 (53.8)	0.615	138 (49.3)	114 (37.5)	465 (37.4)	316 (32.5)	0.758

Central obesity: waist circumference > 88 cm in females and > 102 in males; triglycerides ≥ 1.65 mmol/l and/or those under treatment; HDL-C < 104 mmol/l in men and < 1.3 mmol/l in women; systolic/diastolic blood pressure ≥ 130/80 mm Hg and/or those under treatment; FBS (fasting blood sugar) ≥ 6.1 mmol/l and/or those under treatment; p < 0.001

tion areas after intervention. Table IV shows the association of some variables with the pharmacological treatment in both the intervention and reference areas before and after interventions. Based on the logistic regression analysis, the male sex decreased the medication use 0.69-fold from 2001 to 2007 ($p < 0.001$). The older subjects had approximately 8 times higher use of antihypertensive medications than the younger participants ($p < 0.001$). Education did not show a significant relationship with any type of drug in both the intervention and reference areas in 2001 and 2007.

Living in an urban area increased the rate of using lipid-lowering agents 1.85-fold after interventions in the intervention areas ($p < 0.05$). In the intervention areas, the rate of using antidiabetic agents had not changed after interventions, based on age, sex and education, but living in an urban area increased this figure 2.7-fold from 2001 to 2007 in the intervention area among the study population ($p < 0.05$). Our results revealed a significant relationship between some social determinants and the pharmacological treatment among subjects with the metabolic syndrome between the intervention and reference areas from 2001 to 2007 ($p < 0.001$).

Discussion

The present study aimed to evaluate the efficacy of IHHP on drug compliance in the individuals with the metabolic syndrome after comprehensive intervention in both sexes in an intervention area compared with a reference area. We found that after implementation of a community-based program, the pharmacologic treatment for the management of the different components of the metabolic syndrome increased significantly. These findings suggest that there is national interest in monitoring and managing the CVD risk factors in our population, and it seems that intensive educational programs with a high-risk approach might be successful in increasing the population awareness for screening and control of the CVD risk factors.

The prevalence of the metabolic syndrome is considerably high in Iran [18]. The IHHP study reported that in the urban Iranian populations, the age-adjusted prevalence of the metabolic syndrome was 10.7% in men and 35.1% in women [19]. The age-adjusted prevalence of the metabolic syndrome decreased from 23.3% to 21% in the intervention areas. However, it showed an insignificant increase from 19.9% to 20.2% in the reference area. Primary care physicians and cardiologists in the community practice are on the front lines, when it comes to battling the epidemic of the metabolic syndrome. The first item physicians need to measure the patient's size and the size of waistline at the first visit. Because obesity predisposes individuals to

Table II. The pattern of the pharmacological treatment 2001-2007 by sex in the intervention areas (intervention population – Isfahan and Najaf-Abad)

Variables		Female 1767			Male 785			Total 2552		
		2001 1150	2007 617	Value of p	2001 425	2007 365	Value of p	2001 963	2007 669	Value of p
Anti-hypertensive treatment	Calcium channel blockers	33 (9.1%)	13 (8.0%)	0.683	15 (7.4%)	5 (3.1%)	0.073	48 (8.5%)	18 (5.6%)	0.109
	β-Blockers	142 (30.1%)	111 (42.7%)	0.001	40 (17.6%)	46 (22.8%)	0.183	182 (26.1%)	157 (34.0%)	0.004
	ACE inhibitors	25 (7.1%)	27 (15.3%)	0.003	8 (4.1%)	18 (10.3%)	0.019	33 (6.0%)	45 (12.9%)	< 0.0001
	Thiazides	2 (0.6%)	5 (3.2%)	0.023	0 (0.0%)	5 (3.1%)	0.015	2 (0.4%)	10 (3.2%)	0.001
	A-ARB	0 (0.0%)	4 (2.6%)	0.003	0 (0.0%)	4 (2.5%)	0.030	0 (0.0%)	8 (2.6%)	< 0.0001
Lipid-lowering treatment	Fibrates	65 (6.0%)	31 (5.8%)	0.917	10 (2.6%)	9 (2.8%)	0.882	75 (5.1%)	40 (4.7%)	0.659
	Nicotinic acid	49 (4.6%)	31 (5.8%)	0.271	7 (1.8%)	8 (2.5%)	0.555	56 (3.9%)	39 (4.6%)	0.402
	Statins	30 (2.9%)	99 (16.6%)	< 0.0001	4 (1.1%)	33 (9.1%)	< 0.001	34 (2.4%)	132 (14.0%)	< 0.0001
	Statins, fibrates	69 (6.3%)	99 (16.6%)	< 0.0001	10 (2.6%)	33 (9.5%)	< 0.001	79 (5.4%)	132 (14.0%)	< 0.0001
	Gemfibrozil	32 (3.0%)	40 (7.4%)	< 0.0001	4 (1.1%)	13 (4.0%)	0.012	36 (2.5%)	53 (6.1%)	< 0.0001
Anti-diabetic treatment	Metformin/ phenformin	4 (4.0%)	28 (32.2%)	< 0.0001	2 (3.1%)	12 (19.7%)	0.003	6 (3.7%)	40 (27.0%)	< 0.0001
	Glibenclamide	87 (47.5%)	57 (49.1%)	0.788	48 (43.6%)	42 (46.2%)	0.721	135 (46.1%)	99 (47.8%)	0.699
	Insulin-crystal-NPH	8 (7.7%)	11 (15.7%)	0.096	1 (1.6%)	8 (14.0%)	0.010	9 (5.4%)	19 (15.0%)	0.006
Herbal drugs		49 (4.3%)	11 (1.8%)	0.006	16 (3.8%)	5 (1.4%)	0.034	65 (4.2%)	16 (1.6%)	< 0.0001
Aspirin		80 (7.0%)	93 (15.8%)	< 0.0001	51 (12.1%)	76 (21.8%)	< 0.001	131 (8.3%)	169 (18.0%)	< 0.0001

Value of p < 0.001

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Table III. The pattern of the pharmacological treatment 2001-2007 by sex in the reference area (reference population – Arak)

Variables		Female 1632			Male 586			Total 2218		
		2001 963	2007 669	Value of *p*	2001 282	2007 304	Value of *p*	2001	2007	Value of *p*
Anti-hypertensive treatment	Calcium channel blockers	9 (2.7%)	9 (4.6%)	0.237	2 (1.6%)	3 (2.5%)	0.632	11 (2.4%)	12 (3.8%)	0.260
	β-Blockers	83 (20.3%)	79 (29.8%)	0.005	34 (21.7%)	33 (21.7%)	0.991	117 (20.7%)	112 (26.9%)	0.023
	ACE inhibitors	15 (4.4%)	21 (10.1%)	0.008	8 (6.1%)	15 (11.2%)	0.141	23 (4.9%)	36 (10.6%)	0.002
	Thiazides	0 (0.0%)	2 (1.1%)	0.062	2 (1.6%)	5 (4.0%)	0.246	2 (0.4%)	7 (2.2%)	0.024
	A-ARB	0 (0.0%)	6 (3.1%)	0.001	0 (0.0%)	4 (3.3%)	0.030	0 (0.0%)	10 (3.2%)	< 0.001
Lipid-lowering treatment	Fibrates	59 (6.4%)	28 (4.6%)	0.137	14 (5.4%)	7 (2.5%)	0.088	73 (6.2%)	35 (4.0%)	0.025
	Nicotinic acid	27 (3.0%)	22 (3.7%)	0.511	4 (1.6%)	6 (2.2%)	0.63	31 (2.7%)	28 (3.2%)	0.536
	Statins	25 (2.8%)	68 (10.5%)	< 0.001	4 (1.6%)	23 (7.8%)	0.001	29 (2.6%)	91 (9.7%)	< 0.001
	Statins and fibrates	61 (6.6%)	74 (11.3%)	0.001	15 (5.7%)	24 (8.2%)	0.266	76 (6.4%)	98 (10.3%)	0.001
	Gemfibrozil	24 (2.7%)	29 (4.8%)	0.035	3 (1.2%)	6 (2.2%)	0.393	27 (2.4%)	35 (4.0%)	0.042
Anti-diabetic drugs	Metformin, phenformin	2 (2.5%)	21 (25.6%)	< 0.001	2 (2.4%)	11 (22.9%)	0.010	4 (3.2%)	32 (24.6%)	< 0.001
	Glibenclamide	67 (45.9%)	60 (49.6%)	0.547	26 (37.7%)	32 (46.4%)	0.301	93 (43.3%)	92 (48.4%)	0.298
	Insulin-crystal-NPH	3 (3.7%)	4 (6.2%)	0.480	2 (4.4%)	0 (0.0%)	0.194	5 (3.9%)	4 (3.9%)	0.995
	Herbal drugs	69 (7.2%)	12 (1.8%)	< 0.001	9 (3.2%)	4 (1.3%)	0.117	78 (6.3%)	16 (1.7%)	< 0.001
	Aspirin	44 (4.6%)	49 (7.3%)	0.017	19 (6.7%)	34 (11.2%)	0.059	63 (5.1%)	83 (8.6%)	0.001

Table IV. The relationship between the pharmacological treatment and determinants in 2001-2007 by sex among subjects with the metabolic syndrome

			Anti-hypertensive treatment	Lipid-lowering treatment	Anti-diabetic drugs	Total drugs
Intervention						
2001	Sex	Female	–	–	–	–
		Male	0.44 (0.30-0.64)**	0.37 (0.2-0.67)**	0.82 (0.49-1.36)	0.66 (0.49-0.89)**
	Education	0-5	–	–	–	–
		6-12	1.17 (0.74-1.86)	0.85 (0.48-1.49)	0.69 (0.36-1.34)	0.74 (0.52-1.04)
		> 12	1.41 (0.51-3.88)	0.52 (0.12-2.24)	1.94 (0.4-9.33)	0.69 (0.34-1.43)
	Age group [years]	19-39	–	–	–	–
		40-59	8.72 (3.87-19.65)**	3.2 (1.73-5.92)**	1.01 (0.47-2.16)	5.97 (3.91-9.15)**
		≥ 60	16.07 (7.01-36.89)**	3.46 (1.75-6.87)**	1.97 (0.9-4.32)	15.25 (9.66-24.06)**
	Residency	Urban	–	–	–	–
		Rural	1.17 (0.78-1.74)	1.2 (0.74-1.97)	1.27 (0.69-2.32)	1.15 (0.84-1.57)
2007	Sex	Female	–	–	–	–
		Male	0.41 (0.27-0.62)**	0.55 (0.35-0.86)**	0.81 (0.46-1.41)	0.69 (0.51-0.96)*
	Education	0-5	–	–	–	–
		6-12	1.41 (0.86-2.33)	0.71 (0.51-1.05)	0.83 (0.43-1.6)	0.88 (0.62-1.26)
		> 12	1.11 (0.5-2.45)	0.74 (0.29-1.85)	1.03 (0.24-4.52)	0.87 (0.46-1.64)
	Age group [years]	19-39	–	–	–	–
		40-59	3.54 (1.76-7.11)**	3.52 (1.82-6.78)**	1.65 (0.62-4.36)	3.9 (2.49-6.12)**
		≥ 60	7.24 (3.51-4.94)**	4.65 (2.31-9.35)**	1.1 (0.42-2.9)	10.5 (6.42-17.17)**
	Residency	Urban	–	–	–	–
		Rural	0.58 (0.34-0.99)*	0.54 (0.29-0.99)*	0.37 (0.16-0.89)*	0.45 (0.29-0.7)**
Reference						
2001	Sex	Female	–	–	–	–
		Male	0.99 (0.64-1.56)	0.8 (0.44-1.45)	0.67 (0.37-1.22)	1.19 (0.85-1.67)
	Education	0-5	–	–	–	–
		6-12	1.24 (0.62-2.48)	0.73 (0.34-1.6)	1.55 (0.62-3.86)	1.03 (0.64-1.66)
		> 12	1.77 (0.61-5.15)	0.93 (0.21-4.09)	2.36 (0.35-15.73)	1.45 (0.63-3.36)
	Age group [years]	19-39	–	–	–	–
		40-59	4.47 (1.78-11.2)**	2.18 (1.11-4.28)*	2.94 (1.03-8.36)*	4.91 (2.97-8.09)**
		≥ 60	7.02 (0.36-0.92)**	2.27 (1.08-4.73)*	4.73 (1.56-14.29)**	10.2 (6.02-17.27)**
	Residency	Urban	–	–	–	–
		Rural	0.57 (0.36-0.92)*	0.74 (0.43-1.27)	0.86 (0.44-1.67)	0.68 (0.48-0.95)*
2007	Sex	Female	–	–	–	–
		Male	0.76 (0.49-1.17)	0.7 (0.42-1.16)	0.79 (0.43-1.47)	0.95 (0.68-1.33)
	Education	0-5	–	–	–	–
		6-12	0.95 (0.46-1.97)	0.92 (0.48-1.76)	1.06 (0.46-2.45)	0.77 (0.48-1.24)
		> 12	1.96 (0.49-7.82)	0.48 (0.06-3.87)	5.78 (0.55-60.72)	1.34 (0.51-3.55)
	Age group [years]	19-39	–	–	–	–
		40-59	2.15 (1.08-4.27)*	2.63 (3.84-10.72)**	2.48 (0.98-6.3)	3.06 (1.98-4.74)**
		≥ 60	3.14 (1.57-6.27)**	2.58 (1.28-5.21)**	2.16 (0.81-5.77)	5.47 (3.41-8.78)**
	Residency	Urban	–	–	–	–
		Rural	0.75 (0.5-1.12)	0.51 (0.33-0.79)* *	0.68 (0.37-1.25)	0.62 (0.46-0.85)**

*p < 0.05, **p < 0.001

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several risk factors that comprise the metabolic syndrome [20].

Community interventions in the IHHP program were designed to improve the lifestyle indicators and behavior among the high-risk groups. Our previous studies showed that the improvement in nutritional habits, smoking and physical activity was significantly higher in the high-risk population, such as individuals with the metabolic syndrome, in the interventional areas compared to the reference area [8]. The IHHP holds comprehensive training courses and effective Continuing Medical Education (CME) programs in order to increase the attitude, knowledge and practice related to the cardiovascular disease risk factors among the health professionals including cardiologists, internists, general physicians, and nurses. Continuing Medical Education could help greatly to increase the knowledge and practice in the health professionals. Prevention, early detection, improved management of cardiovascular disease, as well as improvement in healthy lifestyle were our training goals [21].

The strength of the study is that patients and physicians were not trained about the metabolic syndrome and its components in 2001, whereas during IHHP interventions, health professionals underwent extensive training about the lifestyle modification, drug compliance, monitoring and control of CVD risk factors. Given the multiplicity of comprehensive training programs, IHHP has apparently increased drug acceptance in individuals with the metabolic syndrome. We suggest that the increased medication use, has resulted from the improved knowledge about the risk factor control and optimum medication use.

In this study, the most common pharmacologic agents consumed by individuals with the metabolic syndrome were, β-blockers (26.1% and 30.4% in 2001 and 2007, respectively), followed by lipid-lowering agents (5.4% and 14% in 2001 and 2007), with significant differences before and after intervention. On one hand, the prevalence of hypertension was decreased significantly among both sexes from 2001 to 2007, and on the other hand, the percentages of all types of hypertensive drugs, especially β-blockers, increased significantly from 2001 to 2007. It is supposed that on one hand, as hypertension is one of the most common risk factors among our study subjects, the use of antihypertensive drugs is significantly higher than other types of treatment. On the other hand, our population has higher awareness and practice as regards control and treatment of hypertension [22]. This is in line with another study in our population showing that β-blockers were the most prevalent anti-hypertensive drug used by the Iranian hypertensive patients [23]. However, it is established that most β-blockers have adverse effects on insulin sensitivity and carbohy-

drate and lipid metabolism, and are not recommended in the metabolic syndrome. However, it seems that in Iran, most subjects with the metabolic syndrome have been treated for the individual risk factors. Furthermore, the new generation of β-blockers, such as carvedilol and nebivolol, have better effects on metabolism [24].

Lifestyle interventions are crucial for the control and management of major risk factors in the metabolic syndrome, but pharmacological interventions to specifically target all the risk factors are crucial as well. The focus on the individual risk factor medication involves a multipronged strategy to control the borderline high LDL cholesterol (statins, statin-ezetimibe combination); high triglycerides (fibrates, fibrate-statin combination, omega-3 fatty acids); low HDL cholesterol (niacin, fibrates); high blood pressure (ACE inhibitors, angiotensin receptor blockers, β-blockers, and others); and insulin resistance (metformin, acarbose, thiazolidinediones). However, population-based lifestyle interventions are critical, and are the best evidence-based approaches in the Iranian populations as well as South Asian [22-30]. Our results revealed a significant relationship between some social determinants and pharmacological treatment among subjects with the metabolic syndrome between the intervention and reference areas from 2001 to 2007. We found that the rate of treatment increased among the older females with a low level of education who lived in an urban area from 2001 to 2007.

Our results also showed that this community trial succeeded in increasing the pharmacologic treatment among individuals with metabolic syndrome in the intervention areas, whereas the reference population did not follow the same pattern.

This study relies on two sets of cross-sectional data to test hypotheses in the different study phases; thus we cannot conclude about just personal compliance. Finally, we could not determine the comorbid factors affecting individuals with the metabolic syndrome over time.

In conclusion, our results revealed a significant increase in the pharmacologic treatment to control blood pressure and lipid profile among the individuals with the metabolic syndrome. In addition to the population approach, the high-risk approach should be considered in community trials for prevention and control of non-communicable diseases.

Further research is needed to evaluate the impact of community trials on control and prevention of CVD risk factors and compliance behavior of patients who have been diagnosed with the metabolic syndrome.

Acknowledgments

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