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Original Article

Non-physician health workers for improving adherence to medications and healthy lifestyle following acute coronary syndrome: 24-month follow-up study

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ABSTRACT

Objective: To evaluate usefulness of non-physician health workers (NPHW) to improve adherence to medications and lifestyles following acute coronary syndrome (ACS).
Methods: We randomized 100 patients at hospital discharge following ACS to NPHW intervention ($n = 50$) or standard care ($n = 50$) in an open label study. NPHW was trained for interventions to improve adherence to medicines – antiplatelets, β-blockers, renin–angiotensin system (RAS) blockers and statins and healthy lifestyles. Intervention lasted 12 months with passive follow-up for another 12. Both groups were assessed for adherence using a standardized questionnaire.
Results: ST elevation myocardial infarction (STEMI) was in 49 and non-STEMI in 51, mean age was 59.0 ± 11 years. 57% STEMI were thrombolyzed. On admission majority were physically inactive (71%), consumed unhealthy diets (high fat 77%, high salt 58%, low fiber 57%) and 21% were smokers/tobacco users. Coronary revascularization was performed in 90% (percutaneous intervention 79%, bypass surgery 11%). Drugs at discharge were antiplatelets 100%, β-blockers 71%, RAS blockers 71% and statins 99%. Intervention and control groups had similar characteristics. At 12 and 24 months, respectively, in intervention vs control groups adherence (>80%) was: anti platelets 92.0% vs 77.1% and 83.3% vs 40.9%, β blockers 97.2% vs 90.3% and 84.8% vs 45.0%), RAS blockers 95.1% vs 82.3% and 89.5% vs 46.1%, and statins 94.0% vs 70.8% and 87.5% vs 29.5%; smoking rates were 0.0% vs 12.5% and 4.2% vs 20.5%, regular physical activity 96.0% vs 50.0%, and 37.5% vs 34.1%, and healthy diet score 5.0 vs 3.0, and 4.0 vs 2.0 ($p < 0.01$ for

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all). Intervention vs standard group at 12 months had significantly lower mean systolic BP, heart rate, body mass index, waist:hip ratio, total cholesterol, triglyceride, and LDL cholesterol ($p < 0.01$).

Conclusions: NPHW-led educational intervention for 12 months improved adherence to evidence based medicines and healthy lifestyles. Efficacy continued for 24 months with attrition.

1. Introduction

In India, compared to high and middle income countries, a greater mortality from cardiovascular diseases (CVD) has been reported despite having lower cardiovascular risk factors and younger age.[1] This could be due to inadequate control of CVD risk factors, poor management of acute coronary events, poor secondary prevention or a combination of all the three.[2] Although there have been some improvements in acute coronary care in developing countries,[3] including India,[4] current data indicate a higher mortality among such patients in India[5,6] compared to studies from developed countries.[7,8]

International cohort and population-based studies have shown that greater adherence to cardioprotective drug regimens following acute coronary syndromes (ACS) is associated with lower long-term mortality.[9–12] Adherence to evidence based cardioprotective medication in particular to antiplatelets, β-blockers, renin–angiotensin system (RAS) blockers such as angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), and statins following hospital discharge for ACS has been found to be poor worldwide.[9] While Indian registries have reported adequate use of various secondary preventive medicines at hospital discharge,[5,6] studies have reported that their use in the community is low.[13–15] In the Prospective Urban Rural Epidemiology (PURE) study, the long term use of secondary prevention therapies was suboptimal in India and other South Asian countries and at a mean of 4.5 years after diagnosis of coronary heart disease (CHD) and more than 80% of patients were not on any effective secondary prevention drugs.[16] PURE study also reported that only 38% in low and middle income countries had quit smoking compared to 75% in high-income countries and 26% consumed healthy diets compared to 43% in high income countries at the end of 4.5 years.[17] On the other hand, increasing trends in use of secondary preventive lifestyles and drugs have been reported in EUROSPIRE studies.[18]

Interventions led by community health workers (CHW) or non-physician health workers (NPHW) have improved adherence to drug therapies in communicable diseases, e.g., tuberculosis, HIV/AIDS, etc., with considerable success in high-, middle- as well as low-income countries.[19] The utility of trained CHWs or NPHWs has been demonstrated in non-communicable diseases (NCDs) management in developed countries but has not been adequately evaluated in developing countries.[20] The aim of the present study was to assess whether a trained NPHW can improve adherence to proven secondary prevention measures after an ACS event. We performed an open label prospective randomized controlled multisite trial to assess the effect of NPHW based educational intervention among patients and their family members for 12 months to improve adherence to cardioprotective medication and lifestyle modifications (LSM) vs usual care for ACS survivors following hospitalization.[21] In the present study we evaluated the effect of this intervention at 24-months using a passive follow-up of all such patients at our center.

2. Methods

This study was conducted after approval by the institutional ethics committee at the hospital. Written informed consent was obtained from each study participant. Patients with ACS, as the primary reason for admission during the years 2011–2012, were screened for eligibility. ACS was defined as either myocardial infarction (ST elevation or non-ST elevation) or unstable angina using standard definitions.[5] We excluded patients living far (>50 km) from the healthcare facility and those unlikely to survive the study duration due to other serious illnesses, e.g., metastatic cancer, or inability to execute study protocol, lack of telephone or cellphone and pregnancy. The principal multisite study was performed at 12 centers in the country and detailed methodology has been reported earlier.[21,22] The follow-up duration in the national study was 12 months.[22]

Eligible patients with ACS were consecutively randomized using centralized process with a telephone randomization service at national coordinating center in a 1:1 ratio to intervention or standard care arm. The allocation sequence was concealed until a patient consented to participate. All screened hospitalized ACS patients for study were counselled to participate in the study 1–2 days before discharge from hospital and written informed consent obtained form those who agreed to participate. The care provider (spouse or another family member) of each patient was involved in the decision to participate in the study. Patients in both groups received all standard ACS hospital discharge counselling by the admitting physician and other staff. This included follow-up appointments, diet and exercise advice, discharge medication list and educational information about cardiac medications.

For the intervention group, we trained a NPHW to provide follow-up care. Criteria for selection of NPHW were – young male or female with schooling to higher secondary level (12th grade education) and no formal college degree, good communication skills and proficiency in local languages, some knowledge of English and familiarity with a hospital setting.[21,22] These criteria were used to facilitate use of similarly available persons (CHW) in the national health program for chronic diseases in India (National Programme for Cancer,

Diabetes, Cardiovascular Diseases and Stroke, NPCDCS).[21] Each NPHW was provided training at the local hospital by a project manager known as SPREAD Project Officer (SPO). This SPO was a graduate with background in medical sciences (pharmacist, nurse, non-postgraduate medical degree or practitioners of other systems of medicine) with competence inter-personal communications. He was trained at national coordinating center for 3 days and also helped in developing a comprehensive NPHW training manual. He trained the NPHW over a 6-month period. Periodic evaluation of NPHW and SPO was performed. Other details have been reported previously.[21]

The NPHW was intimately involved with the patient and his family and carried out formal discussions and building of rapport with the patient and the family care provider in the initial visit. At this stage the NPHW, caregiver and the patient mutually identified potential barriers to compliance with healthy lifestyle and pharmacological treatment and developed strategies to overcome them. Tools used for improving adherence were a visual calendar and a health diary. We focused on importance of evidence based drugs and healthy lifestyles. For patients randomized to intervention arm follow-up visits were explained with the role and objectives of NPHW over 12 months follow-up. Patients and care-providers were urged to collect empty medication blisters regularly and this was verified by the NPHW at each visit. At the first visit during discharge, the NPHW and patient mutually decided on the schedule for the follow-up visits over one year.

2.1. *Interventions and follow up*

There were a total of 6 follow-up visits in the intervention arm, four at the hospital at 1, 5, 7, and 12 months and two home visits at 3 and 9 months. Home visits were fixed at mutually convenient times when the home caregiver was also available. The key intervention was to have a relaxed discussion over 45–60 min with the patient and the primary caregiver. At this time the NPHW helped to identify barriers for medication adherence (lack of knowledge, attitude regarding medications, cost, access, regimen complexity, side effects and lack of family support) and for making adequate LSMs (lack of knowledge, unfavorable environment, lack of family support).[21] Thereafter the NPHW and patient with the caregiver mutually evolved strategies to overcome the barriers. The interventions were therefore personalized for each patient.[22] At each visit NPHWs assessed risk factors such as blood pressure (BP), tobacco and alcohol use, diet, exercise and adherence to secondary prevention medications that were prescribed. They also verified entries in the visual calendar, empty blisters counts and patient diary to corroborate the oral report from patients and their caregivers. Details of correlation of these parameters for the national study have been reported earlier.[22] During home visits, in addition to the activities at hospital visits, the NPHW involved as many family members as possible in discussions related to the care of the patient, specifically in reviewing the barriers for adherence to medication and lifestyle. At the end of the home visit, the NPHW reviewed the patients' medication adherence, BP and general condition. If the status was unsatisfactory, the NPHW also contacted the treating physician directly for necessary medical advice. In between visits the patient was encouraged to call the NPHW for any health related issue. Furthermore the NPHW made a telephone call every 3 months to inquire on their health status as well as their adherence to medications and LSMs advice. At the final visit the NPHW gave the patient and the caregiver a summary of their adherence level to medications and LSM over the preceding year and advised them to continue regular follow-up with their treating physician. Patients in the standard care group followed treatments in accordance with the hospital's usual practice. At the end of 12-month follow-up the standard care patients had data obtained on adherence to medications and LSM advice over the last one-month and whether any events occurred over the course of the study. If the patient had died, these details were collected from the caregiver. For the next 12 months no contact was maintained by the patient with NPHW and he was provided usual care by the physicians. Details of adherence was inquired at the end of 24 months using the tools reported above.

2.2. *Study outcomes*

The main study outcome was the adherence to secondary prevention medications and LSMs at 12 months and secondary outcome was adherence at 24 months. We estimated adherence to medications using data regarding each of the four types of medications (anti-platelets, β-blockers, RAS inhibitors, and statin) as well a composite medication adherence score (CMAS).[23] The adherence as well as CMAS was calculated for these four types of medications at one month preceding the final follow-up visit at 12 and 24 months. The CMAS is the proportion of all these four medication taken of those prescribed in the last one month. In case the physician stopped a drug sometime during the preceding month, this drug was not considered in the calculation. Patients who took 80% or more of all the prescribed drugs were categorized as adherent. To assess LSM we used patient self-reports and primary caregiver reports for tobacco consumption or smoking. At the one year follow-up visit, patients initially categorized as 'current' consumers were reclassified as 'former' if they quit tobacco at least one month prior to the final visit. Exercise was classified as none/sedentary or moderate. Diet was assessed with a simple 5-point questionnaire and a score was computed using weekly consumption of vegetables and fruits, whole grain and high fiber foods, sweets, refined grains, deep fried and salty foods and red meat.[21] Higher scores indicated a healthier diet. At 24 month, patients were contacted telephonically to assess drug adherence and lifestyles. Details of all deaths, cause of deaths and number of hospitalization were also obtained in both the groups.

2.3. *Statistical analyses*

The primary outcome in the study was adherence to prescribed cardioprotective medications (antiplatelets, β blockers, RAS blockers and statins) based on visual calendar marking. Other methods considered were counting of pills or self report but were not used because of patient

resistance on qualitative study.[21] We estimated that 100 patients (50 patients in each group) would have sufficient power to detect improvement of ≥15% in drug adherence in the intervention arm relative to the usual care. This sample size has 90% power with alpha of 5%. Power was estimated based on prior studies that demonstrated that ≈50–70% of patients will be adherent at 12 months after discharge from hospital.[23–25] Even with 10% loss in follow-up, there will still be 90 patients (45 patients in each group) at the end of study, which is sufficient to assess the primary outcome. All analyses were performed according to the intention to treat principle using a commercially available software (SPSS, Version 13.0, SPSS Inc., Chicago). Between-group comparisons of continuous variables were performed by *t*-test and categorical variables with χ^2 test. We compared continuous variables which were not normally distributed with the Wilcoxon test. p value <0.05 was considered significant.

3. Results

We randomized 100 eligible patients of acute coronary syndrome (intervention group, $n = 50$ and standard care group, $n = 50$). About half (49%) of the patients had an ST elevation myocardial infarction (STEMI) and the rest had a non-STEMI or unstable angina. The mean age of the patients was 59.0 ± 11 years and majority of the patients were men (84%). Details of the baseline demographic and clinical characteristics are in Table 1. About a fifth smoked or used tobacco, half reported

Table 1 – Baseline demographic and clinical characteristic of study subjects.

	Control group ($n = 50$)	Intervention group ($n = 50$)	p value[a]
Demographic variables			
Mean age (years)	60.7 ± 10.8	57.3 ± 10.5	0.177[b]
Time from symptom onset to hospital, median (IQR)	7.0 (9.2–39.2)	16.0 (10.0–38.0)	0.844[c]
Distance of residence to hospital (km)	19.6 ± 17.4	15.8 ± 13.9	0.503[b]
Diagnoses			
Unstable angina	18 (36.0)	20 (40.0)	0.680
Non ST elevation myocardial infarction	11 (22.0)	2 (4.0)	0.007
ST elevation myocardial infarction (STEMI)	21 (42.0)	28 (56.0)	0.161
Thrombolysed STEMI's	12 (57.1)	16 (57.1)	1.00
Lifestyle risk factors			
Smoking/tobacco use	11 (20.0)	10 (22.0)	0.806
High fat diet	40 (80.0)	37 (74.0)	0.476
High salt diet	31 (62.0)	27 (54.0)	0.418
High calorie diet	25 (50.0)	20 (40.0)	0.315
Low fiber diet	29 (58.0)	28 (56.0)	0.855
Low fruits/vegetables intake	27 (54.0)	26 (52.0)	0.841
Physically inactive	40 (80.0)	41 (82.0)	0.799
Risk factors			
Hypertension	28 (56.0)	26 (52.0)	0.688
Diabetes mellitus	12 (24.0)	16 (32.0)	0.373
Known dyslipidemia	4 (8.0)	3 (6.0)	0.695
Family history of coronary artery disease	7 (14.0)	10 (20.0)	0.424
Prior cardiovascular events	5 (10.0)	3 (6.0)	0.460
Previous coronary intervention	5 (10.0)	2 (4.0)	0.239
Medication taken in the month prior to hospitalization			
Antiplatelets	6 (12.0)	9 (18.0)	0.401
Anti-hypertensive	25 (50.0)	23 (46.0)	0.689
Anti-diabetics	10 (20.0)	16 (32.0)	0.171
In-hospital treatments			
Coronary interventions (PCI or CABG)	43 (86.0)	47 (94.0)	0.182
PCI	36 (83.7)	43 (91.5)	0.085
CABG	7 (16.3)	4 (8.5)	0.337
Medical only	7 (16.3)	3 (6.0)	0.182
Medications at discharge			
Aspirin	50 (100)	50 (100.0)	1.000
RAS blockers	33 (66.0)	38 (76.0)	0.270
β blocker	37 (74.0)	34 (68.0)	0.509
Lipid lowering	50 (100.0)	49 (98.0)	0.219
Diuretics	11 (22.0)	8 (16.0)	0.443
Calcium channel blockers	4 (8.0)	3 (6.0)	0.695

IQR, interquartile range; PCI, percutaneous coronary interventions; CABG, coronary artery bypass grafts; RAS, renin–angiotensin system.
[a] p values determined by χ^2 test unless mentioned.
[b] *t*-Test.
[c] Wilcoxon test.

unhealthy diet, and less than a fifth were physically moderately active. Among STEMI patients 57% were thrombolyzed. In the month prior to hospitalization 15% reported taking an anti-platelet agent, 48% an antihypertensive and 26% antidiabetic medication. Patients prescribed a CVD medication prior to the hospitalization admission reported that they forgot to take their medication more than once a week (20%), stopped medications on their own (9%) and reported not taking medications on time (37%). At admission to hospital, majority of patients were physical inactive (81%) and on unhealthy diet (high fat 77%, high salt 58% and low fiber 57%) while 21% were smokers or used tobacco. Before discharge coronary revascularization was performed in 90% (percutaneous coronary intervention 79%, bypass surgery 11%). At discharge the prescription pattern in the study cohort was: any antiplatelet 100%, dual antiplatelets 93%, β-blockers 71%, RAS inhibitors (ACEI or ARB) 71% and statins 99%. There was no significant difference in intervention and control groups in use of cardiovascular medications at baseline (Table 1).

Follow-up was performed according to the protocol in both intervention and control groups and details of all the patients were obtained periodically. At the end of 12 months, 50 patients in the intervention group and 48 in control group were evaluated (2 patients died in the interim). Proportion of patients receiving cardioprotective drugs (antiplatelets, β-blockers, RAS inhibitors, and statins) at baseline, 12 months and 24 months is shown in Fig. 1. While almost all the patients were on antiplatelet agents or statins at discharge, a lower proportion were on β-blockers and RAS blockers. Attrition is observed in both intervention and control groups over time and the use is significantly greater in intervention group at 12 as well as 24 months (Fig. 1). At the end of 12 months, in intervention vs control group, adherence defined as >80% of drug use (among those prescribed a particular medication) to antiplatelets use was 92.0% vs 77.1% ($p = 0.040$), β blockers in 97.2% vs 90.3% ($p = 0.231$), RAS inhibitors (ACEI or ARB) in 95.1% vs 82.3% ($p = 0.074$) and statins in 94.0% vs 70.8% ($p = 0.002$). Patients taking all the four medications, derived using CMAS, were 93.3% in intervention group vs 86.9% in the control group ($p = 0.431$) (Table 2). At the end of 12 months the average monthly consumption (mean ± 1SD, %) of medication (pills taken/prescribed) in intervention vs control group were antiplatelets in 95.0 ± 4.2 vs 84.1 ± 10.5 ($p < 0.001$), β blockers in 95.2 ± 5.1 vs 84.2 ± 11.0 ($p < 0.001$), RAS inhibitors in 94.8 ± 4.6 vs 82.5 ± 13.1 ($p < 0.001$), and statins in 93.7 ± 8.3 vs 83.1 ± 12.4 ($p < 0.001$) (Table 2).

In both intervention and control groups, adherence decreased over the next 12 months of passive follow-up (Table 2). 3 patients were lost to follow-up (2 intervention, 1 control) and 3 more patients in the control group died. At the end of 24 months, the intervention group had significantly greater adherence to antiplatelets use 83.3% vs 40.9% ($p < 0.001$), β blockers 84.8% vs 45.0% ($p = 0.002$), RAS blockers 89.5% vs 46.1% ($p < 0.001$), and statins 87.5% vs 29.5% ($p < 0.001$) (Table 2). The percent monthly consumption was also greater in the intervention vs control group to antiplatelets 88.3 ± 7.5 vs 79.8 ± 8.1, βblockers 86.5 ± 10.1 vs 75.8 ± 11.6, RAS blockers 87.8 ± 8.8 vs 77.8 + 9.3 and statins 87.0 + 11.8 vs 77.2 + 9.4 (all p values <0.001) (Table 2).

We also evaluated adherence to healthy lifestyles at 12 and 24 months (Fig. 2). In intervention vs control groups smoking prevalence at 12 months was 0.0% vs 12.5% ($p = 0.002$) and 4.2% vs 20.5% at 24 months ($p = 0.010$). Moderate or greater regular physical activity at 12 months was 96.0% vs 50.0% ($p < 0.001$) and 24 months was 37.5% vs 34.1% ($p = 0.733$). Median healthy diet score at 12 months was 5.0 vs 3.0 and 24 months was 4.0 vs 2.0) ($p < 0.001$). Differences in specific dietary intake patterns

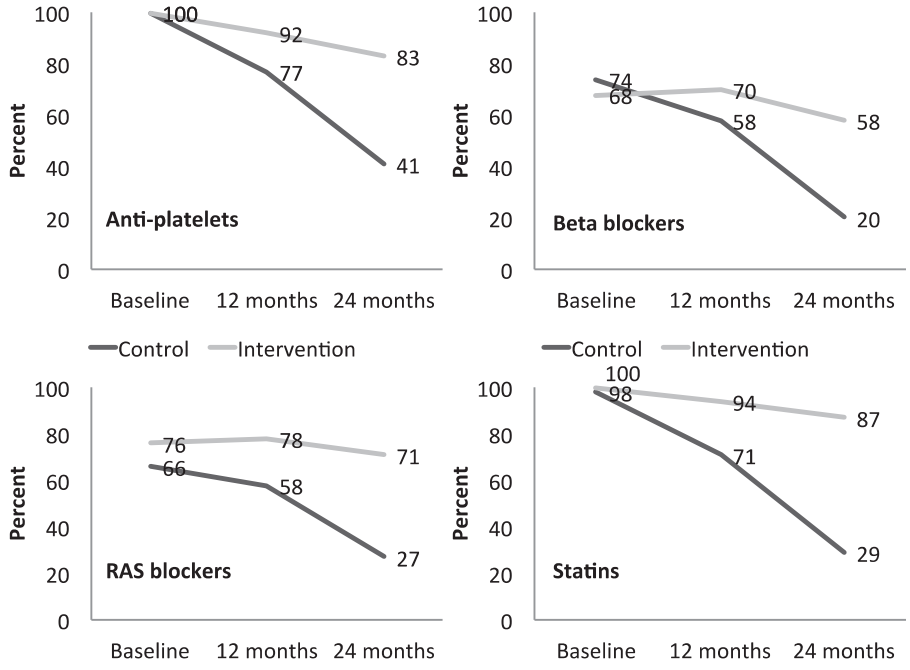

Fig. 1 – Use of various cardioprotective drugs (anti-platelets, β blockers, RAS (renin–angiotensin system) blockers and statins) at 12 months and 24 months in intervention and control groups.

Table 2 – Adherence to various medicines in control and intervention groups at 12 and 24 months.

Drug class		Discharge		At 12 months			At 24 months		
		Control ($n = 50$)	Intervention ($n = 50$)	Control ($n = 48$)	Intervention ($n = 50$)	p value*	Control ($n = 44$)	Intervention ($n = 48$)	p value[a]
Antiplatelets	Prescribed	50	50	48	50		44	48	
	Adherent >80% (n, %)			37 (77.1)	46 (92.0)	0.040	18 (40.9)	40 (83.3)	<0.001
	Average consumption %	–	–	84.1 ± 10.5	95.0 ± 4.2	<0.001	79.8 ± 8.1	88.3 ± 7.5	<0.001
β blockers	Prescribed	37	34	31	36		20	33	
	Adherent >80% (n,%)			28 (90.3)	35 (97.2)	0.231	9 (45.0)	28 (84.8)	0.002
	Average consumption %			84.2 ± 11.0	95.2 ± 5.1	<0.001	75.8 ± 11.6	86.5 ± 10.1	0.001
RAS blockers	Prescribed	33	38	34	41		26	38	
	Adherent >80% (n, %)			28 (82.4)	39 (95.1)	0.074	12 (46.1)	34 (89.5)	<0.001
	Average consumption %			82.5 ± 13.1	94.8 ± 4.6	<0.001	77.8 ± 9.3	87.8 ± 8.8	<0.001
Statins	Prescribed	50	49	48	50		44	48	
	Adherent >80% (n, %)			34 (70.8)	47 (94.0)	0.002	13 (29.5)	42 (87.5)	<0.001
	Average consumption %			83.1 ± 12.4	93.7 ± 8.3	<0.001	77.2 ± 9.4	87.0 ± 11.8	<0.001
All four drugs	Prescribed	29	28	23	30		18	28	
	Adherent >80% (n, %)			20 (86.9)	28 (93.3)	0.431	8 (44.4)	24 (85.7)	0.003
	Average consumption %			76.2 ± 18.8	92.6 ± 5.4	<0.001	66.6 ± 17.4	76.5 ± 17.0	0.015

Numbers in parentheses are percent; Values ± indicate 1 SD; RAS, renin–angiotensin system.
[a] p values derived using χ^2 test for ordinal variables and t-test for continuous variables.

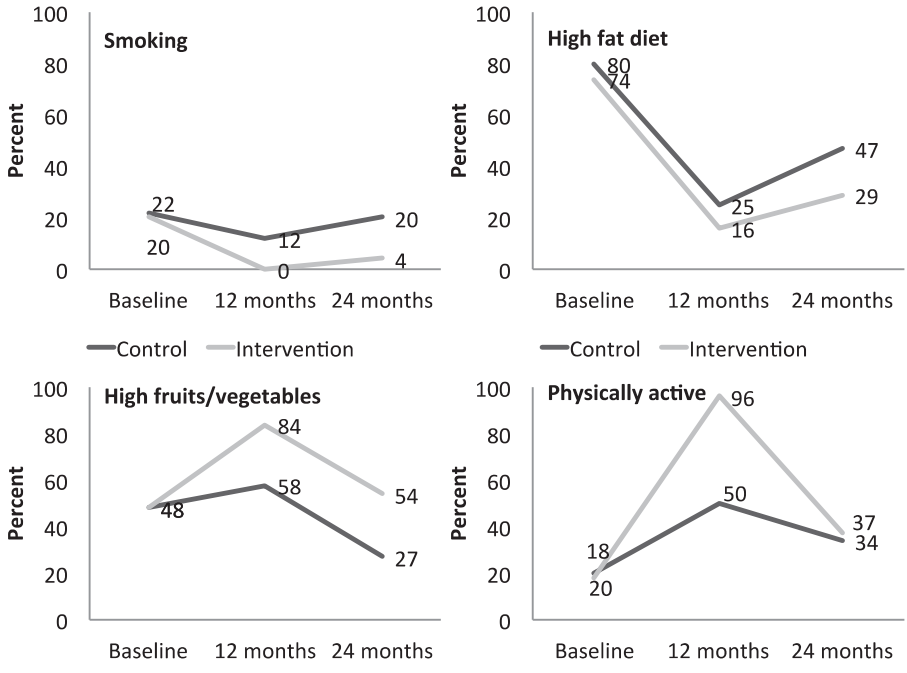

Fig. 2 – Adherence to healthy lifestyles (smoking, high fat diet, high fruits and vegetables consumption and regular physical activity) in control and intervention groups at 12 and 24 months.

in intervention vs control groups at 12 and 24 months, respectively, were high fat diet 16.0 vs 25.0 ($p = 0.269$) and 29.2 vs 47.7 ($p = 0.067$), high calorie food 14.0 vs 27.1 ($p = 0.108$) and 27.1 vs 38.6 ($p = 0.237$), high salt diet 12.0 vs 29.2 ($p = 0.035$) and 22.9 vs 40.9 ($p = 0.063$) and low fruits and vegetable intake 16 vs 43.8 ($p = 0.002$) and 56.3 vs 63.0 ($p = 0.342$) (Table 3).

In the intervention vs control groups, at 12 months, significantly lower values were observed for mean systolic BP (121.2 vs 129.3 mmHg, $p < 0.001$), diastolic BP (79.9 vs 83.8 mmHg, $p < 0.001$), body mass index (23.6 vs 25.8 kg/m^2, $p = 0.006$), waist:hip ratio (0.95 vs 0.99, $p < 0.001$), total cholesterol (152.7 vs 176.7 mg/dL, $p = 0.008$), triglycerides (122.1 vs 152.3 mg/dL, $p = 0.006$) and LDL cholesterol (92.2 vs 106.3 mg/dL, $p = 0.020$) (Table 3). At 24-month follow-up the mean systolic BP and body-mass index increased but significant difference was maintained in intervention vs control group for systolic BP (124.9 vs 135.9 mmHg, $p < 0.001$), diastolic BP (81.9 vs 86.1 mm Hg, $p < 0.001$) and body mass index (24.2 vs

Table 3 – Changes in lifestyle factors, physiological factors and clinical outcomes at 12- and 24-month follow-up.

	12 months			24 months		
	Control group ($n = 48$)	Intervention group ($n = 50$)	p value	Control group ($n = 44$)	Intervention group ($n = 48$)	p value
Lifestyle factors[a]						
Smoking	6 (12.5)	0 (0.0)	0.002	9 (20.5)	02 (4.2)	0.010
High fat intake	12 (25.0)	8 (16.0)	0.269	21 (47.7)	14 (29.2)	0.067
High salt intake	14 (29.2)	6 (12.0)	0.035	18 (40.9)	11 (22.9)	0.064
High calorie intake	13 (27.1)	7 (14.0)	0.108	17 (38.6)	13 (27.1)	0.238
Low fiber intake	8 (16.7)	07 (14.0)	0.714	21 (47.7)	18 (37.5)	0.321
Low fruit/veg intake	21 (43.8)	08 (16.0)	0.003	29 (65.9)	27 (56.3)	0.237
Physical active	24 (50.0)	48 (96.0)	<0.001	15 (34.1)	18 (37.5)	0.733
Physical and biochemical factors[b]						
Systolic BP	129.3 ± 8.0	121.2 ± 5.4	<0.001	135.4 ± 10.8	124.9 ± 6.1	<0.001
Diastolic BP	83.8 ± 5.7	79.9 ± 2.1	<0.001	86.1 ± 6.4	81.9 ± 2.5	<0.001
Heart rate	78.5 ± 7.4	74.9 ± 3.9	0.003	–	–	
Body mass index	25.8 ± 4.3	23.6 ± 3.0	0.006	26.1 ± 3.1	24.2 ± 2.7	0.002
Waist circumference	92.2 ± 17.0	90.5 ± 8.5	0.521	–	–	
Waist:hip ratio	0.99 ± 0.05	0.95 ± 0.03	<0.001	–	–	
Cholesterol	176.7 ± 49.9	152.7 ± 37.5	0.008	–	–	
Triglyceride	152.3 ± 61.2	122.1 ± 44.0	0.006	–	–	
HDL cholesterol	37.2 ± 5.4	39.6 ± 9.5	0.139	–	–	
LDL cholesterol	106.3 ± 28.7	92.2 ± 29.8	0.020	–	–	
Clinical outcomes[a]						
Mortality	2 (4.0)	Nil	0.084	3 (6.2)	Nil	0.032
Hospitalization	4 (8.3)	3 (6.0)	0.680	9 (20.4)	7 (14.6)	0.654

BP, blood pressure.
[a] Comparison using χ^2 test.
[b] Comparison using t-test.

26.1 kg/m^2, $p = 0.002$) (Table 3). We performed a sensitivity analysis comparing changes in systolic BP, body mass index and LDL cholesterol in patients adherent vs non-adherent to therapies at 12 months in both intervention and control groups. In intervention group the decline in systolic BP in adherent vs non-adherent groups was -7.4 ± 17.9 vs -1.5 ± 6.3 mmHg ($p < 0.001$) and in control group was $-3.7 + 16.6$ vs $-2.8 + 15.8$ mmHg ($p = 0.10$). Change in body mass index in adherent vs non-adherent in intervention group was -2.20 ± 0.86 vs -1.65 ± 0.34 kg/m^2 ($p < 0.001$) and in control group was -0.49 ± 1.02 vs -0.47 ± 0.51 ($p = 0.1$). LDL cholesterol also declined more in adherent vs non-adherent in intervention group (-38.1 ± 35.2 vs -5.2 ± 73.5 mg/dL, $p < 0.001$) and not in control group (-18.2 ± 20.8 vs -20.8 ± 34.6 mg/dL, $p = 0.1$). At the end of study period, cumulative incidence of deaths or hospitalization in intervention vs control groups was 3 vs 6 ($p = 0.294$) at 12 months and 7 vs 12 ($p = 0.218$) at 24 months.

4. Discussion

This open-label randomized trial shows that non-physician health worker led educational intervention improves adherence to cardioprotective medications and healthy lifestyles in patients with ACS following hospital discharge. We found that intervention significantly improved adherence to drug therapies as well as lifestyle changes at 12 months of active intervention. The beneficial effects were sustained during passive follow-up for further 12 months although there was significant attrition in adherence to drugs and healthy lifestyles.

There are limited studies that have focused on improving medication adherence among patients following ACS hospitalization using NPHWs or CHWs.[23–25] Most of the studies have used either pharmacist-based approaches,[24–29] individual empowerment,[30–33] or multifacorial approaches.[34–37] In the Netherlands, 754 ACS patients from 11 sites were randomized to a nurse coordinator prevention program with four outpatient visits aimed to improving lifestyle and medication adherence over one year. This trial (RESPONSE) demonstrated a 17.4% ($p = 0.021$) risk reduction as measured by a coronary risk evaluation score.[27] Better adherence to drugs and to LSM led to reductions in heart rate, systolic BP and body mass index at one year. Smith et al. demonstrated that mailed communications to patients after myocardial infarction discharge improved adherence to β-blockers by 4.3%.[30] Ho et al. evaluated a multifactorial approach for patient education led by pharmacists to evaluate adherence to evidence based medications in a study of 253 patients discharged after ACS in the United States.[37] The interventions increased adherence to medications in the year after discharge (89.3% in intervention group vs 73.9% in control group, $p = 0.003$). Similar to our study, the interventions improved adherence to RAS blockers and statins. Unlike our findings there was no improvement in BP and LDL cholesterol levels.

Economic analyses of the studies in developed countries suggest a cost-saving with appropriate secondary prevention.[28] However, all these studies have been performed in developed countries and evaluated trained health workers, e.g., nurses and pharmacists, or used multiple strategies (NPHWs as well as reminders, voice messaging and eliminating insurance co-payments) and demonstrated modest effects

in improving adherence and reducing risk levels. The health systems, patient characteristics and the challenges in India are, however, different from those observed in developed countries and these studies may not be applicable to India or other developing countries.[4] We used a health worker and the results have shown significant improvement in adherence to lifestyles and pharmatherapy at 12 months of intervention which is similar to an earlier study in rural Andhra Pradesh.[38] Uniquely, our study shows that the beneficial effects of this intervention last for a further 12 months showing the legacy effect of our intervention. This legacy effect is similar to long-term protective effects of pharmacological interventions in diabetes and hypercholesterolemia and demonstrates that even non-pharmacological interventions have similar benefits.

The overall adherence rate in our study at one year was more than 90%. This is probably due to the quality of service at the private health care center chosen for the study as well as the motivation level and high education status of the included patients. A very high rate of coronary interventions is observed in our study (90%) compared to previous Indian registries (CREATE 7%, Kerala ACS 12%).[5,6] It is well known that patients who had coronary interventions have better adherence to drug and lifestyle measures, especially following an ACS.[23] NPHW interventions led to high level of adherence to evidence based medications by identifying barriers related to medications (lack of knowledge, cost of drugs, drug side effects and lack of financial support) and by helping the patient find acceptable strategies to overcome them by being a ''health champion''. We observed improvements in all lifestyle parameters in the intervention group. This is likely due to enhanced awareness, support from family and the persistence of the interventions to overcome the barriers. Moreover, we included all patients who consented to participate in the study regardless of their prior adherence behavior and able to comply with the requirements of the interventions, including being able to make the follow-up visits. This could have introduced a selection bias among patients and may explain the high rates of adherence to medications in both groups. High rates of adherence to drug therapies reflect the type of hospitals and quality of physicians, both of which can positively bias the adherence rates. While the medication adherence was evaluated by visual calendar marking patients may still have exaggerated their compliance and this is also a study limitation. We did not use other tools such as pill count, purchase bills or patient diary to document adherence as these likely provide lower specificity as compared to the tools that we designed.

Additional limitations exist in this study. We physically followed up the patients for 12 months and contacted telephonically at 24 month after hospital discharge. It could be important to continue the follow-up of these patients to assess clinical outcomes, however, the sample size is not powered for these measures. Secondly, our intervention included multiple components (physician, hospital counselling, NPHW and family members), all of which have been shown to contribute to improve adherence to medication and lifestyles.[9,20,23,25] Thirdly, our study was conducted within a single non-governmental tertiary care cardiac center and it is not clear whether these results can be replicated in other health care settings in India. And finally, although declines in smoking and other lifestyle measures achieved statistical significance in the intervention group, we are not sure whether these changes would sustain long term as shown by significant attritions (Fig. 2).

In India CVD mortality can be reduced by creation of better healthcare delivery systems and use of NPHW for NCD management.[2,39] Our study demonstrates that non-physician health workers (CHWs) can improve optimal use of evidence-based medications and adequate LSMs following ACS. Use of mobile health technologies to complement efforts of trained NPHWs with lesser number of clinic and home visits may be more effective in improving adherence.[39] Additional studies are needed to assess the association between adherence and clinical outcomes in a larger patient sample with long term follow-up. Our experience and the tools developed for interventions can be adapted and used in similar other hospital settings in India to improve outcomes after an acute coronary event.

Conflicts of interest

The authors have none to declare.

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