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# Effectiveness and medication adherence in patients with ST- elevated myocardial infarction: Persian polypill study

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Original Article

## Abstract

**BACKGROUND:** Polypill or fixed-dose combination has been recognized as an effective secondary prevention strategy for patients with cardiovascular disease (CVD). This study aimed to evaluate the effectiveness of the polypill on one-year medication adherence, patient satisfaction, and lipid profile control in patients with ST-elevation myocardial infarction (STEMI).

**METHODS:** This was an open-label, multicentric, randomized clinical trial study of STEMI patients who were prescribed a polypill (Aspirin 81 mg, Atorvastatin 40 mg, Metoprolol Succinate 47.5 mg, and Valsartan 40 mg) versus usual care (continued with separate medications) for secondary prevention. The primary outcome was to compare one-year medication adherence between groups. Other outcomes included comparing patient satisfaction and lipid profile after 12 months of follow-up, as well as identifying predictor factors of medication adherence.

**RESULTS:** Of 624 STEMI participants, 289 patients were treated with the polypill (79.2% male; mean age 61.67 ± 8.54 years), and 335 patients received usual care (82.7% male; mean age 62.10 ± 9.63 years). After one-year follow-up, no significant differences were detected between groups regarding medication adherence (p-value = 0.351) and cholesterol levels (p-value = 0.808). The polypill strategy was associated with increased patient satisfaction and better control of LDL-C (p-value = 0.043) and HDL-C (p-value < 0.001). Patients with a history of chronic kidney disease (OR: 13.392; p-value = 0.001), cerebrovascular disease (OR: 4.577; p-value = 0.011), and higher waist circumference (OR: 1.01; p-value = 0.002) demonstrated a lower probability of medication adherence. In contrast, in-hospital complications such as arrhythmia (OR: 0.039; p-value = 0.010), bleeding (OR: 0.034; p-value = 0.007), and higher ejection fraction (OR: 0.965; p-value = 0.002) were associated with a higher probability of medication adherence.

**CONCLUSION:** In STEMI patients, participants treated with polypills were more satisfied and showed better lipid profile control. However, a longer follow-up duration is needed to examine the effectiveness of the polypill on medication adherence in this subgroup.

**Keywords:** Polypill; ST Elevation Myocardial Infarction; Medication Adherence; Patient Satisfaction; Lipids

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## Introduction

ST-segment elevation myocardial infarction (STEMI), which accounts for approximately 30% of patients presenting with acute coronary syndrome (ACS), is a clinically time-sensitive fetal condition that results from complete thrombotic occlusion of the infarct-related artery[1,2]. Early reperfusion by percutaneous coronary intervention (PCI) or thrombolytic therapy is the gold standard of treatment for STEM[3]. Despite advancements in long-term survival following STEMI, patients still encounter a heightened risk of recurrent myocardial infarction (MI), stroke, and mortality, particularly in the presence of additional risk factors such as diabetes and hypertension[4]. This underscores the importance of a secondary prevention strategy targeting standard modifiable cardiovascular risk factors[5].

Lipid-lowering drugs, anti-hypertensive agents, and anti-platelet therapy are the guideline-recommended pharmacological treatments for secondary prevention in patients with STEMI[6]. Despite the proven benefits of evidence-based pharmacological secondary prevention, lack of medication adherence remains a significant challenge in STEMI patients due to the complexity of multi-drug prescriptions. Previous studies have shown that adherence to pharmacotherapy was suboptimal in patients after hospital discharge for STEMI[7,8], and medication non-adherence was associated with an increased risk of cardiovascular hospitalizations and mortality, coronary revascularization procedures, and increased costs[9,10].

Wald et al. first described the polypill strategy, which includes combined pharmaceutical components to simultaneously target major cardiovascular risk factors, for both primary and secondary prevention[11]. The concept of the polypill or fixed-dose combination (FDC) has evolved over time to enhance medication adherence and manage CV risk factors. However, several previous studies have provided moderate evidence that the polypill can improve adherence and CV risk factor control in patients with CVD[12-17]. Still, there is a lack of evidence regarding the effectiveness of the polypill in patients with STEMI. Therefore, our study aimed to compare one-year medication adherence, patient satisfaction, and lipid profile control in STEMI patients treated with the polypill versus usual care.

## Methods

### *Study Design*

This was an open-label, multicentric, parallel two-arm, 1:1 allocation randomized clinical trial of polypill treatment compared with usual care in patients with STEMI for 12 months in three referral hospitals (Chamran, Alzahra, and Khorshid) in Isfahan, Iran. This trial has been registered in ClinicalTrials.gov as Persian Polypill Study (Identifier: NCT03541109).

### *Study Participants*

The study included men and women aged over 40 years who were hospitalized in the mentioned hospitals because of their first episode of STEMI, with a clear indication of receiving all components of the polypill (aspirin, statin, ARB/ACE inhibitor, and beta-blocker) and lived in Isfahan city or nearby areas. The indication for drugs was determined by the responsible physician according to the standard guidelines. Patients with mental illness limiting their self-care ability, severe disease with an estimated lifespan of less than 3 years, history of adverse reaction or contraindication to any component of the polypill, secondary hyperlipidemia, serum creatinine $\geq 2$ mg/dl, severe heart failure, childbearing potential, or planning for a procedure (Coronary Artery Bypass Graft Surgery (CABG), PCI, or another surgical procedure) within the following 6 months were excluded from the study.

### *Study Randomization*

Central randomization was used in this study. Blocked randomization with a block size of 5 was used for random sequence generation. An investigator was responsible for randomization, recording a list of patients, and the management of follow-up visits. Responsible physicians in the hospitals assessed patients for eligibility criteria and after obtaining informed consent, they contacted the investigator for the type of intervention allocation. Blinding of investigators and patients was not possible in this study; however, the statistician was blind to the group assignment.

### *Intervention*

The polypill used in this study was available in fixed doses of Aspirin (81mg), Atorvastatin (40mg), Metoprolol Succinate (47.5mg), and Valsartan (40mg) (prepared by Alborz Daroo Company).

The usual care group received regular drug orders at the time of discharge from the hospital. The responsible physician initiated a regimen of polypill drugs in accordance with the current guidelines[18]. If necessary, he/she had the option to switch to a different group of drugs or add a new medication to achieve the treatment objectives. If a patient from the polypill group had been taking any of the four drug classes before hospitalization, the physician could switch to polypill treatment or add individual doses to achieve the desired level of effectiveness. The polypill and those four drug classes were free of charge in this study and were provided to the patients by an individual blind to the two distinct groups.

### *Outcomes*

The primary outcome was to compare the one-year adherence of patients to prescribed medication(s) between the polypill and usual care groups. Additionally, the study aimed to compare patient satisfaction as a secondary outcome. Other outcomes included comparing changes in lipid profile between groups after 12 months and identifying factors associated with medication adherence.

### *Data Collection Methods and Assessments.*

### *Baseline Characteristics*

Baseline demographics (age, sex, marital status, and educational levels), clinical data (past history and family history of diseases, type of treatment, in-hospital complications), and laboratory investigations were collected for each participant using checklists. Waist circumference (WC) and ejection fraction (EF) were collected using appropriate tools and added to the checklist. WC was measured at the narrowest part of the torso between the iliac crest and the xiphoid process or the level of the iliac crest after normal exhalation. EF was determined by a cardiologist using the Philips IE 33 ultrasound machine in the left lateral decubitus position and assessed according to the guidelines[19].

### *Medication Adherence Assessments*

The Persian version of the Morisky Medication Adherence Scale (MMAS-8) was used to assess patients' adherence to medication(s)[20]. It consisted of 8 self-reported questions measuring to what extent the patients follow their doctor's instructions on medication(s) uptake (seven questions with two-choice answers (yes/no) and one Likert question). For the first 7 questions, a score of 0 was given for each "yes" answer and 1 for each "no" answer, except for question 5, which was scored in reverse. Question 8 was a 5-point Likert scale, where "never" = 0, "rarely" = 1, "sometimes" = 2, "often" = 3, and "always" = 4. The total scores ranged from 0 to 8. In this study, scores > 6 were considered good adherence to medication treatment.

### *Patient Satisfaction Assessments*

The Treatment Satisfaction Questionnaire for Medication (TSQM) was used to evaluate patient satisfaction with drug treatment over the previous 2-3 weeks or since the patient's last use. The TSQM comprised 14 items across four domains: effectiveness (three items), side effects (five items), convenience (three items), and global satisfaction (three items). The patients' responses were evaluated using a 5- or 7-point Likert scale, except for question four in the side effects domain, which required a simple yes or no answer. If the response to question 4 was negative, questions 4 to 8 in the side effects domain were not asked. A higher score indicated that patients were more satisfied with their drug treatment. The Persian version of the TSQM has shown acceptable validation and reliability results[21].

### *Lipids Assessments*

Blood sampling and analysis were done in the hospital laboratories for lipid profile (total cholesterol, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C)) after 10 hours of fasting at night.

### *Trial Procedures*

Each participant was followed up for at least 12 months. Laboratory tests, lipid profiles, and questionnaires were obtained six months after recruitment, and at the end of the study.

### *Ethical Statement*

The ethics committee of Isfahan University of Medical Sciences approved the informed consent (approval number: IR.NIMAD.REC.1396.24). The study was conducted in accordance with the Declaration of Helsinki.

### *Statistical Analysis*

Quantitative variables were presented as mean ± standard deviation (SD), and qualitative variables as numbers and percentages (%). The normality assumption was assessed using the Kolmogorov-Smirnov test, with a p-value < 0.05 indicating that the variable did not meet the normality assumption. We used the independent sample t-test and Mann-Whitney test to assess quantitative variables, while categorical variables were compared using the Chi-square test (or Fisher's exact test when appropriate). Variables significantly associated with medication adherence in these analyses were examined using logistic regression, reporting the odds ratios (OR) and confidence intervals (CI) for predictive variables. Good adherence is reference variable. Statistical analysis was performed using IBM SPSS (IBM Corporation, Armonk, NY, USA) statistics for Windows version 20 and was considered significant when the p-value was < 0.05.

## Results

### *Baseline Characteristics*

A total of 624 patients with STEMI (81.1% male; mean age 61.90 ± 9.14 years) who met the inclusion and exclusion criteria were screened: 289 patients treated with polypill (79.2% male; mean age 61.67 ± 8.54 years) and 335 patients with usual care (82.7% male; mean age 62.10 ± 9.63 years). At baseline, patients treated with polypill had higher WC (100.60 ± 11.62 vs 93.39 ± 17.40 cm; p-value < 0.001), HDL-C (41.09 ± 7.97 vs 39.38 ± 6.82 mg/dl; p-value = 0.002) and lower LDL-C (101.86 ± 22.34 vs 106.54 ± 26.40 mg/dl; p-value = 0.028) than patients with usual care. The baseline characteristics of study participants are shown in Table 1.

### *Medication Adherence and Patient Satisfaction Comparison*

At the end of the study, 247 patients (39.58%) were good adherence to medical treatment. One-year medication adherence was similar between the polypill (6.9%) and the usual care group (8.1%) (p-value= 0.351). Patients treated with polypill showed significantly higher satisfaction, especially in the convenience (13.15 ± 1.78 vs 12.23 ± 1.45; p-value < 0.001) and global satisfaction (13.06 ± 1.97 vs 12.75 ± 1.18; p-value < 0.001) domains of TSQM (Table 2). It is important to note that the adverse effects domain score was also higher in the polypill group than in the usual care group (5.65 ± 6.05 vs 2.95 ± 2.75; p-value < 0.001).

### *Lipid Profile Comparison*

At the end of the study, the polypill group showed higher HDL-C (41.40 ± 19.90 vs 37.92 ± 7.6 mg/dl; p-value < 0.001) and lower LDL-C (77.06 ± 17.31 vs 82.89 ± 58.01 mg/dl; p-value = 0.043) than patients in the usual care group (Table 2). However, there was no significant difference in cholesterol levels between groups (144.57 ± 26.86 vs 144.19 ± 41.60 mg/dl; p-value = 0.808).

### *Factors Associated with Medication Adherence*

Using a Multilevel Logistic Regression, a lower probability of adherence was observed in patients with a history of cerebrovascular diseases (OR (95% CI): 4.577 (1.410-14.860); p-value = 0.011), history of CKD (OR (95% CI): 13.392 (2.827-63.435); p-value = 0.001), and patients with higher WC (OR (95% CI): 1.01 (1.004-1.035); p-value = 0.002). In contrast, in-hospital complications such as atrial tachyarrhythmia (OR (95% CI): 0.039 (0.003-0.458); p-value = 0.010) and bleeding (OR (95% CI): 0.034 (0.003-0.399); p-value = 0.007) and higher EF (OR (95% CI): 0.957 (0.930-0.984); p-value = 0.002) were associated with a higher probability of medication adherence (Tables 3 and 4).

## Discussion

To the best of our knowledge, this was the first study to investigate medication adherence, patient satisfaction, and CV risk factor control in patients with STEMI using either a polypill or usual care for secondary prevention. The study found that medication adherence and cholesterol levels were similar between groups after 12 months. However, patients receiving polypill treatment showed higher satisfaction and better lipid profile control compared to those receiving usual care at the end of the study. Additionally, it was demonstrated that a history of CKD, a history of cerebrovascular disease, EF, WC, and in-hospital complications were independent predictors of medication adherence.

The results of our study showed that fewer than forty percent of the participants adhered to their medical treatment, and the one-year medication

**Table 1.** Baseline Characteristics of Study Participants in Polypill and Usual Care Groups.

| Characteristics | | Polypill group n=289 | Usual care group n=335 | Total n=624 | P value |
|---|---|---|---|---|---|
| **Age (years), Mean (SD)** | | 61.67(8.54) | 62.10(9.63) | 61.90(9.14) | 0.576 |
| **Male, n (%)** | | 229(79.20) | 277(82.70) | 506(81.10) | 0.160 |
| **Married, n (%)** | | 265(91.70) | 296(88.40) | 561(90.00) | 0.103 |
| **Educational Levels, n (%)** | 0-5 Years | 69(23.90) | 145(43.30) | 214(34.30) | <0.001 |
| | 6-12 years | 213(73.70) | 140(41.80) | 353(56.60) | |
| | >12 Years | 7(2.40) | 50(14.90) | 57(9.10) | |
| **Past Medical History, n (%)** | | | | | |
| **HTN** | | 84(29.00) | 98(29.30) | 182(29.20) | 0.487 |
| **DM** | | 75(25.90) | 93(27.70) | 168(26.90) | 0.351 |
| **Dyslipidemia** | | 86(29.70) | 111(33.00) | 197(31.60) | 0.221 |
| **Cerebrovascular disease** | | 7(2.40) | 12(3.50) | 19(2.90) | 0.324 |
| **CKD** | | 5(1.70) | 3(0.90) | 8(1.20) | 0.363 |
| **Clinical Manifestation, Mean (SD)** | | | | | |
| **WC (cm)** | | 100.60(11.62) | 93.39(17.40) | 96.73(15.42) | <0.001 |
| **EF** | | 39.25(7.46) | 38.91(9.82) | 39.07(8.80) | 0.300 |
| **Family History, n (%)** | | | | | |
| **HTN** | | 125(43.30) | 160(47.70) | 285(45.70) | 0.164 |
| **DM** | | 118(40.80) | 126(37.60) | 244(39.00) | 0.237 |
| **Dyslipidemia** | | 94(32.50) | 108(32.20) | 202(32.40) | 0.511 |
| **MI** | | 162(56.10) | 172(51.40) | 334(53.50) | 0.135 |
| **Laboratory Data, Mean (SD)** | | | | | |
| **LDL-C (mg/dl)** | | 101.86(22.34) | 106.54(26.40) | 104.37(24.70) | 0.028 |
| **HDL-C (mg/dl)** | | 41.09(7.97) | 39.38(6.82) | 40.17(7.42) | 0.002 |
| **TG (mg/dl)** | | 149.71(60.12) | 147.26(68.94) | 148.39(64.97) | 0.301 |
| **Cholesterol (mg/dl)** | | 175.60(44.33) | 176.15(28.42) | 175.90(36.62) | 0.156 |
| **Creatinine (mg/dl)** | | 1.03(0.52) | 1.07(0.21) | 1.05(0.38) | <0.001 |
| **Type of Treatment, n (%)** | | | | | |
| **Primary PCI & CABG** | | 277 (95.80) | 326 (97.30) | 589 (96.40) | 0.101 |
| **Thrombolysis** | | 2(0.70) | 9(2.70) | 11(1.80) | 0.055 |
| **In-Hospital Complications, n (%)** | | | | | |
| **Atrial tachyarrhythmia** | | 0(0.00) | 4(1.19) | 4(0.64) | |
| **Ventricular tachyarrhythmia** | | 0(0.00) | 12(3.60) | 12(1.92) | 0.151 |
| **Bleeding** | | 5(1.70) | 2(0.60) | 7(1.20) | 0.399 |
| **AF** | | 0(0.00) | 11(3.30) | 11(1.80) | 0.582 |

SD: Standard Deviation, HTN: Hypertension, DM: Diabetes Mellitus, CKD: Chronic Kidney Disease, WC: Waist Circumference, EF: Ejection Fraction, MI: Myocardial Infarction, LDL-C: Low-density Lipoprotein Cholesterol, HDL-C: High-density Lipoprotein Cholesterol, TG: Triglyceride, PCI: Percutaneous Intervention, CABG: Coronary Artery Bypass Graft, AF: Atrial Fibrillation. P value < 0.05 is significant.

adherence rate was similar between the polypill and usual care groups. Castellano et al. conducted a randomized clinical trial, SECURE trial, comparing the efficacy of the polypill-based strategy with the usual care for secondary prevention in patients with MI[22]. The previous RCT reported significant improvement in medication adherence after 6 months in patients receiving polypills compared with patients in the usual care group (70.6 % vs 62.7%; risk ratio (95% CI): 1.13 (1.06-1.20)). At 24 months, medication adherence also increased in the polypill group more than usual care group (74.1% vs 63.2%; risk ratio (95% CI): 1.17 (1.10-1.25))[22].

One possible explanation for the discrepancy in our study could be the characteristics of the participants, as patients with STEMI showed lower adherence rates to optimal medication treatment for secondary prevention[23]. Additionally, the relatively low adherence rate observed in both groups in our study may be attributed to the novelty of the polypill concept in our region, which might influence patients' acceptance of the medication. Factors

**Table 2.** Comparison of Patient Satisfaction and Lipid Profile between Polypill and Usual Care Groups.

| | Polypill group n=289 | Usual care group n=335 | Total n=624 | P value | Treatment effect | 95% CI | | P value |
|---|---|---|---|---|---|---|---|---|
| **Patient Satisfaction** | | | | | | | | |
| **TSQM domain, Mean (SD)** | | | | | | | | |
| **Effectiveness** | 8.94(0.36) | 8.87(0.74) | 8.90(0.60) | 0.681 | 1.016 | 0.998 | 1.034 | 0.081 |
| **Adverse effects** | 5.65(6.06) | 2.95(2.75) | 4.20(4.78) | <0.001 | 0.947 | 0.922 | 0.973 | <0.001 |
| **Convenience** | 13.15(1.78) | 12.23(1.45) | 12.72(1.70) | <0.001 | 0.978 | 0.935 | 0.989 | 0.007 |
| **Global satisfaction** | 13.06(1.97) | 12.75(1.18) | 12.92(1.66) | 0.001 | 0.986 | 0.945 | 0.995 | 0.034 |
| **Lipid Profile** | | | | | | | | |
| **Cholesterol (mg/dl)** | 144.57 (26.86) | 144.19 (41.60) | 144.37 (35.51) | 0.808 | 1.001 | 1.000 | 1.002 | 0.081 |
| **LDL-C (mg/dl)** | 77.06 (17.31) | 82.89 (58.01) | 80.19 (44.17) | 0.043 | 1.002 | 1.000 | 1.004 | 0.018 |
| **HDL-C (mg/dl)** | 41.40 (19.90) | 37.92 (7.6) | 39.78 (15.56) | <0.001 | 0.997 | 0.991 | 0.999 | 0.007 |

TSQM: Treatment Satisfaction Questionnaire for Medication, LDL-C: Low-density Lipoprotein Cholesterol, HDL-C: High-density Lipoprotein Cholesterol, SD: Standard Deviation, CI: Confidence Interval. P value < 0.05 is significant.

**Table 3.** Characteristics of study participants based on adherence levels.

| Characteristics | | Non-Adherence n=377 | Good-Adherence n=247 | Total n=624 | P value |
|---|---|---|---|---|---|
| **Age (years), Mean (SD)** | | 61.77(9.12) | 63.55(9.25) | 61.90(9.14) | 0.130 |
| **Male, n (%)** | | 306(81.16) | 200(80.97) | 506(81.08) | 0.546 |
| **Married, n (%)** | | 341(90.45) | 205(83.00) | 546(87.50) | 0.150 |
| **Educational Levels, n (%)** | 0-5 Years | 129(34.21) | 85(34.41) | 214(34.30) | |
| | 6-12 years | 221(58.62) | 79(31.98) | 300(48.08) | 0.658 |
| | >12 Years | 26(6.89) | 84(34.00) | 110(17.62) | |
| **Past Medical History, n (%)** | | | | | |
| **HTN** | | 108(28.64) | 84(34.00) | 192(30.77) | 0.281 |
| **DM** | | 99(26.25) | 84(34.00) | 183(29.32) | 0.171 |
| **Dyslipidemia** | | 119(31.56) | 73(29.55) | 192(30.76) | 0.454 |
| **Cerebrovascular disease** | | 90(23.87) | 26(10.52) | 116(18.58) | 0.031 |
| **CKD** | | 34(9.01) | 16(6.47) | 50(8.01) | 0.011 |
| **Clinical Manifestation, Mean (SD)** | | | | | |
| **WC (cm)** | | 96.79(15.45) | 96.02(15.13) | 96.73(15.42) | 0.481 |
| **EF** | | 39.22(8.85) | 37.17(7.99) | 39.07(8.80) | 0.091 |
| **Family History, n (%)** | | | | | |
| **HTN** | | 173(45.88) | 105(42.51) | 278(44.55) | 0.544 |
| **DM** | | 145(38.46) | 110(44.53) | 255(40.86) | 0.329 |
| **Dyslipidemia** | | 120(31.83) | 95(38.46) | 215(34.45) | 0.221 |
| **MI** | | 197(52.25) | 163(66.00) | 360(57.69) | 0.059 |
| **Laboratory Data, Mean (SD)** | | | | | |
| **LDL-C (mg/dl)** | | 103.99(24.70) | 109.06(24.50) | 104.37(24.70) | 0.135 |
| **HDL-C (mg/dl)** | | 40.14(7.48) | 40.63(6.58) | 40.17(7.42) | 0.891 |
| **TG (mg/dl)** | | 147.93(65.20) | 154.05(62.35) | 148.39(64.97) | 0.902 |
| **Cholesterol (mg/dl)** | | 175.38(36.75) | 182.12(34.77) | 175.90(36.62) | 0.156 |
| **Creatinine (mg/dl)** | | 1.05(0.39) | 1.09(0.18) | 1.05(0.38) | 0.027 |
| **Type of Treatment, n (%)** | | | | | |
| **Primary PCI & CABG** | | 361 (97.34) | 241 (97.57) | 602 (96.47) | 0.497 |
| **Thrombolysis** | | 6(1.59) | 5(2.02) | 11(1.76) | 0.582 |
| **In-Hospital Complications, n (%)** | | | | | |
| **Atrial tachyarrhythmia** | | 1(0.26) | 16(6.47) | 17(2.72) | 0.022 |
| **Ventricular tachyarrhythmia** | | 11(2.91) | 10(4.04) | 21(3.36) | 0.652 |
| **Bleeding** | | 1(0.26) | 26(10.52) | 27(4.30) | 0.022 |
| **AF** | | 6(1.59) | 11(4.45) | 17(2.72) | 0.486 |

SD: Standard Deviation, HTN: Hypertension, DM: Diabetes Mellitus, CKD: Chronic Kidney Disease, WC: Waist Circumference, EF: Ejection Fraction, MI: Myocardial Infarction, LDL-C: Low-density Lipoprotein Cholesterol, HDL-C: High-density Lipoprotein Cholesterol, TG: Triglyceride, PCI: Percutaneous Intervention, CABG: Coronary Artery Bypass Graft, CHF: Congestive Heart Failure, AF: Atrial Fibrillation. P value < 0.05 is significant.

**Table 4.** Multivariable analysis in determining factors associated with medication adherence (age and sex-adjusted).

| Characteristics | | OR* | 95% CI | | P value |
|---|---|---|---|---|---|
| **Married (vs. other marital status)** | | 1.446 | 0.608 | 3.438 | 0.404 |
| **Educational Levels** | 0-5 Years | Ref. | | | |
| | 6-12 years | 1.331 | 0.715 | 2.475 | 0.366 |
| | >12 Years | 0.930 | 0.344 | 2.506 | 0.886 |
| **Past Medical History** | | | | | |
| **HTN** | | 0.831 | 0.424 | 1.628 | 0.592 |
| **DM** | | 0.747 | 0.380 | 1.470 | 0.400 |
| **Dyslipidemia** | | 1.215 | 0.611 | 2.409 | 0.578 |
| **Cerebrovascular disease** | | 4.577 | 1.410 | 14.860 | 0.011 |
| **CKD** | | 13.392 | 2.827 | 63.435 | 0.001 |
| **Clinical Manifestation** | | | | | |
| **WC (cm)** | | 1.01 | 1.004 | 1.035 | 0.011 |
| **EF** | | 0.957 | 0.930 | 0.984 | 0.002 |
| **Family History** | | | | | |
| **HTN** | | 1.239 | 0.683 | 2.247 | 0.479 |
| **DM** | | 0.976 | 0.535 | 1.782 | 0.938 |
| **Dyslipidemia** | | 0.904 | 0.489 | 1.672 | 0.751 |
| **MI** | | 0.740 | 0.413 | 1.362 | 0.346 |
| **Laboratory Data** | | | | | |
| **LDL-C (mg/dl)** | | 0.996 | 0.986 | 1.006 | 0.482 |
| **HDL-C (mg/dl)** | | 0.968 | 0.934 | 1.003 | 0.076 |
| **TG (mg/dl)** | | 0.999 | 0.994 | 1.004 | 0.632 |
| **Cholesterol (mg/dl)** | | 0.996 | 0.989 | 1.003 | 0.297 |
| **Creatinine (mg/dl)** | | 0.842 | 0.308 | 2.296 | 0.736 |
| **Type of Treatment** | | | | | |
| **Primary PCI & CABG** | | 0.542 | 0.212 | 1.386 | 0.201 |
| **Thrombolysis** | | 0.859 | 0.106 | 6.896 | 0.886 |
| **In-Hospital Complications** | | | | | |
| **Atrial tachyarrhythmia** | | 0.039 | 0.003 | 0.458 | 0.010 |
| **Ventricular tachyarrhythmia** | | 0.903 | 0.111 | 7.378 | 0.924 |
| **Bleeding** | | 0.034 | 0.003 | 0.399 | 0.007 |
| **AF** | | 0.715 | 0.081 | 0.862 | 0.763 |

*Adjusted for Sex and Age. OR: Odds Ratio, CI: Confidence Interval, HTN: Hypertension, DM: Diabetes Mellitus, CKD: Chronic Kidney Disease, WC: Waist Circumference, EF: Ejection Fraction, MI: Myocardial Infarction, LDL-C: Low-density Lipoprotein Cholesterol, HDL-C: High-density Lipoprotein Cholesterol, TG: Triglyceride, PCI: Percutaneous Intervention, CABG: Coronary Artery Bypass Graft, CHF: Congestive Heart Failure, AF: Atrial Fibrillation. P value < 0.05 is significant.

affecting the acceptance of the polypill could include personal beliefs regarding the ineffectiveness of a single pill to manage risk factors such as hyperlipidemia and hypertension, concerns about potential adverse events, and a lack of substantial evidence supporting its effectiveness in preventing cardiovascular events[24]. Furthermore, differences in the duration of follow-up and physicians' concerns regarding the effectiveness of the polypill, which led to discontinuing its use, could explain the differences with the previous study.

In terms of patient satisfaction, our results showed that patients treated with the polypill were more satisfied than the usual care group, with significantly higher scores in the convenience and global satisfaction domains of TSQM. These findings were consistent with the Aurora study, which also showed that polypill patients reported higher satisfaction in effectiveness, convenience, and global satisfaction compared to patients treated with monocomponents[25]. Our findings regarding patient satisfaction align with those of a comparative study evaluating satisfaction levels between a cardiovascular polypill and separate pills. The study demonstrated a significantly higher degree of satisfaction with polypill therapy, and a high proportion of patients receiving the individual components stated that they would prefer the polypill[17].

Dyslipidemia is a major modifiable risk factor for CVD[26]. Previous studies have demonstrated that an increase in triglycerides, total cholesterol, LDL-C, and a decrease in HDL-C are significantly correlated with the risk of CVD[27]. Due to perceptions of various medications among patients with CVD, only a small number of them remain adherent to medical treatment. More than fifty percent of them have uncontrolled hypertension and dyslipidemia rates, posing a significant challenge to global health[28,29]. The use of a polypill seems to be an effective strategy to improve the rates of adequate control of cardiovascular risk factors and reduce cardiovascular mortality by simplifying medication therapy[29].

The polypill-based strategy showed positive effects on lipid profile enhancement[30,31]. Better lipid profile control was achieved in patients treated with the polypill in our study. This finding was in line with a retrospective observational study of 6,117 patients with IHD, which showed a greater reduction in LDL-C in patients treated with the CNIC polypill[32]. It was also demonstrated in the Bacus study that the CV polypill for secondary prevention enhances lipid profile control regardless of the patient's BMI[33].

The FOCUS project identified several factors that predicted non-adherence to polypill medication, including age under 50, depression, low social support, low insurance coverage, and treatment complexity[34]. Our study expanded on these findings by adding a history of CKD, a history of cerebrovascular disease, EF, WC, and in-hospital complications as additional predictors of medication adherence.

Patients with CKD have been shown to have poor medication adherence in previous studies. The high cost of treatment, fear of drug interactions, concerns about multi-drug treatment, and doubts about the real efficacy of some prescribed drugs may explain non-adherence among CKD patients[35,36]. Furthermore, Tanashyan et al. demonstrated inadequate adherence to treatment among patients with cerebrovascular disease. Factors contributing to this condition include cognitive impairment, a higher number of prescribed medications, and the presence of comorbid conditions such as diabetes mellitus and hypertension[37]. Our findings are consistent with prior research, suggesting that comorbidities such as CKD and cerebrovascular disease may increase the probability of medication non-adherence[38,39]. We also found reduced left ventricular EF (LVEF) predicted non-adherence to the polypill strategy. LVEF is a powerful predictor of poor outcomes in patients with STEMI, and patients with lower LVEF are at high risk of mortality[40,41].

The likelihood of medication adherence was higher in patients with in-hospital complications such as atrial tachyarrhythmia and bleeding. It appears that patients who experience complications during their hospital stay are more likely to accept prescribed medication. This is because they want to reduce the risk of re-hospitalization and prevent the recurrence of adverse events.

## Conclusions

According to our results, in STEMI, using the polypill-based approach showed a similar one-year medication adherence rate versus usual care, despite increased patient satisfaction and lipid profile improvement. We also identified CKD, cerebrovascular disease, EF, WC, and in-hospital complications as medication adherence predictors.

### *Strength and Limitations*

This study was the first to assess the effect of the polypill as a secondary prevention strategy on medication adherence, satisfaction, and CV risk factors in a large cohort of STEMI patients, which is a clear strength of the study. However, our analysis has some limitations. Firstly, the follow-up duration was relatively short, and an extended follow-up period is essential to evaluate a more comprehensive analysis of the impact of polypills on medication adherence in this subgroup. Secondly, we were unable to find a reasonable explanation for the significant correlation between waist circumference and medication adherence. Third, 81 percent of participants were male and the results of the study may not be generalized. Given these limitations, the results should be interpreted with caution.

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## Conflict of interests

All authors declare that there is no conflict of interest.

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## Author's Contributions

Conceptualization: MS, ShG, HR; Data Curation: EA, AA, MKA, ZTJ, JN, HS, AKF, MA, KH; Formal Analysis: HR, MM; Funding Acquisition: MS, EA, ESh, ShG; Investigation: MS, Esh; Methodology: MS, HR, ShG, AN; Supervision: MS, ESh, MA; Validation: MS, HR; Writing, Review, Editing & Final approval: all of the authors.

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