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ORIGINAL INVESTIGATIONS

A Polypill Strategy to Improve Adherence

Results From the FOCUS Project

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CME Objective for This Article: After reading this article the reader should be able to explain: 1) the prevalence and significance of medication nonadherence; 2) the factors associated with medication nonadherence; and 3) the efficacy, safety, and tolerability of a fixed-dose combination polypill to improve medication adherence.

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A Polypill Strategy to Improve Adherence

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ABSTRACT

BACKGROUND Adherence to evidence-based cardiovascular (CV) medications after an acute myocardial infarction (MI) is low after the first 6 months. The use of fixed-dose combinations (FDC) has been shown to improve treatment adherence and risk factor control. However, no previous randomized trial has analyzed the impact of a polypill strategy on adherence in post-MI patients.

OBJECTIVES The cross-sectional FOCUS (Fixed-Dose Combination Drug for Secondary Cardiovascular Prevention) study (Phase 1) aimed to elucidate factors that interfere with appropriate adherence to CV medications for secondary prevention after an acute MI. Additionally, 695 patients from Phase 1 were randomized into a controlled trial (Phase 2) to test the effect of a polypill (containing aspirin 100 mg, simvastatin 40 mg, and ramipril 2.5, 5, or 10 mg) compared with the 3 drugs given separately on adherence, blood pressure, and low-density lipoprotein cholesterol, as well as safety and tolerability over a period of 9 months of follow-up.

METHODS In Phase 1, a 5-country cohort of 2,118 patients was analyzed. Patients were randomized to either the polypill or 3 drugs separately for Phase 2. Primary endpoint was adherence to the treatment measured at the final visit by the self-reported Morisky-Green questionnaire (MAQ) and pill count (patients had to meet both criteria for adherence at the in-person visit to be considered adherent).

RESULTS In Phase 1, overall CV medication adherence, defined as an MAQ score of 20, was 45.5%. In a multivariable regression model, the risk of being nonadherent (MAQ <20) was associated with younger age, depression, being on a complex medication regimen, poorer health insurance coverage, and a lower level of social support, with consistent findings across countries.

In Phase 2, the polypill group showed improved adherence compared with the group receiving separate medications after 9 months of follow-up: 50.8% versus 41% ($p = 0.019$; intention-to-treat population) and 65.7% versus 55.7% ($p = 0.012$; per protocol population) when using the primary endpoint, attending the final visit with MAQ $= 20$ and high pill count (80% to 110%) combined, to assess adherence. Adherence also was higher in the FDC group when measured by MAQ alone (68% vs. 59%, $p = 0.049$). No treatment difference was found at follow-up in mean systolic blood pressure (129.6 mm Hg vs. 128.6 mm Hg), mean low-density lipoprotein cholesterol levels (89.9 mg/dl vs. 91.7 mg/dl), serious adverse events (23 vs. 21), or death (1, 0.3% in each group).

CONCLUSIONS For secondary prevention following acute MI, younger age, depression, and a complex drug treatment plan are associated with lower medication adherence. Meanwhile, adherence is increased in patients with higher insurance coverage levels and social support. Compared with the 3 drugs given separately, the use of a polypill strategy met the primary endpoint for adherence for secondary prevention following an acute MI. (Fixed Dose Combination Drug [Polypill] for Secondary Cardiovascular Prevention [FOCUS]; NCT01321255) (J Am Coll Cardiol 2014;64:2071–82)

Mortality due to cardiovascular diseases (CVDs) is still rising in low- and middle-income countries (LMIC), and is expected to surpass communicable diseases as the leading cause of death by 2030 (1). In high-income countries, however, CVD mortality rates are stable or even decreasing, mainly due to the appropriate administration of evidence-based drug treatments (e.g., statins, antihypertensive and antithrombotic agents) in patients at high risk, particularly those recovering from an acute coronary event (2). It has been estimated that one-half of the overall reduction in CVD mortality observed over the past 20 years in western countries could be attributed to appropriate use of cardiovascular (CV) medications for secondary prevention (3).

Despite these advances, significant evidence highlights the existence of a gap in drug treatment and