


**Editorial**

# Use of polypill to improve therapeutic adherence and outcomes in adults with recent acute myocardial infarction: is it an effective strategy?

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## Uso de polipíldora para mejorar la adherencia terapéutica y los resultados en adultos con infarto agudo de miocardio reciente: ¿es una estrategia efectiva?

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Cardiovascular diseases remain the leading cause of morbidity and mortality in the world, generating an

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unsustainable global disease burden [1,2]. The World Health Organization estimates that approximately 18 million people die annually from cardiovascular complications (32% of all deaths worldwide, mainly from acute myocardial infarction and cerebrovascular disorders) and that more than 75% occur in low- and middle-income countries [1]. Because of this, the global health agenda defined as a priority the control of the most prevalent chronic non-communicable diseases, based on primary and secondary prevention strategies [2]. The polypill is a therapeutic strategy aimed at helping drug adherence, studied in depth in cardiovascular diseases [3, 4]. However, due to the social, cultural, economic and health differences in the different regions, it has not been precisely defined whether it is an effective and reproducible strategy, despite having shown promising results.

Very recently, Castellano et al [5] published the results of a randomized controlled trial, where they enrolled 2499 individuals with a history of acute myocardial infarction 6 months prior and administered the polypill strategy (Aspirin 100 mg, Ramipril 2.5/5/10 mg and Atorvastatin 20/40 mg) vs. usual care. Cardiovascular death, nonfatal acute myocardial infarction type 1, myocardial ischemia, or urgent need for revascularization were evaluated as outcomes. During a median follow-up of 36 months, 118/1237 (9.5%) major cardiovascular events occurred in the intervention group vs. 156/1229 (12.7%) in the control group (Hazard Ratio [HR] 0.76; 95% CI 0.60 - 0.96,  $p=0.02$ ). The reported adherence was higher in the polypill group and adverse events were similar between the groups. This allowed the authors to conclude that the polypill was an effective and safe strategy in the prevention of major cardiovascular events in those with a recent history of acute myocardial infarction [5].

The same results have been obtained in other countries such as India [6] and Spain [3, 4], although the evidence supporting these studies is limited. Barrios et al [3] carried out a cost-effectiveness study in Spain on a simulated model, where they evaluated the 10-year cardiovascular outcomes in a male population with an average age of 64 years and a history of infarction, who would be administered polypill. They found that using this strategy would prevent 46 non-fatal events and 11 fatal events per 1000 individuals treated. Probability analysis showed that this strategy would be approximately 90% more effective than multiple monotherapies, saving thousands of euros per quality-adjusted life year [3]. In the same country, Ros-Castelló et al [4] evaluated the potential of the polypill on the secondary prevention of cerebrovascular disease in a cohort of 104 patients (54 received the polypill vs. 50 received conventional treatment). Their results showed a reduction in

systolic blood pressure in the intervention group ( $p=0.002$ ), but without finding superiority in the effect on cholesterol (41% vs. 44%). Adverse events were moderate and similar in both groups, as well as adherence to treatment (93% vs. 88%) and stroke recurrence at 90 days (0% vs. 1%) [4]. This allowed the authors to conclude that there were no significant differences in adherence, as opposed to the reduction in systolic pressure. In India, Singh et al [6] conducted a cost-effectiveness study on the use of the polypill in secondary prevention vs. usual care, observing a significantly lower cost per patient with the polypill (-\$203,  $p < 0.001$ ). According to variations, a price of \$0.94 per polypill was estimated, resulting to be cost-effective due to the outcomes obtained in previous studies [6].

In Latin America, particularly in Colombia [7] and Chile [8], studies have been carried out to measure drug adherence in secondary prevention for cardiovascular diseases, showing that it is less than 70% [7,8]. However, it is necessary to highlight that this adherence is affected by certain dimensions such as socioeconomic, provider-related, therapy experience-related and personal factors of the patient. Thus, 70% adherence cannot be expected in poor communities where out-of-pocket expenses do not allow for the independent cost of drugs, in areas where health systems fall short of providing drugs, where side effects and social myths prevent a rational weighing of the benefit-risk of therapy, and where scientific literacy and health education is scarce, which does not allow the patient to understand the relevance of adherence to treatment [7, 8].

Thus, and according to the current needs of global health that must be matched by evidence-based medicine [9-11], it is necessary to: 1) Design studies to obtain primary data on the behavior of this effect in each region, adapted to its social and health context; 2) To rigorously evaluate the methodological and reporting quality of the evidence on polypills in secondary prevention of cardiovascular disease; 3) Attempt to establish through public policies the use of the polypill, achieving an affordable purchase rate for health systems and providers, so that it can be reproducible and full coverage of the population in need can be obtained. This could be a tool with a substantial positive impact in the medium- and long-term on global cardiovascular health, especially in the regions with the greatest need for cardiometabolic health care.

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## 1. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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