Polypill: The Path from Concept to “Near” Reality in Preventing Cardiovascular Disease

Dear Editor,

In a landmark paper in 2003 Wald and Law coined the term “polypill”, a pill containing antihypertensives, antiplatelet (aspirin), statin, and folic acid. They estimated giving the polypill to those above the age of 55 years irrespective of cardiovascular risk would result in 88% reduction in ischaemic heart disease and 80% reduction in stroke. Principle risk factors lowered by the polypill are blood pressure by anti-hypertensives (such as ACE Inhibitors and thiazide diuretics) and LDL cholesterol by using statins. The rationale relies on the fact there is no threshold below which reduction of such risk factors does not confer a beneficial effect. Although evidence for folic acid, which lowers the homocysteine levels, another marker of cardiovascular disease, has been refuted all other components have proven track record to substantially reduce myocardial infarction and stroke. The polypill concept has important implication for middle and low income countries who will bear 80% of the global cardiovascular disease (CVD) related mortality by year 2020. It is even truer in Iran where cardiovascular disease account for 47.5% of deaths. Limited resources in these countries have resulted in poor access to individual drugs that are part of the polypill for even secondary prevention. Therefore if proven of benefit polypill can have a major public health impact in the primary prevention of CVD. Recent trials reported in India and other parts of the world and a pilot study in Iran have supported the concept, even though the effect size has been much less than the 80% mark reduction in CVD initially estimated by Wald and Law. The Indian study estimated a reduction in cardiovascular heart disease by 62% and stroke by 48%. A similar effect size was reported by the PILL Collaborative Group (PILL study) who estimated 50% reduction in CVD. These findings have necessitated the call for revisiting the question on the need for traditional risk scoring systems like the Framingham prediction model that is complex and uses multiple risk factors to determine need for treatment. Costs are unlikely an issue with these drugs being generic. Further recent surveys and studies have suggested acceptance among patients and physician for use of the polypill approach.

The paper by Sepanlou et al. acknowledges there are limitations and emphasise the need for monitoring adverse events, large scale population based studies with cardiovascular disease as end points and cost effectiveness analysis of the findings of such studies. Irrespective of the outcome on the effectiveness of the polypill saga, key interventions pivotal to prevention of CVD will be in introduction of antismoking legislations that can have greater impact in reduction of CVD outcomes. More work needs to focus on reduction in salt intake, trans-fat and saturated fat intake, sugar and alcohol across the global population. Similarly behavioural change will have an important role but they tend to be difficult to achieve, costly and are often not sustainable. It is in this context polypill provides a simplistic alternative until substantial progress is made on these fronts.

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References


Polypill for Primary Prevention: Has The Time Arrived?

Authors’ Reply

Since the introduction of the concept of Polypill for cardiovascular disease (CVD) prevention, many studies have been conducted to determine whether it can be recommended as routine primary prevention of CVD. In the previous issue of the *Arch Iran Med* ( 2012; 15(9): 531 – 537) we reported the estimated effectiveness of such a combination using updated meta-analyses of the component drugs.1 Our estimates of the relative reduction in CVD mortality are more conservative than those previously reported,2-5 because we estimated the effects of Polypill components on clinical endpoints rather than modeling their effects through reductions in blood pressure and serum cholesterol and we used a more conservative assumption for the combined effects of multiple endpoints rather than modeling their effects through reduction in blood pressure and serum cholesterol.

We also reiterate our emphasis that medical interventions and health system characteristics in Iran may need to be strengthened (possibly using family physicians) before such a national strategy can be successfully implemented. We also reiterate our emphasis that medical interventions should be combined and balanced with effective lifestyle interventions in a comprehensive national CVD prevention strategy.

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References


Letters to the Editor

Particular aspects of the cardiovascular disease epidemiology and health system characteristics in Iran may support large scale population-based administration of Polypill: CVD constitute 53% of deaths above age 30 in Iran;2-5 54% of these deaths are attributable to high blood pressure and 22% to high serum cholesterol.7 The pills are produced locally at a low cost and an extensive primary health care network can enhance the feasibility and coverage of the policy.

However, we agree with Nirantharakumar and Marshall that before the use of Polypill can be recommended as a strategy for primary prevention of CVD on a national scale, its safety and acceptability should be evaluated in large scale randomized trials and its cost-effectiveness should be rigorously examined. It should also be noted that the coverage of the primary health care system in urban areas may need to be strengthened (possibly using family physicians) before such a national strategy can be successfully implemented. We also reiterate our emphasis that medical interventions should be combined and balanced with effective lifestyle interventions in a comprehensive national CVD prevention strategy.