



Letter to the Editor

Exercise as the master polypill of the 21st century for the prevention of cardiovascular disease



Fabian Sanchis-Gomar^{a,*}, Carmen Fiuza-Luces^b, Alejandro Lucia^b

^a Department of Physiology, Faculty of Medicine, University of Valencia, Fundación Investigación Hospital Clínico Universitario/INCLIVA, Spain

^b Universidad Europea and Research Institute of Hospital 12 de Octubre ('i+12'), Spain

ARTICLE INFO

Article history:

Received 18 December 2014

Accepted 20 December 2014

Available online 23 December 2014

Keywords:

Polypill

Cardiovascular diseases

Mortality

Myocardial infarction

To the Editor,

The growing pandemic of cardiovascular diseases (CVD) has paradoxically paralleled advances in pharmacology, and CVD remains the leading cause of death worldwide. Therapeutic strategies aiming at controlling several CVD risk factors simultaneously in individuals without evidence of CVD are expensive and difficult to implement. Thus, the development of fixed-dose drug combinations of antiplatelet together with blood pressure (BP) and cholesterol-lowering drugs, i.e., polypills, is gaining attention to prevent CVD [1,2] and all-cause mortality [3], even after an acute coronary syndrome [4]. Despite the potential of polypills to increase adherence at a lower cost [5], people randomized to this therapy are 20% more likely to report an adverse event compared with those receiving placebo, single-drug therapy, or usual care [6]. Further, the association of polypills with lower all-cause mortality or CVD events is still uncertain [5]. Yet the evidence that regular exercise and one of its main consequences, high cardiorespiratory fitness (CRF), are associated with reduced rates of all-cause and especially CVD mortality is irrefutable [7].

Exercise is available at low cost and relatively free of adverse events [8]. Exercise interventions, especially endurance activities (jogging,

brisk walking), have drug-like effects on CVD risk factors, particularly in reducing systolic BP and LDL/total cholesterol [8]. An additional exercise benefit that further decreases CVD risk (together with the risk of other major diseases, particularly multiple cancer types) and cannot be achieved by drug therapies is a significant decrease and increase in adiposity and CRF, respectively [8,9]. Rates of tolerability/adherence seem to favor exercise interventions vs. most drugs, with an average dropout from the exercise programs of 10% [9]. Further, exercise can decrease CVD risk beyond traditional risk factors, notably by attenuating aging autonomic dysfunction [8].

Exercising muscles can produce several hundred secreted factors, collectively known as 'myokines'. These molecules travel through the bloodstream to tissues where they exert beneficial drug-like effects but without adverse effects. For instance, *secreted protein acidic and rich in cysteine* (SPARC) can inhibit colon cancer proliferation, muscle-released *interleukin-6* can promote a healthy anti-inflammatory milieu and improve glucose homeostasis or *irisin* can induce thermogenesis in adipocytes [8].

Advances in cardiovascular medicine are welcome and in fact urgent. Ongoing research might hopefully show that polypills represent a step forward in CVD prevention. But why not putting more emphasis on exercise interventions? Starting from medical schools, physicians should be taught to prescribe exercise, that is, the right dosage for each individual.

Conflicts of interests

The authors declare that no conflicts of interest exist.

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* Corresponding author at: Department of Physiology, Faculty of Medicine, University of Valencia, Fundación Investigación Hospital Clínico Universitario/INCLIVA, Av. Blasco Ibañez 15, Valencia 46010, Spain.

E-mail address: fabian.sanchis@uv.es (F. Sanchis-Gomar).

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