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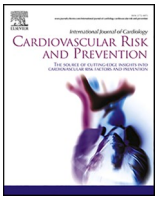

The use of polypills in cardiovascular disease management: Benefits vs challenges

Cardiovascular disease (CVD) refers to a class of diseases that involve the heart or the blood vessels and is a leading cause of disability and death worldwide, accounting for 18 million deaths, a third of all-cause annual deaths [1]. Hence, It is important to implement primary and secondary prevention strategies to alleviate the widespread occurrence of CVD. The risk of CVD could be potentially explained by major risk factors that include hypertension, diabetes, and dyslipidemia with the absence of protective factors such as exercise and adequate diet.

In response to the increasing risk of CVD, the concept of polypills was introduced which involves combining multiple medications with different therapeutic objectives into a single pill. There are two major groups of polypills in clinical studies. The first one is more expensive and combines multiple medications to lower only one CVD risk such as high cholesterol or high blood pressure. This type of polypill is called a "single-purpose" polypill. The other type combines 3–4 pharmaceutical components to reduce more than one CVD risk and is called a "multi-purpose polypill" or a "cardiovascular polypill" [2]. In 2003, Wald and Law published a modeling analysis proposing the formation of a cardiovascular polypill that reduces ischemic heart disease events by 88 % and stroke by 80 %. It is believed that this polypill strategy could largely prevent heart attacks and strokes if taken by everyone aged 55 or more [3].

CVD patients often face challenges regarding medication adherence as it is difficult to manage the daily intake of multiple oral medications. Additionally, people in low-income countries face multiple obstacles including limited access to affordable healthcare as well as a lack of awareness regarding cardiovascular diseases [4]. In response to these challenges, the polypill-based strategy offers simplified medication regimens which leads to better medication adherence and a reduction in risks associated with polypharmacy. A randomized clinical trial was conducted which included the use of a fixed-dose combination strategy. At the end of the study, it was concluded that this strategy resulted in significantly higher medication adherence at 15 months [5].

Hypertension is one of the most modifiable CVD risk factors with the highest contribution to premature cardiovascular deaths. Moreover, the persistently low success rate in reaching treatment objectives makes it even more challenging to manage hypertension. In the past, most hypertension management guidelines included an initial use of an antihypertensive drug as mono-therapy and emphasized increasing the dose or substituting it with a different drug. However, this led to very little effect on lowering blood pressure and increased risk of side effects. A meta-analysis concluded that combination therapy is better than increasing the dose of a single pill, as it results in a greater reduction in blood pressure. A low-dose combination therapy that combines any two antihypertensive drug classes was 5 times more effective than mono-therapy [6].

Polypills proved to be a better solution to other CVD risk factors such as dyslipidemia. Combinations such as statins/ezetimibe and bempedioc acid/ezetimibe control LDL-C levels by inhibiting cholesterol synthesis and gastrointestinal absorption. Their hypolipidemic effect is believed to be additive [7].

Other than this, using polypills is potentially beneficial for reducing Major Adverse Cardiovascular Events (MACE), particularly in secondary prevention. A randomized clinical trial was conducted in which patients with myocardial infarction in the previous six months were assigned to a polypill-based strategy. It was concluded that treatment with a polypill containing aspirin, ramipril, and atorvastatin resulted in a lower risk of MACE as compared to usual care [8].

Based on its impressive results, the polypill-based strategy seems promising for treating cardiovascular diseases. However, there are certain challenges to its implementation such as the lack of confidence in the available scientific evidence among physicians which leads to a low trend in prescription [9]. Moreover, there are still questions about whether aspirin should be a part of the combination. A meta-analysis of 15 randomized trials highlighted the extracranial side effects of low-dose aspirin. Of all the components, aspirin had the most adverse side effects mainly due to hemorrhage [3]. Other challenges include inconsistency with the modern direction of precision medicine, which develops specific treatments for individuals based on lifestyle and genomic factors.

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Yamaan Adil*
Dow University of Health Sciences, Karachi, Pakistan

Shanezehra Siddiqui
Dow University of Health Sciences, Karachi, Pakistan
E-mail address: shanezehrasiddiqui@gmail.com.

* Corresponding author. Mission Rd, New Labour Colony Nanakwara, Karachi, 74600, Pakistan.
E-mail address: yamaanadilqureshi@gmail.com (Y. Adil).