Editorial Article

Polypill For Patients with Heart Failure

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Heart failure (HF) is a leading global public health problem with a higher disease burden in the low and middle-income countries due to population growth, aging, and increasing prevalence of HF risk factors **(**1**)**. One-year mortality rates in chronic HF continue to be around 10%, even in well-treated patients enrolled in contemporary clinical trials **(**2**)**. Large intercontinental differences exist regarding risk profiles and responses to therapies, with socioeconomic influences being among the strongest predictors of early HF readmissions **(**2**)**.

The drug armamentarium for chronic HF with reduced ejection fraction (HFrEF) has rapidly evolved and expanded over the past two decades to include several effective therapies, including beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), mineralocorticoid receptor antagonists (MRAs) and the recent SGLT2 inhibitors **(**3, 4**)**.

These regimens reduce mortality by over 60% **(**3**)**. Combining these drugs into a single dosage form (polypill) could have benefits for patients with HF. Polypill provides a simple, convenient, and effective treatment strategy to meet the increasing burden of HF, especially among the elderly, and address the issue of drug non-compliance in the outpatient treatment of HF thereby improving the patient outcomes in HF.

An ideal polypill for HFrEF patients possibly must include a β-blocker, ACE inhibitor/ARB, a mineralocorticoid receptor antagonist, and an SGLT2 inhibitor as these drugs have demonstrated to have an independent benefit in reducing morbidity and mortality in HF patients **(**3,4**)**.

Patients most likely to benefit from HFrEF polypills are likely to be inadequately treated, have low baseline adherence to polypill component drugs, and live in areas where frequent follow-up visits for sequential initiation and titration of medications may be impractical, such as in rural settings.

Various pharmacokinetic and pharmacodynamics variables will be vital in determining the preliminary efficacy and safety of these polypills. Because of the favorable cost-effectiveness with increased compliance rates polypill must be recommended as the "highest priority" intervention among patients with HFrEF.

The polypill strategy has a few notable drawbacks. Many of the agents in an HFrEF polypill would have fixed doses that may be higher than the starting dose. Increased risk for adverse events due to synergy, notably hyperkalemia.

Depending on the ultimate formulations of the polypills, clinicians may have to negate the possible reductions in clinical efficacy with potential gains in compliance and affordability. Screening and selection of appropriate patient groups may help to achieve the maximum clinical benefit with minimal risk of potential adverse effects.

Randomized trials evaluating these HFrEF polypills' outcomes should include evaluation of efficacy among various patient subgroups and the differences in outcomes across age, sex, racial/ethnic, and geographic subgroups. If these polypills are shown to be superior to usual care in clinical trials, integration into current clinical practices would become mandatory.

In conclusion, the polypills represent a novel, inexpensive and convenient option for mortality reduction for patients with HFrEF in countries without adequate access to specialized cardiology follow-up care. Regardless, high-quality research is mandatory to evaluate this approach and understand its safety and efficacy in patients with HFrEF.

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