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Research Article

TO STUDY THE BENEFITS AND CHALLENGES INVOLVED IN THE USE OF POLYPILL PROPHYLACTICALLY FOR THE CARDIO-VASCULAR DISEASES

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ABSTRACT
Introduction of Polypill for prophylactic use to curb the risk factors, can be a step forward to decrease the burden of cardiovascular diseases like ischaemic heart disease and stroke, but it must be used along with the non-pharmacological measures like diet control and exercise. Polypill is a combination pill of following drugs-hydro-chlorthiazide(12.5mg),atenolol (50mg), ramipril(5mg), simvastatin (20 mg), aspirin(100 mg). A large phase III trial is required along with the follow-ups to assess the feasibility of the use of polypill . Full safety profile needs to be studied before this is accepted.

Key Words: *Polypill, Cardiovascular Risks, Prophylactic Use*

INTRODUCTION

The mortality due to cardiovascular diseases is increasing day by day, worldwide. The people in developing countries are suffering more from these, due to limited health resources (Lloyd Jones *et al.*,2006).The multiple risk factors associated with these diseases particularly ischaemic heart disease and stroke include dyslipidemia, hypertension, diabetes, smoking and obesity (Eva lonn *et al.*, 2010). There is a good amount of evidence available to support the use of pharmacological treatment for the prevention of cardiovascular deaths in these patients, including anti-platelet drugs, beta blockers, lipid lowering agents and angiotensin converting enzyme inhibitors and the beneficial effects of these on morbidity and mortality have been clearly demonstrated (Soliman *et al.*,2011). But there may be problems of poor adherence to treatment regimens and the reason may be high cost of treatment in low and middle income countries (Fuster and Sanz 2011).

The development and introduction of Polypill for prophylactic use to curb some of the above risk factors can be a step forward to decrease the burden of cardiovascular diseases like ischaemic heart disease and stroke, but it must always be used along with the non-pharmacological measures like diet control and exercise. Polypill is a combination pill of following drugs- hydro-chlorthiazide (12.5mg), atenolol (50mg), ramipril(5mg), simvastatin (20 mg),aspirin(100 mg)(Wald, Law 2003).

MATERIALS AND METHODS

The present study analysed the various benefits and challenges involved in the prophylactic use of polypill to prevent the cardiovascular diseases like ischemic heart disease and stroke by reviewing various studies. Pubmed searches were conducted for articles and abstracts .There was no limit to the time of publication of these articles.

RESULTS

A Study by Wald & Law (2003) claimed that taking a daily pill containing six active ingredients would reduce ischemic heart disease events by 88% and stroke by 80% in individuals of 55 years and older. The proposed polypill contained aspirin, simvastatin, a combination of three blood pressure lowering drugs i.e. ramipril, atenolol and hydrochlorthiazide and folic acid (not included now) to reduce homocysteine to decrease cardiovascular disease.

A large phase II randomized trial (The Indian Polypill Study,TIPS)was conducted in 50 centers in India including 2053 patients to assess the effects of a fixed dose formulation polypill containing thiazide , atenolol , ramipril , simvastatin, aspirin on blood pressure, serum lipids, heart rate and urinary thromboxane B_2 to measure its effect on risk factors as well as tolerability in individuals not having CVS disease but have at least one risk factor(Yusuf *et al* 2009). TIPS concluded that the polypill could be used to reduce multiple risk factors and cardiovascular risk. It could potentially reduce ischaemic heart disease by 62 % and stroke by 48 %. The degree of cholesterol lowering was

less with the polypill than in patients using simvastatin alone the reason for which is not very clear. A lower dose of simvastatin (20 mg) was used than that suggested by Wald & Law (40 mg).The next polypill might shift to a larger dose of simvastatin or might include a more potent statin.
The polypill reduced systolic blood pressure by 7.4 mm Hg and diastolic blood pressure by 5.6 mm Hg which was similar when three blood pressure lowering drugs were used with or without aspirin. There were 3-8% of patients who had increases in creatinine and potassium and in liver function tests. So the full safety profile is required.
Another study argues against the use of statins in diabetic patients on a generalized basis and indiscriminate large-scale treatment with a polypill. It endorses the use of aspirin in all diabetic patients ≥ 21 years of age and the life-style interventions. It also proposes the use of 'Polymeal' containing wine, fish, dark chocolate, fruits, vegetables, garlic, and almonds.(Stirban,Diethelm 2008).
An open-label, parallel-group, randomized clinical trial involving 216 patients without established cardiovascular disease (CVD) was conducted in Sri lanka. The trial compared a Polypill (75 mg aspirin, 20 mg simvastatin,10 mg lisinopril and 25 mg hydrochlorthiazide) to standard practice.The patient acceptability of treatment was high.90 % patients completed the trial. Both the Polypill and standard treatment resulted in significant reductions in systolic blood pressure, total cholesterol and 10-year risk of CVD (Soliman *et al*., 2011).
A study conducted among US adults has projected, by published meta-analyses and three large population - based cohort studies that the Polypill use by people aged ≥55 years is projected to potentially prevent 3.2 million coronary heart disease events and 1.7 million strokes over 10 years(Muntner *et al*., 2011).
A large clinical trial has been begun in five countries to investigate the beneficial effects of treatment using a Polypill, on ischemic heart disease recurrence and its results could become a basis of a new therapeutic approach to the management of CVD, diabetes and stroke (Sanz,Fuster 2011) .
Another study emphasizes on patient selection for Polypill prescription and according to it the age alone is effective and simpler means of selecting people for preventive treatment using the polypill (Wald & Wald 2010).

DISCUSSION

There are certain questions which still remain unanswered and have been raised time and again by various authors also(Stirban, Diethelm 2008),(Rafter Woodward2005),(Cannon 2009).The cardiovascular polypill contains just one dose of each ingredient while regulatory authorities require a combination pill to be available in every dose combination of each drug. Should a patient with single risk factor like diabetes or smoking, without high blood pressure be put on three anti-hypertensives exposing him to the side effects of these drugs? Why Cholesterol lowering with simvastatin was less when given in combination than when given alone? The pill size may also be too big to swallow? Adverse effects, drug interactions, inter individual variations in drug metabolism and the underlying causes of hypertension that differ between patients may require individualized therapy? Would one size-fits-all approach be safe and effective?
The availability of single 'magic bullet' for the prevention of heart disease might not lead people to abandon exercise and diet control? The benefit of polypill in being cost-effective and showing better patient compliance has also been raised by some studies, but it is yet to be proved. Inclusion of folic acid in the polypill as suggested by Wald and Law has not been established and has been refuted by some studies(Clarke *et al* 2010).Another important point to ponder is that, low-dose aspirin is beneficial in secondary prevention,but if used for long term for primary prevention of CVD as a part of polypill could lead to increased risk of bleeding tendancies(Baigent *et al*.,2009).

Conclusion

The polypill strategy could prove effective in carefully selected populations with poor compliance or at high risk, old patients and also in patients requiring numerous medications. The fact that lifestyle interventions are the basis of primary prevention of CVD, should never be forgotten. An indiscriminative population- based therapy does not seem to be suitable regarding use of polypill. A large phase III trial is required along with the follow-ups to assess the feasibility of the use of polypill.

Full safety profile needs to be studied before this is accepted. It is suggested that that it might be better to first target secondary prevention with this strategy.

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